Clinical Cases in Dermatology
Series Editor: Robert A. Norman

Fabio Arcangeli
Torello M. Lotti *Editors*

Clinical Cases in Neonatal and Infant Dermatology

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Clinical Cases in Dermatology

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Robert A. Norman
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Clinical Cases in Neonatal and Infant Dermatology

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Chapter 1
1-Year-Old Male with Erythema, Scales and İtching

Zhou Yang, Zhe Xu, and Lin Ma

An 1-year-old male infant was characterized by whitish scales on an erythematous background with slight ectropion and sparse hair after birth. On the basis of erythema with white scales, red papules, scales, scratches appeared intermittently on his face, trunk, arm and leg (Fig. 1.1a–c), accompanied by obvious itching. After the treatment of topical glucocorticoids, the itching skin lesions could be relieved. He had mild blepharitis and conjunctivitis, and was allergic to seafood, eggs, beef and mutton. No other members of his family had similar skin manifestations.

Laboratory examinations: the total serum IgE was 1000.58 IU/mL, the eosinophil count was 2.75×10^9/L (normal range $0.05–0.5 \times 10^9$/L), and the percentage of eosinophil was 15.8% (normal range 0.5–5.0%). Histopathological examination showed epidermal hypokeratosis, intraepidermal abscess formation, thickening of the spinous layer, and spongy edema. There was a little lymphocyte infiltration and occasional eosinophilic infiltration around the vessels in the dermis (Fig. 1.1d).

Based on the Case Description and Photograph, What İs Your Diagnosis?

1. Atopic dermatitis
2. Congenital ichthyosiform erythroderma
3. Netherton syndrome
4. Drug reactions

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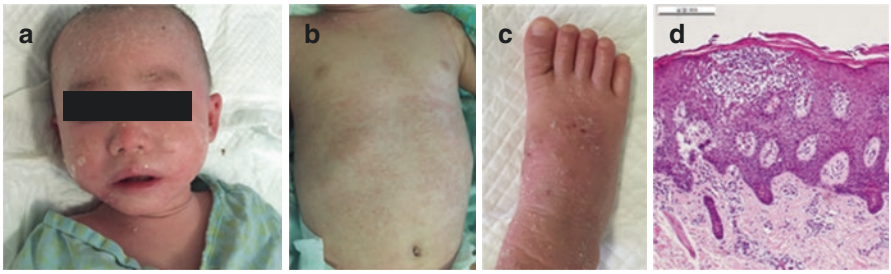


Fig. 1.1 (**a**–**c**) Desquamed lesions on erythematous background of the face, trunk and foot, sparse hair and slight ectropion. Red macular papules, papules, and scratches on the erythematous background; (**d**) Skin histopathology (HE×20): epidermal hypokeratosis, intraepidermal abscess formation, thickening of the spinous layer, and spongy edema. There was a little lymphocyte infiltration and occasional eosinophilic infiltration around the vessels in the dermis

Gene detection: a homozygous mutation c.433C>T, p.Arg145Ter was found in the NIPAL4 gene, and both parents were heterozygous carriers. No FLG gene mutations which associated with atopic dermatitis were found in this patient.

Diagnosis

Congenital ichthyosiform erythroderma accompanied by atopic dermatitis

Discussion

Congenital ichthyosiform erythroderma (CIE) belongs to autosomal recessive congenital ichthyosis which is a heterogeneous group of nonsyndromic disorders of keratinization. CIE can be caused by mutations in ABCA12, ALOX12B, ALOXE3, CERS3, CYP4F22, NIPAL4, PNPLA1, TGM1 and other unidentified genes [1]. NIPAL4 (nipa-like domain-containing 4) gene is considered to encode Ichthyin as a Mg2+ transporter. It is highly expressed in the granular layer of the epidermis, and also in the brain, lung, stomach, and white blood cells. The ultrastructure shows abnormal lamellar bodies and prolonged perinuclear membranes in the granular layer, which may indicate the role of NIPAL4 in lipid processing, or the cytotoxic effect of accumulated metabolites, but its precise function is still unclear [2].

Most patients with NIPAL4 mutations have CIE at birth, and may be accompanied by ectropion or focal palmoplantar keratosis, or have a history of psoriasis [1, 2]. In our case, in addition to the typical erythema with fine scales of CIE, the

patient also showed atopic dermatitis skin lesions such as red macula papules, papules, scales, scratches, accompanied by obvious itching, and were effective to topical glucocorticoids. Combined with his histopathological characteristics and a history of various food allergies, significantly elevated serum total IgE and eosinophils, this patient was diagnosed with CIE accompanied by atopic dermatitis.

The homozygous mutation p.Arg145Ter in NIPAL4 may cause the loss of normal protein function through protein truncation or nonsense-mediated mRNA decay, but patients with the same mutation have not been associated with atopic dermatitis in the past. In addition to the typical CIE features, our patient had atopic features, and no FLG gene mutations were found. It may be speculated that the NIPAL4 mutation plays a role in epidermal lipid processing, which may lead to skin barrier dysfunction, causing accelerated transdermal sensitization to multiple allergens, and increasing the risk of atopic dermatitis. In the literature, there were two mutations in the NIPAL4 gene have been found in ichthyosis accompanied with atopic dermatitis: the missense mutation p.Ala176Asp in a Pakistani family and the homozygous partial deletion of exon 3–4 in two cousins in Saudi Arabia [3, 4].

Common causes of erythema, scales and itching are skin diseases such as atopic dermatitis, Netherton syndrome, drug reactions and others. Among them, Netherton syndrome is also characterized by congenital ichthyosiform erythroderma and atopic diathesis, which needs to be distinguished from the characteristics of this patient. Netherton syndrome is a rare autosomal recessive genetic disease caused by mutations in the serine protease inhibitor of Kazal type 5 (SPINK5) gene [5]. Patients with Netherton syndrome also have trichorrhexis invaginata, and can be associated with immunodeficiency, susceptible to recurrent bacterial skin infections or systemic infections such as bacteremia and lung infections [6]. Other system syndromes may be related to short stature, developmental delay, intellectual disability and growth hormone deficiency [5]. As the patients grow older, most skin lesions gradually become milder, and linear ichthyosis of varying severities often appears after the age of 2 years, which is characterized by migratory creeping erythema with bilateral scales around [5]. Eczema-like or pustular psoriasis-like rash may also occur [7]. Drug reaction's lesions usually have a history of medication before the onset, and are not presented at birth. When clinical and histopathological findings are non-specific, gene detection may be helpful for diagnosis.

Key points

- Congenital ichthyosiform erythroderma is characterized by fine, whitish scales on a background of erythematous skin over the whole body.
- Homozygous missense mutations (c.433C>T, p.Arg145Ter) in NIPAL4 might lead to a congenital ichthyosiform erythroderma phenotype accompanied by atopic dermatitis.
- When clinical and histopathological findings are nonspecific, gene detection may be helpful for diagnosis.

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Chapter 2
A 1-Year-Old Boy with Multiple Papules

Ya-xiang Li, Long-fei Zhu, and Songmei Geng

A 1-year-old boy presented dome-shaped papules on his face with size about 2–3 mm in diameter. The lesions were first seen 3 months earlier which grew slowly (Fig. 2.1).



Fig. 2.1 A 1-year-old boy with dome-shaped papules on his face

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Based on the Case Description and the Photographs, What Is Your Diagnosis?

1. Langerhans cell histiocytosis
2. Benign cephalic histiocytosis
3. Juvenile xanthogranuloma
4. Molluscum contagiosum

Physical examination and routine laboratory work-up didn't provide the evidence of internal organs involved. His parents had no records of similar family history including allergy. A biopsy of the fully developed skin lesion showed the infiltration of predominantly histiocytic cells mixed with lymphocytes in the superficial to midreticular dermis. Most of the histiocytes were well-defined without mitosis that had pale cytoplasm and bland round to oval nuclei. The area of the papule also could be observed mild focal vacuolar degeneration at the dermoepidermal junction and a slightly spongiotic epidermis.

Diagnosis

Benign cephalic histiocytosis

Discussion

Belonging to the family of non-Langerhans cell histiocytosis, Benign cephalic histiocytosis (BCH) is an orphan disease that mainly affects infants or children [1]. In 2014 Aikaterini Patsatsi et al. had reviewed 55 cases in Europe since the first case of BCH was reported in 1971 [2]. Owing to its low incidence, the pathophysiology and etiology may still require further clarification.

The classical manifestations of BCH are asymptomatic macules and papules with size less than 1 cm in diameter usually restricted on head and neck, occasionally trunk or other parts of the body are involved [3]. Still, some reports described the extremities as the sole location of the BCH [4]. The color of the round or oval lesions may range from tan to reddish yellow. The lesions may regress without any treatment. Normally, BCH don't leave scar or hyperpigmentation.

Biopsy is a necessity to diagnose BCH. The lesions are abundant in well-defined histiocytic cells with low rates of mitosis from superficial to midreticular dermis. The nuclei of the cells are bland round to oval in shape, while the cytoplasm are vacuolated. Mixed inflammatory cells including lymphocytes and scattered eosinophils can be found as well. In most cases, the immunohistochemistry staining for CD 68 and factor XIIIa are positive, whereas CD1a and CD207 (langerin) that

commonly used as the Langerhans cell markers are negative. Ultrastructural studies conducted by electron microscopy may find desmosome-like structures, coated vesicles, and comma-shaped bodies which may be characteristic of BCH. Immunohistochemistry and electron microscopy contribute more clues to diagnose BCH accurately.

Langerhans cell histiocytosis (LCH) is the most common histiocytic disorder that mainly affects mononuclear phagocyte system. This disease has the ability to influence any organ system which shows higher affinity in skeleton, skin, spleen, liver, and lung. The skin lesions of LCH also present varied manifestations, while a vast majority are seborrheic eczema. Biopsy shows the infiltration of numerous neoplastic cells with a coffee-bean nuclear grove and pale cytoplasm which are positive for CD207 (langerin) and CD1a in epidermis and dermis. When visualized by electron microscopy, rod-shaped inclusions with pentalaminar cytoplasm (Birbeck granules) are helpful to distinguish LCH [5].

Compared with BCH, juvenile xanthogranuloma (JXG) has a much higher incidence in the spectrum of non-Langerhans cell histiocytosis. Patients who suffered from JXG are usually infants (40–70%) and children. However, adults whose ages range from 20 to 30 may also have JXG without spontaneous regression. BCH and JXG share many similarities in clinical and histological features. Thus, there are points that BCH may be a variant of JXG. Nevertheless, the traits followed can be helpful to distinguish between BCH and JXG. For instance, JXG is not confined to neck and face and can appear over the entire body. In biopsy specimens, markedly xanthomized cells, ample eosinophils, and Touton-type giant cells may be clues to diagnose JXG rather than BCH. Of note, JXG can have extracutaneous involvement, particularly eye manifestations [6].

Molluscum contagiosum has been considered as the only member of the Molluscipoxvirus genus in the family Poxviridae that mainly affects children. Patients' trunks, faces, and other anatomic sites except mucous membranes may present skin-colored to tan papules with the average diameters of 2–5 mm. The cheesy material can come out of the umbilicated top when squeezed. These lesions are usually transmitted by skin contact including scratch. Histologically, the typical results always show a crater-like inverted lobules with large, eosinophilic, intracytoplasmic inclusion bodies (molluscum bodies) and keratin fragments in prickle cell layer of the epidermis [7].

According to patient's clinical features and biopsy results, the diagnosis of Benign cephalic histiocytosis was made. Due to the self-healing trait of BCH, we suggested the patient should be followed up without any treatment. Subsequently, his lesions spontaneously regressed after 3 months. In 2 years follow-up, there was no recurrence of similar lesions.

Key Points

- Benign cephalic histiocytosis is a rare non-Langerhans histiocytosis characterized by asymptomatic macules and papules restricted on head and neck.
- BCH has trait of self-healing and should be followed up.

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Chapter 3
A 2-Year-Old Girl with Erythema on the Face, Trunk and Arms, Associated with Fever, Conjuntivitis and Nasal Discharge

Alfonso Delgado Rubio and Fabio Arcangeli

A 2-year-old girl was referred because of a for 4 day erythematous rash which involved the face, with a "butterfly" shape (Fig. 3.1), the trunk and arms. Fever, headache, sore throat, coryza and moderate conjunctivitis occurred a few days before the rash.

Nothing significant could be detected in the remote, personal and family anamnestic investigation.

The clinical examination showed weight and height in normal percentiles and good general conditions. There was fever above 38 °C, conjunctivitis, catarrh of the upper airways and minimal cervical, axillary and inguinal lymphadenopathy. The erythema on the face was well defined and indurated with a butterfly shape.

Laboratory tests, a chest x-ray and an abdominal ultrasound were all normal.

Based on the Case Description and the Photograph Which Is Your Diagnosis?

1. Infectious mononucleosis
2. Erythema infectiosum (Megalo erythema, fifth disease, Sticker's disease)
3. Roseola infantum (sixth disease)
4. Kawasaki disease

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Fig. 3.1 Butterfly erythema on the face

Diagnosis

Erythema infectiosum

Viral serology performed on two consecutive samples 3 weeks apart revealed the presence of high level IgM and IgG against Parvovirus B19.

Discussion

Infectious mononucleosis due to Epstein-Barr virus (EBV) or mononucleosis-like syndromes can present with sore throat, headache, fever and exanthematous rash. Children younger than 4 years have not only a rash and symptoms of an upper respiratory tract infection. They are frequently affected by splenomegaly or hepatomegaly and important lymphadenopathies. Transaminases usually increase. Our patient was in good health and laboratory tests were normal. Furthermore, the serology for parvovirus B19 was positive.

Roseola infantum (also called “3-day fever”) is a common childhood disease. The cause is primary infection with human herpesvirus 6 (HHV-6). The classic presentation is a 9- to 12-month-old infant who acutely develops a high fever (39–40 °C). After 3 days, it suddenly resolves and a morbilliform rash appears. Both clinical manifestations and serology rule out this diagnosis.

Table 3.1 Other illnesses that occasionally may be linked to or triggered by parvovirus B19 [4]

Meningoencephalitis	Systemic lupus erythematosus (SLE)
Plexobrachial neuropathy	Kawasaki disease
Acute myocarditis	Vasculitis. Angioedema
Glomerulonephritis	Rheumatoid arthritis
Thrombopenic purpura	Gloves and socks syndrome
Neutropenia. Pancytopenia	Paroxysmal cold hemoglobinuria
Hemophagocytic syndrome	Schönlein-Henoch syndrome
Behçet's disease	Chronic fatigue syndrome
Acute hepatitis	Fibromyalgia
Mononucleosis-like syndrome	Pneumonia

Kawasaki disease is characterized by very high persistent fever over 5 days. Moreover, except erythema, no other diagnostic criteria of this disease were present in our case.

The presence of a butterfly indurated erythematous rash on the face (like slapped-cheeks) followed by macular erythema on the trunk and limbs, associated with flu-like symptoms and moderate fever should suggest a diagnosis of Erythema infectiosum.

Erythema infectiosum, often referred to as fifth disease, is caused by human parvovirus B19. It occurs mostly during the spring, commonly causing mild constitutional symptoms and a maculopapular rash beginning on the cheeks [1]. The initial manifestations are nonspecific flu-like symptoms. Several days later, an indurated erythema appears over the cheeks ("slapped-cheeks" appearance) and a symmetric maculopapular rash spreads to the trunk and to the limbs, usually sparing the palms and soles [2]. The illness spontaneously heals within 5–10 days. Only symptomatic treatment is needed [3, 4]. Because children with Erythema infectiosum are contagious prior to the onset of the rash, preventing the spread of this common childhood exanthem is very difficult [4].

Parvovirus B19 is the cause of Erythema infectiosum and other different clinical entities (Table 3.1).

Key Points

- Low-grade fever and slight malaise followed by an indurated erythema on the cheeks ("slapped-cheeks" appearance) and a symmetric rash on the trunk and limbs suggesting a diagnosis of Erythema infectiosum
- Diagnosis of Erythema infectiosum is usually based on clinical presentation. Viral serology may be helpful if detected IgG and IgM against Parvovirus B19
- Treatment of Erythema infectiosum is symptomatic because the disease is self-healing

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Chapter 4
A 2-Year-Old Girl with Erythroderma

Lei Jiao, Yuan Liang, Zi-Gang Xu, and Lin Ma

A 2-year-old girl was admitted to our hospital because of fever and a generalized rash. 15 days before admission, the girl presented with erythematous macules and papules on the face with pruritus. The rash progressed to the trunk and limbs with a fever of 39 °C 2 days later. The rash subsided and the body temperature returned to normal after 1 week with intravenous methylprednisolone and azithromycin. But the patient had a fever (38.5 °C) again after stopping the treatment, and the rash coalesced and involved more than 90% of the body surface, accompanied by facial edema and exfoliative cheilitis (Fig. 4.1a, b), in addition, examination revealed 1-cm mobile lymph nodes in the bilateral cervical and inguinal distributions and hepatomegaly. Her parents reported that she got pneumonia 4 weeks before admission and was treated with mezlocillin/sulbactam for 10 days. Other past medical history was unremarkable.

Based on the Case Description and the Photograph, What Is Your Diagnosis?

1. Drug reaction with eosinophilia and systemic symptoms syndrome
2. Infectious mononucleosis
3. Erythrodermic psoriasis
4. Primary biotin deficiency
5. Omenn syndrome

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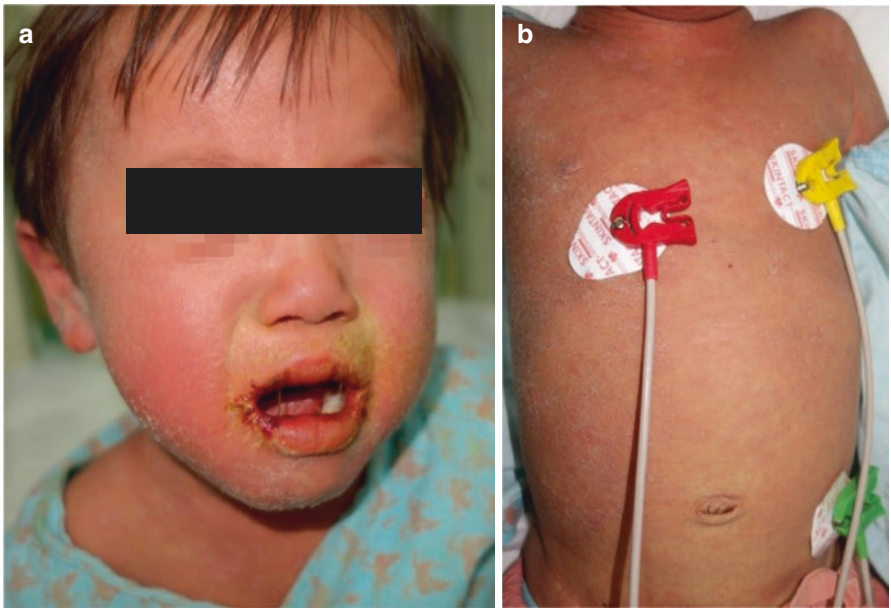


Fig. 4.1 A 2-year old girl presented with exfoliative erythroderma (**b**), accompanied by facial edema and exfoliative cheilitis (**a**)

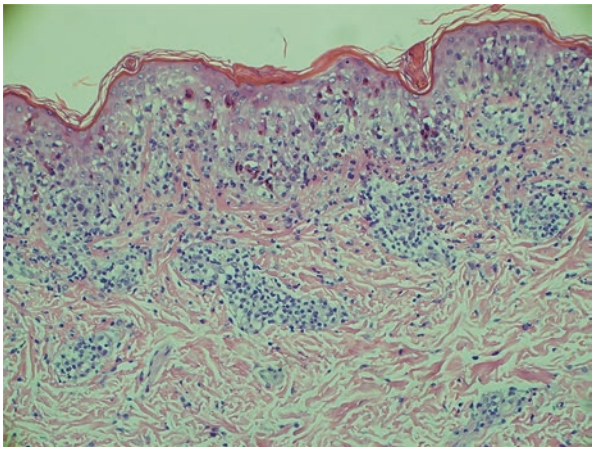


Fig. 4.2 Histopathological examination showing necrotic keratinocytes, vacuolar alteration at the dermoepidermal junction, and perivascular lymphocytic infiltrate in the dermis, with eosinophils (HE×20)

Laboratory evaluation was notable for an absolute eosinophil count of 1611 per cubic millimeter (reference range, 0–500), elevated levels on liver-function tests (alanine aminotransferase level of 175.6 U/L, aspartate aminotransferase level of 195.9 IU/L, total bilirubin level of 152.16 μmol/L, direct bilirubin level of 136.18 μmol/L), and a coagulation dysfunction (prothrombin time 15.1 s, fibrinogen 0.74 g/L). Tests of the blood for hepatitis A, B and C virus, EB virus, Cytomegalovirus, and Antinuclear antibody were negative. Histopathological examination (Fig. 4.2)

revealed necrotic keratinocytes, vacuolar alteration at the dermoepidermal junction, and perivascular lymphocytic infiltrate in the dermis, with eosinophils.

Diagnosis

Drug reaction with eosinophilia and systemic symptoms syndrome

Discussion

Erythroderma also known as exfoliative dermatitis is an extreme state of anatomic and physiologic dysfunction of skin, characterized by extensive erythema and scaling involving more than 90% of body surface area [1]. Different diseases can appear as, or progress to erythroderma, including infections, pre-existing chronic dermatosis such as psoriasis and atopic dermatitis, drug eruptions, lymphoma and internal malignancies. In children, metabolic diseases and primary immunodeficiency diseases must be considered.

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a rare, severe, potentially life-threatening adverse drug reaction with both cutaneous and visceral involvement [2]. It is characterized by the development of fever, skin eruption, lymphadenopathy and internal organ involvement. The time interval between drug exposure and onset of symptoms in DRESS can be 2–8 weeks [3]. The most common manifestation is an erythematous morbilliform rash. It usually spreads to be widespread and confluent, evolving to exfoliative erythroderma. Facial edema often accompanies the skin eruption, mucosa can be involved. Multiple organ systems can be involved in DRESS syndrome. Haematological abnormalities occur in the majority of patients, including peripheral leucocytosis, atypical lymphocytosis and eosinophilia. The most common affected internal organ is liver, followed by renal, pulmonary, cardiac, and nervous system manifestations. These clinical features may remain for weeks even months after discontinuing the culprit drug.

Infectious mononucleosis is a viral disease that classically presents with the triad of fever, lymphadenopathy, and pharyngitis [4]. Most acute infections are caused by the Epstein-Barr virus (EBV). Facial edema, hepatomegaly, splenomegaly and jaundice can occur in some patients. So it needs to be considered in the differential diagnosis. However, the rash is usually exanthematous (Fig. 4.3a, b), and rarely appears as exfoliative dermatitis in infectious mononucleosis. In addition, EBV-specific antibody and EBV-DNA testing are negative in this patient, which is not support this diagnosis. It is worth mentioning that drug eruption may occur after treatment of penicillin or cephalosporin antibiotics for infectious mononucleosis, which can make the diagnosis complicated.

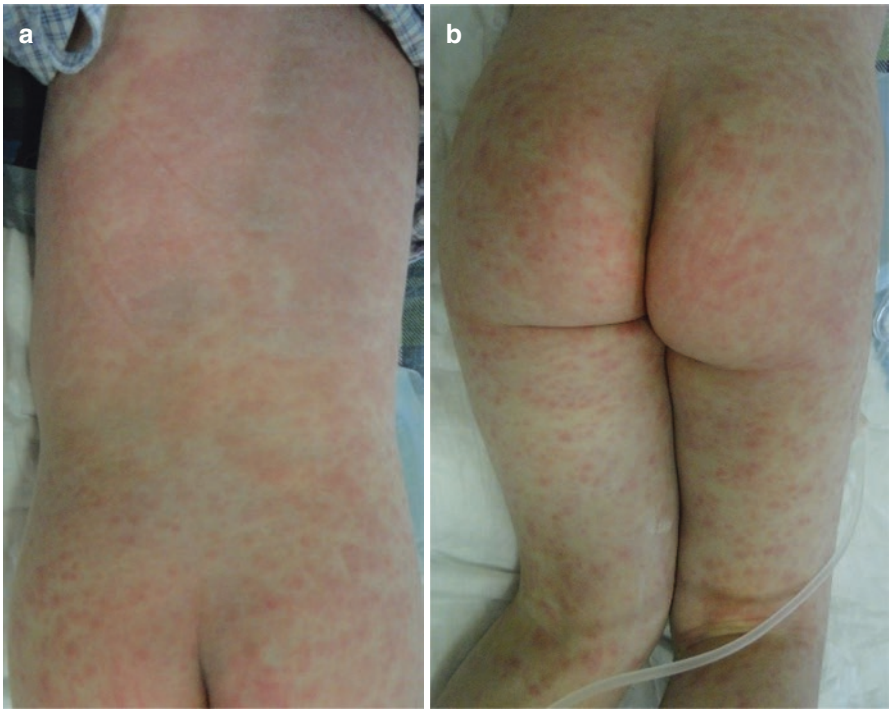


Fig. 4.3 Exanthematous rash on a 3-year-old girl with infectious mononucleosis. Generalized confluent erythematous papules on trunk (**a**) and limbs (**b**)

Erythrodermic psoriasis can be seen in a few pediatric patients (Fig. 4.4). But patients with it may have a recurrent history of psoriasis and it's usually secondary to drug stimulation, psoriasis vulgaris and pustular psoriasis. Thickened plaques and tough lamellar scales like the outside of an oyster shell may present on erythroderma.

