Clinical Cases in Dermatology
Series Editor: Robert A. Norman

Torello M. Lotti
Uwe Wollina
Olga Olisova
Mohammad Jafferany *Editors*

Clinical Cases in Exfoliative Dermatitis

Springer

Clinical Cases in Dermatology

Series Editor
Robert A. Norman, Tampa, FL, USA

This series of concise practical guides is designed to facilitate the clinical decision-making process by reviewing a number of cases and defining the various diagnostic and management decisions open to clinicians.

Each title is illustrated and diverse in scope, enabling the reader to obtain relevant clinical information regarding both standard and unusual cases in a rapid, easy to digest format. Each focuses on one disease or patient group, and includes common cases to allow readers to know they are doing things right if they follow the case guidelines.

Torello M. Lotti • Uwe Wollina
Olga Olisova • Mohammad Jafferany
Editors

Clinical Cases in Exfoliative Dermatitis

Springer

Editors
Torello M. Lotti
Dermatology
Marconi University
Rome, Roma, Italy

Olga Olisova
Department of Dermatology & Venereology
Sechenov First Moscow State Medical
University (Setchenov University)
Moscow, Russia

Uwe Wollina
Dermatologie & Allergologie
Städtisches Klinikum Dresden
Dresden, Sachsen, Germany

Mohammad Jafferany
Psychodermatology, Psychiatry
& Behavioral Sciences
Central Michigan University College
of Medicine
Saginaw, MI, USA

ISSN 2730-6178 ISSN 2730-6186 (electronic)
Clinical Cases in Dermatology

ISBN 978-3-031-08465-2 ISBN 978-3-031-08466-9 (eBook)
https://doi.org/10.1007/978-3-031-08466-9

This Springer imprint is published by the registered company Springer Nature Switzerland AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

Contents

Chapter 1
A 25-Year-Old Woman with the Pruritic and Bullous Lesions on the Skin Developed in the Third Trimester of Pregnancy 3 Days Before the Delivery

Olga Olisova, N. P. Teplyuk, A. A. Lepekhova, and V. Varshavsky

A 25-year-old woman presented to the Dermatology clinic with the itching pruritic and bullous lesions on the skin (Fig. 1.1a, b).

She had no concomitant disease. Pregnancy was uncomplicated. Three days before the delivery the woman noted the first pruritic lesion became generalized during next three days and followed by vesicles and finally small tense bullae on an erythematous background. Skin lesions developed on the ears, abdomen, back, arms and palms, and thighs. Face, scalp, palms and mucous membranes were free of rashes. Histopathologic findings in biopsy of urticarial lesions were characterized by edema of the epidermis, upper and mid-dermis with a perivascular infiltrate by lymphocytes, histiocytes, and eosinophils (Fig. 1.2).

Direct immunofluorescence (DIF) showed a linear deposition of C3 (complement 3) and IgG autoantibodies at the dermo-epidermal junction (Fig. 1.3a, b), enzyme-linked immunosorbent assay (ELISA) showed circulating IgG autoantibodies against BP180.

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

Polymorphic eruption of pregnancy

O. Olisova · N. P. Teplyuk · A. A. Lepekhova (✉)
Department of Dermatology and Venereology, Sechenov University, Moscow, Russia

V. Varshavsky
Department of Dermatology and Venereology, Sechenov University, Moscow, Russia

Department of Pathology, Sechenov University, Moscow, Russian Federation

T. M. Lotti et al. (eds.), *Clinical Cases in Exfoliative Dermatitis*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08466-9_1

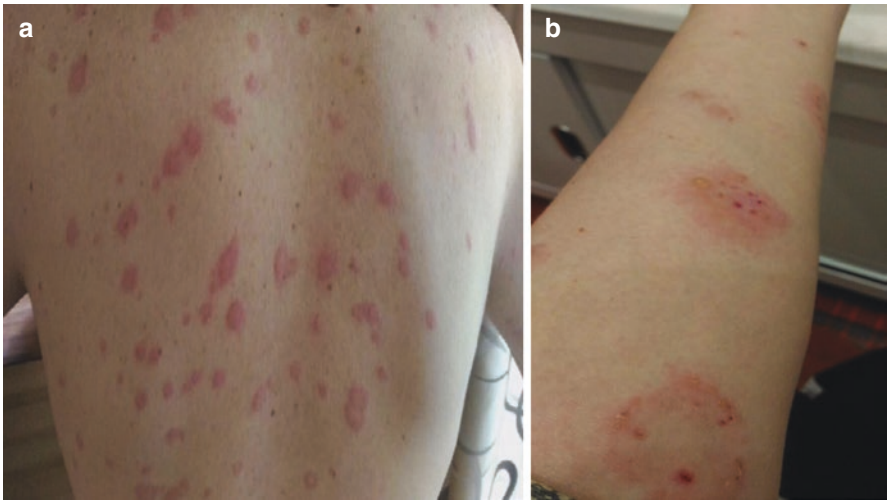

Fig. 1.1 (**a**, **b**) Pruritic plaques and blisters on the trunk and extremities

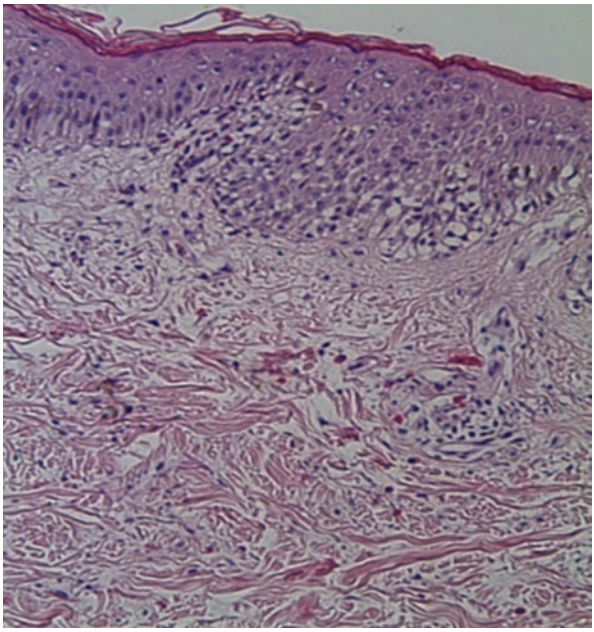

Fig. 1.2 Edema of the epidermis, upper and mid-dermis with a perivascular infiltrate by eosinophils, lymphocytes and histiocytes

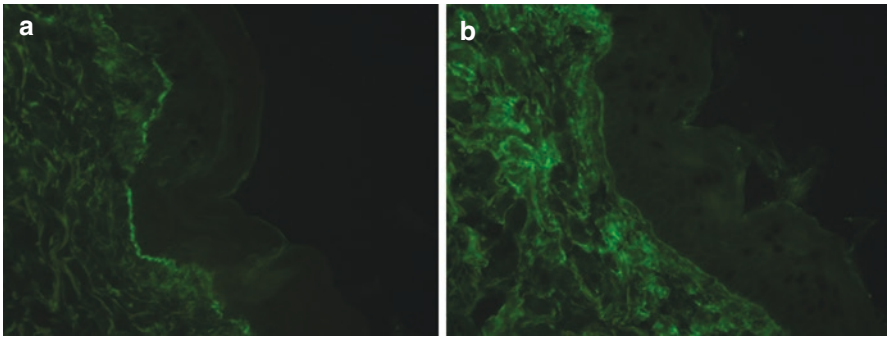

Fig. 1.3 (**a**, **b**) Direct immunofluorescence (DIF) showed a linear deposition of C3 and IgG autoantibodies at the dermo-epidermal junction

Intrahepatic cholestasis of pregnancy
Atopic eruption of pregnancy
Erythema multiforme

Diagnosis

Pemphigoid gestations

Discussion

Pemphigoid gestations (PG) (Herpes Gestationis) is a rare pregnancy-associated blistering autoimmune skin disease, typically occurring in the second and third trimesters of pregnancy, immunologically and clinically similar to the pemphigoid group of autoimmune blistering skin disorders. The disease manifests with severe pruritus, then polymorphic lesions appear that include erythematous urticarial papules and annular plaques, erythema multiforme-like target lesions, papulovesicles, followed by vesicles and finally tense bullae on an erythematous background. In several cases pruritus may remain the only symptom of PG [1]. Skin lesions usually firstly appear around the umbilicus and subsequently spread to the abdomen and the extremities; the face and mucous membranes are affected very rarely. In early stages histopathology is nonspecific and showed an edema of the epidermis, upper and mid-dermis with eosinophilic spongiosis and an inflammatory infiltrate consisting of lymphocytes, histiocytes, and eosinophils. In later stages, subepidermal split formation and blistering develop [2]. DIF shows a linear deposition of C3 and IgG autoantibodies at the dermo-epidermal junction and sometimes remains positive even after 6 months to 4 years of clinical remission. Indirect immunofluorescence

(IIF) and ELISA and BIOCHIP (Biochip-based test-system) assays can corroborate the diagnosis of PG [3].

Differential diagnosis includes polymorphic eruption of pregnancy (PEP), intrahepatic cholestasis of pregnancy (ICP), atopic eruption of pregnancy (AEP).

Polymorphic Eruption of Pregnancy (PEP) is a benign skin inflammatory dermatosis associated with pregnancy and appears in the third trimester of pregnancy like PG. Clinical features especially at the beginning of PEP mimic PG and are characterized by an abrupt eruption of intensively pruritic papules that can coalesce to form plaques. Papulovesicles, target-like or eczematous lesions, and even blisters can develop [4]. The first lesions also appear on abdominal wall, then they can spread to other parts of the body and become generalized. Histological examination of skin biopsies is also nonspecific and usually demonstrates epidermal and upper dermal edema and perivascular infiltrate by neutrophils, lymphocytes, mast cells, and occasionally eosinophils. The gold standard test in differential diagnosis between PEP and PG is DIF that doesn't show a linear deposition of C3 and IgG autoantibodies at the dermo-epidermal junction; IIF and ELISA also show negative results [5].

Intrahepatic cholestasis of pregnancy (ICP) presents with pruritus, increased serum levels of bile acids, liver transaminases, and occasionally bilirubin. It has an onset during late pregnancy and might increase the stillbirth risk. Skin lesions are secondary to scratching. There are no other clinical features on skin, allowing an easy differential diagnosis of PG and ICP [6].

Atopic eruption of pregnancy (AEP) is a common dermatosis of pregnancy, usually developing in early childhood and is characterized by excoriated papules, papulovesicles, and lichenification with pruritus, with no specific histopathological or laboratory findings. AEP was called atopic eczema of pregnancy, prurigo of pregnancy, and pruritic folliculitis of pregnancy. Several authors consider PEP a late form of AEP [4].

Erythema multiforme (EM) is a hypersensitivity reaction with a history of herpes simplex infection or drug allergy. There are two clinical variants of EM: "EM minor" with only skin involvement and "EM major" with similar skin features and additional involvement of mucosae (e.g. lips, inside of the mouth, windpipe, gullet, anus, genital area, and eyes) and usually some associated symptoms, such as fever or joint pain [5]. "EM minor" is characterized by the sudden development of red spots in several days changing to raised patches and then to typical target-shaped lesions with a dusky red center and small blisters surrounded by a paler area, and resulting in a dark red ring. The first lesions appear very often on the hands and feet, spread up the limbs to the trunk and face. Histopathological or laboratory findings are nonspecific.

Key Points

- PG is a rare pregnancy-associated blistering autoimmune skin disease, typically occurring in the second and third trimesters of pregnancy
- The disease manifests with severe pruritus, followed by polymorphic lesions
- Diagnosis is based on DIF that shows a linear deposition of C3 and IgG autoantibodies at the dermo-epidermal junction. IIF detects IgG autoantibodies targeting the basement membrane of the skin, ELISA typically reveals circulating IgG antibodies against BP180. Also, anti-BP180 IgG autoantibodies can be detected by BIOCHIP technology

References

1. Sävervall C, Sand FL, Thomsen SF. Pemphigoid gestationis: current perspectives. Clin Cosmet Investig Dermatol. 2017;10:441–9.
2. Sadik CD, Lima AL, Zillikens D. Pemphigoid gestationis: towards a better understanding of the etiopathogenesis. Clin Dermatol. 2016;34(3):378–82. https://doi.org/10.1016/j.clindermatol.2016.02.01.
3. Sadik CD, Pas HH, Bohlmann MK, Mousavi S, Benoit S, Sárdy M, Terra JB, Lima AL, Hammers CM, van Beek N, Bangert C, Zillikens D, Schmidt E. Value of BIOCHIP technology in the serological diagnosis of pemphigoid gestationis. Acta Derm Venereol. 2017;97(1):128–30. https://doi.org/10.2340/00015555-2460.
4. Brandao P, Sousa-Faria B, Marinho C, Vieira-Enes P, Melo A, Mota L. Polymorphic eruption of pregnancy: review of literature. J Obstet Gynaecol. 2017;37(2):137–40. https://doi.org/10.1080/01443615.2016.1225019.
5. Sirikudta W, Silpa-archa N. Polymorphic eruption of pregnancy presented with targetoid lesions: a report of two cases. Case Rep Dermatol. 2013;5:138–43. https://doi.org/10.1159/000351259.
6. Palmer KR, Xiaohua L, Mol BW. Management of intrahepatic cholestasis in pregnancy. 2019. www.thelancet.com. vol. 393, March 2.

Chapter 2
A 49-Year-Old Woman with Chronic Recurrent Vesicles, Erosions, and Fissures in Flexural Areas

O. Yu Olisova, N. P. Teplyuk, and A. A. Lepekhova

A 49-year-old woman presented in the Dermatology Clinic with burning and painful chronic rashes (recurrent vesicles, erosions, and fissures) in flexural areas (axilla and groin). Physical examination revealed well-demarcated erythematous patches and plaques with fissures (rhagades) and peripherally extending weeping crusted erosions of ripped vesicles; postinflammatory hyperpigmentation is found in the groin area (Fig. 2.1a–d).

In the family history, an aunt and elder sister have the same disease. The disease started about ten years ago. During the first years, the patient had been diagnosed with intertrigo. Three years later she came to the Dermatology Clinic for excisional biopsy that revealed intraepidermal bullae with the "dilapidated brick wall" appearance of epidermis, mild dyskeratosis. Immunofluorescence (IF) was negative. Then she was treated by systemic and topical corticosteroids and doxycycline with remissions from half to over a year.

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

- Intertrigo
- Pemphigus
- Darier disease

O. Y. Olisova · N. P. Teplyuk · A. A. Lepekhova (✉)
Department of Dermatology and Venereology, Sechenov University, Moscow, Russia

T. M. Lotti et al. (eds.), *Clinical Cases in Exfoliative Dermatitis*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08466-9_2

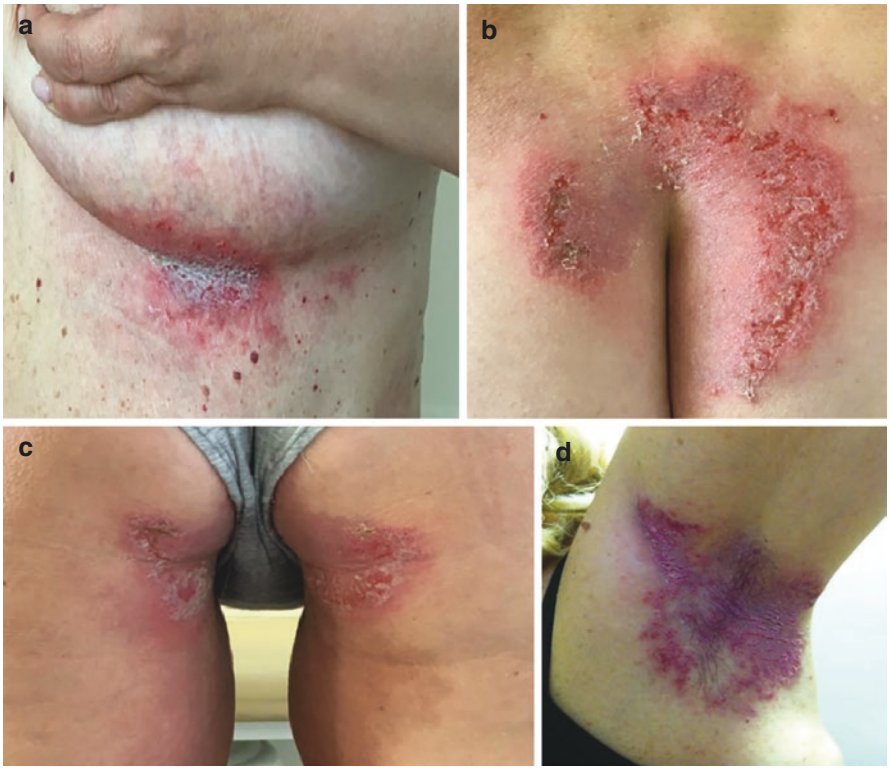

Fig. 2.1 Recurrent vesicles, erosions, fissures and well-demarcated erythematous patches and plaques with rhagades in the trunk (**a**), intergluteal cleft (**b**, **c**) and axillary folds (**d**)

Diagnosis

Hailey-Hailey disease

Discussions

Hailey-Hailey disease (HHD) also known as familial benign chronic pemphigus is a rare blistering genodermatosis with autosomal dominant defects in the ATP2C1 gene with incomplete penetrance [1]. The disease begins between 20 and 40 years of age. HHD always begins from small loose blisters on erythematous ground, but they quickly transform to erosions. Also, it is characterized by painful or burning recurrent erythematous patches and/or plaques with crusted weeping erosions and fissures (rhagades) with peripheral scaly borders, sometime with small blisters and vesicopustules on periphery of the rashes [2]. There is post-inflammatory hyperpigmentation. Typical localization of rashes is axillary, inguinal, perianal regions, and

laterals of the neck. Less frequently affected areas are scalp, trunk, antecubital and popliteal fossae. In female patients there are vulvar lesions. But buccal, conjunctival, and vaginal mucous membrane are rarely involved. Histopathology shows hyperparakeratosis with inclusions of fibrinous exudate, neutrophils and bacteria; broad-based transepidermal acantholysis ("dilapidated brick wall"); scattered dyskeratotic keratinocytes, and superficial perivascular lymphocytic infiltrate. Antibodies to the components of the epidermis are absent in IF [3]. Treatment includes doxycycline, systemic steroids (not only in tablet but also as intralesional injections), or combination of systemic steroids and cyclosporine. An article described successful treatment of HHD with oral alitretinoin but others noted that oral retinoids were not effective. Except systemic treatments, topical corticosteroids, antimicrobial agents, or botulinum toxin injections provided remission.

Differential diagnosis includes intertrigo, pemphigus, Darier disease.