To young children, metabolic diseases such as primary biotin deficiency (Fig. 4.5a, b) and primary immunodeficiency diseases such as Omenn syndrome are worth mentioning in the differential diagnosis. Apart with exfoliative erythroderma, patient with these diseases may have an earlier onset and prominent systemic symptoms. Alopecia, optic atrophy, conjunctivitis, hearing loss and neurologic symptoms may present in biotin deficiency. hepatosplenomegaly, lymphadenopathy, recurrent infections, elevated Eosnophils and high serum IgE may present in Omenn syndrome. It's a form of severe combined immunodeficiency and the prognosis is poor [5].

Based on the patient's medical history, physical examination, laboratory tests and biopsy, the diagnosis of DRESS syndrome induced by mezlocillin/sulbactam was confirmed. The patient was admitted for treatment with intravenous methylprednisolone pulse treatment of 100 mg (10 mg/kg) for 3 days, and intravenous immunoglobulin of 10 g (1 g/kg) for 2 days. Plasma and fibrinogen was infused



Fig. 4.4 Exfoliative erythema of erythrodermic psoriasis in a 18-month-old girl

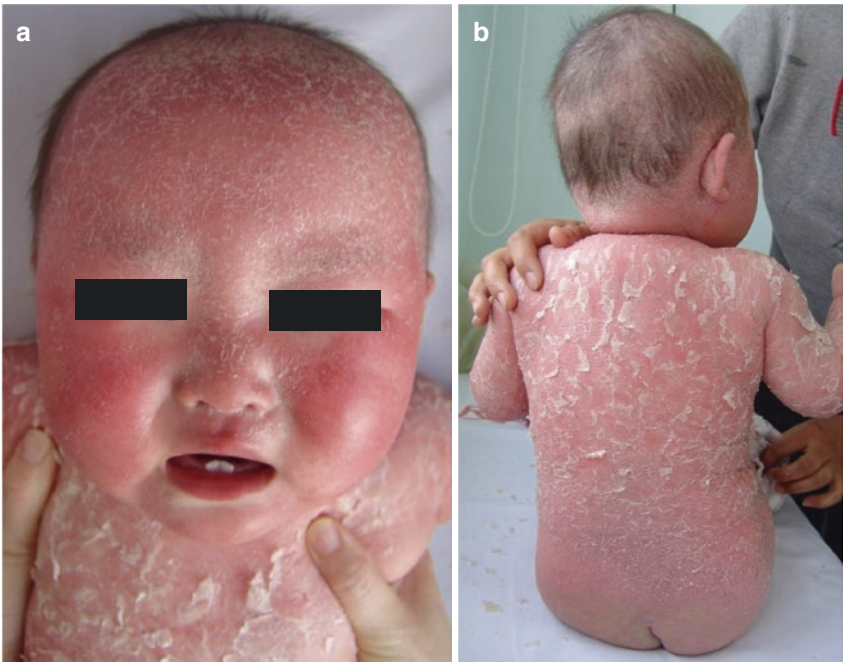


Fig. 4.5 Exfoliative dermatitis resulted from primary biotin deficiency in a 1-year-old girl. (**a**, **b**): Large dry scales on generalized edematous and erythematous background of the whole body

intermittent to improve coagulation. The clinical manifestation and the result of laboratory tests improved 3 days later, methylprednisolone was tapered. The rash subsided after 1 month and liver function was normal after 50 days. Glucocorticoid was reduced gradual and stopped after 60 days.

Key points

- DRESS syndrome is a severe adverse drug reaction with both cutaneous and visceral involvement.
- The most common dermatologic manifestation of DRESS syndrome is an erythematous morbilliform rash, which may evolve to exfoliative erythroderma.
- The liver is the most frequently affected visceral organ.

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Chapter 5
A Case of High Risk Multisystem Langerhans Cell Histiocytosis in 22-Month-Old Boy

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A 22 months old boy was consulted to Department of Dermatovenereology with chief complaints multiple reddish spots accompanied by thick yellowish scales and blackish-red crusts that felt itchy on the scalp, neck, face, chest, back, both hands and both feet, started since he was 4-month-old. Patient had received several kinds of topical therapy. Complaints were reduced but reddish spots kept reappearing. Patient also suffered a bump on the forehead without prior history of trauma and protrusion of the eyeballs. Patient often had fever since 1-year-old. There was also a history of gums that bleed easily, teeth that are prone to loose and arranged untidy.

On examination we observed protrusion on the forehead, exophthalmos and a widespread erythematous plaque, erythematous papules accompanied by thick yellowish scales on the scalp and forehead, erythematous papules with reddish black crusts, erosions and excoriations in the area around the eyes, ear, neck, chest, back and waist (Fig. 5.1). Almost all the fingers have pruritic linear lesions (Fig. 5.2). On intraoral examination, there was a change in tooth arrangement due to infiltrative lesions on the jaw (Fig. 5.3). Based on the case description and photographs, the differential diagnosis for this patient were LCH, seborrheic dermatitis and atopic dermatitis. Several investigations were needed to establish a definitive diagnosis.

Laboratory investigations revealed severe anemia, leukocytosis, low level of hematocrit, erythrocytes and serum iron and thrombocytosis. Bone marrow puncture (BMP) resulted in normocytic normochromic anemia with possibility of

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Fig. 5.1 There were protrusion of forehead with size 10 × 7 × 3 cm, followed by protrusion in both eyes and multiple itchy erythematous papules and plaque accompanied by thick yellowish scales on the scalp and forehead, erythematous papules with reddish black crusts, erosions and excoriations in the area around the eyes, ear, neck, chest, back and waist

histiocytosis (easily found histiocyte cell in preparation). Skull X-ray showed osteolytic lesions in different areas. Head computed tomography (CT) scan showed multiple bone lytic lesions (destruction) (Fig. 5.4). Histopathological examination supported histiocytosis along with immunohistochemistry of S-100 protein gave positive staining (Figs. 5.5 and 5.6).

Based on medical history, physical examination, laboratory examination, bone marrow puncture, skull X-ray, head CT scan, histopathology and immunohistochemistry, the patient was diagnosed as high-risk multisystem LCH. Pediatric Department treated this patient with IVFD vinblastin 2.8 mg/week and etoposide



Fig. 5.2 There were pruritic linear lesions on the fingernails



Fig. 5.3 There were a change in tooth arrangement

70 mg/mg (initial therapy for 6 weeks), vinblastine 2.8 mg/3 weeks, etoposide 70 mg/3 weeks/6-mercaptopurine 25 mg/day, prednisone 17.5 mg/during the week/every 3 weeks (advanced therapy for 18 weeks). For topical medication, patient was treated with lanolin anhydrous cream twice a day (30 min before taking a bath), hydrocortisone cream 2.5% twice daily on erythematous plaques and erythematous papules, natrium fucidin cream 2% twice daily on erosions and excoriations. The patient is currently under periodic follow up and showed improvement during the treatment.



Fig. 5.4 Skull X-ray showed osteolytic lesions on calvaria and head CT scan showed areas of destruction

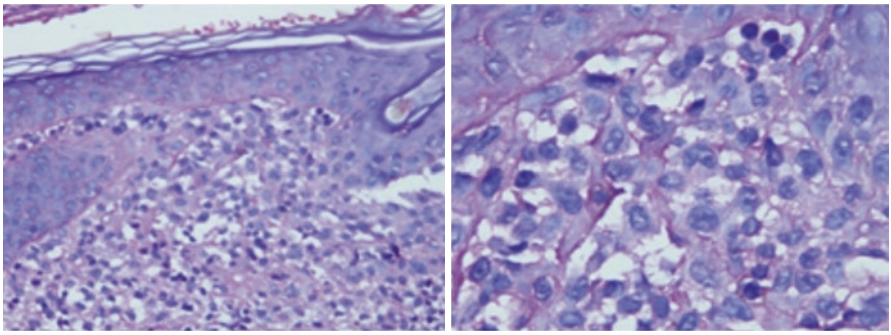


Fig. 5.5 Histopathology examination showed proliferation of histiocytes with indistinct cytoplasmic borders and rounded vesicular nuclei

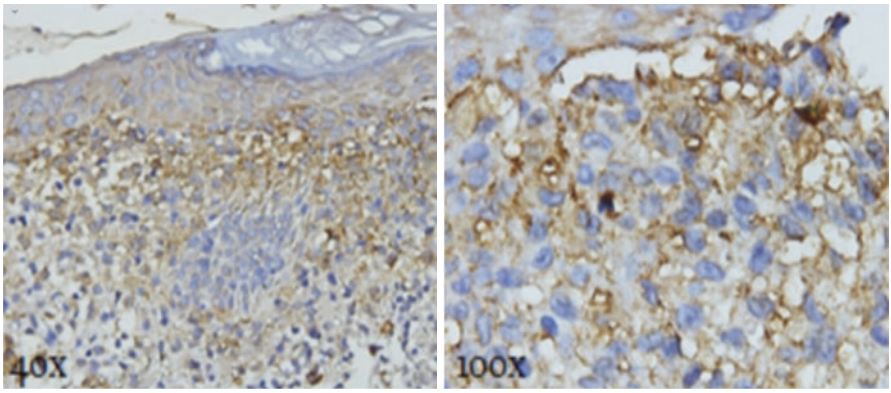


Fig. 5.6 Immunohistochemistry examination showed positive results for S-100 protein

Discussion

Langerhans cell histiocytosis (LCH) is an uncommon hematological disorder that generally affects infants and young children. Langerhans cell histiocytosis (LCH) is more frequent in males than in females with a ratio ranging from 1.1:1 to 4:1. The incidence of LCH is relatively low with an estimation of 2–5 cases per million per year in children under 15 years old, with peak incidence in children aged 1–2 years [1–3].

Langerhans cell histiocytosis (LCH) is classified into single system LCH (SS-LCH) and multisystem LCH (MS-LCH), according to the organs involved. Single system LCH affects one of the following organs, which are bones (80%), skin (33%), lymph nodes (5–10%), lungs (15%), spleen (15%), liver (15%) and central nervous system (2–4%). Single-system LCH can be unifocal or multifocal. Multisystem LCH (MS-LCH) involves two or more organs with or without involvement of a risk organ. Risk organ involvement is defined as the presence of at least one of the following: hematopoietic system (bi- or pancytopenia), liver (hepatomegaly and/or dysfunction), and/or spleen (splenomegaly). Multisystem LCH is differentiated into three categories, low-risk MS-LCH (without involvement of risk organ), high-risk MS-LCH (with involvement of risk organ) and very high-risk (high risk patients without response to 6 weeks of standard treatment) [4, 5].

The front-line treatment based on the association is vinblastine bolus 6 mg/m^2 i.v. weekly for 6 weeks, with prednisone 40 mg/m^2/day orally in three-divided doses for 4 weeks and then tapered over the following 2 weeks. After the first 6 weeks of treatment, disease's status should be re-evaluated. Evaluation of treatment response is usually classified into three classifications: better, intermediate, or worse. Evaluation is classified as "better" if patient shows complete resolution (non-active disease) or if there was disease regression (better active disease); "intermediate" in cases with stable (unchanged) or mixed responses with new lesions in one location, and/or regression in another site; and "worse" in cases of disease progression [5].

The prognosis of LCH is determined by several factors, namely, age at diagnosis, initial therapy response, number of organs involved and involvement of risk organs (hematopoietic, pulmonary, liver, spleen and bone marrow). The prognosis becomes poor when there is a dysfunction of lung, liver, spleen, and bone marrow, and no response to initial treatment. Patients with severe disease but respond quickly to therapy and without the involvement of the risk organs have a good prognosis with a mortality rate of 4%. Whereas patients with the risk organs involvement have a mortality rate of 66%. The number of organs involved also affects the prognosis: patients with 1–2 organ involvements have 0% mortality rate, patients with 3–4 organs involved have 35%, patients with 5–6 organs involved have 60% and patients with 7–8 organs involved have 100% mortality rates [5].

Key points

- Langerhans cell histiocytosis (LCH) often resembles many skin diseases, making it difficult to diagnose.
- A proper medical history, physical examination, laboratory examination, bone marrow puncture, skull X-ray, head CT scan, histopathology and immunohistochemistry are necessary for a diagnosis.
- LCH also has a low survival rate so it is necessary to understand how to establish diagnosis and take immediate appropriate treatment.

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Chapter 6
A Case of Lamellar Ichthyosis in 2-Year-Old Boy with History of Collodion Baby

I. G. A. A. Praharsini, Ketut Kwartantaya Winaya, Monica Rosalind Kawilarang, and Marrietta Sugiarti Sadeli

A 2-year-old Indonesian boy was referred to the Pediatric Dermatology Department with dry and brown scaly skin over his entire body (Fig. 6.1). He was born preterm and encased in thin, translucent membrane. Over the first 4 weeks, the membrane was shed and replaced by large, plate-like scales in generalized distribution. No redness or fine scales. He never sweats. His eyes could not close completely and sometimes there was redness. No other anomalies or symptoms. Family history was taken and pedigree analysis was done. No dermatological-related disorder or any genetic disease. No history of consanguinity. No maternal complications or any drug exposure during pregnancy.



Fig. 6.1 Dry and brown scaly skin over his entire body

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Based upon history and clinical appearance, what is your diagnosis?

1. Lamellar Ichthyosis
2. Non-Bullous Congenital Ichthyosiform Erythroderma
3. Ichthyosis Vulgaris

On examination there were scarring alopecia on the scalp, crumpled left ear, madarosis on the eyebrows, eclabium on the mouth and ectropion on the eyes. Dermatology examination showed large, brown, polygonal scales over the entire body with plate-like appearance. We also found hyperkeratotic and hyperlinear palmaris and plantaris. Dermoscopy examination showed quadrilateral brownish structures with fine white scale around arranged in lamellar pattern (Fig. 6.2). Genetic examination is the standard diagnosis but it is expensive and the treatment is not based on the ichthyosis types.

The final diagnosis for this patient is lamellar ichthyosis.

Treatment of this patient consists of urea 10% cream applied twice a day over the entire skin. The parents were advised to keep the surroundings cool and avoid heavy activities to prevent the increase of body temperature, also genetic counselling. We also consulted the patient to the ophthalmologic department and were given artificial tear drops to prevent dryness and keratitis.

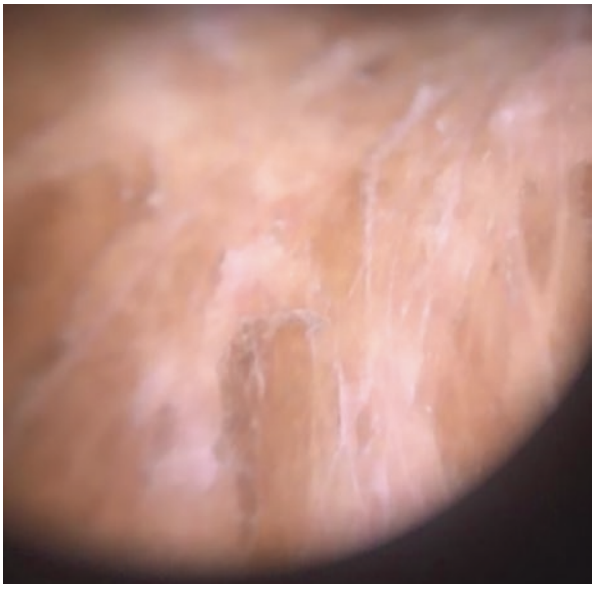


Fig. 6.2 Dermoscopy examination

Discussion

Collodion baby is a rare congenital disorder characterized by parchment-like taut membrane covering the whole body, often resulting in ectropion and eversion of the lips. Primary pathology in ichthyosis is disordered cornification, which leads to formation of collodion membranes. In the long term course, approximately 75% of collodion baby cases will develop an Autosomal Recessive Congenital Ichthyosis (ARCI) [1]. In rest 15% cases association with various entities is seen like ichthyosis vulgaris, trichothiodystrophy, metabolic and endocrine disorders which involve keratinization disorders [2]. So far, six genes have been associated with mutations with transglutaminase-1 accounting for approximately 40% cases [1]. In our case, the patient was born as collodion baby and later the membrane shed and showed the abnormalities beneath which are large, plate-like scales in generalized distribution, no redness.

All types of ichthyosis show abnormalities of the two outermost skin layers, stratum granulosum and stratum corneum, causing impairments of the skin barrier function. The molecular defects differences determine the patient's signs and symptoms. ARCI is a heterogeneous group of recessively inherited disorders with congenitally appearing ichthyosis but no extra-cutaneous involvement. The most common mature phenotypes are generalized Lamellar Ichthyosis (LI) and Congenital Ichthyosiform Erythroderma (CIE). It is often combined with palmoplantar keratoderma, ectropion, and anhidrosis. Clinical subtyping by looking at the relationship between ichthyosis and erythema severity is needed to differentiate it [2]. Ichthyosis Vulgaris is the mildest form of hereditary non-syndromic ichthyosis. Predilection areas are the extensor sides of the lower legs and the back, sparring chest and abdomen and often combined with keratosis pilaris and palmoplantar hyperlinearity [3]. In our case, the clinical signs support lamellar ichthyosis diagnosis.

Observational study by Gajjar et al. on pediatric patients shows that the dermoscopy findings of ichthyosis is hyperkeratosis and widened intercellular space. Scaling pattern observed clinically as well as dermoscopically helps in differentiating disorders of cornification like ichthyosis. Ichthyosis vulgaris is characterized by a criss-cross pattern of fine white scale and LI is characterized by quadrilateral brownish structures with fine white scale around arranged in lamellar pattern [4]. In our case, the dermoscopy findings also support lamellar ichthyosis diagnosis.

Symptomatic treatment with emollients and topical keratolytics remains the mainstay therapy for ichthyosis. By mixing hydrating and keratolytic agents in the right combinations, surprisingly effective creams can be obtained. However, the risk of systemic absorption of the ingredient, especially in infants treated over the whole body, must always be considered· Patients with LI often have profound hypohydrosis and are at risk for hyperpyrexia in hot climates [2, 4, 5]. In our case, we give urea 10% cream which acts as a hydrating agent, and also we give genetic counselling and education for the parents.

Key points:

- Most patients with lamellar ichthyosis are born as collodion babies.
- It is difficult to diagnose just by the clinical appearances, and dermoscopy can help to differentiate some types of ichthyosis.
- There is no cure for lamellar ichthyosis, symptomatic and supportive treatments remain the mainstay therapy.

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Chapter 7
A Newborn with a Large Facial Segmental Vascular Lesion

Maurizio Parisi and Fabio Arcangeli

A baby born full term after a normal pregnancy presented a large erythematous area on the right side of the face at 6 days of life (Fig. 7.1). Its colour is mostly uniform but teleangectatic striae were present. The little girl was in good health and no other skin manifestations were present.



Fig. 7.1 Large flat erythematous lesion on the right half of the face

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Based on the history and the photograph, which is your diagnosis?

1. Capillary malformation (CM)
2. Sturge-Weber syndrome (SWS)
3. Infantile Hemangioma (IH)
4. PHACES syndrome (PS)

Diagnosis

Infantile Hemangioma (macular phase)

Discussion

In the hypothesis of a capillary malformation (CM) an expert dermatologist specializing in pulsed dye laser treatment was consulted. At the same time a brain MRI was performed with a normal result.

The appearance of the lesion after the birth suggested a diagnosis of IH. Large facial hemangiomas frequently arise with a flat feature, so much so as to create differential diagnosis problems with CM.

Within 2 weeks, the lesion became raised suggesting a diagnosis of IH (Fig. 7.2).

Due to of dyspnoic crises, the child was admitted to a specialized hospital where a laryngotracheoscopy was performed revealing a subglottic hemangioma.

Local (depomedrol) and systemic (prednisone 3 mg/kg/day) corticosteroid therapy was started, but the lesion continued to grow in the following weeks (Fig. 7.3).

After 3 months of steroid therapy, not only the clinical picture and dyspnea didn't improve, but intubation was necessary during two critical respiratory episodes.



Fig. 7.2 The raised erythematous lesion after 2 weeks



Fig. 7.3 The three-dimensional growth of the lesion which appeared more and more prominent

It was therefore decided to add vincristina to prednisone, which the baby began at the age of 5 months.

Unfortunately, the therapy didn't bring about any improvement. Furthermore, the little girl had a serious episode of worsening dyspnea, caused by the appearance of a voluminous paratracheal hemangioma. In an attempt to reduce its volume steroid infiltration and arterial embolization was carried out.

Immunosuppressive therapy that proved unsuccessful resulted in severe muscular dystrophy with arrested weight and statural growth. After the first report about the effectiveness of systemic propranolol in reducing IH [1] was published, we immediately started the treatment of propranolol at the dosage of 2 mg/kg/day, three times a day. A few days after starting the propanolol therapy there was an impressive involution of the hemangioma which appeared bluish in colour and less consistent. Two months later it had considerably reduced in volume in all its districts, especially in the right periorbital (Fig. 7.4). The laryngotracheoscopy showed a complete involution of the subglottic and paratracheal hemangiomas.

Therapy with propanolol was continued until the 18th month of life with the almost complete regression of the hemangioma (Fig. 7.5).

It is of great importance to distinguish IH from CM as soon as possible because of evolution is different and the therapeutic approach too (Table 7.1).

Infantile hemangiomas are benign vascular lesions that have a characteristic clinical course. They usually appear after the birth, increase their size early due to endothelial proliferation, then slowly spontaneously regress. Hemangiomas are the most common tumors of infancy. The estimated incidence is between 4 and 5%. Propranolol has become the treatment of choice for disfiguring or functionally significant hemangiomas [2].



Fig. 7.4 Improvement of the ehemangioma, mainly on the periorbital area



Fig. 7.5 Advanced regression of the face hemangioma

Table 7.1 Differences between IH and CM

Infantile hemangioma	Capillary malformation
Usually appears in the early neonatal period (1 week after the birth)	Usually presents at birth
Is a vascular tumor due to endothelial cells proliferation	Is a vascular malformation due to embryogenetic defects
Usually disomogeneous in colour or with teleangectasias or raised areas inside	Usually its colour is uniform, without teleangectasias and raised areas
Two phases 1. rapid three-dimensional growth 2. slow regression by the age of 5–10 years	Continues to grow with flat appearance, with the growth of the patient, without a tendency towards regression
When segmental localized on the face and >5 cm in diameter possible PHACES syndrome Necessary: • MRI with and without intravenous gadolinium	When localized on the face possible Sturge-Weber syndrome. Necessary: • MRI with intravenous gadolinium and/or single-photon emission computed tomography (SPECT) or positron emission tomography (PET) scanning • Complete eye examination
Early medical therapy with oral propranolol (2–3 mg/kg/day)	No medical therapy, early treatment with Pulsed Dye Laser

A large facial segmental hemangioma has associations with PHACES syndrome (PS). The name PHACES is an acronym of *P*osterior fossa malformations, *H*emangioma of the cervicofacial region, *A*rterial anomalies, *C*ardiac anomalies, *E*ye anomalies, and *S*ternal or abdominal clefting or ectopia cordis [3].

Capillary malformation, also called port-wine stain or nevus flammeus, is generally present at birth. It can grow in size but only commensurate with the child and remain flat. Capillary malformations are present for life and have no tendency toward involution [4]. Pulsed dye laser is the treatment of choice for capillary malformation. It is safe and effective when performed every 2 weeks or every 3 months early in infancy [5].