Intertrigo is a common inflammatory skin disorder that occurs because of skin-on-skin friction in the skin folds (including inframammary, intergluteal, axillary, and interdigital areas, the so called intertriginous regions), moisture trapped owing to poor air circulation [4]. It has often association with obesity (body mass index over 30 kg per m^2), diabetes mellitus, or human immunodeficiency virus infection, and in bedridden patients [5]. The etiology is often connected with a fungal superinfection (more often with Candida albicans and dermatophytes such as Trichophyton). A bacterial superinfection may coexist with Candida, Staphylococci, Streptococci (especially group A beta-haemolytic streptococci), Pseudomonas, Proteus mirabilis, and C. minutissimum (leading to erythrasma), gut bacteria (enterococci or Escherichia coli) [4]. Typical localization of HHD rashes is like intertrigo. In intertrigo, there are intense erythema and desquamation, copious or purulent discharge, sometime ulceration. But unlike HHD, small serous tense blisters, vesicles, and fissures (rhagades) are never observed in this disease. The Wood's light shows a coral-red fluorescence with erythrasma and a green fluorescence with Pseudomonas infection. Fungal infection may be identified by potassium hydroxide examination and a mycologic culture, bacterial superinfection—by a bacterial culture. But in HHD there are different secondary infection. Biopsy may be performed for the differential diagnosis. In intertrigo, histopathological examination shows no characteristic features. Some cases can present with mild acanthosis, exocytosis of neutrophils, spongiosis in the epidermis, and superficial lymphocytic perivascular infiltrate with occasional neutrophils, plasma cells, solitary eosinophils, and sometimes with multinucleated giant cells. But there are no broad-based trans-epidermal acantholysis ("dilapidated brick wall"). PAS-stained histopathological samples for Candida reveals septa-free hyphae and yeast forms.

Pemphigus are a group of rare autoimmune bullous diseases with the production of pathogenic autoantibodies (usually of the IgG class) against different desmosome proteins (desmogleins) that affects the skin and mucous membranes [6]. The major forms are pemphigus vulgaris (PV) and pemphigus foliaceus (PF) . In pemphigus, cutaneous rashes can be localized or generalized, but not only in flexural areas like in HHD. Nearly all patients with PV present with mucosal lesions, very rare in HHD. Histologically PV can overlap with HHD. But in PV there is more often

suprabasal acantholysis, while HHD shows full-thickness acantholysis. The differential diagnosis is based on direct immunofluorescence (DIF), as PV shows epidermal intercellular deposits of IgG and C3 directed against desmogleins, components of the hemidesmosome, and HHV is invariably negative [7]. Indirect immunofluorescence or ELIZA demonstrate circulating IgG-autoantibodies.

Darier disease (DD), also known as keratosis follicularis, is a rare autosomal dominant genodermatosis that occurs because of a mutation in the ATP2A2 gene on chromosome 12q23-24. Typical clinical manifestations of DD differ from HHD and include dense follicular papules mainly on scalp, upper arms, elbows, back, chest, or knees [8]. Solely flexural localization of DD with predominant involvement of flexures is extremely rare. The lesions may be on axillae and groin, nape of neck, submammary area, lower abdominal folds, ventral aspect of elbows, and knees. DD is characterized by minimal itching hyperkeratotic verrucous lesions over large skin folds. Microscopic examination shows dyskeratotic keratinocytes ("corps ronds" and "grains") with hyperparakeratosis and focal suprabasal acantholysis with formation of lacunae or clefts and villi lined by a single layer of basal cells. DIF is negative [9].

Key Points

- Hailey-Hailey disease (HHD) also known as familial benign chronic pemphigus is a rare blistering genodermatosis with autosomal dominant defects in the ATP2C1 gene with incomplete penetrance.
- HHD has predominant involvement of flexures with painful or burning recurrent erythematous patches and/or plaques, crusted weeping erosions, and fissures (rhagades), small blisters, and vesicopustules.
- Histopathology shows hyperparakeratosis with inclusions of fibrinous exudate, neutrophils, and bacteria; broad-based transepidermal acantholysis ("dilapidated brick wall"); scattered dyskeratotic keratinocytes; and superficial perivascular lymphocytic infiltrate.
- HHD is resistant to therapy and is often exacerbated.

References

1. Thompson LDR. Hailey-Hailey disease. ENT-Ear, Nose Throat J. 2016, p. 370. www.entjournal.com.
2. Engin B, Kutlubay Z, Çelik U, Serdaroğlu S, Tüzün Y. Hailey-Hailey disease: a fold (intertriginous) dermatosis. Clin Dermatol. 2015; https://doi.org/10.1016/j.clindermatol.2015.04.00.
3. Kempf W, Hantschke M, Kutzner H, Burgdorf WHC. Dermatopathology. Steinkopff Verlag; 2008. p. 40–1.
4. Voegeli D. Intertrigo: causes, prevention and management. Br J Nurs. 2020;29(12):S16–22.
5. Kalra MG, Higgins KE, Kinney BS. Intertrigo and secondary skin infections. Am Fam Phys. 2014;89(7):569–73.
6. Porro AM, Seque CA, Ferreira MCC, Silva Enokihara MMS e. Pemphigus vulgaris. An Bras Dermatol. 2019;94(3):264–78. https://doi.org/10.1590/abd1806-4841.20199011.

7. Kempf W, Hantschke M, Kutzner H, Burgdorf WHC. Dermatopathology. Steinkopff Verlag; 2008. p. 66–8.
8. Teplyuk NP, Olisova OY, Grabovskaya OV, et al. Successful Darier disease treatment in Russian patients. Dermatol Ther. 2020;33(6):e14028. https://doi.org/10.1111/dth.14028.
9. Sharma N, Negi SR. multiple flexural presentation of Darier disease. J Case Rep. 2018;8(2):154–6. https://doi.org/10.17659/01.2018.0041.

Chapter 3
A 51-Year-Old Male with the Coexistence of Lichenoid and Blister Lesions

Xiao-Qun Luo, Jie Ren, Qin-Yuan Zhu, Hu-Yan Chen, and Zi-Hua Chen

A 51-year-old male patient presented to the hospital with his daughter complaining of widespread skin lesions for 1 month. The lesions developed from the hands to the trunk, and finally to the mucous membranes. Before visiting our hospital, the patient had received topical steroid and narrowband UVB. but the skin lesions continued to expand. On physical examination, widespread lichenoid plaques and scattered blisters were seen on hands (Figs. 3.1 and 3.2); pinhead-sized papules were noticed on genital mucosa; Bilateral white streaks were found on the buccal mucous membrane (Fig. 3.3). He had no fever, alopecia, joint pain. The patient was admitted to the hospital.

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

1. Bullous lichen planus
2. Lichen planus pemphigoides
3. Bullous pemphigoid
4. Erythema multiforme
5. Atypical subacute cutaneous lupus erythematosus

Following his hospitalization, the skin biopsy showed hyperkeratosis and focal hypergranulosis, basal cell liquefaction degeneration, subepidermal band-like lymphocytic inflammatory infiltration. Direct immunofluorescent studies were obtained

X.-Q. Luo (✉) · J. Ren · Q.-Y. Zhu · H.-Y. Chen · Z.-H. Chen
Department of Dermatology, Huashan Hospital, Fudan University, Shanghai, China
e-mail: 10301010236@fudan.edu.cn

T. M. Lotti et al. (eds.), *Clinical Cases in Exfoliative Dermatitis*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08466-9_3

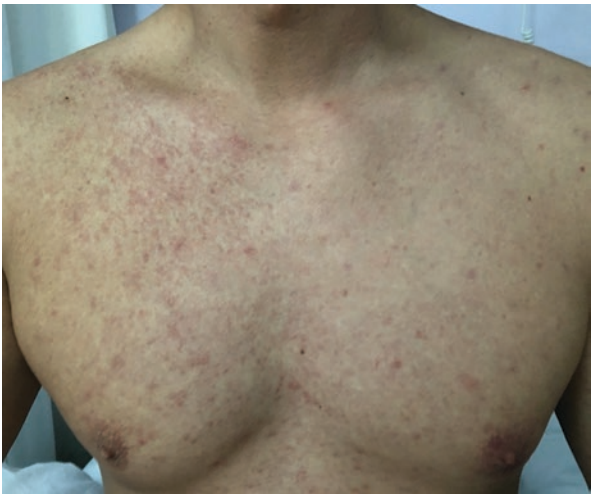

Fig. 3.1 A 51-year-old male presented with widespread pruritic violaceous polygonal papules and plaques with a shiny surface

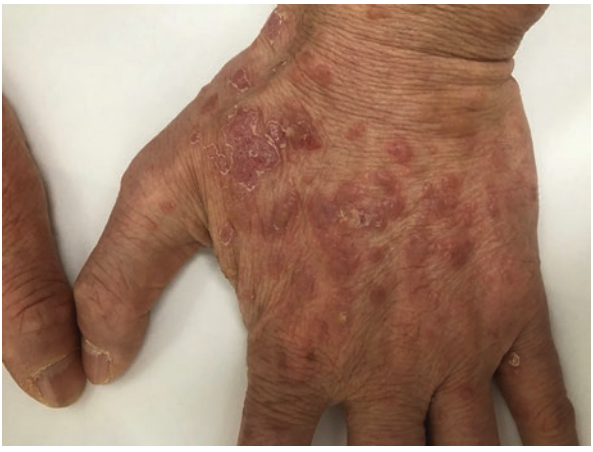

Fig. 3.2 A 51-year-old male presented with scattered blisters on hands, Nikolsky sign (−)

from the perilesional skin and showed deposition of immunoglobulin G (IgG) and C3 on the basement membrane zone (BMZ). His ANA, ENA, and anti-desmoglein results were negative. The titers of BP180 autoantibodies were 17 U/mL, for which a result >9 U/mL was defined as abnormal.

Diagnosis

Lichen planus pemphigoides

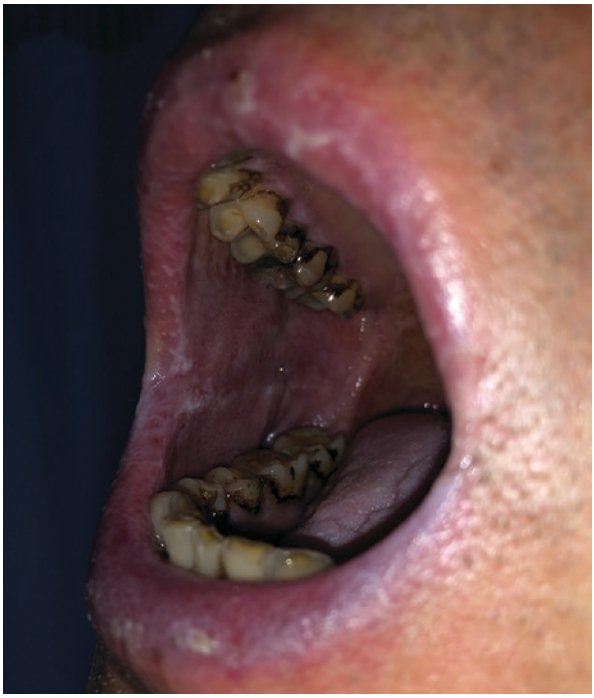

Fig. 3.3 A 51-year-old male presented with bilateral white streaks on buccal mucous membrane

Discussion

Lichen planus pemphigoides is a rare cross-over syndrome between lichen planus and bullous pemphigoid. Clinical manifestations of the disease include lichenoid papules, plaques, and tense blisters on the skin. Nail atrophy, loss of the nail plate, and white streaks on the buccal or outer genital mucosa can be found. Histopathology of a lichenoid lesion shows band-like lymphocytic inflammatory infiltrate in the upper dermis, while that of a bullous lesion shows a subepidermal blister. On immunology, IgG and C3 deposition are found at the dermal-epidermal junction zone; BP180 reveals a positive outcome [1].

Differential diagnosis includes bullous lichen planus, bullous pemphigoid, erythema multiforme, and atypical subacute cutaneous lupus erythematosus. Lichen planus is an acute or chronic inflammatory dermatosis involving skin and/or mucous membranes [2]. Lichen planus usually appears as flat topped papules with a violaceous appearance on the ankle. The epidermis is acanthotic with hyperkeratosis on the surface. The acanthosis is irregular and has a saw-tooth appearance. Areas of wedge-shaped hypergranulosis are present. The lichenoid and interface changes are illustrated by the presence of ‘civatte bodies’ (apoptotic cells). A lichenoid band of lymphocytes and histiocytes is also present. Erythema multiforme is a common reaction pattern of blood vessels in the dermis with secondary epidermal changes. Manifests clinically as characteristic erythematous iris-shaped popular and

vesiculobullous lesions. The histopathology of erythema multiforme is characterized by prominent interface changes with frequent clusters of keratinocyte necrosis, atrophy of the epidermis. There is an early formation of a subepidermal cleft.

Based on the patient's medical history, clinical manifestations, and skin biopsy, and immunology, the diagnosis of lichen planus pemphigoides was made. After comprehensive medical examination, including positron emission tomography-computed tomography (PET-CT), no malignant disease was found. After the treatment of glycyrrhizin (2.8 mg/kg body weight/daily) in combination with acitretin (0.25 mg/kg body weight/daily), the patient had gradually improved.

Key Points

- Lichen planus pemphigoides is a rare cross-over syndrome between lichen planus and bullous pemphigoid.
- Clinical manifestations of lichen planus pemphigoides include lichenoid papules, plaques, and tense blisters on the skin. Nail atrophy, loss of the nail plate, and white streaks on the buccal or outer genital mucosa can be found.

References

1. Zaraa I, et al. Lichen planus pemphigoides: four new cases and a review of the literature. Int J Dermatol. 2013;52(4):406–12.
2. Wolff K, et al. Fitzpatrick's Color Atlas & synopsis of clinical dermatology. 7th ed. New York: McGraw-Hill; 2012. p. 320.

Chapter 4
A Female with Plaques and Nodules

Ma-Liang Juan

A Case

A 43-year-old female patient.

Chief Complaint Scattered red papules and nodules on the right neck and shoulder for 3 months.

Current Medical History Scattered erythema and papules appeared on the right neck and shoulder 3 months ago. The papules gradually increased, 0.5–1 cm in diameter, red hemispherical, medium hardness (Fig. 4.1). The patient had no systemic symptoms and no joint changes.

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

1. Fibrous histiocytoma
2. Xanthoma
3. Lymphoma
4. Infection (tuberculosis, fungi)
5. Reticulohistiocytoma

Histopathological Examination In the dermis and the subcutaneous tissue, the histiocytes showed granulomatous proliferation, with more multinucleated giant

M.-L. Juan (✉)
Department of Dermatology, The Second Affiliated Hospital of Harbin Medical University, Harbin, China

T. M. Lotti et al. (eds.), *Clinical Cases in Exfoliative Dermatitis*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08466-9_4

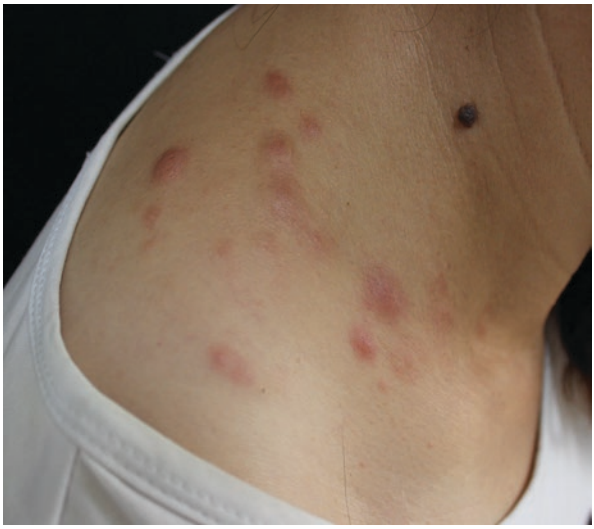

Fig. 4.1 Erythema, papules and nodules scattered on the right neck and shoulder. The nodule is 0.5–1 cm in diameter, red hemispherical, medium hardness

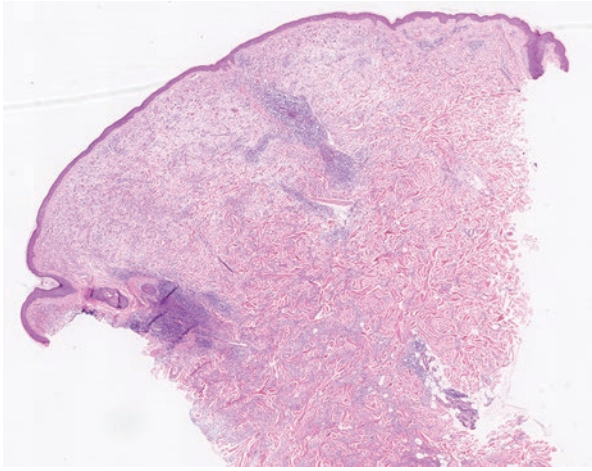

Fig. 4.2 Diffuse mononuclear cell infiltration from dermis to subcutaneous tissue, with more multinucleated giant cells (HE×10)

cells. The histiocytes were pink and uniform in shape. The cytoplasm of multinucleated cells was eosinophilic ground glass, with more lymphocytes (Figs. 4.2 and 4.3). IHC: CD68(+), S-100(−), CD1a(−), CD4(−), CD45(+), CD4(−), Ki67 < 1%, Alcian blue staining(−).

Diagnosis Multiple cutaneous reticulohistiocytoma.

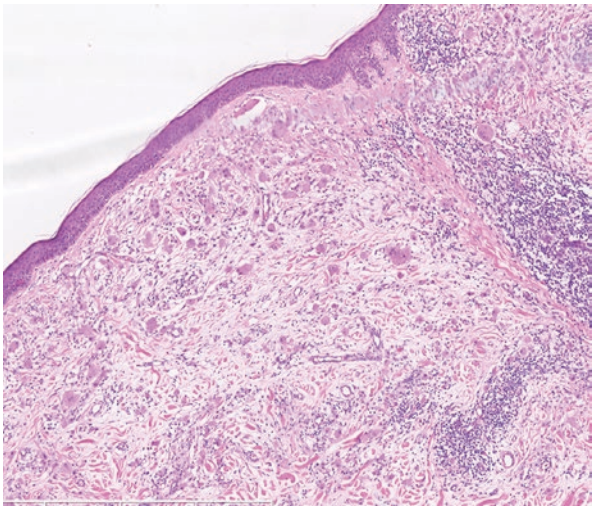

Fig. 4.3 Diffuse infiltration of histiocytes and lymphocytes from dermis to subcutaneous tissue, with more multinucleated giant cells, pink histiocytes and uniform morphology, and eosinophilic ground glass like cytoplasm of multinucleated cells (HE×40)

Discussion

Multiple cutaneous reticulohistiocytoma (reticulocytic granuloma) is a unique pattern of reticulocytic disease spectrum. The spectrum of the reticulohistiocytoses can be divided into three clinically distinct patterns: (1) solitary cutaneous reticulohistiocytoma (reticulohistiocytic granuloma) (SCR), (2) multiple cutaneous reticulohistiocytomas (reticulohistiocytic granulomas) (MCRs), (3) multicentric reticulohistiocytosis (MR). SCR and MCRs are more common in men, characterized by single or multiple granulomas confined to the skin, without obvious arthritis or potential systemic diseases [1]. MR, the disease mainly affects middle-aged women, in addition to skin lesions, multiple arthritis is an important clinical feature, and can also be combined with malignant tumor [2]. The three types have the same histopathological characteristics. Our patient best fits the second mode (MCRs) because it has multiple skin lesions, no evidence of arthritis or potential systemic disease.