The CM can associate with other malformations. In the case of large capillary malformation on the half of the face it is important to consider the possibility of a Sturge-Weber syndrome. The classic trisymptomatic type of SWS is characterized by a congenital facial capillary malformation, an ipsilateral vascular anomaly in the brain (leptomeningeal hemangioma), and an ocular hemangioma. In every case of large CM on the upper face early brain MRI with gadolimum and a complete eye examination is needed [6].

Key Points

- Sometimes a large facial IH may appear as a flat lesion at the initial stage and may mimic a CM
- Clinical markers of IH in flat appearance are teleangectasias and raised areas inside
- The medical therapies for IH in the pre-Propanolol era were ineffective and with side effects
- The use of Propanolol for IH has dramatically changed its natural history

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Chapter 8
A Newborn with Several White Spots on the Forehead

Maurizio Parisi and Fabio Arcangeli

A 3-month-old girl came to our observation because her mother had noticed the presence of some white spots on her forehead. The little girl was in good health and her birth occurred at full term without any problems.

The clinical examination showed several greyish white spots on her forehead (Fig. 8.1) and also clear signs of seborrheic dermatitis on the scalp, especially at the hairline.

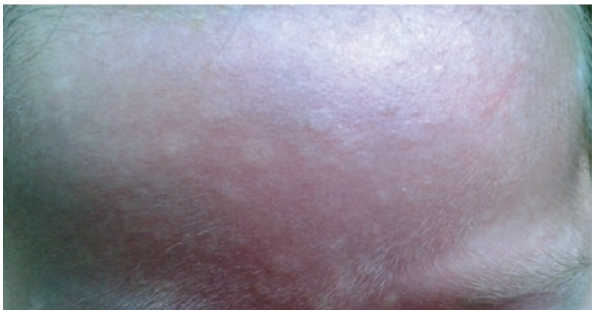


Fig. 8.1 Hypopigmented round macules on the forehead

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Based on the history and the photograph, which is your diagnosis?

1. Vitiligo
2. Tinea versicolor (achromians)
3. Pityriasis alba

Diagnosis

Tinea versicolor (TV)

Discussion

Tinea versicolor (also known as Pityriasis versicolor) is a benign superficial cutaneous mycosis very frequent in young people and adults and less common in pediatric age.

Tinea versicolor is caused by Malassezia, a lipophilic yeast which naturally colonizes on the human skin and occasionally becomes pathogenic.

Some factors that lead to the conversion of the saprophytic yeast to the parasitic, mycelial morphologic form, include a genetic predisposition, warm, humid environments and seborrheic skin. Sometimes immunosuppressive diseases or immunosuppressive drugs can play a causative role [1].

TV is asymptomatic and is not considered contagious because the responsible pathogen is a normal inhabitant of the skin.

The cutaneous manifestations of the TV (achromians type) consist of hypochromic spots that are rounded or oval, with well defined borders (Table 8.1). The surface is smooth or covered with thin scales. The preferred location is the trunk in young people and adults, the face, particularly the frontal region, in newborns and infants [1, 2].

In fair-skinned patients, the disease is often diagnosed in the summer months as the lesions do not darken and become more noticeable than tanned skin.

The hypopigmentation of the spots is due to the inhibition of tyrosinase caused by azelaic acid produced by Malassezia [2].

Table 8.1 The main clinical differences and different Wood's light pattern in tinea versicolor, vitiligio and pityriasi alba

Disease	Shape	Margins	Wood's lamp pattern
Tinea versicolor	Rounded or oval	Well defined	Greyish white Yellow-green fluorescence
Vitiligo	Irregular	Well defined	Milky white Blue fluorescent
Pityriasis alba	Rounded or oval	Poorly defined	Greyish white No fluorescence

Occasionally, the TV lesions may be hyperpigmented (chromians type).

The clinical presentation of TV is distinctive, and the diagnosis is often made without any laboratory documentation. Clinical diagnosis is based on:

- typical appearance and location of the lesions
- Wood's lamp examination (Table 8.1)

The Wood's lamp emits an ultraviolet light with a wavelength between 320 and 400 nm. It is usually absorbed from the dermo-epidermic junction melanic pigment.

The Wood's lamp examination must be carried out in an absolutely dark environment. It is successfully used in dermatology, with diagnostic purposes, especially in pigmentation disorders [3].

The low cost of the device, the simplicity of execution and the immediacy of the result make it the first choice when TV is suspected.

The Wood's lamp examination of the hypopigmented lesions of TV shows a dull white colour. Infact, because the epidermis melanin is reduced but not absent in TV, the Wood's light is partially reflected and a partially absorbed. In the case of complete absence of epidermis melanin, as happens in vitiligo lesions, the Wood's light is completed reflected and the macules appear milky white with a slight blue fluorescence. Furthermore, in TV the parasitic lesions show a typical yellow-green fluorescence (Fig. 8.2).

The therapy consists of the use of topical antifungals in different formulations: creams, lotions, sprays or shampoos. Treatment leads to the disappearance of scaling within a few days, but discoloration may last for weeks to months [1].

Parents and caregivers need to realize that TV is caused by a fungus that is normally present on the skin surface; thus, it is not considered a contagious disease. Sequelae from the disease are not permanent, and any pigmentary alterations resolve entirely 1–2 months after treatment is initiated [1].

Relapses are very frequent due to the predisponent factors and a permanent cure may be difficult to achieve. Consequently, a prophylactic treatment regimen—such as an intermittent use of topical antifungals—may help to prevent its recurrences.

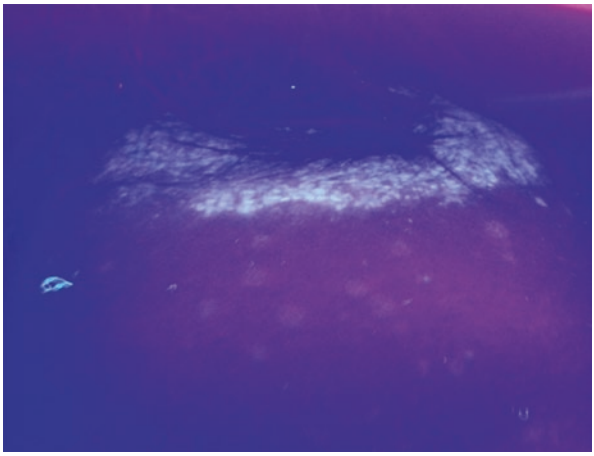


Fig. 8.2 Hypopigmented grayish white macules on the forehead and yellow fluorescence on the scalp

The main differential diagnosis include:

- Vitiligo

Vitiligo is an immune-mediated skin condition resulting in a loss of pigmentation. Acral or acrofacial vitiligo typically involves the face and distal extremities, generally with a symmetrical appearance. The macules presents well defined margins as TV but the Wood's lamp examination shows a milk white pattern with common blue fluorescence [2].

- Pityriasis alba

Pityriasis alba is a disorder commonly associated with atopic dermatitis, usually presenting as hypopigmented, irregular patches on the face, forearms, thighs and less frequently on the trunk, in children and young adults. Excessive unprotected sun exposure may be a trigger. A fine scale with itching is occasionally present. The macules always have ill defined margins and the Wood's lamp examination shows a greyish white pattern without any fluorescence [2].

Key Points

- Tinea versicolor usually affects young people and adults but it is non infrequent in infants and children
- Although tinea versicolor can occur in immunosuppressed patients, the most affected patients are usually healthy
- The disease is often diagnosed in the summer months because hypopigmented lesions become more prominent than tanned skin
- To confirm the diagnosis the Wood's lamp examination is usefull
- The first line treatment is topical antifungals

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Chapter 9
A One-and-a-Half-Month-Old Boy with Recurrent Fever, Heat Intolerance and Diminished Sweating

Alfonso Delgado Rubio and Fabio Arcangeli

A 1½-month-old boy is presented for a visit because of recurrent febrile episodes since he was 2 weeks old. Previously he was hospitalized in another pediatric clinic where all investigations performed (laboratory tests, microbiological tests, bone marrow examination, x-rays, ultrasound scans, etc.) were negative. The family reported that the child was irritable and didn't tolerate heat, cried with few or no tears, and seemed not to sweat. The family history was negative, the pregnancy had been normal, with physiological delivery at full term.

On physical examination, the child presented normal growth percentiles. His appearance was abnormal (Fig. 9.1), his hair was sparse, eyelashes and eyebrows were absent. His skin, thin and very pale, was particularly wrinkled on the eyelids and lips. No other abnormalities were observed, in particularly the nails was normal.

At that time, we made no further investigations. We recommended avoiding high environmental temperatures, dressing him lightly and washing him frequently on hot days, without drying him. We also prescribed the use of artificial tears and a physiological solution to moisten the nose and ears. We informed the family that later dental prostheses would be needed and we put them in contact with other specialists to better address any foreseeable aesthetic, functional and psychological problems.

At 6, the boy had normal body weight and regular psychomotor development. The appearance of the face remained the same: the forehead was very wide, the root of the nose was deformed like a "saddle", eyelashes and eyebrows were absent, the

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Fig. 9.1 Sparse scalp hair, absent eyelashes and eyebrows, wrinkled eyelids and lips

lips was everted (Fig. 9.2). His hair was sparse with areas of alopecia (Fig. 9.3). The teeth were few and conical (Fig. 9.4).

Based on the clinical history and the photographs which is your diagnosis?

1. Congenital Syphilis
2. Ellis van Creveld syndrome
3. Tricho-dento-osseous (TDO) syndrome
4. Ectodermal dysplasia anhydrotic

Diagnosis

Ectodermal dysplasia anhydrotic



Fig. 9.2 Typical face with wide forehead, "saddle" nose, absence of eyelashes and eyebrows, everted lips

Discussion

The "saddle" nose and the alterations of the lips could suggest a diagnosis of syphilis. However, these sequelae in the case of syphilis tend to appear later. Furthermore the particular phenotype of our patient, as well as hypodontia, conical teeth and other clinical features described ruled out the diagnosis of congenital syphilis.

In Ellis van Creveld syndrome, dental changes with partial agenesis or conical teeth can be observed. However, this syndrome is also characterized by short stature, congenital heart disease, typical skeletal manifestations and polydactyly [1] which are absent in our case.

Tricho-dento-osseous (TDO) syndrome is an autosomal dominant disorder characterised by curly hair at infancy, anomalies of the eyelashes and eyebrows, hypoplasia and taurodontism of teeth, sclerotic bone, palmar and plantar keratosis, "café au lait" spots with normal sweating [2]. Our patient presented only some of these manifestations.



Fig. 9.3 Sparse hair with areas of alopecia



Fig. 9.4 Hypodontia and conical teeth

Ectodermal dysplasias (Eds) is a genetic heterogeneous group of disorders characterized by developmental dystrophies of ectodermal structures. They mainly affect the hair, nails, teeth and sweat glands. Over 190 varieties have been described [3–5].

Ectodermal dysplasia anhydrotic (EDA) is the most common among Eds.

It includes three subtypes, not clinically differentiable, which show, as a cardinal sign, a sweating disorder:

1. Christ-Siemens-Touraine syndrome (X-linked). Associated with EDA gene (Xq12-q13.1)
2. Autosomal dominant EDA. Associated with the EDAR gene (2q13)
3. Autosomal recessive EDA. Associated with the EDARADD gene (1q42.3)

A fourth rare subtype is known, EDA with immunodeficiency.

Christ-Siemens-Touraine syndrome (CST) is the most common subtype (80%) and its incidence in males is estimated at 1 in 50,000–100,000 births [5].

It is characterized by the triad of signs comprising sparse hair (atrichosis or hypotrichosis), abnormal or missing teeth (anodontia or hypodontia) and inability to sweat due to lack of sweat glands (anhidrosis or hypohidrosis). All these symptoms were present in our patient.

The autosomic recessive and dominant forms affect both sexes equally. In the X-linked form, carrier females may be asymptomatic or have a milder phenotype: oligodontia, conical incisors, hypotrichosis, and reduced sweating.

The defective sweating ability often leads to recurrent hyperthermic episodes (recurrent fever not otherwise explained) and heat intolerance. The recurrent hyperthermic episodes are commonly the initial presentation causing the request for medical intervention [6]. Dry skin and eczematous dermatitis, decreased teas, and photophobia are common while onychodystrophy is not frequent.

Most patients with EDA have a normal life expectancy. However, the hyperthermia may be followed by brain damage in early infancy, if unrecognized. Thus an early diagnosis is very important. The aim of the treatment is to restore the function and the aesthetics of the teeth [7]. As long as there are no physical, psychological or social burdens, no treatment is necessary.

Key Points

- Recurrent fever, secondary to anhidrosis or hypohidrosis,, may occur in the neonatal period as the first sign of Ectodermal dysplasia anhydrotic
- Infant affected may show typical face with wide forehead, “saddle” nose, absence of eyelashes and eyebrows, everted lips early
- Most patients with EDA have a normal life expectancy. However, the hyperthermia may be followed by brain damage in early infancy, if unrecognized.

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Chapter 10
A Red Nodule on the Cheek

Miriam Anna Carpanese, Giulia Veronesi, Marco Adriano Chessa, Alba Guglielmo, and Iria Neri

A 2-year-old child presented with a painless non tender red nodule located on his cheek (Figs. 10.1 and 10.2). The parent reported that the nodule had appeared 1 month before. They also reported recurrent chalazia during the last year.



Fig. 10.1 A red nodule on the cheek

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Fig. 10.2 Detail of the red nodule of the cheek

Based upon history and clinical appearance, what is your diagnosis?

1. Spitz nevus.
2. Cutaneous leishmaniasis.
3. Idiopathic Facial Aseptic Granuloma (IFAG).
4. Pilomatricoma.
5. Pyogenic granuloma.

Diagnosis: Idiopathic Facial Aseptic Granuloma (IFAG)

The physical examination showed a solitary non tender erythematous nodule of about 1 cm in diameter, located on the left cheek. No systemic symptoms or enlarged regional lymph nodes were observed.

Dermoscopic findings: erythematous background with non-branching vessels, whitish perifollicular halo, follicular plugs. A cheek ultrasound scan showed hypoechoic central lesion with hyperechoic peripheral signals.

Discussion

Idiopathic Facial Aseptic Granuloma (IFAG) is an uncommon pediatric disease characterized by one, rarely more, asymptomatic reddish-violaceous nodules usually located on a specific triangle-shaped area of the cheek, delimited by the external limit of the orbit, the labial angle, and the ear lobe. The most cases are young infants and toddler-aged children under 4 years of age [1]. Although the pathogenesis of IFAG remains unclear the most current hypothesis is that it may be a form of granulomatous rosacea, due to the similar histopathologic features, the association with recurrent chalazia and the response to same medications [2]. IFAG has a prolonged

course with a spontaneous resolution within months. Differential diagnosis include nodular infantile acne, localized infectious pyodermas, pyogenic granulomas, xanthogranulomas, vascular malformations, dermoid or epidermoid cysts, and benign tumors such as pilomatricomas [3]. In several cases, clinical characteristic could not be sufficient to confirm the diagnosis, and dermoscopy, ultrasonography and histology are needed. Dermoscopy reveals perifollicular hypopigmentation, follicular plugging and nonbranching vessel on an erythematous background [4]. Ultrasound is a non-invasive technique that can improve the diagnosis and the follow-up of IFAG, showing an oval-shaped hypoechogenic dermal lesions with irregular margins and surrounding hyperechogenicity and hypervascularization [5]. Histology is characterized by inflammatory granulomatous infiltrate of the dermis with lymphocytes, neutrophils and plasma cells around epithelioid histiocytes. There is no agreement on the treatment of IFAG. Due to its benign and auto-resolutive course a conservative approach should be preferred. Local and systemic antibiotics such as metronidazole, oral doxycycline, clarithromycin can be prescribed. In our patient we prescribed topical ivermectina twice daily with a complete resolution [6]. Drainage and surgical excision represent a second-line treatment in persistant cases [7].

Key points

- IFAG is a rare disease that presents with one or more reddish-violaceous nodules located on the cheeks
- Main differential diagnosis are nodular acne, infectious pyodermas, pyogenic granulomas, xanthogranulomas, vascular malformations, dermoid or epidermoid cysts, pilomatricomas
- Dermoscopic and ultrasound features can help confirming the diagnosis in order to avoid skin biopsy

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Chapter 11
Acrodermatitis Enteropathica in a 7-Month-Old Baby Boy

Luh Made Mas Rusyati, Made Wardhana, and Dewi Gotama

A 7-month-old baby boy, was referred to the department of dermatology and venereology because of redness with skin peeling. Redness and exfoliation were found in the back of the head, back of the neck, around the mouth, both of palms and soles, groin, buttocks, and scrotum (Fig. 11.1). No history of diarrhea. He received exclusive breastfeeding for the first 6 months of life, followed by breast milk and solid foods in the form of porridge. His parents have not had similar complaints, and they were not blood-related. However, there was a marriage with blood relations between the grandfather and grandmother on the mother's side. There was no history of similar complaints from other family members.

Based on the case description and photographs, what is your diagnosis?

1. Acrodermatitis Enteropathica
2. Necrolytic migratory erythema
3. Atypical psoriasis
4. Epidermolysis bullosa

On examination we observed multiple erythematous patches with marginal scaling on the back of head and neck, perioral region, anogenital region, both of palms and soles.

We also found the zinc serum level was 14 μg/dL (29–131 μg/dL) and the biopsy result was representative for acrodermatitis enteropathica (Fig. 11.2).

The final diagnosis for this patient is acrodermatitis enteropathica.

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Fig. 11.1 Erythematous lesion with marginal scaling

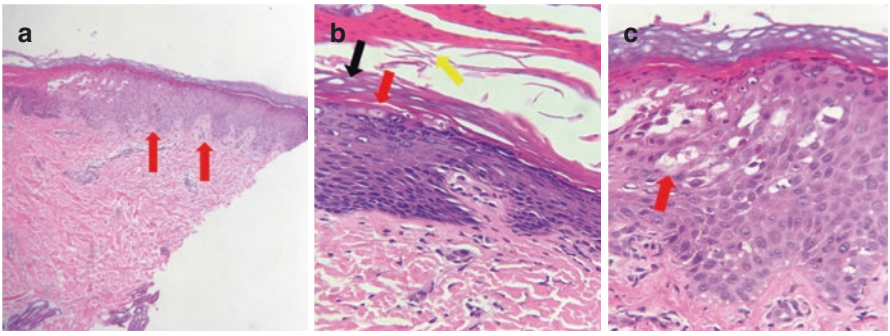


Fig. 11.2 Biopsy results. (**a**) On epidermis and dermis layers found psoriasiform. (**b**) The appearance of parakeratosis, orthokeratosis, pale keratinocyte (degenerative keratinocyte) (magnification of 10× and 40×, H&E). (**c**) The appearance of ballooning degeneration (spongiosis) (magnification of 40×, H&E). No sign of subepidermal bullae

The treatment consists of zinc supplementation orally and found the rapid and progressive clinical improvement.

Discussion

Acrodermatitis enteropathica (AE) is a rare disease inherited through autosomal recessive. This condition occurs because mutation from a zinc transporter causes a disruption in zinc absorption in the intestines, which is the zinc-ligand binding

protein 4 (ZIP4), coded for the SLC39A4 gene. Acrodermatitis enteropathica usually occurs after switching breastmilk to formula milk or cereals, or if within the fourth or tenth week of age, the infant did not receive breastmilk [1]. The classic clinical manifestations of AE are alopecia, diarrhea accompanied by lethargy, and periorificial dermatitis (perioral, periocular, and anogenital), and acral areas (hands and legs) [1]. The skin lesion starts as a vesiculobullous eruption on the skin surface with an erythematous base. The bullae will rupture quickly and turn into crust [2]. In this case, skin manifestations of lesions around the perioral area, neck, anogenital, and acral accompanied by alopecia on the back of the head were found. There was no sign of diarrhea or nail abnormality.

To aid in establishing a diagnosis, an adjunctive examination of zinc serum level and biopsy was conducted. In acrodermatitis enteropathica, zinc serum level examination is the gold standard. It will result in a low serum level in plasma. The histopathological characteristics of acrodermatitis enteropathica include various psoriasiform hyperplasia with parakeratosis, spongiosis, and paleness on the upper part of the epidermis [1]. In this case, the results found that low zinc serum level and biopsy were in accordance with the characteristics of acrodermatitis enteropathica.

Acrodermatitis enteropathica requires lifetime continuous therapy of zinc supplementation. The clinical response is usually fast with early improvement within days to weeks. There are several zinc formulas available, but the most common one is the zinc sulfate enteral formula [1]. The dose of zinc in acrodermatitis enteropathica is usually 1–3 mg/kg body weight/day per oral [3]. In this case, the patient was given 2 mg/kg body weight of zinc supplementation orally. An improvement was seen after a week of zinc therapy.

Key points

- Acrodermatitis enteropathica (AE) is a rare disease inherited through autosomal recessive.
- The classic clinical manifestations of AE are alopecia, diarrhea and dermatitis
- Acrodermatitis enteropathica requires lifetime continuous therapy of zinc supplementation.

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Chapter 12
An 11-Month-Old Child with a Nodular Lesion on Her Right Buttock

Giuseppe Ruggiero and Cosimo Ruggiero

An 11-month-old caucasian girl presented with a single-like asymptomatic lesion which appeared on the right buttock at 7 months. Physical examination revealed a sharply-defined erythematous plaque 15 mm in diameter with a smooth surface and hard consistency (Fig. 12.1).



Fig. 12.1 Erythematous plaque on the right buttock

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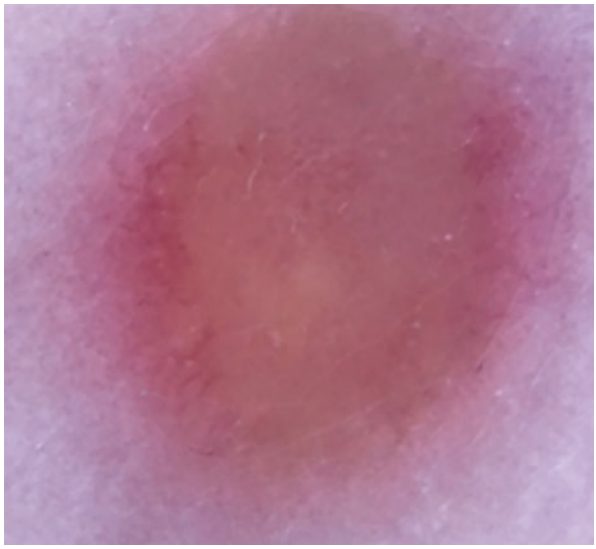


Fig. 12.2 Light central patch with a surrounded pigment network by dermoscopic examination

The family did not report any medical conditions or triggering events such as trauma, insect bites or similar findings.

The dermoscopic examination showed a lighter central patch, surrounded by a thin but regular pigment network, which is gradually fading towards the periphery (Fig. 12.2).

Based on the Case Description and the Photographs, Which Is Your Diagnosis?

1. Dermatofibroma
2. Spitz nevus
3. Xanthogranuloma

Diagnosis

Dermatofibroma

Discussion

Dermatofibroma is one of the most common soft tissue tumors of the skin in adults. A study evidenced 80% of cases between 20 and 49 years [1]. The presentation can vary from 2 months to 77 years [2, 3]. Cases before the first year of age are very

rare. Over 70% of the lesions occur on the extremities (only 6% of cases are found on the buttocks) and they are brown with a smooth surface. About 2–3% of the skin tumors occur at sites of insect bites and most of them are asymptomatic (58.2%). In addition, more than two lesions are present in 14.7% of the patients [2–4].

Dermatofibromas are entirely contained in the thickness of the dermis and on palpation they give the sensation of a hard nodule, the so-called pastille fibroids.

The Fitzpatrick sign or "dimple sign" is a typical dermatological sign in which lateral pressure on the skin produces a depression should it be a dermatofibroma.

The most common dermoscopic pattern associated with dermatofibroma shows a pigment network and a central white patch. Nevertheless this tumor has a wide range of dermoscopic appearances.

Dermatofibromas tend to persist throughout life or sometimes they spontaneously regress over the years. Ulcerated and growing lesions must be surgically removed for an histopathologic evaluation. Excision is generally recommended in all patients, including children, to clarify the diagnosis and minimize the possibility of recurrence [5].

Differential Diagnosis

1. The Spitz nevus presents clinically as a plaque or nodule, usually amelanic, pink or red, mainly on the face and lower limbs. It is characterized by a rapid initial growth, followed by a phase of stabilization until its disappearance. The dermoscopic examination reveals an angiomatoid appearance with little or no melanic pigment. A differential diagnostic evaluation should be considered for growing lesions after their onset with a biopsy specimen [6].
2. Xanthogranuloma presents like a nodular lesion ranging in size from a few mm to 4–5 cm, brown, asymptomatic, apparently stable. Dermoscopically the lesion appears like a "setting sun" with an yellow, homogeneous and diffuse pattern and a typical vascular crown periphery.

Key Points

- Dermatofibroma is rare in pediatric age
- Hard consistency and "dimple sign" are suggestive for a clinical diagnosis of dermatofibroma
- The classical dermoscopic pattern with a white patch and periferic pigment network supports the diagnosis of dermatofibroma
- Ulcerated and growing lesions must be surgically removed for an histopathologic evaluation

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Chapter 13
An Annular Facial Erythema in a 2-Year-Old Girl

Ya-Bin Zhou, Ying Liu, Zi-Gang Xu, and Lin Ma

A 2-year-old girl presented with an annular erythema on the face. The lesion began 7 days ago as a small itchy macula with a gradually increased size. On physical examination, an annular erythema with scaling and crust measuring 1.0 × 1.2 cm was observed on the right cheek (Fig. 13.1). She was treated with topical mupirocin ointment for 2 days without any improvement. Her parents denied any history of preceding injury or insect bite and had a 2-month-old British shorthair cat at home. Her pet cat had an annular patch of alopecia, mild scaling on the trunk. She often played with the cat. She had a history of eczema from 3-month-old to 1-year-old. Her mother had a history of systemic lupus erythematosus for 1 year and was receiving oral prednisone therapy. The results of an antinuclear antibody profile (including antibodies to SS-A/Ro, SS-B/La, and ribonucleoprotein) were negative. Direct fungal microscopic examination of the lesion with calcofluor white revealed numerous fungal hyphae (Fig. 13.2). Fungal culture grew *Microsporum canis* (Fig. 13.3). She was treated with topical terbinafine hydrochloride cream for 4 weeks with complete remission of the lesion. No recurrence was reported at a 2-month follow-up visit. Her pet cat was diagnosed with dermatophytosis by a veterinarian and also treated with topical terbinafine.

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Fig. 13.1 A 1.0 × 1.2 cm annular erythema with scaling and crust was observed on the right cheek

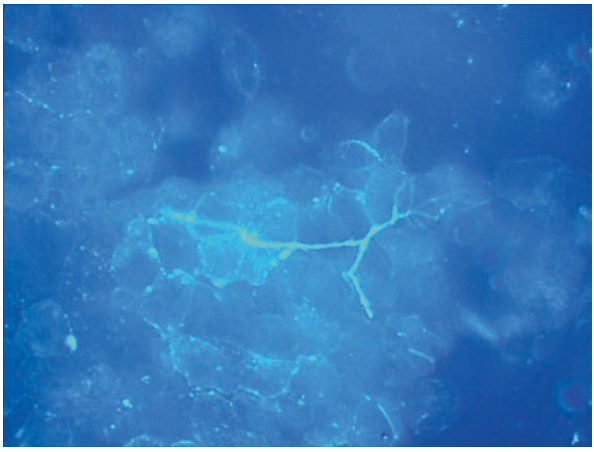


Fig. 13.2 Microscopy of the lesion, showing numerous fungal hyphae (calcofluor white staining, original magnification ×400)

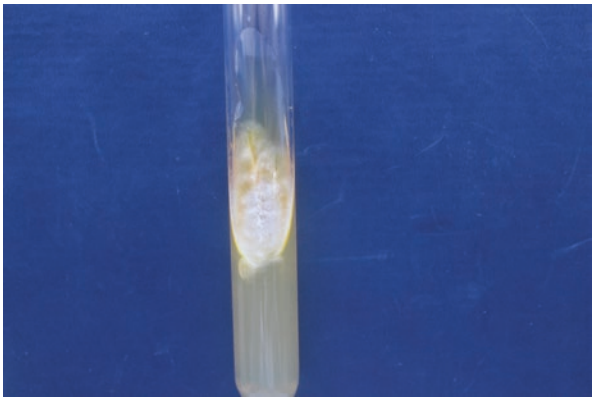


Fig. 13.3 Rapid growth, velvety or downy, yellowish colonies on Sabouraud dextrose agar after 2 weeks incubation

Based on the Case Description and the Photograph, What Is Your Diagnosis?

- Impetigo
- Nummular eczema
- Subacute cutaneous lupus erythematosus
- Granuloma annulare

Diagnosis

Tinea faciei

Discussions

Tinea faciei is a relatively uncommon superficial dermatophytosis that occurs on the glabrous skin of the face. The causative agent varies according to the geographic region and the potential environment reservoirs. In the USA, *Trichophyton tonsurans*, *Trichophyton rubrum*, and *Microsporum canis* are the most common causative agents [1]. Whereas in China, *Trichophyton mentagrophytes* is the most predominant species [2]. Two age peaks are observed in tinea faciei [3]. One peak involves children, often due to direct contact with pets. The other peak occurs in those aged 20–40 years. This may be due to the occupational exposure or leisure activities in this age group. Typical lesions of tinea faciei are single or multiple annular scaling patches with central clearing. Compared with other forms of tinea, tinea faciei has a high potential for misdiagnosis, possibly due to the complex anatomy of the face [1]. Direct fungal microscopic examination along with fungal culture of the lesions remains the gold standard for establishing the diagnosis of tinea faciei. Histopathological examination can also be performed, but special stains such as periodic acid–Schiff (PAS) stain are usually needed to detect fungal elements [1]. Topical antifungals are the first-line treatment for most cases of tinea faciei. The most common used antifungal drugs are azoles and allylamines [1]. Systemic antifungal treatment is needed for those with co-existence of vellum hairs infection, very atypical forms or multiple affected cutaneous areas. Alternative drugs include terbinafine, itraconazole, fluconazole and griseofulvin. Oral antifungal treatment usually needs 1–2 weeks.

Impetigo is a common, contagious infection of the superficial layers of the epidermis that can present in non-bullous and bullous forms. Non-bullous impetigo is usually caused by *Staphylococcus aureus* and *Streptococcus pyogenes*. The bullous impetigo is usually caused by *S. aureus* [4]. It is often located on the face but can also occur in any other part of the body with crusting erythematous plaques. The

diagnosis is usually clinically. Bacterial culture of the exudate from beneath the crust or fluid from intact bullae can help confirm the diagnosis.

Nummular eczema presents as multiple coin-shaped, pruritic, erythematous lesions. It may occur as a feature of atopic dermatitis. It usually presents on the extensor surfaces of the extremities and trunk. Face lesions are rare. The diagnosis is based on its classical presentation. Nummular eczema is often mistaken for tinea, and direct fungal microscopic examination of skin scrapings may help rule out tinea [5].

Subacute cutaneous lupus erythematosus (SCLE) is a subtype of cutaneous lupus erythematosus presenting as photosensitive erythematous rash confined to sun-exposed skin. Lesions of SCLE may have annular lesions with central clearing, or papulosquamous lesions with an eczematous or psoriasiform appearance. SCLE has a strong association with anti-Ro antibody, about 70% of the patients have anti-Ro antibody [6]. The lesions typically heal without scarring but with dyspigmentation.

Granuloma annulare is a benign, usually self-limited, cutaneous disease of unknown etiology. It is often located on the lateral and dorsal hands and feet presenting as arciform to annular plaques. There is usually no pruritus or pain associated with the lesions. Histologically granuloma annulare is characterized by focal degeneration of collagen and elastic fibers, inflammation with interstitial histiocytes, and mucin deposition in the upper and mid dermis. Despite being a benign disease, it can be associated with HIV infection or malignancy [7].

Key Points

- Tinea faciei is a relatively uncommon superficial dermatophytosis and has a high potential for misdiagnosis.
- Direct fungal microscopic examination along with fungal culture of the lesions remains the gold standard for establishing the diagnosis of tinea faciei.
- Animal contact history is a significant diagnostic clue of tinea.

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Chapter 14
An Eczematous Lesion on the Forehead of a 3-Month-Old Child

Giuseppe Ruggiero and Luca Ruggiero

A 3-month-old child presented with a 1 month history of a non-itchy single lesion of the forehead. A physical examination revealed an annular and eczematous-like lesion with sharply defined and raised borders (Fig. 14.1). The dermoscopic examination showed a lighter central area and an erythematous edge (Fig. 14.2). Topical treatment with emollient and low-potency corticosteroids for 7 days was unsuccessful for the recurrence of the lesion after 10 days from the discontinuation therapy.

Based on the Case Description and the Photographs, Which Is Your Diagnosis?

1. Tinea Facei incognita
2. Atopic Dermatitis
3. Contact dermatitis

Diagnosis

Tinea facei incognita

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Fig. 14.1 Eczematous lesion on the forehead

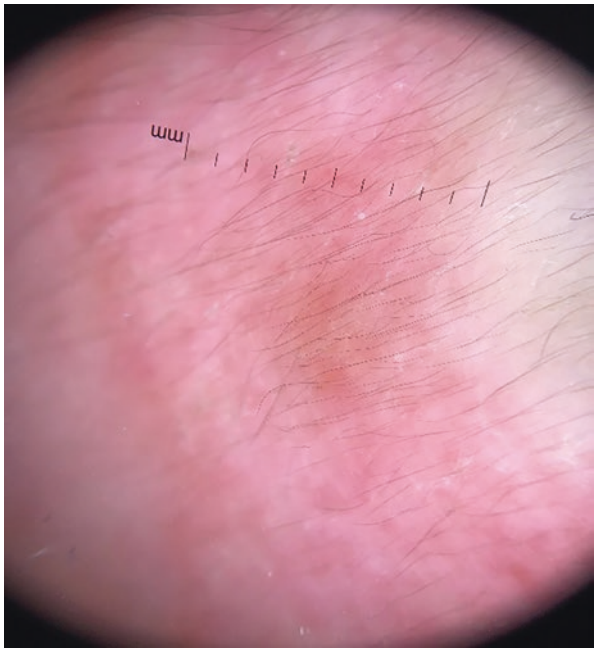


Fig. 14.2 Erythematous borders and lighter central area on dermoscopic examination



Fig. 14.3 The complete healing after 3 weeks' therapy

Discussion

Tinea facei is a facial dermatophytosis, first described in 1968 [1]. It is typically rounded, erythematous and with scaling patches. It represents about 3–4% of the dermatophytosis of glabrous skin and is very rare under 1 year. Only a few cases are reported in literature [2, 3]. The term "incognita" is used to define a clinical modified lesion after unsuitable treatment such as topical corticosteroids, antibiotics or calcineurin inhibitors [4, 5]. These medications reduce symptoms and signs of inflammation (itching, erythema and vesiculations), losing original clinical-morphological features. A direct microscopy and a culture test of scale are necessary to confirm diagnosis and to identify the etiologic agent for an appropriate treatment. In our patient due to SARS-CoV-2 pandemic, an empiric therapy with 1% topical ciclopiroxolamine was administered with complete healing after 3 weeks (Fig. 14.3).

Differential Diagnosis

1. Atopic dermatitis: the lesions are multiple, different in shape and symmetricon typical sites and often associated with desquamation and scabs. Usually they are very itchy.
2. Contact dermatitis: the lesion is erythematous and uniform without raised borders, often with a positive anamnesis.

Key Points

- If atopic dermatitis does not improve with adequate therapy, diagnosis could be different.
- Eczema is primarily included for differential diagnosis with "tinea incognita". Allergic contact dermatitis, atopic dermatitis and nummular eczema are the most frequently compared [6, 7].

- Microscopic and cultural examinations are necessary to obtain a certain diagnosis of “Tinea incognita”.
- Therapy of “tinea incognita” firstly requires to stop the use of the topical steroid and start a specific antifungal.

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Chapter 15
An Infant with Disseminated Red Scaling Papules

Jiahui Hu, Lihong Zhao, and Songmei Geng

A 6-month-old infant presented to our dermatology clinic with disseminated red scaling papules covering yellow to brown crusts for 2 months. Scars and hypopigmentation were left after healing (Fig. 15.1).

Based on the Case Description and the Photograph, What Is Your Diagnosis?

1. Eczema
2. Pityriasis lichenoides et varioliformis acuta
3. Lymphomatoid papulosis
4. Langerhans cell histiocytosis

No other systemic abnormalities were documented. She was born healthy through vaginal delivery after an uneventful pregnancy. No family history of similar lesions was recorded. The parents denied history of genetic diseases or drugs intake during pregnancy.

Physical examination showed no mucosal and other internal organs involvement. No lymphadenopathy or hepatosplenomegaly was found. Dermatological examination demonstrated multiple red scaling papules on the trunk and extremities, covering with yellow to brown crusts. Scars and hypopigmentation could be seen after healing.

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Fig. 15.1 Clinical manifestation of the patient: a 6-month-old infant presented with numerous red scaling papules, covering yellow to brown crusts. Scars and hypopigmentation were left after healing

Routing laboratory investigations, including peripheral blood examination as well as biochemistry analysis were all in normal limits, autoantibody series and the erythrocyte sedimentation rate also showed no abnormalities. Systemic involvement texts including electrocardiograph, chest X-ray, and skeletal X-ray examination were all negative.

Histopathologic examination demonstrated epidermal atrophy and invaded by a subcutaneous diffuse infiltrate extending into the deep reticular dermis. Higher power magnification showed large heteromorphic histocytes, with reniform nuclei, fine chromatin and abundant pale eosinophilic cytoplasm, accompanied by large eosinophils (Fig. 15.2). Immunohistochemical analysis revealed large histocytes were positive for CD1a and S100 protein (Fig. 15.3).

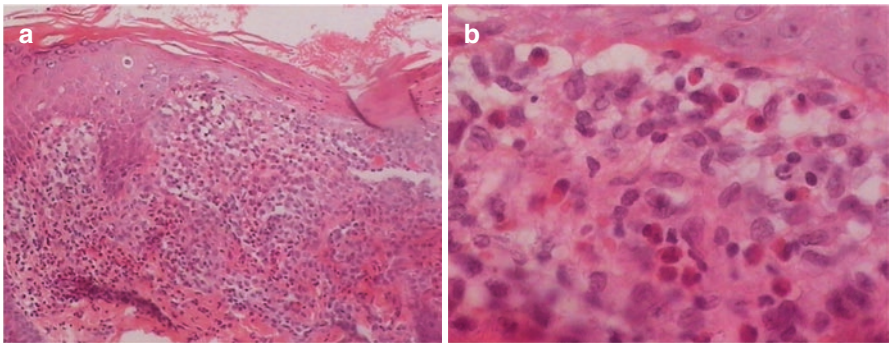


Fig. 15.2 Epidermal was atrophy and invaded by large heteromorphic histocytes with reniform nuclei, fine chromatin and abundant pale eosinophilic cytoplasm, accompanied by large eosinophils throughout dermis (**a**, HE ×10; **b**, HE ×40)

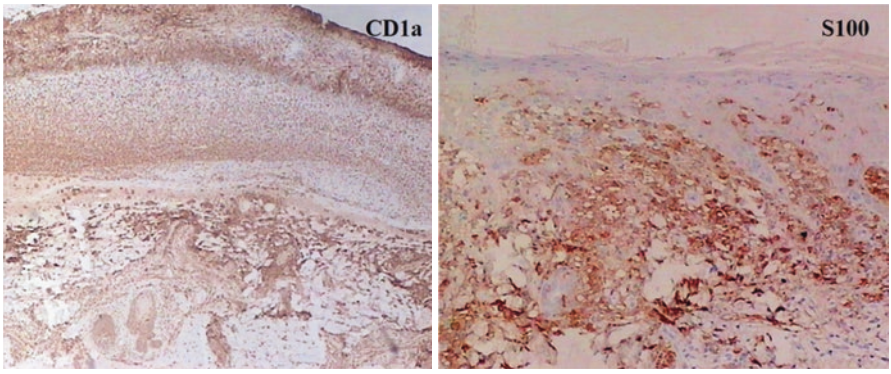


Fig. 15.3 Positive immunohistochemistry for CD1a and S-100 protein in infiltrating histocytes

Diagnosis

Langerhans cell histiocytosis

Discussion

Langerhans cell histiocytosis (LCH) is a rare heterogeneous disease more prominent in children than adults. LCH is characterized by the pathologic proliferation and excessive accumulation in a variety of organs with Langerhans cells that normally derived from epidermal and mucosal dendritic cells [1, 2]. The disease can be localized in a single organ or multi-organs involvement [3].

LCH has traditionally been described as four separate syndromes with different clinical severity: Hashimoto-Pritzker disease, Eosinophilic granuloma, Hand-Schüller-Christian disease and Letterer-Siwe disease. Currently, LCH patients are generally categorized as single system LCH (SS-LCH) and multi-system LCH (MS-LCH). MS-LCH can be categorized as high-risk type LCH and low-risk type LCH based on whether the organs at risk, including liver, spleen and bone marrow, are involved. The clinical severity of LCH ranges from benign skin lesions to invasive multi-organ disease [4].

Pityriasis lichenoides et varioliformis acuta (PLEVA) is believed to be an inflammatory reaction caused by certain infective factors or secondary to T cell clonal proliferative [5]. Clinical manifestations are multiple erythematous ulcerative necrotic lesions, which usually occur on the flexural side of extremities and the trunk. Scaly papules usually have a central punctum and develop into small vesicular with hemorrhagic necrosis, ulcers, and brown scabs, often leaving varioliformis scarring. Histologic analysis shows parakeratosis, basal layer vacuolization, extravasation of lymphocytes and erythrocytes extending into the epidermis, perivascular lymphocytic and histiocytic infiltration in the dermis. Immunohistochemistry reveals that the infiltrating cells are mainly $CD3^+$ and $CD8^+$ T lymphocytes.

Lymphomatoid papulosis (LyP) is a non-aggressive skin disorder with a tendency to self-regression. LyP is characterized by a variety of clinical features with solitary or aggregated papules and nodules, accompanied by central hemorrhage, necrosis and crusts, half of which remain superficial atrophic scars after healing [6]. There are five typical histopathologic subtypes of LyP: A, B, C, D and E, which vary according to the predominant cell type and tropism. The most common form is type A, which demonstrates the wedge-shaped dermal cellular infiltrate containing large anaplastic cells, plasma cells, pleomorphic lymphocytes and histiocytes. Immunohistochemistry shows CD30 expression in large anaplastic or pleomorphic lymphoid cells.

Treatment strategies of LCH depend on the site, extent and severity of the disease. In the cases of single lesion, topical steroids, surgical excision, thalidomide, methotrexate and phototherapy have all been used. Combined chemotherapy is recommended in a diffuse multi systemic disease or when disease relapses or progresses. Recently, BRAF V600E mutations has been found in nearly half of LCH cases, which is a significant implications for both molecular diagnostics and targeted therapies using specific BRAF oncogenic kinase inhibitors such as vemurafenib or dabrafenib, especially for refractory and relapsed cases.

Considering the age and severity of the disease, we prescribed topical corticosteroids, twice per day, and moisturizers to the patient. After 2 weeks treatment, the pruritus and scaling papules lesions improved obviously. Full blood count, internal organs' function, growth and development were all in normal ranges without life-threatening complications during the 6-month follow-up.

Key Points

- Langerhans cell histiocytosis (LCH) is regarded as a heterogeneous disease, with remarkably diverse clinical spectrum, ranging from isolated skin or bone lesions to a diffuse disease that can affect nearly any organ.
- Histopathologically, LCH is characterized by diffuse infiltrate of heteromorphic histocytes with reniform nuclei, fine chromatin and abundant pale eosinophilic cytoplasm, accompanied by large eosinophils.
- LCH is currently categorized as single system LCH (SS-LCH) and multi-system LCH (MS-LCH) by extent of single or multiple systems involvement and the presence of risk organ involvement. Specific BRAF oncogenic kinase inhibitors such as vemurafenib or dabrafenib, which has become a new targeted therapy for refractory and relapsed LCH patients.

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Chapter 16
An Infant with Generalized Pimples and Nodules

Jin-lan Tian, Ya-hui Jiang, and Chun-shui Yu

A 7-month-old boy was evaluated for a 10-day history of severe diffuse pruritus. He was crying and restless at night, treated with glucocorticoid ointment, but the skin lesions were not significantly relieved or even worsened. Physical examination revealed the presence of many erythematous papules and several nodules on his trunk and limbs (Fig. 16.1).

Based on the Case Description and the Photograph, What Is Your Diagnosis?

1. Eczema
2. Papular urticaria
3. Scabies

Examination with a hand-held epiluminescent stereomicroscope (dermoscope) revealed the several brown, triangular shapes (scabies mites) on the palm (Fig. 16.2), At 200 magnification, it showed clearly evidence of scabies mites and a burrow containing lots of ovoid, translucent eggs and the feces of the parasite (Fig. 16.3).

Diagnosis

Scabies

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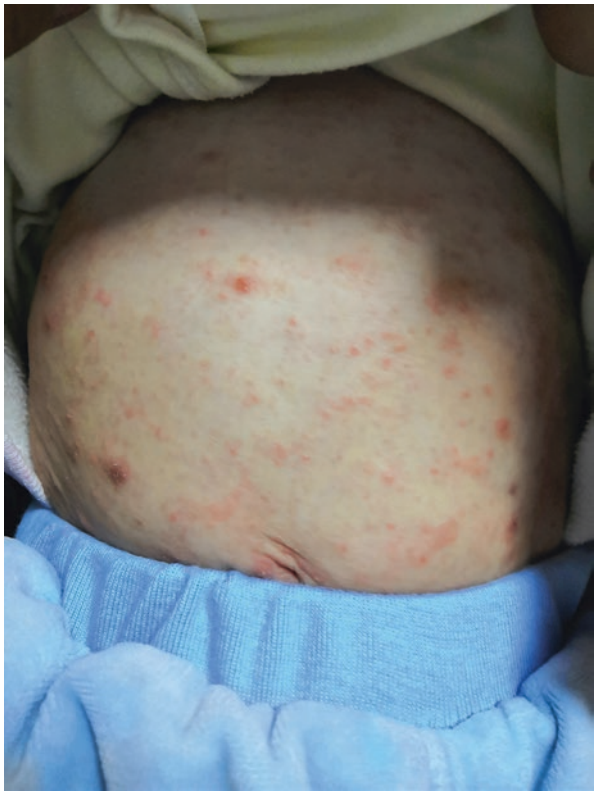


Fig. 16.1 Many erythematous papules and several nodules on his trunk



Fig. 16.2 Observed by dermatoscopy at ×50 magnification, it revealed the several brown, triangular shapes (scabies mites)

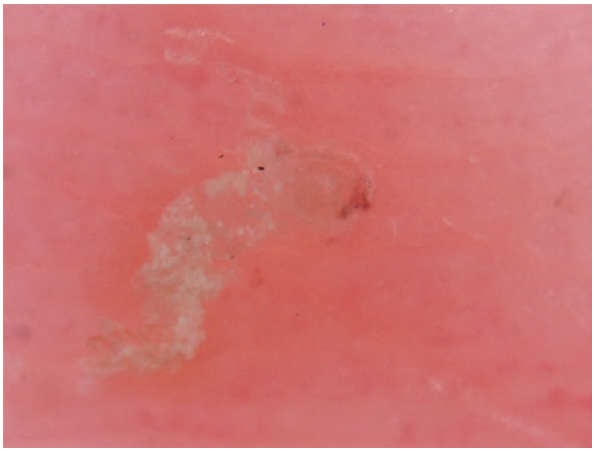


Fig. 16.3 Observed by dermatoscopy at ×200 magnification, it showed clearly evidence of scabies mites and a burrow containing lots of ovoid, translucent eggs and the feces of the parasite

Discussion

Scabies is a contagious skin infestation caused by Sarcoptes scabiei hominis, which invading the epidermal layer of human skin. With flat and oval shape body, scabies mites are characteristically found in thin and tender areas such as the finger webs, scrotum and under the breasts [1]. Different from adults, infants skin have the characteristic of thin and tender, it is easier invaded by mites, the symptoms often more serious and spread quickly the whole body. The areas of the palm is rarely infected in adults. Infantile scabies is easily misdiagnosed as eczema and papular urticaria, resulting in repeating treatment and not effective, increasing the infection rate. Because baby skin is more suitable for the growth of scabies mites, it leads to the proliferation of scabies mites which are easily found under a dermatoscope at 50 magnification, especially on the surface of the nodules, at the same time, we found that the mites and eggs can be better identified at 200 microscope, similar report is also reported in the another study [2]. Therefore, Observation area can be preferentially selected at the nodules and palms for the infant scabies mites, first under a low-power microscope, later adjusted to a higher-power microscope to observe the form of the scabies mites more clearly.