Reticulohistiocytosis is a granulomatous disorder of unknown cause. Although previously believed to be a neoplasia, it is now classified as a reactive process. The primary lesion is characterized by slow growth, hard, fleshy or yellow to reddish brown papules or nodules. The most common sites are the head and neck. 50% of the cases involved oral and nasal mucosa [2, 3]. 25% of patients may have itching, burning or pain. Histopathologic examination reveals a moderately well-circumscribed dermal granulomatous infiltrate composed of foreign body multinucleated giant cells with abundant cytoplasm that has a “groundglass” appearance, large histiocytes with eosinophilic, finely granular cytoplasm, and inflammatory cells, usually lymphocytes and plasma cells. Many giant cells demonstrate phagocytosis of leukocytes. Histochemical analysis reveals that the “groundglass”

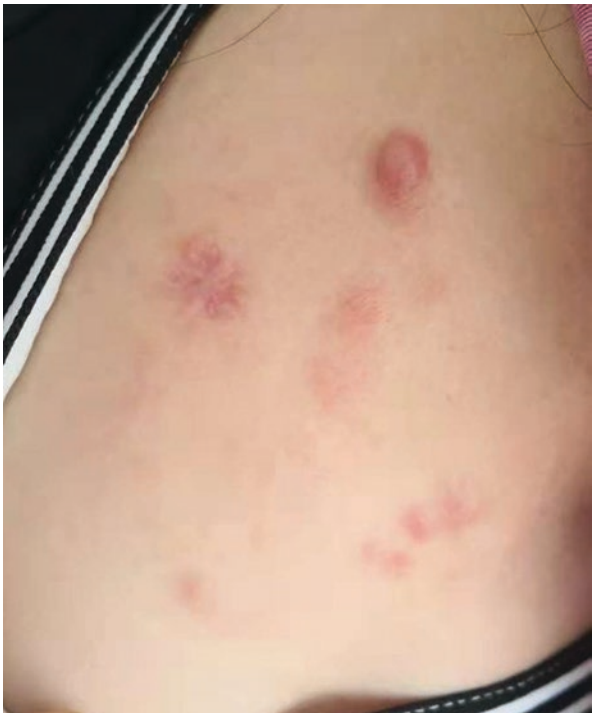

Fig. 4.4 Three months after treatment, most of the erythema of the original skin rash on the right neck and shoulder subsided, and the nodules became smaller and some subsided

material within the histiocytes is a glycoprotein [1]. Immunohistochemically, the cells were positive for CD68, but negative for S-100 and CD1a.

Appropriate therapies for MR remain challenging, and use oral prednisolone, immunosuppressants, and the latest biological agents [2, 4]. The lesions of MCRs can spontaneously subside in some patients. The symptomatic lesions can be treated by surgical resection and electrodrying. Our patient was treated with intralesional injection of Diprospan, and the regression was obvious 3 months later (Fig. 4.4).

Key Points

- Multiple cutaneous reticulohistiocytoma is a unique pattern of reticulocytic disease spectrum.
- Multiple cutaneous reticulohistiocytoma is characterized by multiple granulomas confined to the skin, without obvious arthritis or potential systemic diseases.

References

1. Toporcer MB, et al. Multiple cutaneous reticulohistiocytomas (reticulohistiocytic granulomas). J Am Acad Dermatol. 1991;25(5 Pt 2):948–51.
2. Yamamoto TJ. Skin manifestation associated with multicentric reticulohistiocytosis. Clin Rheumatol. 2020;28(1):e234–9. https://doi.org/10.1097/RHU.0000000000001679.
3. Markopoulos AK, et al. Reticulohistiocytic granuloma of the tongue: a case report. Quintessence Int. 1993;24(11):807–8.
4. Izu CB, et al. Multicentric reticulohistiocytosis: A case report treated with tofacitinib. Med Clin (Barc). 2020;156(6):310–1.

Chapter 5
A Man with Recurrent Fever and Erythema Nodosum

Jing Zhang, Bo Cheng, and Chao Ji

A 52-year-old man presented to the dermatology clinic with recurrent painful purulent skin lesions for 4 years. He experienced episodes of lymphadenopathy and new lesions that are painful accompanied by fever as well. He used to be diagnosed with Sweet syndrome which was sensitive to corticosteroid therapy. Physical examination revealed diffused infiltrated erythematous plaques and nodules on the trunk and extremities, some of which had pus points with mild tenderness (Fig. 5.1a, b).

Based on the Medical History and the Physical Examination, What Is Your Diagnosis?

1. Sweet syndrome
2. Sarcoidosis
3. Adverse cutaneous drug reactions

Skin biopsy from his back of invasive nodule showed an intense perivascular infiltrate of foamy histiocytes mixed with neutrophils and lymphocytes throughout the dermis (Fig. 5.2a, b). Numerous acid-fast bacilli (AFB) in vacuolated histiocytes (Fig. 5.2c). Smears taken from physical cooler areas, such as the earlobes, superior orbital and underjaw, where the acid-fast bacilli of smear were strong positive (Fig. 5.2d).

J. Zhang · B. Cheng · C. Ji (✉)
Department of Dermatology, The First Affiliated Hospital of Fujian Medical University, Fuzhou, China

T. M. Lotti et al. (eds.), *Clinical Cases in Exfoliative Dermatitis*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08466-9_5

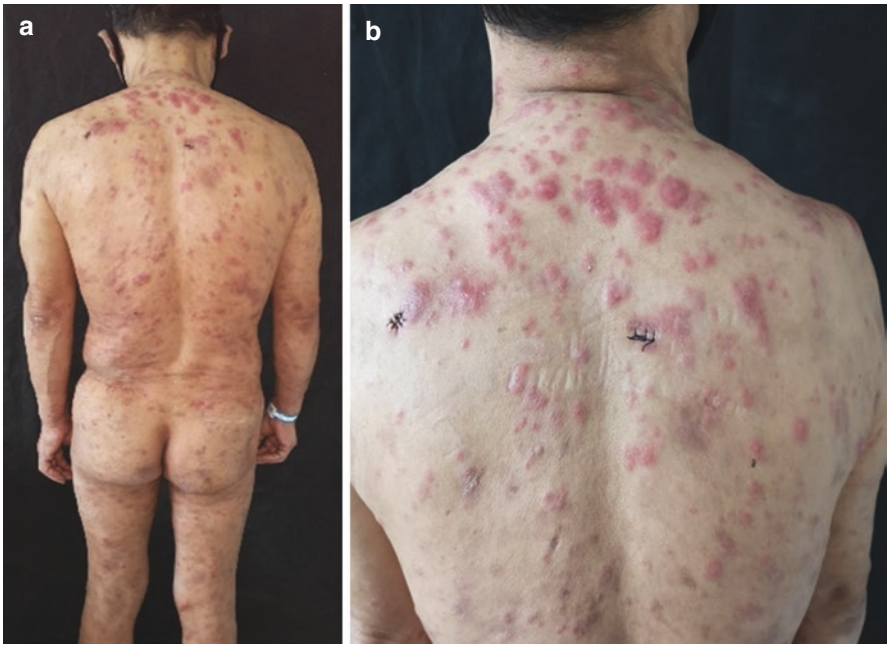

Fig. 5.1 The clinical manifestation. (**a**) Patient with generalized nodules, papules and erythematous edematous plaques; (**b**) Some with pseudo vesicles aspect and others with central pallor, affecting arms, chest and back

Diagnosis

Type 2 leprosy reaction with Sweets syndrome-like presentation.

Discussion

Leprosy is a chronic disease characterized by manifestations in the peripheral nerves and skin. The course of the disease may be interrupted by acute phenomena called reactions. The varied manifestations are well known to mimic other chronic dermatoses. The inflammatory bouts may cause considerable tissue damage and are attributed to immunological changes. Type 1 reactions occur in borderline patients and are due to variations in cellular immunity. Type 2 reactions are mediated by immune complexes, occur in multibacillary patients and are characterized by diverse clinical manifestations, being stereotypical the erythema nodosum leprosum (ENL). Reactions usually appear during or after the treatment of leprosy, but they can also represent the first manifestation of the disease, making diagnosis more difficult. Sweet's syndrome-like leprosy reaction was first described in 1987 by Kuo and Chan [1]. The authors reported a case clinically suggestive of Sweet's syndrome,

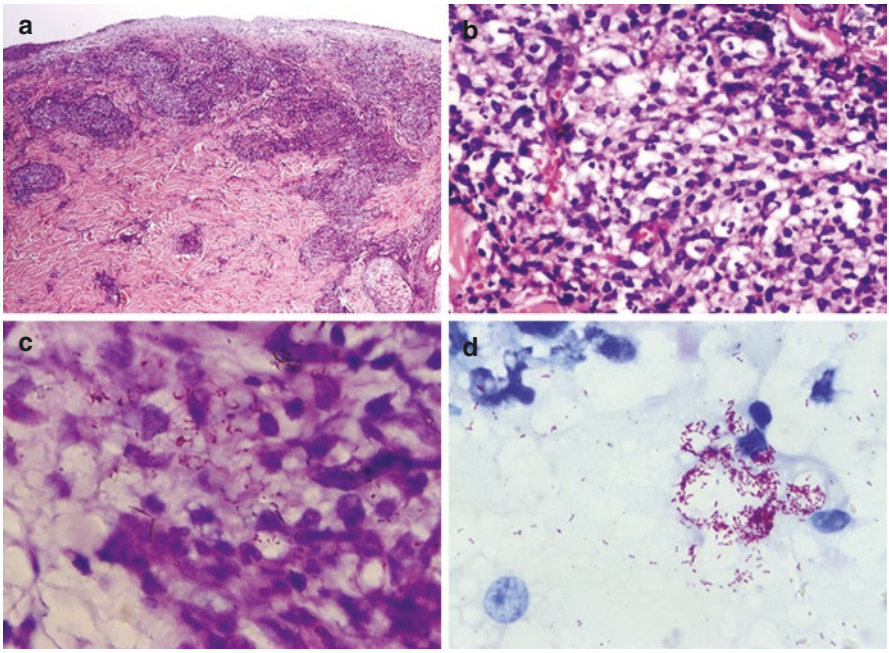

Fig. 5.2 The histopathology of skin biopsy and acid-fast stained. (**a**) Histopathology showing marked inflammatory infiltrate rich in neutrophils around the vessels and cutaneous appendages (HE×10); (**b**) Deep nodular infiltrate, rich in vacuolated histiocytes and the fragmented remains of neutrophilic nuclei (karyorrhexis) (HE×40); (**c**) Numerous acid-fast bacilli (AFB) in vacuolated histiocytes (Fite's 400×); (**d**) The AFB from the left earlobes was positive (5+) (Fite's 400×)

but with histopathological features of lepromatous leprosy, associated with edema of the papillary dermis and dense dermal neutrophilic infiltrate. Since then, few cases have been published [2]. It is classified as a subtype of type 2 reaction and occurs more often in borderline-lepromatous patients. In this case, the histopathological analysis was indicated due to the clinical setting with disseminated skin lesions and prolonged evolution. In this case, the acid-fast bacilli smear (AFB) positive (5+) and numerous acid-fast bacilli (AFB) in vacuolated histiocytes. The histopathological analysis was indicated due to the clinical setting with disseminated skin lesions and prolonged evolution.

Sweet's syndrome is an acute febrile neutrophilic dermatosis, first described in 1964 by Robert Douglas Sweet [3]. Its characteristics are fever, neutrophilia and painful purplish erythematous plaques. These plaques may contain pseudo vesicles due to severe edema of the papillary dermis. With the evolution of the lesions, there may be a central clearing, resulting in target aspect similar to erythema multiforme. The most commonly affected sites are face, neck, chest, back and upper extremities. Histopathology is characterized by dense infiltrate of intact and fragmented neutrophils in the superficial and middle dermis and marked edema in the papillary skin layer. According to the etiology, the syndrome can be divided into 3 groups:

classical (or idiopathic), associated with malignant disease and drug-induced. The classic form predominates in females and may be associated with inflammatory and autoimmune diseases, infections–the most common occurring in the gastrointestinal and upper respiratory tracts—and pregnancy.

Sarcoidosis was first described in 1877 by the dermatologist Jonathan Hutchinson who described violaceous skin lesions, which were called "sarcoid" by Caesar Boeck because of their histologic resemblance to sarcoma. Sarcoidosis is a multisystemic disease that mostly affects the lungs (90% of cases), but can involve any organ in the body. It has a variable clinical presentation that depends on organ involvement and the severity of involvement. The diagnosis is made based on history, physical examination, appropriate radiologic and pathologic findings, and the exclusion of other causes. Sarcoidosis is known as the great mimicker; as such, a thorough history, especially an exposure history, is crucial to exclude other causes of granulomatous disorders. The skin is the second most common organ involved in sarcoidosis [4]. Cutaneous manifestations include maculopapular lesions, hypopigmented and hyperpigmented lesions, subcutaneous nodules, localized alopecia, ulcers, and pustules. Skin biopsy of sarcoidosis skin lesions reveals noncaseating granulomas. This patient has none of lung lesions and his dermatopathology don't support the diagnosis of sarcoidosis.

Adverse cutaneous drug reactions (ADR) are recognized as being major health problems worldwide causing considerable costs for health care systems. Most adverse cutaneous drug reactions follow a benign course. A thorough drug history, including prescribed and non-prescribed medication, is essential for diagnosis. Of all organs affected by ADR, the skin is most frequently involved [5]. Cutaneous exanthematous drug reactions most frequently present themselves clinically as a maculopapular rash (MPR) , but they can also present in eczematoid-, psoriasiform-, or lichenoid-like pattern. The patients has none of medical history and the atypical persistent polymorphic cutaneous rash didn't support the diagnosis of MPR.

Based on the patient's medical history, clinical manifestation and biopsy result, the diagnosis of type 2 leprosy reaction with Sweets syndrome-like presentation was made.

Then this patient was referred to designated hospitals for leprosy. This patient reported remission of skin lesions and symptoms after several months of multiple anti-leprosy treatment through telephone follow-up.

Key Points

- In the case of Sweet's syndrome-like leprosy reaction, the identification of vacuolated histiocytes containing bacilli in the midst of an infiltrate rich in neutrophils is of fundamental importance.
- The early diagnosis of reactions and immediate initiation of treatment are essential, in order to prevent the nerves and disabilities triggered by leprosy.

References

1. Kou TT, Chan HL. Severe reactional state in lepromatous leprosy simulating Sweet's syndrome. Int J Dermatol. 1987;26(8):518–20.
2. Das T, Ghosh S, Kundu AK, Maity A. Reactional state in lepromatous leprosy simulating Sweet's syndrome. J Assoc Physicians India. 2013;61(11):856–8.
3. Sweet RD. An acute febrile neutrophilic dermatosis. Br J Dermatol. 1964;76(1):349.
4. Mañá J, Marcoval J, Graells J, Salazar A, Pujol R. Cutaneous involvement in sarcoidosis: relationship to systemic disease. Arch Dermatol. 1997;133(7):882–8.
5. Adverse cutaneous drug eruptions: current understanding. Semin Immunopathol 2015;38(1):1–12.

Chapter 6
A Middle-Age Female with a Nodule in Her Posterior Chest Wall

Rui-Jiao Liu, Rui-Qun Qi, Shi-Fa Zhang, and Xing-Hua Gao

A 42-year-old female presented with a mass on the left posterior chest wall for about 1 year. As the mass was asymptomatic, the patient was untreated. The past history, drug allergy history and family history were not special. Color Doppler ultrasound revealed a mixed nodule in muscle layer of left posterior chest wall. The mass was completely excised under local anesthesia. During the operation, it was found that the boundary between the mass and surrounding tissues was unclear. The mass was hard, without an obvious capsule. The mass was cut off, found to be a yellow white solid mass. No bleeding was found (Fig. 6.1). The central part of the mass was taken for examination.

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

1. Dermatofibroma
2. Xanthomas
3. Granular cell tumor
4. Schwannoma

R.-J. Liu · R.-Q. Qi (✉) · X.-H. Gao
Department of Dermatology, The First Hospital of China Medical University, Shenyang, China

S.-F. Zhang
Department of Dermatology, Northeast International Hospital, Shenyang, China

T. M. Lotti et al. (eds.), *Clinical Cases in Exfoliative Dermatitis*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08466-9_6

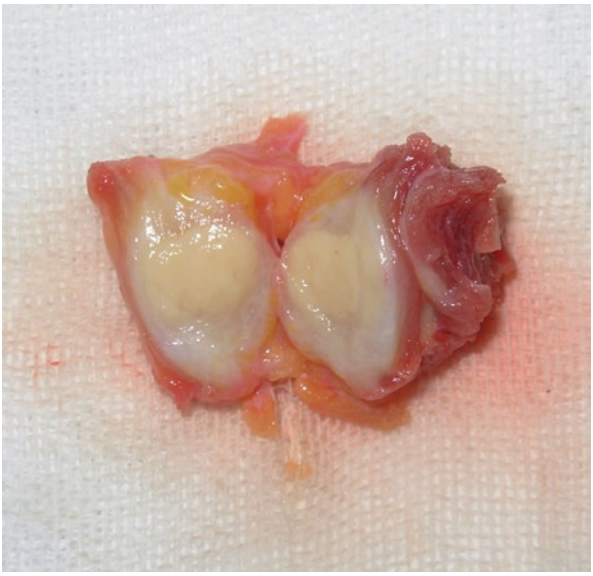

Fig. 6.1 A 42-year-old female presented with a mass on the left posterior chest wall for about 1 year. The mass was completely excised

Pathology

The dermis contains a circumscribed nodule composed of large polygonal cells, It may infiltrate into the adjacent dermis. The tumor cells have abundant, granular, faintly eosinophilic cytoplasm with small, dark, and uniform nuclei. Characteristic larger cytoplasmic granules, called pustule-ovoid bodies of Milian (eosinophilic globule surrounded by a clear halo) have been observed. There was no mitotic activity, necrosis, or pleomorphism. The boundary of the cells was unclear, and it was separated into lumps by fibrous tissue, and showed aggressive growth to the surrounding soft tissue and transverse striated muscle tissue (Fig. 6.2).

Immunohistochemistry

NSE (+), S-100 (+), CD68 (+), Vimentin (+), SOX10 (+), Ki67 (−).

Diagnosis

Granular cell tumor

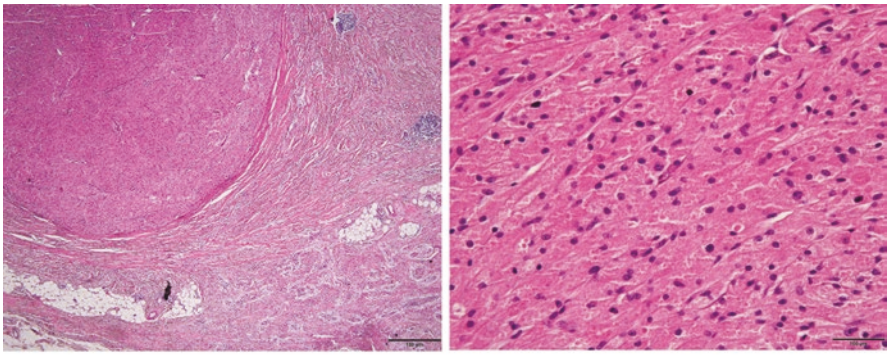

Fig. 6.2 Pathology: The dermis contains a circumscribed nodule composed of large polygonal cells, It may infiltrate into the adjacent dermis. The tumor cells have abundant, granular, faintly eosinophilic cytoplasm with small, dark, and uniform nuclei. Characteristic larger cytoplasmic granules, called pustule-ovoid bodies of Milian (eosinophilic globule surrounded by a clear halo) have been observed. There was no mitotic activity, necrosis, or pleomorphism. The boundary of the cells was unclear, and it was separated into lumps by fibrous tissue, and showed aggressive growth to the surrounding soft tissue and transverse striated muscle tissue

Discussion

Granular cell tumors (GCT), previously designated myoblastoma, was first described by Abrikossoff in 1926. The tumor cells are named for cytoplasmic eosinophilic granules, due to the accumulation of lysosomal granules. Accumulation of immunohistochemical and ultrastructural evidence over the past years have supported the notion that that GCT cells are derived from Schwann cells [1]. Most cutaneous granular cell tumors are of neural origin, but granular cell change occurs in a variety of neoplasms.