Dermoscopy is a simple, accurate and rapid technique in the dermatology department, which is non-invasive and no discomfort. Scabies is confirmed by microscopic examination of burrow skin scrapings in the past, however compared with dermoscopy, it cannot detect mites rapidly and effectively dermoscopy can easily detected Scabies with a brown triangle structure and a white tunnel [3], and the triangle structure is caused by the mouthparts and two pairs of forelegs of the mites, the contour of the round body of the mite can also be identified the hang-glider-like triangle of the mite's head and round body. Moreover the ovoid, translucent eggs and the feces of the parasite are evident in brown of the female mite [4].

Finally, we suggest that dermatoscopy should be recommended for children with suspicious scabies or pruritic skin diseases in the future clinical diagnosis. Because

dermoscopy has high clinical application value for the diagnosis of scabies, especially in infants and young children, with the skin lesions are often atypical, and the etiological examination of scabies is often negative. Dermatoscopy can greatly reduce the rate of misdiagnosis and improve the level of diagnosis of the dermatologists.

Key Points

- Infantile scabies is easily misdiagnosed as eczema and papular urticaria.
- Dermoscopy has high clinical application value for the diagnosis of scabies.

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Chapter 17
Asymptomatic Skin Colored Nodule of the Buttocks

Mohamed Saeed Mohamed, Shady M. Ibrahim, and Mohamed L. Elsaie

Case Presentation

Male patient 2 years old presented in the dermatologic clinic with single asymptomatic nodule on his left buttock (Fig. 17.1). The lesion had history of 6 months; the patient mother told he had no relevant familial or personal medical history. On physical examination of the skin, he had single asymptomatic yellow-brown, well-defined, soft to stiff, pedunculated papulo-nodular lesion with size 2 × 2 cm and some subcutaneous patterns. The examination of mucous membranes, palms, other areas of the skin, eyes and soles revealed normal findings. There was no evidence of apparent inguinal lymph node enlargement. Initially the patient tried topical steroids and antibiotic with no response.

Dermoscopic examination revealed a red-yellow center and a discrete erythematous halo, characterizing the "setting sun" pattern (Fig. 17.2).

Based on the Case Description, Clinical and Dermoscopic Photographs, What Is Your Diagnosis?

1. Hemangioma.
2. Xanthogranuloma.
3. Gluteal abscess.
4. Rosai-Dorfman disease

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Fig. 17.1 Single asymptomatic nodule on the left buttock of male patient 2 years old

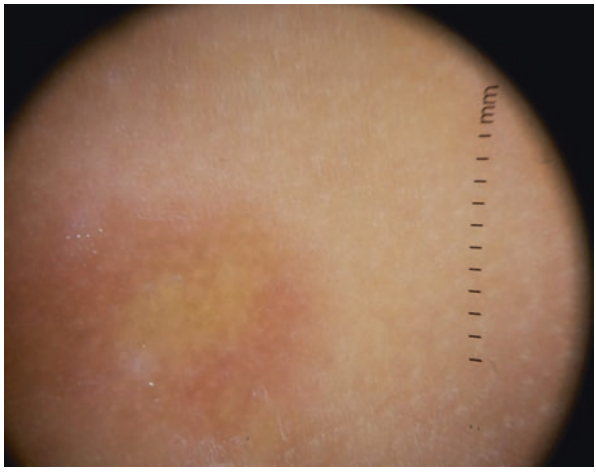


Fig. 17.2 Dermoscopic examination revealed "setting sun" pattern: a red-yellow center and a discrete erythematous halo (Dermoscopy 3gen DermLite 3, magnification 10×)

Diagnosis

Juvenile xanthogranuloma

Discussion

Juvenile Xanthogranuloma (JXG) is a non-Langerhans cell histiocytosis disorder [1]. The lesions usually present as asymptomatic yellow-brown papules and nodules that are mostly self-limited. JXG can present anywhere in the body but primarily occurs as a solitary lesion on the head, the neck, or upper trunk [1].

Skin lesions of JXG are categorized into the three main forms of small nodular/popular (2–5 mm), large nodular (5–20 mm), and giant xanthogranuloma (>20 mm) [2]. In most juvenile cases, lesions regress markedly by a year [3].

Dermoscopy of juvenile Xanthogranuloma revealed characteristic pattern, the pattern described as setting sun is characterized by a yellow-orange central area, which may show areas of lighter yellow, correlating with the dermal xanthogranulomatous infiltrate, and an erythematous halo, which may occur at any stage of evolution [4]. Linear telangiectasias have also been described. Other non-specific characteristics found include discrete pigment network, whitish streaks indicating areas of fibrosis, and fine, branched vessels [4].

Key Points

- Juvenile Xanthogranuloma (JXG) is a relatively uncommon non-Langerhans cell histiocytosis disorder.
- Dermoscopy can help in diagnosis and differnate it from other diseases by characteristic sunset pattern.

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Chapter 18
Axillary Dermatitis in a Newborn

Antonio Iannone, Laura Ciulli, and Fabio Arcangeli

We present the case of a 25-day-old newborn in good health with a well-defined, deep red erythematous patch in the right axilla. It was partly covered with foul-smelling exudate and no satellite lesions were evident (Fig. 18.1). No other family members were affected.

Based on the Case Description and the Photographs Which Is Your Diagnosis?

1. Bacterial intertrigo
2. Candida albicans infection
3. Seborrheic dermatitis
4. Inverse psoriasis

Bacterial culture of the affected region was obtained by a skin swab. Until response was available an empirical treatment with both topical fusidic acid and systemic amoxicillin and clavulanic acid was started, admitting probable bacterial aetiology. The culture yielded a growth of penicillin sensitive Streptococcus pyogenes. After only 3 days of treatment the eruption had already started improving, and after 1 week complete resolution was obtained (Fig. 18.2).

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Fig. 18.1 An area of erythema and maceration on the right axilla



Fig. 18.2 Complete resolution of the erythema after 7 days of antibiotic therapy

Diagnosis

Bacterial intertrigo

Discussion

Intertrigo is an inflammatory dermatitis of the skin folds caused by friction. Opposing skin surfaces rub against each other, at times causing erosion and inflammation. It is usually found in infants and children due to the humidity of the folds, the flexed posture, the short neck, the lack of air circulation and the relative plumpness [1]. Generally the most affected folds, often asymmetrically, are those of the neck, groin and axillary region. These areas can be more easily colonized by Candida Albicans. Other infectious agents such as group A streptococci and Staphylococcus aureus may be involved. Streptococcal intertrigo usually manifests itself with a well-defined erythematous patch, bright red in colour, partly covered with foul-smelling exudate and with an absence of satellite lesions [2].

Candida Albicans intertrigo shows a bright red, exuding, well demarcated patch commonly surrounded by papulo-pustular satellite lesions. The typical foul odour of bacterial intertrigo is usually absent.

Infantile seborrheic dermatitis appears between the second week and the sixth month of life. It manifests with erythematous-squamous-crusted, yellowish and greasy lesions, symmetrically distributed to the face and scalp [3]. According to most of authors it can also affect the diaper area, the neck and axillary folds. It usually resolves spontaneously by the sixth month of life [4]. The typical foul odour of bacterial intertrigo is usually absent.

Inverse psoriasis (fold psoriasis) is a variety of psoriasis less frequent than the classic one, but relatively common in children. It typically affects the folds of the limbs, the armpits, the neck, the groin and the perigenital regions. The lesions appear as erythematous patches, with sharp edges and shiny surfaces, sometimes covered with dry scales [5]. Diagnosis can be facilitated by the simultaneous presence of psoris in other sites. The dermoscopic examination usually shows microscaling and homogeneously distributed red dots. The typical foul odour of bacterial intertrigo is usually absent.

Key Points

- Intertrigo is an inflammatory dermatitis of skin folds commonly observed in newborn and small children. It is frequently aggravated by candida albicans or bacterial infection.
- Group A beta-hemolytic streptococci infection is still a poorly recognized cause of intertrigo.
- The absence of papulo-pustular satellite lesions and the presence of a badly smelling exudate are two important elements in the differential diagnosis.

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Chapter 19
Baby Girl with Widespread Lesions on the Face and Alopecic Nodules of the Scalp

Nora Pollozhani, Katerina Damevska, Anita Najdova, and Maja Dimova

A 6-month-old girl was presented with a 3-month history of papulopustular lesions with an advancing border and mild scaling and erythema spreading from the left cheek to the periocular and the forehead. Lesions were treated with topical corticosteroids (TCS) for 1 month, but the lesion became larger. The infant was in good general health, with no history of recent fever or any other symptoms. Family history was positive for an erythematous annular lesion on the wrist of the father.

On dermatological examination, widespread papulopustular lesions were observed on her left cheek, periocular area, and forehead (Fig. 19.1). Well-demarcated nodular lesions with a diameter of around 2 cm were noticed on the baby's frontoparietal scalp (Fig. 19.2). The Wood's light examination of scalp lesions revealed a brilliant green fluorescence.

Laboratory studies revealed no abnormal findings.

Based on the Case Descriptions and Photographs, What Is Your Diagnosis?

1. Seborrheic dermatitis
2. Demodiciosis
3. Tinea incognito
4. Lupus vulgaris
5. Annular psoriasis

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Fig. 19.1 Grouped papules and pustules with discrete scaling



Fig. 19.2 Alopecic nodular lesions on the hairy scalp with malodorous discharge

Diagnosis

Tinea incognito

Discussion

Mycological analysis of all lesions was performed. Hair and scale samples were collected with scraping and examined under a light microscope with 20% KOH solution, detecting spindle-shaped multicellular macroconidia. The source of infection was demonstrated to be a dog kept as a pet by the family for several years. The dog had no evidence of clinical lesions.

Tinea faciei presents a dermatophytic infection of the facial region. The dermatophytes are fungal infections caused by three genera (Tichphyton spp; Microsporum spp. Epidermophyton spp), with the ability to invade and multiply within the keratinized tissue (hair, skin, nails). The typical clinical presentation is erythematous annular plaques with scaling borders, pustules, and crusts may be present too. Lesions may assume other shapes also, such as the oval, circinate, and arcuate. Typically the lesions spread centrifugally with central clearing, and an advancing inflammatory border is seen in most cases. The lesions can be single, presenting as a plaque or patch, or they can be multiple. Tinea corporis might result in a spread from human to human, animal to human, and soil to human. Domestic animals are an important factor in transmitting the infection, especially the zoophilic species. Infections due to zoophilic organisms such as *Microsporum canis* tend to be associated with severe inflammatory changes. In contrast, anthropophilic organisms such as *Trichophyton tonsurans* may be associated with minimal inflammation and fine scaling [1].

Tinea faciei accounts for about 3–4% of all cases of tinea corporis, frequently reported in tropical countries. It affects all age groups, with two peaks in children between 2 and 14 years and adults between 20 and 40 years of age. Both trichophyton and microsporum species can cause tinea facie [1, 2].

Dermatophytic infections are common during childhood, but they can be misdiagnosed because of their polymorphic clinical appearance [3, 4]. A typical clinical presentation, e.g., annular configuration, scales, pustules in the borders, usually does not pose a challenge in being diagnosed by a trained eye. Atypical forms may lead to misdiagnosis and delayed recovery [5].

An Italian study analyzed 154 cases of atypical tinea. The authors concluded that clinical atypia is not a consequence of TCS but present at the onset of the illness due to the variable dermatophyte's invasive capacity, the site of the invasion, and acquired conditions such as excessive washing or sun exposure. Therefore *Azori et al.* suggest that "tinea atypica" rather than "tinea incognito" includes all forms of dermatophytosis that do not present the classic features for both primary and secondary pathomorphosis [6].

The variations in the clinical presentation result from the dermatophyte's characteristics and a combination of patients' immunity response. Other factors may also contribute, including excessive washing, sun exposure, and the use of cosmetic products. The eventual prescription of TCS or calcineurin inhibitors further induces pathomorphosis (tinea incognito), leading to longstanding disease.

The factors responsible for the increase in the disease incidence are untreated contacts with superficial dermatophytosis, inappropriate treatment with incorrectly prescribed or over-the-counter steroid-containing triple/quadruple combination creams, and inadequate dosing and duration of antifungal therapy. Clinical presentation with large patches and extensive body surface area involvement is common.

The differential diagnosis of tinea faciei includes lupus vulgaris, granuloma annulare, demodicosis, erythema chronicum migrans, annular psoriasis, subacute lupus cutaneous, perioral dermatitis, seborrheic dermatitis.

In tropical countries, where epidemiologically tuberculosis is very common, tinea atypica or tinea incognito can lead to suspect lupus vulgaris. Typically lupus vulgaris presents as a slowly progressive irregular and an infiltrative plaque with central atrophic scarring and advancing borders. However, the early evolving lesions may not show scarring. Granuloma annulare is also characterized by the annular erythematous plaques with an elevated periphery and a depressed center. The lesions are mostly localized in the hands, feet, and wrists, but can also be located anywhere in the body, including the face. Annular psoriasis typically presents as plaques with diffuse thick, white scales, but it can also present as annular lesions with scale only on the borders. Erythema chronicum migrans is the cutaneous hallmark of Lyme disease. One or more large erythematous patches may appear anywhere on the skin. The lesions expand centrifugally, sometimes with central clearing, giving rise to annular patches. The neonatal cutaneous lupus erythematosus may present with polycyclic annular lesions. In the literature, cases of tinea are described as mimicking impetiginized eczema, rosacea-like dermatitis, and seborrhoic dermatitis [3].

Tinea facei should be suspected not just in children with annular lesions but also papulopustular eruptions, infiltrated plaques, eczema-like, and impetigo-like lesions. The diagnosis of tinea is quickly confirmed using a potassium hydroxide (KOH) microscopic slide preparation or culture, which provides precise identification of the species [2].

Tinea corporis is generally responsive to topical creams such as terbinafine; oral antifungal agents may be indicated for extensive disease, failed topical treatment, or for immunocompromised patients. Tinea capitis must be treated with systemic antifungal agents because topical agents do not penetrate the hair shaft. However, concomitant treatment with 1% or 2.5% selenium sulfide shampoo or 2% ketoconazole shampoo should be used for the first 2 weeks because it may reduce transmission. For many years, the first-line treatment for tinea capitis has been griseofulvin because it has a long track record of safety and effectiveness. However, randomized clinical trials have confirmed that newer agents, such as terbinafine and fluconazole, have equal efficacy, safety, and shorter treatment courses [5, 6].

Key Points

- Tinea is a common disease in the pediatric population, but it is rare in the first year of life.
- Differential diagnosis may include seborrheic dermatitis, atopic dermatitis, neonatal lupus, Langerhans cell histiocytosis, and syphilis.
- Parents and close contacts should be carefully examined for superficial fungal infections.

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Chapter 20
Benign Cephalic Histiocytosis

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An 11-month-old boy attended a pediatric dermatology clinic with chief complaints of brownish-yellow nodules on the hairy scalp, face, and chest which was neither painful nor pruritic. The onset of the complaint was when the patient was aged 6 months old in forms of brown papule on the scalp. The papule increased in number and some enlarged into red bean-sized nodules within 2 months. The color of the papules changed into brownish-yellow. One month prior to consult, the preexisting papules multiplied and spread throughout the body. History of previous treatment was admitted; the patient was treated with topical antibiotics by a dermatovenereologist, but without significant improvement. Systemic involvement and history of metabolic disease on the patient and family were denied.

Physical examination revealed multiple lesions on the hairy scalp, retroauricular area, face, and chest in forms of multiple brownish-yellow papules, plaques, and nodules; some with sanguineous and serous crusts on the surface (Fig. 20.1). Dermoscopy examination of the hairy scalp skin revealed brownish-yellow hue on the edge resembling "setting sun appearance" (Fig. 20.2).

Based on the case description and the photographs, what is your diagnosis?

1. Benign cephalic histiocytosis (BCH)
2. Juvenile xanthogranuloma (JXG)

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Fig. 20.1 Brownish-yellow papules, plaques, and nodules; some with sanguineous and serous crusts on the surface found on the hairy scalp, retroauricular area, face, and chest



Fig. 20.1 (continued)

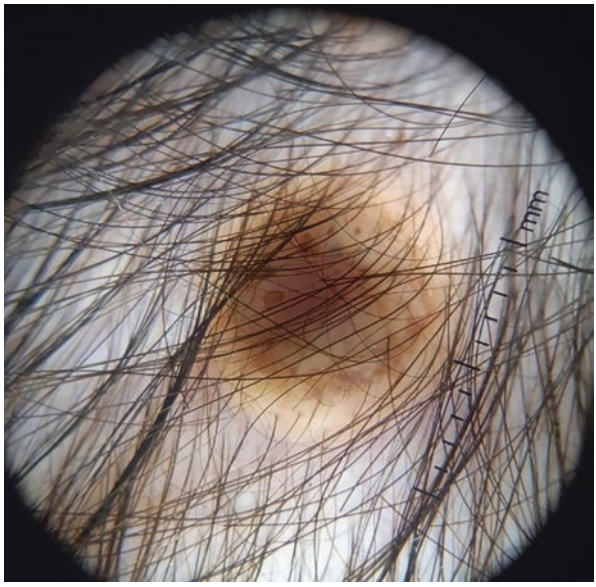


Fig. 20.2 Dermoscopy examination revealed brownish-yellow hue resembling "setting sun appearance"

3. Xanthoma disseminatum (XD)
4. Generalized eruptive histiocytosis (GEH)

Laboratory investigations: revealed iron deficiency anemia.

Hemoglobin 9.5 g/dl; hematocrit 32.2%; erythrocyte 5.23 × 10^6/uL; leucocyte 14.91 × 10^3/uL; thrombocyte 768 × 10^3/uL; mean corpuscular volume 61.6 fL; mean corpuscular hemoglobin 18.2 pg; mean corpuscular hemoglobin concentration 29,5%; basophil 0%; eosinophil 1%; rod neutrophil 0%; segment neutrophil 25%; lymphocyte 65%; monocyte 9%; PT 10.5 s; APTT 30.4 s; INR 0.91; total cholesterol 228 mg/dL; high-density lipoprotein 31 mg/dL; 144 mg/dL; triglyceride 175 mg/dL; aspartate aminotransferase 36 U/L; alanine transaminase 23 U/L; ureum 14 mg/dL; creatinine 0.23 mg/dL; serum Iron 27 ug/dL; total iron binding capacity 355 ug/L; ferritin 28 pg/ml.

Histopathological examination: Fibrocollagenous connective tissue on the dermis with massive histiocytic infiltration.

Immunohistochemistry examination: positive CD68, weak positive S100, and negative CD1a.

Diagnosis: Benign cephalic histiocytosis.

Treatment: Topical 1% rapamycin application on scalp provided satisfactory result.

Discussion

Histiocytosis is a disease marked by accumulation of histiocytes in the tissue [1, 2]. In 2016, Emile, et al. suggested a new categorization of histiocytosis, dividing the disease into five categories: Langerhans-related histiocytosis (L); cutaneous and mucocutaneous non-LCH (C); malignant histiocytosis (M); Rosai-Dorfman disease (R); and hemophagocytic lymphohistiocytosis and macrophage activation syndrome (H). On this latest classification, BCH is included into group C [2, 3].

The incidence of BCH was higher on boys than girls, i.e., 1.2:1. On BCH, the skin lesion might appear between the age of 3–36 months; most frequently before 6 months of age (45%) [4]. This disease was presumed to occur due to infection or physical trigger causing histiocytic granulomatous reaction [5].

The diagnosis of BCH was established based on physical examination and histopathological examination. The initial lesion was a brownish-red nodule on head and neck; furthermore, the color of the lesion might change into yellow nodules which would multiply and spread throughout the body. The most frequently affected body parts were cheeks (22%), eyelids (13%), and ears (10%) [2, 6]. There was one reported BCH case on the scalp [6]. Systemic involvement in BCH has never been reported [1, 2, 7]. However, there were reports which associated BCH with diabetes insipidus and diabetes mellitus [2, 7]. There is no literature that discusses dermoscopic examination in BCH.

Histopathological feature of BCH is diffuse histiocytic infiltration, especially on upper dermis and lower epidermis. In BCH, there was no lipid on the cytoplasm, but xanthomatization might be observed for quite a long time. Multinucleated histiocytes could also be observed [8]. Several literatures stated that BCH is a histopathological variant or part of JXG spectrum [8, 9].

Benign cephalic histiocytosis is a self-limiting disease which does not require specific treatment. Certain treatment might be administered should the disease yield cosmetic problem or if the cutaneous lesion was progressing rapidly [10]. Several therapeutic options including cryosurgery, intralesional corticosteroid injection, laser, and excisional surgery [1, 2]. Topical treatment in BCH cases were rarely prescribed. However, a study reported a case which prescribed topical rapamycin treatment for BCH and yielded satisfactory results marked by thinning of the lesion. Rapamycin is an immunosuppressant that has an antineoplastic effect. Rapamycin can be one of the alternative non-invasive topical therapy options for BCH. However, long-term observations are still needed to assess the effectiveness and side effects of the drug [11].

Key Points

- The diagnosis of BCH requires proper clinical and histopathology examination, because it often overlaps with other diseases.
- Treatment can be considered if the patient has cosmetic problems or if the cutaneous lesion is progressing rapidly.
- Rapamycin can be one of the alternative non-invasive topical therapy options for BCH.

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Chapter 21
Congenital Skin Scars

Alfonso Delgado Rubio and Fabio Arcangeli

A newborn female was admitted to the Neonatal Unit for presenting scar lesions on the scalp and trunk at the time of delivery.

On clinical examination of the skin two circular lesions were observed on the vertex of the scalp in "bites" with absence of hair (Fig. 21.1).

At the chest level, bilateral erosive lesions with dermis exposed and partially covered by necrotic epidermis were observed at the mid-axillary line (Figs. 21.2 and 21.3).

Delivery was full term without signs of fetal distress. Apgar test was 8/10, weight was 400 g. No dysmorphic signs were evident and the face was normal. There was no family history of skin lesions.

Based on the clinical history and the photographs what is your diagnosis?

1. Injuries secondary to amniocentesis or obstetric trauma
2. Prenatal infection by varicella zoster virus (VZV) (Varicella embryopathy)
3. Oculo-cerebro-cutaneous syndrome
4. Aplasia cutis congenita

Chickenpox, herpes and also drugs or other embryo-fetal harmful agents during pregnancy were ruled out. Laboratory blood tests resulted normal. Microbiological, serological and immunological investigations made it possible to rule out prenatal infections. In particular the serology for VZV, herpes virus (HSV), cytomegalovirus

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Fig. 21.1 Two circular wounds on the vertex of the scalp

(CMV) and lues was negative. Skull and extremities radiographs, cerebral and abdominal sonography were normal. The patient proceded normally, without any serious problems.

Diagnosis

Aplasia cutis congenita (ACC).

Discussion

Congenital scarred skin lesions, distributed on the scalp and symmetrically on the trunk, in the absence of other malformations, suggest a diagnosis of ACC, although the most common is that ACC is observed only on the scalp.



Fig. 21.2 Bilateral erosive lesions on the trunk



Fig. 21.3 Dermis exposed and partially covered by necrotic epidermis at the right mid-axillary line

1. The appearance of the lesions, the sites involved and the absence of potential injuries in the pre or perinatal period (amniocentesis, obstetric trauma etc.) have to exclude their traumatic origin.
2. Infection due to HSV or VZV (congenital varicella syndrome) was ruled out, and the absence of maternal chickenpox during pregnancy, the negativity of the IgM in the newborn and serological studies also exclude them.

3. In oculo-cerebro-cutaneous syndrome or Delleman's syndrome, ACC is associated with orbital cysts, brain malformations, microphthalmia, etc. absent in our patient.

Aplasia cutis congenita is a rare condition characterized by the congenital absence of epidermis, dermis and in some cases, subcutaneous tissues. It was first described by Cordon in 1767. Its precise incidence is unknown but has been thought to be around 1 to 3 in 10,000 births [1]. Approximately 85% of ACC cases manifest as isolated lesions on the scalp but any body surface may be involved [2]. Although in most cases ACC is a benign isolated defect, healing with scarring within few months, it can be associated with other malformations or genetic syndromes, such as trisomy 13, 4p deletion syndrome, epidermolysis bullosa, ectodermal dysplasias, Adams-Oliver syndrome, and amniotic band sequence [2, 3]. No specific laboratory abnormalities are consistently found in ACC, chromosome analysis or genetic testing may be indicated only if a pattern of abnormalities suggests a genetic disorder.

Frieden proposed to classified ACC in nine groups based mainly on the presence or absence of associated malformations [4].

Frieden classification of ACC.

Group 1	Scalp ACC without multiple anomalies
Group 2	Scalp ACC with limb anomalies (Adams-Oliver syndrome)
Group 3	Scalp ACC with epidermal and sebaceous (organoid) nevi (Epidermal Nevus syndrome)
Group 4	ACC overlying deeper embryologic malformations (e.g. meningomyelocele, porencephaly, leptomeningeal angiomatosis, cranial stenosis, spinal dysraphism, gastroschisis, omphalocele)
Group 5	ACC associated with fetus papyraceous or placental infarct
Group 6	ACC associated with epidermolysis bullosa (Bart syndrome)
Group 7	ACC localized to the extremities without epidermolysis bullosa
Group 8	ACC linked to intrauterine infection with herpes simplex virus or varicella zoster virus or to exposure to methimazole
Group 9	ACC associated with malformation syndromes (Patau syndrome, Wolf-Hirschhorn syndrome, Johanson-Blizzard syndrome, Goltz syndrome, Delleman syndrome, Finlay-Mark syndrome, Kabuki syndrome, 46XY gonadal dysgenesis)

Key Points

1. ACC may involve not only the scalp but every body surface
2. ACC must alert the clinician to potential association with other congenital anomalies and genetic syndromes

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Chapter 22
Cryotherapy Treatment in Infantile Hemangioma: A Case Report

Muhammad Zuldan Karami, Devy Caroline, Puguh Riyanto, Muslimin, Buwono Puruhito, and Widyawati

A 3-month-old female infant presented with a rapidly growing bright red tumor on the forehead since 1 week of age was brought to Diponegoro National Hospital (Fig. 22.1). There was no complaint of tenderness and bleeding. There was no sign of fever, bleeding, and lymph node enlargement. The patient has been given propranolol without any improvement.



Fig. 22.1 A smooth-surfaced bright red tumor on the patient's forehead

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Based on the case description and the photographs, what is your diagnosis?

1. Infantile hemangioma
2. Pyogenic granuloma
3. Tufted angioma

On physical examination we observed a sharply-demarcated, smooth-surfaced bright red tumor on the patient's forehead with the size of 3 × 2 cm. The infant was born through spontaneous delivery with no history of preterm birth and low birth weight from a mother who was 31 years old at that time. The patient had normal birth weight, had no previous medical history, and was not on any other medication.

The patient was diagnosed with infantile hemangioma and was treated with cryotherapy and prescribed oral analgesic and topical antibiotic before the patient was discharged (Fig. 22.2). A 6-month follow-up presented the lesion as a post-inflammatory hypopigmented macule on the patient's forehead (Fig. 22.3).

Discussion

Infantile hemangioma is estimated in 4–5% of children and more likely to be observed in female infants. According to the literature, the superficial infantile hemangioma is the most often to be found from all three subtypes, with the



Fig. 22.2 A post-inflammatory hypopigmentation on the patient's forehead after second cryotherapy



Fig. 22.3 A post-inflammatory hypopigmentation on the patient's forehead on a 6-month follow-up after first cryotherapy

characteristics of pink to bright-red strawberry plaque or nodule, on the head or neck region. Superficial infantile hemangioma is identified since the first month of age and will grow bigger the next month. The lesion will stop expanding after 5 months of age and starts to go through the involution phase until 3.5–4 years old in 90% of all children [1–4].

The patient was born from a full-term pregnancy with no history of low birth weight, from a 31-year-old mother. According to the references, pregnancy above 30 years old is one of the risk factors for infantile hemangioma [1].

The diagnosis of infantile hemangioma was established based on history taking and physical examination. Histopathologic examination was not performed since the patient was planned to be subjected to cryotherapy.

The differential diagnosis of infantile hemangioma was ruled out because the lesion was not in accordance with pyogenic granuloma which is covered in scales, prone to erosions and bleeding, and does not undergo involution phase [1, 2, 4, 5]. The lesion was also not befitting as tufted angioma since the latter is located on a subcutaneous layer, proliferates slowly, and commonly found on the neck, shoulders, and upper body region. Spontaneous regression is expected if the onset of disease is before 6 months old [1, 6].

Intervention is recommended for infants with infantile hemangioma which does not respond to medical therapy, life-threatening hemangioma, lesion with malignancy tendency, and progressive hemangioma with recurrent infections [1, 4]. The patient was subjected to surgical intervention because the lesion showed no improvement despite having been treated with oral propranolol and topical timolol. Propranolol was prescribed with the dosage of 1.5–3 mg/kg/day, 2 to 3 times a day. Topical beta-blockers such as timolol 0.5% were given two times a day for superficial hemangioma [7, 8]. Cryotherapy was decided due to parental preference and the location of involvement which was favorable for resection [4]. After second cryotherapy, a 6-month follow-up presented the patient with a post-inflammatory hypopigmentation on the forehead as expected of a wound healing following an uncomplicated resection.

The prognosis in this patient is *quo ad vitam ad bonam, quo ad sanam ad bonam, quo ad cosmeticam dubia ad bonam (the prognosis of this patient is good and the post-procedure scar is minimal).*

Key Points

- Superficial infantile hemangioma is one of the most common benign vascular malformations with the characteristics of pink to bright-red strawberry plaque or nodule, on the head or neck region
- Cryotherapy is one of the interventional modalities regarding infantile hemangioma which does not respond to medical therapy

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Chapter 23
Epidermolytic Ichthyosis

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A 20-month-old girl patient attended the Pediatric Dermatology outpatient clinic with yellowish brown scales with an erythematous macule based on almost the entire body that felt itchy. At the age of 40 days, the scales appeared on both hands and feet, the longer it became thicker and yellowish brown with an erythematous macule based. These complaints also accompanied by avulsion of the both fingernails. Since the patient was 12-month-old, the erythematous macules developed on the scalp, face and nape. Over time, the skin lesion increases and extends to the chest, back, arms and legs, accompanied by hyperkeratosis of the fingernails and toes and the hair did not grow thick or grew longer since birth. Six months after, the erythematous macules have been increasing and extending to almost all parts of the body. On the nose, the earlobes, elbows, hands, knees, feet and buttocks develop a yellowish brown scale with an erythematous macules base (Fig. 23.1). The patient was the only child of healthy and non-consanguineous parents, normal full-term delivery with no complications, no history of blistering or generalized cutaneous redness at or after birth, no collodion membrane. There is a history of treatment without improvement under topical treatment alone because her parents sometimes seek for self medication. There is a history of hyperperspiration without a history of tooth deformation or teeth fall off easily. Moreover, the patient had no medical problems and showed normal growth and development. No other family member was affected by a similar skin condition.

Based on the case description and the photographs, what is your diagnosis?

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Fig. 23.1 Yellowish-brown scales on erythematous base with hyperkeratotic scales on nose, both ear lobes, elbows, hands, knees, feet, and buttocks, with no history of bullae or erosion, thin and sparse hair, hypohidrosis, and onychodystrophy on the entire nails of the hands and feet

1. *Autosomal recessive congenital ichthyosis* (ARCI) type *congenital ichthyosis erythroderma* (CIE)
2. Epidermolytic ichthyosis (EI)
3. Palmoplantar keratoderma (PPK) diffuse type Vörner (Unna-Thost)
4. Papillon Lefèvre syndrome (PLS)

On examination the patient presented yellowish-brown scales on an erythematous base with hyperkeratotic scales on nose, both ear lobes, elbows, hands, knees, feet, and buttocks, with no history of bullae or erosion. Moreover, accompanied by thin and sparse hair, hypohidrosis, and onychodystrophy on the entire nails of the hands and feet.

Laboratory investigations: within normal limit.

Histopathological examination: hyperkeratosis, parakeratosis, vacuolization and acantholysis of stratum granulosum. Dermal papillae appear as inflammatory lymphocyte cells and the dermis appears hyalinized fibrocollagenous connective tissue stroma.

Diagnosis: Epidermolytic Ichthyosis (EI).

Treatment: A retinoid assessment was performed and the patient was treated with acitretin at a dose of 1 mg/kg/day in combination with topical moisturizer and keratolytic, with slight clinical improvement.

Discussion

In 1902, Broq described EI for the first time based on a characteristic histopathological picture, namely the presence of vacuolar degeneration in epidermal keratinocytes accompanied by hyperkeratosis [1]. EI was previously known as bullous congenital ichthyosiform erythroderma (BCIE) or epidermolytic hyperkeratosis (EHK) [1–3]. EI is inherited in an autosomal dominant hereditary disorder, [1, 4] with an incidence of 1:200,000–300,000 per birth, but spontaneous mutations can occur in 50% of patients who do not have a family history of EI [1, 5, 6]. There is no difference in the incidence of EI in males and females [5, 6].

Epidermolytic ichthyosis is a genodermatosis caused by mutations in the KRT1 or KRT10 [1, 4, 7] gene which is expressed in the suprabasal epidermis [1, 6, 8, 9]. These two genes play a role in inhibiting the proliferation of cells and cells that move up the suprabasal layer to become post-mitotic and differentiate progressively towards the surface of the epidermis. KRT1 and KRT10 mutations cause the epidermis to hyperproliferative so that the stratum corneum becomes very thick and produces clinical symptoms in the form of ichthyosis [6, 8–10]. The absence of KRT1 and KRT10 causes keratinocytes from the superficial epidermis become more fragile and break easily, resulting in clinical symptoms in the form of bullae [4, 6]. Some researchers state that mutations in EI occur on chromosomes 12q11–13 and 17q12–21, [5, 6, 11, 12] and are influenced by consanguinity [1].

Epidermolytic ichthyosis usually appears at birth with manifestations of bullae, erythroderma, and desquamation of the skin [1, 4, 7, 13] which is difficult to distinguish from epidermolysis bullosa (EB) or staphylococcal scalded skin syndrome (S4) based solely on clinical manifestation [1, 5, 14]. Neonates with EI is at higher risk of experiencing electrolyte imbalance and susceptibility to infection which can increase the risk of developing sepsis [5]. As they get older, the clinical manifestations of bullae can diminish and then clinical manifestations of hyperkeratosis may or may not become erythroderma [1, 5, 7]. Skin disorders in EI usually odor which is thought to be associated with bacterial superinfection [1, 4, 5]. Skin disorders in EI also have characteristics in the form of scale with accentuation pattern in the body folds, thick palmoplantar hyperkeratosis, generalized verrucous hyperkeratosis, erythrokeratoderma, keratoderma with a superficial scale, and erythroderma [4, 7, 13]. Involvement of palms and soles occur in about 60% of patients with EI and it causes recurrent pain and contractures, which can cause functional impairment.

In general, the diagnosis of EI can be established based on clinical symptoms and histopathological examination of the skin [4, 11]. Molecular biology examinations with sequencing can be performed to determine mutations in KRT [6, 11]. Prenatal diagnosis can be made through fetal skin biopsy or amniocentesis after 19 weeks of gestation to determine KRT1 or KRT 10 mutations [11, 15]. Histopathological examination of EI shows hyperkeratosis, [1, 4, 7, 11, 16] parakeratosis, perinuclear vacuolization of keratinocytes in the stratum granulosum and stratum corneum, increased keratohyalin, [4, 11, 15, 16] and intraepidermal bullae [7, 13, 16, 17].

The principle treatment of ichthyosis is to reduce symptoms by reducing discomfort due to dry skin [18, 19]. First-line therapy is the application of ingredients with hydrating and lubricating properties to improve skin barrier function and reduce scales [19]. Topical therapies-materials that have hydration (NaCl, urea, and glycerin), lubrication (petrolatum or other fatty substances), keratolytics (α-hydroxyacids or AHA, urea with a concentration of >5%, propylene glycol, salicylic acid, and N-acetylcysteinamide), [5, 11, 18, 20] topical retinoids, and topical analogues of vitamin D [4–6, 11, 12]. Glycerol or glycerin is a trihydroxy alcohol which has a role in hydration of the stratum corneum, skin elasticity, repair of skin barrier function, anti-irritation, and accelerates the wound healing process [21]. The maximum concentration of glycerin in infants and children is 10% [22]. Based on research by Fluhr et al. [21] it was reported that a glycerin concentration of 10% proved to be effective in clinical improvement after 3 weeks of use.

For systemic therapy, retinoids can be given, namely acitretin at a dose of 0.5–1 mg/kg/day with a maximum dose of 35 mg per day [4, 6, 23, 24]. Clinical improvement can be seen after 4 week of treatment included reduced scale and palmoplantar hyperkeratosis [22]. Retinoids can cause worsening desquamation and blistering and should be used with caution.

Key Points

- EI is a rare genodermatosis most commonly caused by autosomal dominant mutations in KRT1 and KRT10.

- Thorough clinical examination followed by histopathological investigation are crucial for the diagnosis of EI
- Regular follow-up and age-appropriate management of the patient is important.

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Chapter 24
Incontinentia Pigmenti with Ocular Involvement

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A 4 month-old baby girl presented to the hospital by her parents with complaint of hyperpigmented macules appears as whorls and streaks without pain or itch on almost the entire body (Fig. 24.1). The skin lesion started as small vesicles on her right arm when she was 2 days-old, which then spread to both extremities, trunk and buttocks. Two weeks later, the lesions evolved to become hyperpigmented papules and several verrucous lesions which in a short time turned into hyperpigmented macules.

Based on the case description and the photograph, what is your diagnosis?

1. Incontinentia pigmenti
2. Linear whorled nevoid hypermelanosis

There was no history or complaint of seizures. She is the youngest of two children. Her older sister, mother, grandmother and great grandmother all had the similar disease as the patient. There was no consanguinity between parents.

The patient was consulted to the ophthalmology department with a result of microphthalmia on her right eye (Fig. 24.2) with persistent fetal vasculature and slight vitreus fibrosis.

Histopathology examination showed hyperkeratosis, dyskeratosis, spongiosis accompanied by whorl keratin and eosinophilic infiltrate.

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Fig. 24.1 Hyperpigmented macules along Blaschko lines

Diagnosis

Incontinentia pigmenti with ocular involvement.

Discussion

Incontinentia pigmenti is a rare genetic multi organ disorder with X-linked dominant inheritance, characterized by various cutaneous lesions from infancy to adulthood, and extracutaneous symptoms such as eye, CNS, and musculoskeletal



Fig. 24.2 Microphthalmia of left eye

abnormalities. Skin lesions include erythema, vesicle, hyperkeratotic papule, and hyperpigmentation, and usually heal spontaneously with focal hypopigmentation [1].

Review of pedigrees with familial IP suggests that the condition is due to an X-linked dominant gene, with lethality in affected males. This mode of inheritance is supported by the high female to male ratio, female–female transmission and by the increased incidence of miscarriage [2].

In 2000 an international consortium found a recurrent deletion mutation in 80% of index cases in the *IKBKG* gene (inhibitor of kappa polypeptide gene enhancer in B cells kinase gamma)—previously known as the *NEMO* gene. Cells in which the active X carries the mutated gene are more liable to undergo cell death. In males, extensive cellular apoptosis usually results in early fetal lethality. However, IP has been reported in liveborn males. In such cases, the male may have Klinefelter syndrome or somatic mosaicism [3].

Cutaneous lesions are classified into four stages based on clinical findings. Stage I (vesiculobullous stage) is characterized by vesicular/bullous eruptions and erythema distributed in a linear or whorled pattern on the trunk and extremities (the face is usually spared) that appear within 1 week of birth. Stage II (verrucous stage) follows stage I, and is characterized by verrucous or lichen planus-like keratosis eruptions on the extremities, particularly the dorsal hand and foot. The lesions of stage III (hyperpigmentation stage) appear when individuals are 12–16 weeks old, and these are characterized by brown to gray-brown pigmentation distributed in whorled or linear patterns, respecting the Blaschko line. The pigmentation disappears almost completely by 4 or 5 years of age and may leave focal hypopigmentation, atrophic scar, or alopecia [1]. Classically, the dermatological features are

described in four stages, but all stages do not necessarily occur; they may arise out of order, and several stages may overlap [3].

This case is a classic presentation of incontinentia pigmenti with skin lesions evolving from stage I, II and III.

Histopathology. In the early vesicular cutaneous stage there is massive infiltration of eosinophils into the epidermis and marked peripheral blood leucocytosis with up to 65% eosinophils. Hyperkeratosis, papillomatosis and mild dyskeratosis are seen in the verrucous stage and the pigmentary stage shows degeneration of the basal cells and melanin-loaded macrophages in the dermis, giving the condition its name [4].

Eye abnormalities are seen in 36% to 77% of patients with IP including both retinal and non-retinal lesions, such as retinal detachment, retinal hemorrhage, strabismus, nystagmus, and uveitis [5]. Occasionally microphthalmos, cataract and optic atrophy are seen [3]. Various vitreoretinal manifestations can be found in paediatric patients with IP and classified into five stages, which are characterized by retinal vasculopathy [5].

Skin lesions of IP tend to be self-healing but may leave scars or hair loss at the affected areas. Secondary infection and strong inflammation may be possible, particularly in the stage I lesions, requiring topical treatment based on the skin condition. Eye and CNS abnormalities can cause serious impacts to the patients including blindness and death. Routine regular follow-up study for extracutaneous lesions including those affecting the eyes and CNS is needed to allow early initiation of appropriate interventions [1].

Key Points

- Incontinentia pigmenti is a rare genetic multi organ disorder with X-linked dominant inheritance
- Cutaneous lesions are classified into four stages: vesiculobullous, verrucous, hyperpigmentation and hypopigmentation
- Up to 77% patients with IP have ocular involvements

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Chapter 25
Infantile Erythroderma Caused by Focal Infection

Inda Astri Aryani, Fitriani Fitriani, Soenarto K, and Grady Garfendo

A 2-month-old male Asian infant was referred to a dermatology and venereology clinic with generalized erythema and scales almost on the entire body (Fig. 25.1). Two weeks earlier, his mother noticed erythematous patches with scales on the patient's scalp, neck and trunk. Skin lesions then progressed to envelop his upper and lower extremities. No fever nor watery stools were reported. Patient was bottle-fed since birth and as yet, still feeds well. Patient was born full-term with normal delivery, showing normal growth for his age. No other family member was suffering from similar skin lesion; previous family history of atopy, seborrheic or familial skin disease were absent. Several diseases were considered as underlying causes

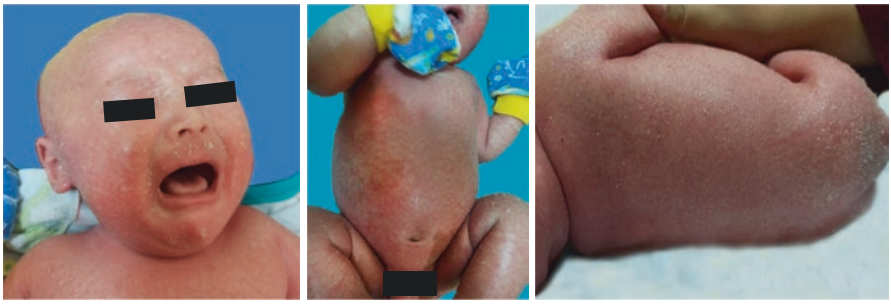


Fig. 25.1 Wide body surface area involvement in IE

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such as seborrheic dermatitis, atopic dermatitis and acrodermatitis enteropathica. Coincidentally, his mother mentioned yellow, foul-odored discharge from a patient's ears after bathing prior to current skin condition. Consultation to the Otorhinolaryngology department was indicated and the patient was diagnosed with otitis media in both ears.

On physical examination, we observed a non-homogenous, diffuse erythema with white thin scales almost on the entire body. palmoplantar skin was spared. He presented with ectropion on both eyelids.

Blood sample examination result: Erythrocyte count $3.70 \times 10^3/mm^3$ (normal range: 3.75–4.95), hematocrit 32% (38–52), mean corpuscular volume 86.8 fL (93–115), neutrophil 28% (50–70), lymphocyte 63% (20–40), blood glucose 111 mg/dl (50–90). Natrium 140 mEq/L (135–155), Kalium 5.4 mEq/L (3–7), Zinc serum 64 µg/dL (26–141). ASTO non-reactive (reactive), normal zinc serum level.

Based on case history and clinical examination, differential diagnosis of this case was based on causative underlying causes of infantile erythroderma which were:

1. focal infection in otitis media,
2. seborrheic dermatitis
3. atopic dermatitis.

Considering further clinical findings and laboratory examination, we diagnose this patient with infantile erythroderma caused by focal infection in otitis media.

Treatment: Patient was started with hydrogen peroxide ear drops and oral antibiotics amoxicillin-clavulanate were prescribed from the Otorhinolaryngology department. Topical medications such as ceramide cream and hydrocortisone cream were also prescribed. Intake and output of electrolytes and diet were monitored. The patient showed marked improvement during 1 month follow-up (Fig. 25.2).



Fig. 25.2 Clinical improvements shown after 1 month follow-up

Discussion

Although uncommon and rarely studied, IE is considered a life-threatening condition. Mortality rate may be varied from 16–26% and depend on underlying causes [1]. Etiology is frequently difficult to establish and usually delayed due to nonspecific clinical and histological findings [1, 2]. Most common are atopic dermatitis and seborrheic dermatitis. Infection is rarely suspected but diseases such *Staphylococcal Scalded Skin Syndrome* (SSSS), candidiasis, herpes simplex and congenital syphilis may pose a significant problem [1]. Pruszkowski et al. found 51 cases of IE during the first year of life, with average age of onset at 7 weeks. Underlying causes determined to be immunodeficiency (30%), simple or complex ichthyosis (24%), Netherton syndrome (18%), and eczematous or papulosquamous dermatitis (20%) [3]. In the contrary, Sarkar et al. found 20 cases of IE with underlying causes of infections (40%), ichthyosiform erythroderma (25%), atopic dermatitis (15%), seborrheic dermatitis (10%), and unidentified (10%) [4].

Metabolic and nutritional causes such as zinc deficiency should be suspected especially in bottle-fed infants [1]. Congenital zinc deficiency (acrodermatitis enteropathica) is an autosomal recessive disorder that generally appears in early infancy and is characterized by a triad of sacral and periorificial skin lesions, diarrhea, and alopecia. The condition may manifest days to weeks after bottle-fed and after weaning if breast-fed [5]. Diagnosis is based upon typical clinical findings and low zinc serum levels. Patients usually achieved rapid clinical response to zinc supplementation [5, 6].

To our knowledge, non-cutaneous focal infection as an underlying cause of IE has never been reported. However, otitis media (OM) is the most common pediatric bacterial infection, affecting up to 75% children before the age of 5 years old. Liese et al. found 5764 cases of OM in major European countries and showed that 55% of cases were found in the age range of 0–2 years old [7]. Another study by Usonis et al. found higher incidence in patients fed with formula milk than breast milk [8]. Most common bacterial causes are *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis* and less commonly, *Streptococcus pyogenes*. Although usually of single bacterial cause, co-infection may also occur [9]. Antibiotics were beneficial in children younger than 2 years old with bilateral OM based on a meta-analysis study. Amoxicillin is the drug of choice; amoxicillin-clavulanate is indicated if there is concurrent purulent conjunctivitis, a history of amoxicillin treatment within the previous 30 days, relapse of a recent infection, or nonresponse to amoxicillin. Patients with a history of amoxicillin allergy should be prescribed second-generation or third-generation cephalosporin [10].

Guidelines regarding evaluation and diagnosis of IE have yet been established. Detailed history taking and examination are imperative. Complete blood exam and electrolytes serum should be indicated. Unless suspected, additional exams such as histopathology and zinc serum must be spared to avoid unnecessary manipulation of the infant [1, 11]. Severe complications such as secondary infection, hypoalbuminemia and dehydration, are life-threatening [1]. Supportive and symptomatic

treatment must be swiftly initiated to maintain fluid and electrolyte balance with adequate calorie intake. Topical application of emollients and low-potency corticosteroids may be utilized to maintain skin barrier function and hydration [1, 2]. Treatments of choice were topical ceramide cream and hydrocortisone cream while hydrogen peroxide ear drops and oral antibiotics were used to treat OM. Overall prognosis was good, considering marked improvement in patients during 1 month follow-up.