GCT can occur in any part of the body, frequently occurs in the tongue (40%), skin, subcutaneous tissues, breast (15%), vulva (7%) and bladder. It occurs primarily in adults (age 30–50 years) with a 1:3 males-female ratio. The majority of cases behaved in a benign fashion, mainly occurred in head and neck regions, especially the tongue. These malignant cases mere account for 1–2% of all GCTs, usually in the skin and the deep soft tissue, especially in the thigh [2].

GCT mostly presents a well-circumscribed, solitary and firm nodule, ranging in diameter from 0.5 to 3.0 cm, with a brownish red or flesh tint. However, in about 10% of the cases, lesions are multiple. It behaves as an asymptomatic or occasionally tender or pruritic. Some examples are verrucous at the surface. The cut surface is often faintly yellow and homogeneous. The tumor may show a well-limited or infiltrative growth pattern. The histologic picture of GCT is distinctive. Tumors composed of nests and sheets of large polygonal cells with uniform nuclei and abundant eosinophilic granular cytoplasm. The so-called

pustule-ovoid bodies of Milian, defined as an eosinophilic globule surrounded by a clear halo, have also been described as a characteristic histopathological finding of GCTs. Meanwhile, pseudoepitheliomatous hyperplasia is also a regular feature. The neoplastic cells stain usually positively with neuron-specific enolase (NSE), S-100, vimentin, SOX10, CD68, myelin protein, NKI/C3, and PGP9.5 [3].

Although most lesions with granular cell features behave in a benign fashion, it may be difficult to predict biologic behavior in GCT, because they may show abundant mitotic figures and infiltrative pattern. Fanburg-Smith et al. [4] proposed a classification of GCTs into 3 categories benign, atypical and malignant based on six histologic criteria: necrosis, spindling, vesicular nuclei with large nucleoli, increased mitotic activity (>2 mitoses/10 high-power fields at 200× magnification), high nuclear to cytoplasmic (N:C) ratio, and pleomorphism. Tumors were considered as benign if none or only focal nuclear pleomorphism was seen, atypical when 1 or 2 features present and malignant if 3 or more features were observed.

Differential diagnosis of GCT includes a wide spectrum of benign and malignant lesions such as dermatofibroma, xanthomas, leiomyoma, schwannoma, carcinoma [5]. Xanthomas are excluded by the identification of cytoplasmic granules (rather than vacuoles) in GCT. GCT can induce considerable pseudocarcinomatous hyperplasia of the overlying epithelium, and superficial biopsy samples have been mistaken for squamous cell carcinoma. A variety of epithelial and mesenchyma neoplasms can show granular cell change, including basal cell carcinoma, dermatofibroma and leiomyomas. Immunohistochemistry and some special staining will be helpful to differentiate and diagnose diseases. Based on the clinical manifestation, histopathological features and immunohistochemical findings, the diagnosis of benign GCT was made.

GCT should be completely excised. The large majority of GCT behaves in a benign fashion, with few reports in the literature describing metastasis and local aggressiveness, and does not usually recur after excision. While local recurrence and metastasis are relatively common in MGCT, therefore extensive surgical excision combined with regional lymph node dissection should be performed as primary therapy. GCT tumor is not sensitive to chemotherapy and radiotherapy. The patient in this case was completely excised by surgical operation, and has no metastasis and recurrence so for.

Key Points

- Granular cell tumor (GCT) was a rare soft tissue tumor of Schwann cell origin, the majority of which behaved in a benign fashion, with rare malignant transformation.
- The tumor is characteristically solitary, and frequently occur in the head and neck regions, especially in the tongue.

References

1. Pergel A, Yucel AF, Karaca AS, Aydin I, Sahin DA, Demirbag N. A therapeutic and diagnostic dilemma: granular cell tumor of the breast. Case Rep Med. 2011;2011:972168.
2. Mobarki M, Dumollard JM, Dal Col P, Camy F, Peoc'h M, Karpathiou G. Granular cell tumor a study of 42 cases and systemic review of the literature. Pathol Res Pract. 2020;216(4):152865.
3. Cui Y, Tong SS, Zhang YH, Li HT. Granular cell tumor: a report of three cases and review of literature. Cancer Biomark. 2018;23(2):173–8.
4. Fanburg-Smith JC, Meis-Kindblom JM, Fante R, Kindblom LG. Malignant granular cell tumor of soft tissue: diagnostic criteria and clinicopathologic correlation. Am J Surg Pathol. 1998;22(7):779–94.
5. Cardis MA, Ni J, Bhawan J. Granular cell differentiation: a review of the published work. J Dermatol. 2017;44(3):251–8.

Chapter 7
A Middle-Aged Men with Plaques on Hands

Yuan-Yuan Wu and Feng-Li Xiao

A 46-year-old man came to the dermatology clinic for the bilateral violaceus, red-brown and yellowish plaques on his hands with slight itch and pain one year (Fig. 7.1). He is a delivery man and touched all kinds of goods every day, so he thought his rash might be caused by some harmful chemicals.

According to the case description and the photograph, what diagnosis are you going to define?

- Hand Keratosis
- Erythema Elevatum Diutinum (EED)
- Mycobacteriosis
- Dermatomycosis

The rash began at the joints of his right hand one year ago and spread increasingly to the palm, and developed to the contralateral hand in 1 to 2 months. With the aggravation of the lesions, his hands felt mild itchy and uncomfortable, and other clinical systemic enquiry was not remarkable. No involvement was in his mucous membrane, hair, nails. Patient's medical history was negative for internal and cutaneous diseases and also without trauma or family history.

There was no abnormality in system examination. The multiple thickened and hardened red-purplish plaques with different sizes distributed at the bilateral hands with irregular borders. Laboratory investigations showed that white blood cell count was raised (11.08 × 109/L, normal: 3.5~9.5 × 109/L) in blood routine examination, and serum immunoglobulins M was slightly decreased (0.39 g/L, normal: 0.48~2.12 g/L). Other test were normal including liver function, renal function, blood glucose, serum lipid, antinuclear antibodies, antineutrophil cytoplasmic

Y.-Y. Wu · F.-L. Xiao (✉)
Department of Dermatology, First Affiliated Hospital of Anhui Medical University, Hefei, China

T. M. Lotti et al. (eds.), *Clinical Cases in Exfoliative Dermatitis*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08466-9_7

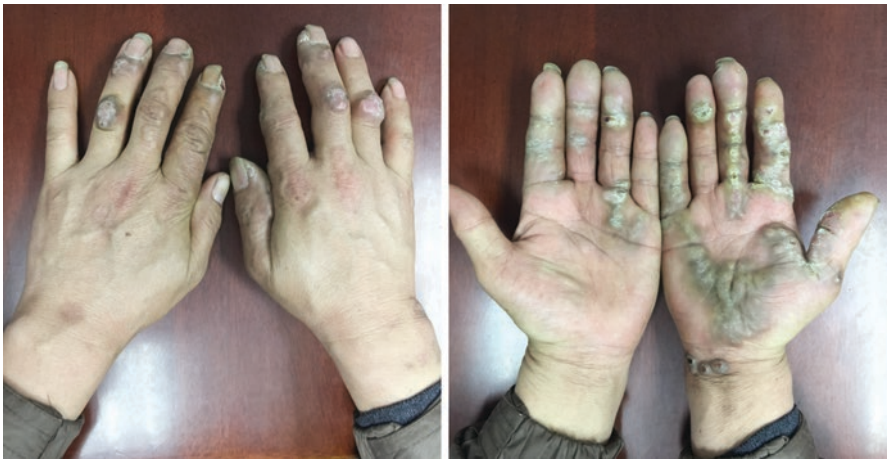

Fig. 7.1 The lesions at hands of the patient

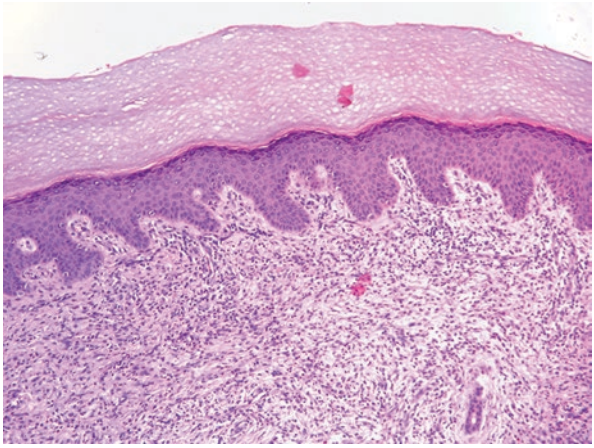

Fig. 7.2 The pathological findings of lesion at hand. Epidermal hyperkeratosis, stratum spinosum acanthosis in epidermis, fibroblasts and myofibroblast proliferation, dermal mixed inflammatory cells infiltrates including neutrophils, lymphocytes, histiocytes and eosinophils in dermis. (Hematoxylin & eosin, original magnification ×100)

antibodies, alexin C3 and alexin C4, and toluidine red unheated serum test (TRUST). The fungus microscopic examination and culture was negative for his scrapings and lesions, further *Mycobacterium* culture of lesion was also negative. The pathological examination for lesion of thenar eminence at right palm revealed that hyperkeratosis and acanthosis in the epidermis, and fibroblasts and myofibroblast proliferation, leukocytoclastic vasculitis with neutrophilic infiltration around small vessels in the dermis (Fig. 7.2).