Key Points

- Previous publications regarding IE caused by focal infection have never been reported.
- Meticulous examination should be encouraged, since common focal infections in an infant has the potential to become an underlying cause in IE.
- Supportive and causative management proved to be vital in achieving clinical improvement in IE cases.

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Chapter 26
Infantile Hemangioma: Successful Treatment with Topical Treatment

Fitriani Fitriani, Inda Astri Aryani, Soenarto Kartowigno, and Indri Widya Sari

A 9-months-old girl was referred to the department of dermatology and venereology because of swelling and dark reddish slightly elevated plaque on the genital after 2 months of birth without functional impairment. No birthmark was present at her birth, discoloration and swelling increased in size gradually (Fig. 26.1a).

Treatment with topical timolol maleate 0.5% solution for 24 weeks changed size and skin texture. Erythema had disappeared. The thickness of plaque had decreased (Fig. 26.1b).

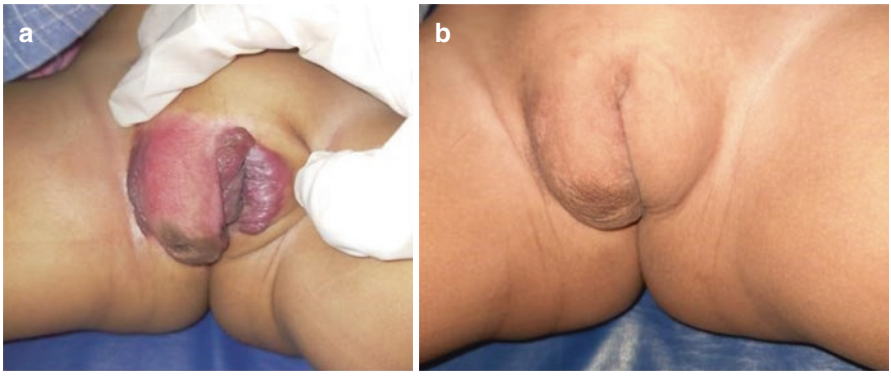


Fig. 26.1 Superficial IH treated with topical timolol maleate 0.5% solution; (**a**) Baseline; (**b**) The lesion had resolved after 24 weeks of treatment

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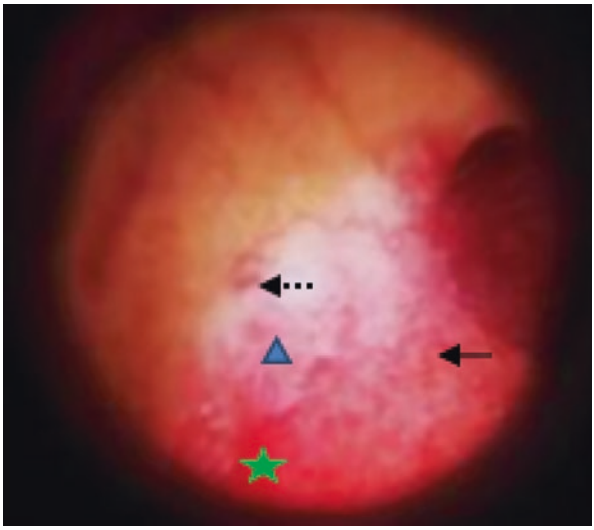


Fig. 26.2 Dermoscopic appearance showed reddish lesion (star), pinkish structure (triangle), red wavy vessel (fine arrow), and red linear vessel (fine dotted arrow)

On physical examination, we observed the swelling and dark reddish plaque 5 × 4 × 0.3 cm in size on the genital region.On dermoscopic examination, we found reddish lesion, pinkish structure, polymorphic vascular patterns of red wavy vessels, and red linear vessels (Fig. 26.2).

Based on the case description and the photographs, what is your diagnosis?

1. Infantile hemangioma
2. Port-wine stains
3. Congenital hemangioma

And due to further clinical and dermoscopic appearance, we diagnose this patient with infantile hemangioma.

Treatment: We applied one drop (0.25 mg) of timolol maleate 0.5% solution twice daily which resulted in a marked improvement within 24 weeks.

Discussion

Infantile hemangioma is a common benign vascular tumor. In neonates, its prevalence is 30% of premature infants, weigh <2500 g, and the ratio of girls 2 to 3:1 [1].

Etiopathogenesis remains unknown. Several theories describe the development of IH. One of the theories about an imbalance of angiogenic and antiangiogenic factors. Level of matrix metalloproteinases (MMPs) 2 and 9, vascular endothelial growth factor (VEGF), basic growth factor of fibroblast (bFGF) has increased significantly [2].

Infantile hemangioma is divided into four stages of growth pattern: nascent (0–3 months), proliferative (<1 year), involution (1–5 years), and involuted (5–10 years) [1].

The diagnosis of IH is based on anamnesis and physical examination. Atypical features with complications and potentially life-threatening need supportive analysis [1]. Dermoscopic examination significantly supported diagnosing vascular skin lesions. The dermoscopic appearance of IH includes polymorphic vascular patterns, such as red globular vessels, red comma-like vessels, and red linear vessels. Capillary malformations have different features, such as port-wine stain shows monotonous vascular pattern [3].

Management of IH has two approaches, active non-intervention, and active intervention. Commonly, IH only requires a non-intervention approach, caused by spontaneous remission. Choice of active intervention base on location of IH (facial, beard, lumbosacral, and genital), and potential local or systemic complications. Treatment of IH considers functional aspects, size, location, risks, benefits, also psychosocial aspects [4].

Application of timolol maleate can be effective for IH, with the characteristic of small superficial lesions, thickness <1 mm. Recommendation dose is limited to <0.25 mg/kg/day [5]. Timolol as a non-selective beta-blocker inhibits angiogenesis. The level of MMP-2, and MMP-9, VEGF, bFGF have reduced, and cause apoptosis of endothelial cells [6]. Chan et al reported effective and safe therapy of timolol 0.5% gel forming solution for infants 5–24 weeks of age, with characteristic size <2.5 cm, thin, nonulcerated cutaneous lesion. Resolution occurred after 8–16 weeks of therapy [7].

Key Points

- Diagnosis of IH can be based on anamnesis, physical examination, and dermoscopic examination.
- Management of IH has two approaches, active non-intervention, and active intervention.
- Timolol maleate 0.5% solution can be effective and safe treatment for superficial IH.

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Chapter 27
Infantile Type Atopic Dermatitis

Rina Gustia and Miranda Ashar

A 5-month-old baby girl patient was referred to outpatient clinic of Dermatology and Venereology Dr. M. Djamil Hospital Padang with chief complain there were erythema plaque and reddish spots with white scales and erosion on face, neck, chest, stomach, back, both arms, both legs which increasing since 3 weeks ago (Figs. 27.1 and 27.2). Initially, ±3 months ago, the patient's mother complained of reddish spots on both of her baby's cheeks. ±3 weeks ago, the patient's mother ate crab, then reddish spots and erythema plaque were increased on both cheeks, forehead, chest, stomach, back, both of arms, both of legs, both of fold the elbows, both of fold the knees. There was erosion on the back of the neck. The patient is still drinking breastmilk and has never received formula milk. The patient was also not given any additional food. The patient's mother likes to eat cheese and it causes reddish spots on the patient's skin. The patient's father had rhinitis allergy and urticaria.

On examination, we found erythema plaque and reddish spots with white scales on face, forehead, chest, stomach, back, both arms, both legs, and erosion on back on the neck. Hanifin-Radjka criteria included four major criteria (pruritus, typical morphology and distribution: facial and extensor involvement during infancy, and family history of atopy, chronic dermatitis) and three minor criteria (xerosis, itchy when sweating, and early age at onset). The SCORAD was 44.9 (moderate degree). We diagnosed infantile type atopic dermatitis with moderate degree in patients.

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Fig. 27.1 Erythema plaque and white scales on face, chest, and stomach



Fig. 27.2 Erythema plaque and white scales on back of the neck, back, both arms, and both of legs. Erosion on back of the neck

Based on the case description and photograph, what is your diagnosis?

1. Infantile type atopic dermatitis
2. Irritant Contact Dermatitis
3. Infantile Seborrheic
4. Scabies

Based on medical history, physical examination, and Hanifin-Radjka criteria, diagnosis for this patient is Infantile type atopic dermatitis.

Treatment: we started hydrocortisone cream 1% twice daily on erythema plaque and reddish spot, fusidic acid cream 2% on erosion, and urea cream 10% twice daily on dry skin and scales. After 1 month of therapy, the patient showed improvement.

Discussion

Atopic dermatitis (AD) is a skin disorder that often occurs in infants and children. 45% of all cases of atopic dermatitis begin within the first 6 months of life, 60% begin in the first year, and 85% begin before 5 years of age [1]. In infantile phase atopic dermatitis, the lesions usually begin to appear on the cheeks and scalp, and may also affect the forehead, ears, neck and sometimes the body. With increasing age, the lesion can appear in the extensor part of the limb with a symmetrical distribution. Generalized dry skin is common [2].

The goal of therapy for AD is to focus on improving quality of life by keeping skin healthy—repairing barrier function, minimizing pruritus, and preventing flare of disease. The five "A's" of AD care include: avoidance of triggers, application of cleanser and moisturizer, anti-inflammatory, anti-itch, and antibacterial [3]. Based on the International Consensus Conference on Atopic Dermatitis (ICCAD) 2002–2003, in the acute phase: AD control is aimed at pruritus and inflammation, the treatment is administering topical corticosteroids and calcineurin inhibitors (pimecrolimus and tacrolimus). Steroids decrease production of proinflammatory cytokines and can help control both local irritation as well as pruritus [4].

Patients with AD have abnormal skin barrier function with increased transepidermal water loss and decreased water content and dry skin (xerosis) contributing to disease morbidity by the development of microfissures and cracks in the skin. These microfissures may serve as portals of entry for skin pathogens, irritants, and allergens. The daily use of an effective emollient helps to restore and preserve the stratum corneum barrier, decreases the need for topical glucocorticoids and NSAIDs and improves outcomes [5].

The subject of skin cleansing is a much-debated topic for patients with AD. Harsh soaps and hot water temperature during bathing or showering can further irritate already inflamed skin, though non-soap-based surfactants, synthetic detergents with an acidic or neutral pH, and lipid-free cleansing lotions may be used. The duration of the cleansing ritual should be limited to 10–15 min and the frequency of bathing 1–2 times a day and should avoid doing scrubbing. Patient with AD should wear soft, sweat-absorbent clothing (cotton) and comfortable to wear [6].

In order to minimize the ongoing stimulus for the underlying inflammation of AD, patients are advised to avoid triggers such as specific foods, seasonal or perennial allergens, and irritants. Because each patient may not display flares in response to any or all of these triggers, the list should be tailored to the individual patient [7].

Key Points

- Atopic dermatitis is an inflammatory skin disease that is chronic and relapsing. It often occurs in infants and children.
- Knowing the risk factors is very important to prevent recurrence.
- One of the important therapies for atopic dermatitis patients is to keep the skin moist, so that patients and their families are encouraged to always use a moisturizer.

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Chapter 28
Juvenile Xanthogranuloma

Raden Mohamad Rendy Ariezal Effendi, Trustia Rizqandaru, Reiva Farah Dwiyana, Srie Prihianti Gondokaryono, and Inne Arline Diana

A 2-year-old boy attended a pediatric dermatology clinic with chief complaints of brownish-yellow papules and plaque on face, trunk, both upper arms, and legs which were neither painful nor pruritic. The onset of the complaint was when the patient was aged 1 year old as a reddish-brown papule on the right cheek. Within 1 month, the papule increased in number, spread to the left cheek and became brownish-yellow in color. The lesion spread to the trunk and legs within 2 months. The patient admitted history of previous treatment, i.e., moisturizer from a dermatovenereologist but the skin lesion remained unchanged. Systemic involvement and history of metabolic disease on the patient and family were denied. Physical examination revealed multiple lesions in forms of brownish-yellow papules and plaques on the face, ears, trunk, both upper arms and legs (Fig. 28.1). Dermoscopy examination revealed brownish-yellow hue resembling "setting sun appearance" (Fig. 28.2).

Based upon history and clinical appearance, what is your diagnosis?

1. Juvenile xanthogranuloma (JXG)
2. Benign cephalic histiocytosis (BCH)
3. Xanthoma disseminatum (XD)
4. Generalized eruptive histiocytosis (GEH)

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Fig. 28.1 Brownish-yellow papules and plaques on face, ears, trunk, both upper arms and legs

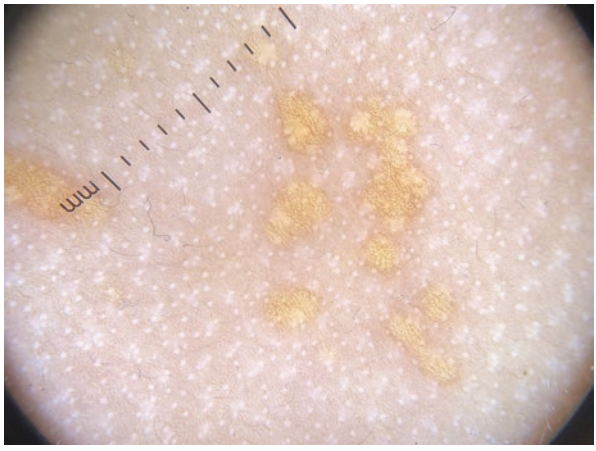


Fig. 28.2 Dermoscopy examination revealed brownish-yellow hue resembling "setting sun appearance"

Laboratory investigations: within normal limit

Histopathological examination: Inflammatory cells consisting of lymphocytes, foam cells and histiocytes on upper dermis. Clustered histiocytes were observed, forming the Touton giant cell.

Immunohistochemistry examination: CD68 positive, S100 positive on Langerhans cells and neurons, with negative CD1a.

Diagnosis: Juvenile xanthogranuloma.

Treatment: Topical 1% rapamycin application on both sides of the face provided satisfactory results.

Discussion

Histiocytosis is a disease marked by accumulation of histiocytes in the tissue [1, 2]. In 2016, Emile, et al. suggested a new categorization of histiocytosis, dividing the disease into five categories: Langerhans-related histiocytosis (L); cutaneous and mucocutaneous non-LCH (C); malignant histiocytosis (M); Rosai-Dorfman disease (R); and hemophagocytic lymphohistiocytosis and macrophage activation syndrome (H). On this latest classification, JXG is included into group C [2, 3].

Based on tumor registry data for 35 years in University of Kiel, Germany, the incidence of JXG was 129 cases out of 24,600 childhood tumor cases (0.5%) [4]. The incidence of JXG was higher on boys than girls, i.e. 1.4:1 [5]. The skin lesion on JXG might appear for the first time around the age of 0–12 years, but most frequently before 1 year of age (71.3%) [4]. The underlying etiology of JXG was not yet clearly determined [2]. This disease was presumed to occur due to infection or physical trigger causing histiocytic granulomatous reaction [6].

The diagnosis of JXG was established by physical examination, dermoscopy, and histopathological examination. The initial lesion of JXG might be in form of solitary or multiple reddish brown papule or nodule on head and neck (33%), trunk (33%), or extremities (18%) [1, 2, 7]. The lesion would then turn into reddish yellow in color [1, 2]. Clinically, JXG could be categorized into micronodular and macronodular form. Micronodular form was represented with lesion less than 10 mm in size while macronodular form has lesion bigger than 10 mm in size [2, 7].

Involvement of other organ apart from the skin in JXG was frequently observed on the eyes [1, 7]. Ocular lesion occurred on 10% cases and most frequently found on the iris, causing hyphema, glaucoma, and blindness [2, 7]. Most frequent ocular complaints in JXG were red eye (40%) and hyphema (13%). Involved ocular parts including the iris (68%), conjunctiva (19%), eyelid and choroid (6%) [2, 8]. Systemic involvement on JXG was found on 5 cases, which involved the liver (2.4%), central nervous system (2.4%), spleen (1.6%), lungs (1.6%), heart (0.8%), and kidney (0.8%) [2, 4]. JXG was associated with several other diseases, including neurofibromatosis (NF) and juvenile chronic myelogenous leukemia (JCML) [1, 7]. Child with NF and JXG has 20–32 fold risk of having JCML compared to child with NF but without JXG [7].

Histopathological examination on early JXG lesions may reveal histiocyte accumulation without lipid infiltration and very scarce lymphocytes and eosinophil. Mature lesions contained foam cells, Touton giant cells, histiocytes, lymphocyte and eosinophil. Older lesions revealed proliferation of fibroblast and fibrosis on infiltration sites [8–10].

Dermoscopy might be utilized as a supporting examination to help establish the diagnosis of JXG [11, 12]. Dermoscopy appearance of JXG might vary based on the evolution of lesions. Initial lesions might exhibit the appearance of an xanthomatous cell which was pathognomonic for JXG, known as "setting sun appearance". More advance lesion might show pale yellow to yellowish orange globules and whitish streaks [12].

Juvenile xanthogranuloma is a self-limiting disease which does not require specific treatment. Certain treatment might be administered should the disease yield cosmetic problems or if the cutaneous lesion was progressing rapidly [13]. Several therapeutic options including cryosurgery, intralesional corticosteroid injection, laser, and excisional surgery [1, 2, 7]. Topical treatments in JXG cases were rarely prescribed. However, there was a reported case in which topical treatment was administered for a non-LCH case, i.e. benign cephalic histiocytosis (BCH) which yielded satisfactory results marked by thinning of lesion. Rapamycin is an immunosuppressant that has an antineoplastic effect. Rapamycin can be one of the alternative non-invasive topical therapy options for JXG. However, long-term observations are still needed to assess the effectiveness and side effects of the drug [14].

Key Points

- Juvenile xanthogranuloma can overlap with other non-LCH forms; hence, diagnosis of JXG requires proper clinical and histopathology examination.
- Treatment can be considered if the patient has a cosmetic problem or if the cutaneous lesion is progressing rapidly, although JXG is self-limiting disease which does not require specific treatment.

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Chapter 29
Kasabach-Merritt Syndrome

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A 2-months-old male was referred to the Dermatology and Venereology clinic in Sanglah General Hospital, Denpasar, Bali, with suspect haemangioma. The patient's family complained of a red lump arising on the right leg, abdomen and back. Initially the lump was on the right leg, then spread to the abdomen and back 2 weeks ago after receiving an immunization injection at that site. The lump is getting bigger and very painful when touched and it makes the baby cry even more. The family said, there were already non-swollen, painless and flat red spots that were visible from birth at the right thigh, right side of abdomen, and right side of the lower back (Fig. 29.1).

Based on the case description and the photograph, what is your diagnosis?

1. Infantile haemangioma with bilateral hydrocele
2. Kaposiform hemangioendothelioma
3. Tufted angioma
4. Kasabach-Merritt syndrome

From physical examination we observed a purplish red solitary tumor with smooth and shiny surface, unclear borders, size 15 × 27 cm, with a dense consistency, petechiae scattered around the tumor on the right leg, scrotum, abdomen and the right side of lower back.

Laboratory investigations: we found abnormality of lymphocytes count 1.43 ($1.8–9 \times 10^3$/L), erythrocyte 1.27 ($4.10–5.3 \times 10^6/\lceil$L), hemoglobin 3.2 (12.0–16.0 g/dL), haematocrit 11.2 (37.0–48.0%), thrombocyte 11 ($140–440 \times 10^3$/μL).

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Fig. 29.1 A purplish red solitary tumor with smooth and shiny surface, unclear borders, size 15 × 27 cm, with a dense consistency, petechiae scattered around the tumor on the right leg, scrotum, abdomen and the right side of lower back

The final diagnosis for this patient is Kasabach-Merritt syndrome.

The treatment consists of methylprednisolone 2 mg/kgBW/day (3 × 3.5 mg) intraorally for 14 days. We also plan to give transfusion of 35 ml packed red blood cells (PRC) and a 50 ml transfusion of fresh frozen plasma (FFP) immediately.

Discussion

Kasabach-Merritt syndrome (KMS) is a rare case and early suspicion is required for an early treatment especially in coagulopathy which is a life threatening condition to patients. This condition needs supportive care and medication choices before proceeding with surgical or other interventional medications [1]. In this patient we found the count of platelet, erythrocyte haemoglobin and haematocrit were in critical value.

Recently, there were no specific guidelines established to treat the KMS. The medication choices in KMS are varied, such as early management of coagulopathy and aggressive supportive care, systemic corticosteroids, systemic chemotherapy, immunomodulators, and surgical management [2].

Efficacy of corticosteroids in management of KMS has been validated in multiple clinical trials. Infantile haemangioma derived stem cells demonstrated that corticosteroids lead to suppression of the factors that are known as targets of nuclear factor κ-light-chain-enhancer of activated B cells (NF-κB) such as vascular endothelial growth factor, monocyte chemoattractant protein-1, urokinase plasminogen activator receptor, and interleukin-6. The initial dosing and the type of corticosteroids used in KMS vary based on the case series or case reports published [3, 4].

In this patient we give supportive care such as PRC and FFP transfusion immediately to recover the general condition. We also give systemic corticosteroid

(methylprednisolone). From 7 days of follow up, the clinical symptoms show that KMS was improved and responsive to our management. It can be seen by increased platelet count and reduced tumor size. The patient is surviving and still needs an advanced treatment modality such as surgery. Recently, the treatment of KMS is still challenging, and more studies are required to summarize a clearly successful treatment as a guideline in the future [5].

Key Points

- Kasabach-Merritt syndrome (KMS) is a rare case and early suspicion is required for an early treatment especially in coagulopathy which is a life threatening condition to patients
- The medication choices in KMS are varied, such as early management of coagulopathy and aggressive supportive care, systemic corticosteroids, systemic chemotherapy, immunomodulators, and surgical management

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Chapter 30
Oral Isotretinoin Treatment of Harlequin Ichthyosis

Hanny Tanasal, Rita Sugiono Tanamal, Antonio Orson Ongkowidjojo, and Ferra Olivia Mawu

A newborn baby was presented to the department of dermatology and venereology right after he was born. The clinical manifestation showed a hard, thick (armor-like plate) on every body surface, severe bilateral ectropion and eclabium on both lips, nose and ear appeared to be flattened, fingers are closed and appeared to be constricted (Fig. 30.1).

Based on the case description and the photographs, what is your diagnosis?

1. Harlequin Ichthyosis
2. Collodion Baby
3. Bullous Congenital Ichthyosiform Erythroderma

The newborn was immediately diagnosed with Harlequin ichthyosis and then treated by the dermatology, pediatric, and ophthalmology departments.

Treatment: the patient was treated with topical emollient and oral isotretinoin. Oral isotretinoin was started on the fifth day of treatment with a dose of 1 mg/kg body weight/day. After 2 weeks of oral isotretinoin, the patient showed improvement on the skin thickness (Fig. 30.2). After 3 months (Fig. 30.3), hard and thick

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Fig. 30.1 "Armor-like" plate on body surface soon after birth



Fig. 30.2 2 months old, showed improvement on skin thickness



Fig. 30.3 3 months old, no visible hard and thick skin



Fig. 30.4 9 months old, erythroderma ichthyosiform

skin are hardly visible, physical findings showed fine scales and there was improvement on eclabium and ectropion. Physical findings after 9 months of treatment showed redness of skin, fine scales and dry skin which is the characteristic of erythroderma ichthyosiform (Fig. 30.4). Oral isotretinoin dose was reduced to 3 times a week for 10 months and the clinical manifestation did not get worse. The dose was then reduced to 2 times a week, as we considered the strain on the liver due to the long term use of isotretinoin. The patient is 22 months old now and the physical findings show that thick scales have started to form and erythroderma ichthyosiform still persists (Fig. 30.5). The dose of oral isotretinoin has been increased to 3 times a week taking into consideration that the patient's liver function test is normal (SGOT:39 u/L, SGPT:21 u/L).

Discussion

Harlequin Ichthyosis (HI) is the most severe form of Autosomal Recessive Congenital Ichthyosis (ACRI) that is caused by ABCA12 gene mutation. The clinical manifestation of HI consists of thick and rigid skin, skin fissure, and yellow-brown armor like plate that covers every part of the body's surface. Nose and lips appear flattened and rudiment, there are constrictive scales on extremities that may lead to autoamputation. Because of the high mortality rate, HI patients have to be treated intensively and as soon as possible. HI patients that have survived this condition can develop exfoliative ichthyosiform erythroderma, palmoplantar keratoderma and nail dystrophy [1–5].

Oral retinoid can improve HI prognosis significantly. In general, oral retinoid regulates skin growth and differentiation. Oral retinoids have a keratolytic/shedding effect that is used to treat HI. 4-oxo-metabolite is the end product of oral retinoid on skin that is known to affect transcription regulation activity of Normal Human Epidermal Keratocytes (differentiation and hyperproliferation) and dermal fibroblast.



Fig. 30.5 22 months old, erythroderma ichthyosiform has persisted

Initial dose of isotretinoin is 0.5 mg–1 mg/kg body weight/day, it is advised to use an isotretinoin dose as small and effective as possible for long term use. It is advised to give a retinoid-free period [4, 6, 7].

In this case, the patient was given 1 mg/kg body weight/day and it was proven effective as the patient clinical manifestation improved after 2 weeks of treatment. The thick, rigid, armor like plates, and skin fissures became less. After 9 months, the patient was given oral isotretinoin 3 times a week for 10 months. The dose was reduced to 2 times a week for 3 months, but it has now been increased to 3 times a week because the patient has started to show thick scales and taking into consideration that the patient's liver function test is within normal limits. At the moment the patient is 22 months old and is still alive.

Key Points

- Harlequin Ichthyosis lesion consists of thick and rigid skin, skin fissure, and yellow-brown armor like plate that covers every part of the body's surface.
- Harlequin ichthyosis can be treated with oral isotretinoin which has a keratolytic effect in controlling the thickness of the skin.
- Oral isotretinoin dose given to the patient is 1 mg/kg body weight/day showed good results and the patient is still alive

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Chapter 31
Oral Propranolol Treatment for Infantile Hemangioma: A Case Report

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A 2-month-old girl, Javanese, visited the Dermatology and Venereology Department of Dr. Soetomo Hospital in East Java with a complaint of irregular red lesions on her face (Fig. 31.1). The symptoms were initially appeared as few red dots in the face at 1 months of age which gradually increased to this present size.

In gestation history, the patient was first child born from the 39 year-old-parent, premature at 34/35 weeks, and delivered by the caesarean section with 2000 g birth weight. The patient also had a cleft lip palate since birth but has not been operated until the age of 10 months old. The mother had a history of preeclampsia during pregnancy that was forced to be operated.

Based on the case description and the photographs, what is your diagnosis?

1. Infantile hemangioma
2. Congenital hemangioma
3. Vascular malformation
4. Hemangiosarcoma

In the facial region there were irregular red colored facial lesions present on the left, middle, and right side of the face also involving the lower lip, with the biggest diameter 4 cm. No ulceration and nor bleeding were noted on the lesion. Physical examination revealed my normal condition. Dermoscopy examination showed cerebriform components (yellow arrow), including dilated red vessels surrounded by pinkish structure (blue arrow) (Fig. 31.2).

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Fig. 31.1 The physical examination of the patient when the first administration

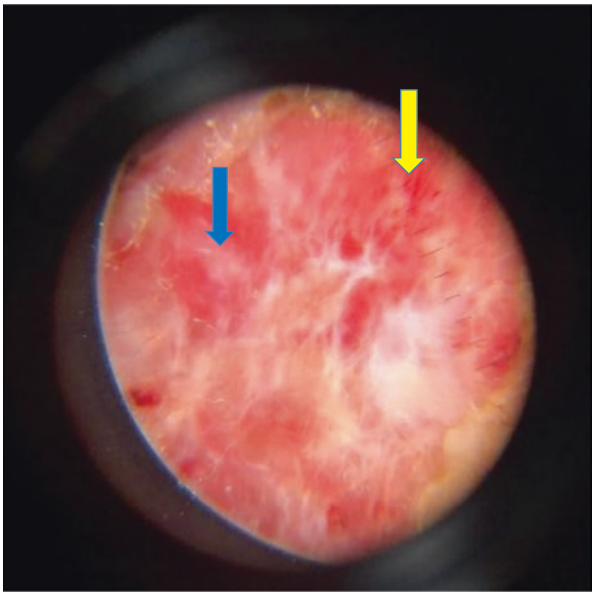


Fig. 31.2 Dermoscopy of the lesion

Laboratory complete blood count examination was within the normal limit. Echocardiography examination resulted in mild atrial septal defect that was not a contraindication for propranolol treatment.

Diagnosis: Infantile Hemangioma.

Treatment: We used oral propranolol 0.5 mg/kg daily for the first week, and gradually tapered up to 0.5 mg/kg daily every week until the dose reached 2 mg/kg/day and being evaluated at first, third, and sixth month. The evaluation of the therapy is presented below, first month (Fig. 31.3), third month (Fig. 31.4), and sixth month (Fig. 31.5).



Fig. 31.3 Physical examination of first month



Fig. 31.4 Physical examination of third month



Fig. 31.5 Physical examination of sixth month

Discussion

Hemangiomas are the most common benign soft tissue tumor of infancy and childhood, mainly arise in the head and neck area, trunk and the extremities. Because mostly happen in infant patients, they are classified as infantile and congenital hemangiomas [1].

Dermoscopy is a good tool to evaluate vascular structures and dermis distribution. In infantile hemangioma, dermoscopy examination is presented as red globular vessels and varied other form vessels that look alike in this case [2]. Although it is specific to evaluate infantile hemangioma (IH), it could strengthen the diagnosis in order to eliminate other differential diagnosis [3].

Actually infantile hemangioma is a self-limiting disease and does not need to be treated. But in some cases, like at periocular, airway, and eyelid because of the risk of complications, will need active treatment [1]. Propranolol is a nonselective beta blocker which has become the first line therapy for most IH requiring therapy. The mechanism of propranolol to treat hemangiomas is unclear but it is hypothesized that beta-blocker activity induces vasoconstriction and can cause discoloration and softening of the hemangioma [4]. In addition, there are suspicions about propranolol's ability to inhibit growth factors and stimulate apoptosis that could degenerate hemangioma [5].

However, propranolol also has side effects that need special attention, especially for neonates and those with congenital heart disease. Beta-blocker activity causes hypoglycemia in neonates undetectable, consequently it is necessary to pay extra attention to neonates who are given propranolol therapy [6]. It is important to evaluate the patient's heart condition before giving propranolol therapy. Because bradycardia activity can be burdensome for individuals with heart failure [7]. In our case the patient suffered from a mild atrial septal defect and was consulted by a cardiologist beforehand.

The management of propranolol administration for infantile hemangioma varies widely and this decision is determined by looking at the patient's condition. Some studies suggest that the initial dose is 1 mg/kg three times daily in the majority of patients [8], but some are directly using 2 mg/kg three times a day [9]. This decision is based on the patient's hemodynamic condition and blood sugar level [10]. The duration of administration also varies, depending on the response to therapy and the size of the lesions that occur in the patient. The fastest administration ever recorded was 3.5 months and the longest was up to 14 months [8]. In our case the treatment of 6-month propranolol is giving excellent response with no side effects.

Key Points

- Infantile hemangioma is a soft tissue tumor of infancy and childhood which could manifest into a high risk case
- Oral propranolol is a systemic drug of choice in high risk infantile hemangiomas because it has a good efficacy and availability

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Chapter 32
Perianal Dermatitis

Amalia Licordari and Fabio Arcangeli

A 9-month-old baby in good general condition came to our observation because for a few days he had a bright red erythema on the perianal area, extending up to the coccygeal region (Fig. 32.1). The lesions were exudative with not exactly clear limits and there were some satellite papular elements. Other polymorphic lesions (maculo-papules, some vesicles, some crusts) were present on the lateral region of the neck (Fig. 32.2) and on the abdominal region (Fig. 32.3).

Based on the Case Description and the Photographs Which Is Your Diagnosis?

1. Streptococcal perianal dermatitis
2. Staphylococcal perianal dermatitis
3. Inverse psoriasis
4. Perianal candidiasis

We performed a culture test for bacteria and yeasts and pending the outcome we started empiric oral antibiotic therapy with amoxicillin and clavulanic acid. After just 2 days we observed a marked improvement and after 7 days the disappearance of all lesions.

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Fig. 32.1 Erythema on the anal and perianal areas



Fig. 32.2 Erythematous exudative lesions on the right of the neck

Diagnosis

Staphilococcal perianal dermatitis.

The outcome of the microbiological investigations was negative for yeasts (Candida Albicans) and positive for staphylococcus aureus.

Discussion

Perianal infectious dermatitis (PID) represents a superficial inflammation of the perianal skin of bacterial origin. The clinical hallmark of PID is represented by a characteristic well-demarcated perianal erythema, extending 2–4 cm around the anus [1].



Fig. 32.3 Erythematous exudative lesions on the abdominal region

PID is frequently observed in children. The most commonly responsible agent is group A beta-hemolytic streptococci, while staphylococcus aureus is involved in a small percentage of cases [2].

The clinical presentation is the same for both and is characterized by an intense perianal erythema with well-defined margins and a circular or oval shape. Superficial erosions, anal fissures, excoriations, and purulent discharge may also be present [3]. Pain or itching are often present (78%–100%) and complications such as constipation (47%–58%), blood-streaked stools (21%–60%) can occur, especially in the absence of treatment [4]. The infection rarely extends to genital organs, resulting in vulvo-vaginitis or balanitis [4].

In our case, papulo-vesicular erythematous manifestations in other sites were associated with perianal dermatitis. All caused by staphylococcus aureus, all resolved after a short course of systemic antibiotic therapy with amoxicillin and clavulanic acid.

The extension of the erythema to the adjacent skin and the concomitance of papules and pustules on the buttocks or on other sites is the clinical feature that distinguishes staphylococcal from sterptococcal perianal dermatitis [2, 4].

Differential Diagnosis

Perianal candidiasis. Candidiasis mainly affects the folds and diaper area in children. It presents more often exuding erythematous lesions, sometimes macerated. Vesicular, pustular or papular satellite elements are commonly observed.

Inverse psoriasis. The erythematous lesions are slightly infiltrated and well demarcated, sometimes covered with fine scales. No vesicular or pustular elements are observed.

Key Points

- Perianal infectious dermatitis is frequent in children and the most common cause is group A beta-hemolytic streptococci but staphylococcal aureus must be kept in mind too.
- The clinical presentation as a bright red and well defined edematous-erythematous lesion is similar in both cases
- The diagnosis is not so obvious and a microbiological study is often necessary
- The extension of the erythema from the perianal area to the adjacent skin and the concomitance of papules and pustules in other sites is the clinical feature that distinguishes staphylococcal perianal dermatitis from the streptococcal one.

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Chapter 33
Staphylococcal Scalded Skin Syndrome

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A 11-month-old girl was referred to the Dermatology Emergency Room of Dr. Soetomo General Hospital Surabaya because of scalded skin in her face, trunk, arm and external genitalia area since 1 day before. The scalded skin started to appear in her waist when her parents tried to carry her and then spread to all over her body including the skin of external genitalia. There was also a small blister appearing near her nose and mouth. The blister ruptured easily with minimal pressure and covered with crust. The lesion started with redness and tender skin 2 days before and the patient was irritable, refusing to be touched. The next day the skin started to be scalded when touched.

She also had fever along with erythematous skin lesions. Five weeks before she had a cough and cold. She went to the public health center and got some medicine, but the parents forgot the name of the drugs given. There was no history of redness on her eyes, pain and infection on her ears, nose and any other site of her skin (Fig. 33.1).

Based upon history and clinical appearance, what is your diagnosis?

1. Staphylococcal scalded skin syndrome
2. Steven-Johnson syndrome
3. Toxic epidermal necrolysis

On examination we observed diffuse erythema with a large area of erosion and desquamation on her face, trunk, arms, legs and also external genitalia skin. Nikolsky's sign was positive all over her skin. There was secret in both eyes.

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Fig. 33.1 Diffuse erythema with large area of erosions and desquamations almost all over the body. Nikolsky's sign was positive

Laboratory examination: Hemoglobin 12.8 g/dL (normal range: 13.3–16.6), leucocyte 13.640/uL (3370–10,000), thrombocyte 418.000/uL (150,000–450,000), SGOT 49 U/L (0–50), SGPT 26 U/L (0–50), BUN 5.0 mg/dL (7–18), creatinine serum 0.49 mg/dL (0.6–1.3) and albumin 4.0 g/dL (3.4–5.0). Urine examination was normal. The bacterial culture from nasopharyngeal swab showed the growth of *Staphylococcus pasteuri* that is sensitive to ciprofloxacin, levofloxacin, moxifloxacin.

Diagnosis: Staphylococcal scalded skin syndrome.

Treatment: Intravenous Ampicillin sulbactam 200 mg four times daily was immediately given. After 6 days, the antibiotic was changed to Levofloxacin 70 mg two times daily according to the bacterial culture result and the antibiotic was continued until 5 days. Topical fusidic acid 2% cream was given twice daily for the erosion lesions (Fig. 33.2).

Discussion

Evidence indicates that the incidence and prevalence of SSSS is increasing. SSSS is most commonly observed in neonates and children younger than 5 years with a peak between 2 and 3 years of age due to their decreased immunity and immature renal



Fig. 33.2 The progression of patients after 7 days of antibiotics therapy

clearance of toxins [1]. Exfoliation of the skin in this disease is caused by an exfoliative toxin released by the *Staphylococcus aureus*, particularly ETA and ETB [2]. An infection with *Staphylococcus aureus* usually precedes SSSS [3]. Those exfoliative toxin (ETs) are thought to lyse desmoglein-1 leading to loss of cell to cell adhesion between the stratum spinosum and stratum granulosum. This disruption is clinically seen as an epidermolysis. The desmoglein-1 can be found in the superficial epidermis but not in the mucosal membrane [2, 3].

The incubation period from skin infection to the appearance of the syndrome ranges from 1 to 10 days. The diagnosis of SSSS can be made based on the history and clinical manifestation. The findings of tender erythroderma followed by flaccid bullae formation, and desquamation with a scalded appearance especially in friction zones, periorificial scabs/crusting, positive Nikolsky's sign, and absence of mucosal involvement can form the basis of diagnosis [4]. It preceded by a prodromal phase in which there maybe fever, general malaise, and the child may become irritable. Large sheets of epidermal surface are typically shed, revealing a moist underlying erythematous base. The exfoliation first appear around the mouth, neck, and subsequently on the body and limbs [2, 5]. SSSS is caused by circulating exfoliative toxin and *S. aureus* does not occur in the skin lesions thus culturing exfoliative lesions and bullae are not helpful. *S. aureus* culture from any suspected primary focus of infection, such as the nasopharynx, conjunctiva, umbilicus, and diaper area, can help to confirm the diagnosis. The histopathology examination is typically not necessary, but if it is performed, superficial intraepidermal separation along the granular cell layer may be shown [6].

SSSS can resemble other epidermolytic diseases such as Toxic epidermal necrolysis (TEN) and Steven-Johnson Syndrome (SJS). The mucosal involvement is the key to differentiate these diseases. TEN and SJS are characterized by a sudden onset of cutaneous erythema and inflammatory bullous lesions on the skin with full thickness epidermal detachment accompanied by involvement of two or more mucosal surfaces [7]. The lesions initially appear as confluent erythematous, pruritic macular

rash that progresses into bulla and epidermal detachment on face, trunk, and extremities. Palms and soles are involved. There are painful oral lesions on lips and buccal mucosa, conjunctival lesions, and corneal erosions. Most cases of TEN and SJS are clearly linked to medications such as sulfonamides, penicillins, cephalosporins, quinolones, anticonvulsants, and non-steroidal anti-inflammatory agents [1, 6].

The treatment includes the administration of anti-staphylococcal antibiotics, liquids, electrolytes and the local treatment of the denuded areas. Anti-staphylococcal antibiotics administered by vein for a minimum of 7 days. Patients need fluid rehydration, topical wound care similar to the care for thermal burns. Morbidity in children who develop cellulitis, sepsis, and pneumonia can be significant [1]. In this case, the patient's condition improved as we immediately gave the antibiotic therapy and no complications arose.

Key Points

- Staphylococcal scalded skin syndrome is one of the emergency conditions in the dermatological field.
- Early diagnosis and treatment is imperative to reduce the morbidity and mortality of this condition.
- We have to exclude other differential diagnosis such as Steven-Johnson syndrome (SJS) and Toxic epidermal necrolysis (TEN) due to their clinical features similarities.

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Chapter 34
Subcutaneous Indurated Plaques in a Newborn

Ana Rebeca Neves Calado, Ana Isabel Barros Ramos Martins, Maria Teresa Dionísio, Maria Francisca Jacome Morgado, Leonor Isabel Castendo Ramos, and Américo Manuel Costa Figueiredo

Clinical Story

A male newborn weighing 4 kg was delivered at full-term (37 weeks, 4 days) by emergency caesarian section for decreased fetal movements. The mother had a history of diabetes type I and Graves disease. The baby was hypotonic at birth, with apnoea and bradycardia (10-min Agar Score 5), requiring endotracheal intubation and therapeutic hypothermia for 72 h, due to severe hypoxic-ischemic encephalopathy (HIE).

During his second week of life, he developed red-violet indurated plaques and nodules on his back and shoulders, with multiple fluctuation areas (Fig. 34.1). He was on day seven of ampicillin and gentamicin. Incision and drainage of one of the plaques revealed culture-negative purulent material.

Skin biopsy of one plaque was performed, showing predominantly lobular panniculitis with a mixed inflammatory infiltrate composed of lymphocytes, histiocytes, and multinucleated giant cells. Needle-shaped clefts in a radial configuration were seen within the giant cells (Fig. 34.2).

Maximum serum calcium level was 11.5 mg/dL (normal range 8.6–9.7 mg/dL), 10 days after the onset of cutaneous lesions. He was managed conservatively, with hydration and dietary restriction of both calcium and vitamin D. Serum calcium was closely monitored (twice weekly). A normalization in calcium level was observed and subcutaneous nodules resolved gradually in 3 months.

The renal ultrasound didn't find any sign of nephrocalcinosis.

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Fig. 34.1 Neonate with a large tumoral lesion over the dorsum

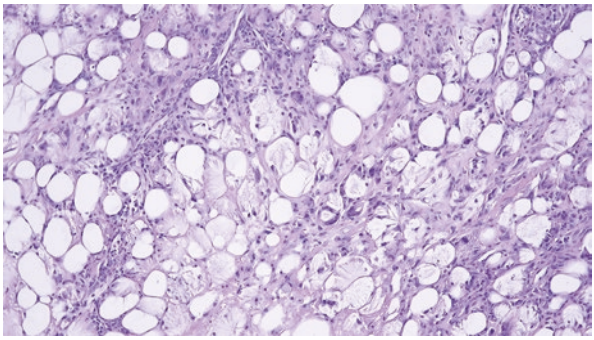


Fig. 34.2 Lobular panniculitis with a lymphohistiocytic inflammatory infiltrate. Needle-shaped crystals within giant cells can be observed

Based on the Case Description and the Photographs, What Is Your Diagnosis?

- Cold panniculitis
- Cellulitis complicated by skin abscess
- Sclerema neonatorum
- Subcutaneous fat necrosis of the newborn

Diagnosis: Subcutaneous fat necrosis of the newborn.

Discussion

Subcutaneous fat necrosis (SFN) of the newborn (NB) is a rare disorder characterized by symmetrically distributed red-brown nodules and indurated plaques, that primarily develops in the first few weeks of life in full-term neonates [1, 2].

Precipitating factors may include perinatal distress (such as asphyxia, hypothermia, hypoxemia, hypoglycemia) or maternal conditions (such as preeclampsia, diabetes and hypothyroidism) [3]. In our case, therapeutic hypothermia and maternal diabetes seemed to predispose to this condition.

The pathogenesis remains unclear, but the high amounts of saturated fatty acids in neonatal adipose tissue may result in crystallization under low temperature, leading to adipocyte necrosis and subsequently, panniculitis [3, 4].

A definitive diagnosis can be made by correlating clinical and histological findings [3].

The histopathology demonstrates a lobular panniculitis and granulomatous inflammatory reaction, as well as needle-shaped clefts in a radial array in lipocytes, macrophages and giant cells (Fig. 34.2) [3].

The differential diagnosis includes sclerema neonatorum (SN), cold-induced panniculitis, post-steroid panniculitis and cellulitis [4].

The distinction with SN is of particular relevance, once the mortality is severely higher in SN. Contrarily to SFN, SN is almost restricted to preterm newborns with low birth weight. These infants are usually severely ill and skin involvement is more diffuse [3, 4].

In general, SFN is a self-limiting condition resolving over weeks to months. Though, recognizing it is paramount as important complications can occur, such as hypercalcemia, thrombocytopenia and dyslipidemia. The most significant complication is hypercalcemia (occurring in up to half of the cases). It is partly explained by the excessive intestinal absorption of calcium from unregulated production of 25-hydroxyvitamin D by activated macrophages within adipose tissue. Other mechanisms involving bone reabsorption and renal failure may also play a role [3, 5].

SFN-associated hypercalcemia can lead to other serious complications such as nephrocalcinosis or metastatic calcification [5, 6].

Monitoring calcium serum levels for up to 6 months after the onset of skin lesions is recommended, as a late presentation of SFN-associated hypercalcemia has been reported. However, these guidelines lack solid evidence and the frequency of calcium serum evaluation may be better dictated by the severity of SFN and by the presence of clinical symptoms of hypercalcemia [2, 3].

The treatment is mainly supportive. Hyperhydration and calcium-wasting diuretic, as well as dietary restriction of calcium and vitamin D, may be sufficient to treat moderate hypercalcemia, but higher values of serum calcium may require treatment with bisphosphonates or corticosteroids [4, 5].

Key Points

- SFN is characterized by symmetrically distributed, firm subcutaneous nodules or plaques.
- Typically occurs in full term neonates, with a history of perinatal stress or maternal gestational pathology.
- Infants who undergo therapeutic hypothermia should be examined for SFN.
- Usually SFN is a self-limited condition with good prognosis.
- The most important complication is hypercalcemia and serum calcium levels should be monitored.

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Chapter 35
Vesicles on the Tongue of a 3-Months-Old Baby

Virginia Botta, Fabio Arcangeli, and Torello M. Lotti

Case Presentation

A 3 months old boy with multiple tiny vesicles on the dorsum of the tongue was referred by a dentist surgeon to our clinic for assessment and treatment (Figs. 35.1 and 35.2).

Systemic symptoms of fever (38 °C) and malaise were reported 3 days before the clinical signs on the dorsal tongue.

The intraoral cavity appeared normal while the vermillion border of the lips was swollen and erythematous.

Cervical lymphadenopathy was not present.

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Fig. 35.1 Multiple vesicles on the dorsum of the tongue of a 3 months old boy



Fig. 35.2 Closer view of multiple vesicles on the dorsum of the tongue of a 3 months old boy

Based on the Case Description and the Photographs, What Is Your Diagnosis?

1. Herpangina
2. Hand, Foot and Mouth disease
3. Varicella
4. Primary herpetic gingivostomatitis (PHGS)
5. Infection mononucleosis

Diagnosis

Primary herpetic gingivostomatitis (PHGS).

Discussion [1–3]

PHGS is the most common clinical presentation of primary Herpes Simplex Virus 1 infection in over 90% of the cases (HSV-2 in less than 10%). The presentation of the disease is usually involving the different mucosal membranes of the oral cavity.

The infection is acquired by direct contact.

The case here reported is quite peculiar for different reasons:

1. PHGS most often occurs at the age of 5 months to 6 years;
2. The overall oral mucosa and the lips are usually involved:
3. Cervical lymphadenopathy is typically present since the beginning.

The parents of the child denied the permission of any kind of saliva and blood examination reporting that the grandmother of the child kissed him 12 days before the clinical signs while being affected by herpes labialis.

They only accepted to keep the child at rest and to improve hydration.

After 14 days the child was examined again in our clinic and we could appreciate that the lesions healed spontaneously and the child was in good health.

Key Points

1. Primary herpetic gingivostomatitis is the most common viral infection of the oral cavity, mainly affecting children aged 5 months to 6 years.
2. PHGS is caused in over 90% of cases by HSV-1 infection while HSV-2 accounts for less than 10% of cases.
3. Clinical diagnosis is easy in immunocompetent children with typical systemic and local presentation.
4. Rest, hydration and health diet are the first level treatment.
5. Oral and/or systemic antibiotics and antifungal drugs and corticosteroids are contraindicated

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