His disease did not alleviate after high-potency topical steroids one month, oral MTX therapy four months and then oral methylprednisolone two months in turn. However his lesions improved significantly after oral dapsone 50 mg per day for one month.

Diagnosis

Erythema Elevatum Diutinum (EED).

Discussion

EED is a rare distinctive form of cutaneous leukocytoclastic vasculitis of the mid-upper dermis. Hutchinson described it in 1878 firstly, and it was subsequently coined by Radcliffe-Crocker and Williams in 1894 [1, 2]. It can occur in any age and has no population bias in gender or race. The age of EED patients was commonly in the third to sixth decade [3]. The most cases resolve within 5–10 years, but an individual case of EED lasted for up to 39 years [4]. The underlying pathogenesis of EED is not entirely understood. The most widely accepted theory for it is that the raised levels of circulating immune complexes continuously deposit in perivascular area, which cause damage and lead inflammatory cell infiltration and eventually fibrosis.

EED begin classically as soft papules or plaques and progress to violaceous, red-brown or purple firmer plaques and fibrotic nodules at extensor surfaces over time. The atypical lesions of EED may appear at trunk. The lesions are generally asymptomatic or mildly feeling, and sometimes progress to vesicular, bullous and ulcer which lead to pain and the bacterial superinfection. This disease usually follows a chronic and recurrent course. Extracutaneous manifestations of EED are less common, including ocular disease or arthralgias. EED may be idiopathic and do not involved generally in systemic diseases, but it also has been reported to be linked to other disorders, such as infection including streptococcus, tuberculosis, viral hepatitis, herpes virus, HIV and syphilis, bone marrow hypoplasia, multiple myeloma, arthralgias, scleritis, peripheral ulcerative keratitis, neutrophilic dermatoses, inflammatory bowel diseases and so on [5]. Therefore, it is necessary to exclude the underlying diseases through a complete investigation.

The histologic findings of EED show a constellation of nonspecific and polymorphic signs, depending on stage of the cutaneous lesions. In early stage of EED, it shows a leukocytoclastic vasculitis of the superficial and mid-dermal vessels with a marked perivascular infiltration of polymorphonuclear neutrophils, fibrin deposition within vessel walls, and endothelial cell swelling. As the lesion progresses, mature lesions can exhibit granulation tissue, perivascular fibrosis with mixed inflammation, and extracellular lipidosis [5].

It is a challenge to diagnose EED, it's uncommon condition clinically resembles many other diseases, such as keratosis, fungal infections, tuberculosis, non-tuberculous mycobacteriosis, and rheumatoid neutrophilic dermatosis and et al. [6]. The keratosis of hand was first considered for at friction stimulation with bilateral symmetrical distribution as the patient was a delivery man. The common feature is hyperkeratosis of the stratum corneum and well-defined hyperkeratotic rashes. The

inflammatory cell infiltration was not seen in simple skin keratosis, so this diagnosis was excluded. The Mycobacteriosis was also suspected, especially tuberculosis verrucosa cutis. It is exogenous inoculation of *tuberculous bacillus* into the skin. It is characterized by chronic reddish brown or red, wart-like plague on the body unilateral exposed distribution. The *Mycobacterium* culture and Tuberculin Purified Protein Derivative (PPD) is positive. EED can be differentiated from it based on the bilateral lesion, pathological evidence and negative *Mycobacterium* culture [7]. Dermatomycosis is widespread condition characterized by both superficial and subcutaneous infections caused by a variety of fungal agents. It appears as erythema, nodule and plaque at the exposed part of body with a history of trauma. Fungus laboratory investigation is positive, but it was negative for the patient.

In this patient, the red-purple nodules and plaques distributed widely only on dorsal and palmar surface of bilateral hands, and his other medical history was negative. Based on the clinical manifestation, laboratory investigations and the histopathologic examination of the lesion, the diagnosis of EED was made.

Dapsone is regarded as the first-line treatment for EED, with good response in 80% of cases, and higher response prior to the onset of nodular lesions [8]. The limited lesions of fibrotic nodules responding poorly to dapsone can be considered to receive surgical excision. In addition, other medications such as corticosteroids, colchicine and sulfapyridine can also be used for second-line treatment. This patient only responded better to dapsone while the disease did not alleviate after oral MTX and methylprednisolone.

Key Points

- Erythema elevatum diutinum (EED) is a rare distinctive form of cutaneous leukocytoclastic vasculitis of the mid-upper dermis.
- Erythema elevatum diutinum is manifested by red to violaceous, yellowish, or brown papules, plaques, and nodules distributed symmetrically over joints on the extensor surfaces of the hand, feet, elbows, or knees.

References

1. Hutchinson J. On two remarkable cases of symmetrical purple congestion of the skin in patches, with induration. Br J Dermatol. 1980;1:10.
2. Radcliffe-Crocker HW, Williams C. Erythema elevatum diutinum. Br J Dermatol. 1894;6:33–8.
3. Bansal R, Aron J, Rajnish I. Erythema elevatum diutinum. Am J Med Sci. 2017;353(2):189.
4. Wilkinson SM, English JSC, Smith NP, Wilson-Jones E, Winkelmann RKJC, Dermatology E. Erythema elevatum diutinum: a clinicopathological study. Clin Exp Dermatol. 1992;17(2):87–93.
5. Sandhu JK, Albrecht J, Agnihotri G, Tsoukas MM. Erythema elevatum et diutinum as a systemic disease. Clin Dermatol. 2019;37(6):679–83.

6. Magri F, Chello C, Pranteda G, Muscianese M, Careri R, Pranteda G, Quaglino P. Erythema elevatum diutinum of the hand: a peculiar case, successfully treated with tetracyclines. Ital J Dermatol Venerol. 2021;156(6):722–24. https://doi.org/10.23736/S2784-8671.20.06536-0. Epub 2020 Mar 4. PMID: 32129588.
7. van Zyl L, du Plessis J, Viljoen J. Cutaneous tuberculosis overview and current treatment regimens. Tuberculosis (Edinb). 2015;95(6):629–38.
8. Murad A, O'Regan G, Watson R, McDermott M, O'Sullivan M, Irvine AD. Erythema elevatum diutinum in a healthy child. Clin Exp Dermatol. 2017;42(4):434–6.

Chapter 8
A Red Man with Scale

Chengbei Bao, Chao Ji, and Bo Cheng

A 50 year-old male presented to our department complaining of generalized scaly erythema for 1 week. The patient experienced recurrent, local, slightly pruritic erythema, plaque and scale that covered about 40% of body surface area for 10 years, which was worsen in winter and improve in summer. The patient received irregular treatment in the clinic. One week ago, the eruptions progressed into diffuse scaly erythema (Fig. 8.1a, b) secondary to an unknown misused topical formulation. He became hospitalized with headache and general discomfort.

Based on the Medical History and the Photograph, What Is Your Diagnosis?

1. Erythrodermic psoriasis
2. Mycosis fungoides
3. Atopic dermatitis
4. Drug reaction

Physical examination showed diffuse scaly, nontender erythema covering more than 90% of the body surface area, with sparse scaly plaque. Onycholysis and subungual hyperkeratosis were observed. Laboratory investigations revealed the following: leukocytes 11.2×10^9/L, eosinophils 0.29×10^9/L, neutrophils 5.11×10^9/L, atypical lymphocyte not detected, normal IgE antibody level. Specimen from abdomen for biopsy was obtained, which revealed hyperkeratosis, neutrophils within the stratum

C. Bao · C. Ji · B. Cheng (✉)
Department of Dermatology, The First Affiliated Hospital of Fujian Medical University, Fuzhou, Fujian, China

T. M. Lotti et al. (eds.), *Clinical Cases in Exfoliative Dermatitis*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08466-9_8

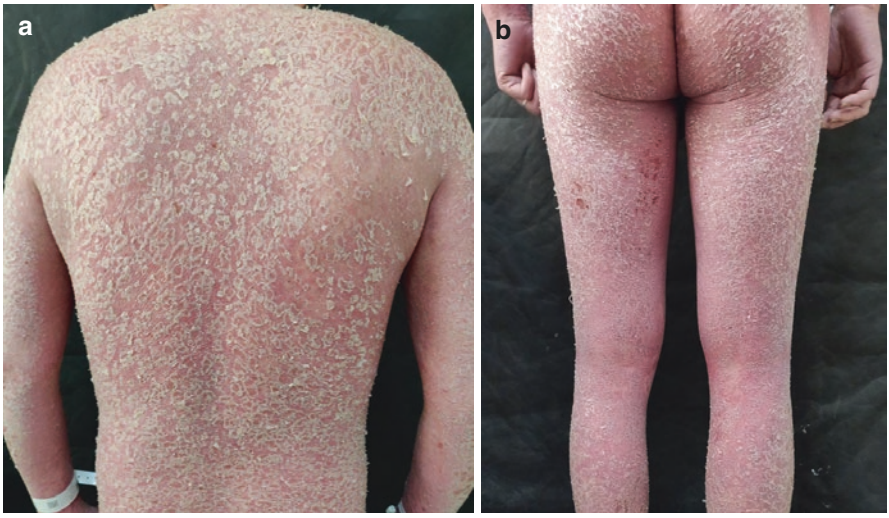

Fig. 8.1 A 50 year-old male presented with generalized scaly erythema, on the trunk, upper limbs (**a**) and lower limbs (**b**), covering more than 90% of body surface area

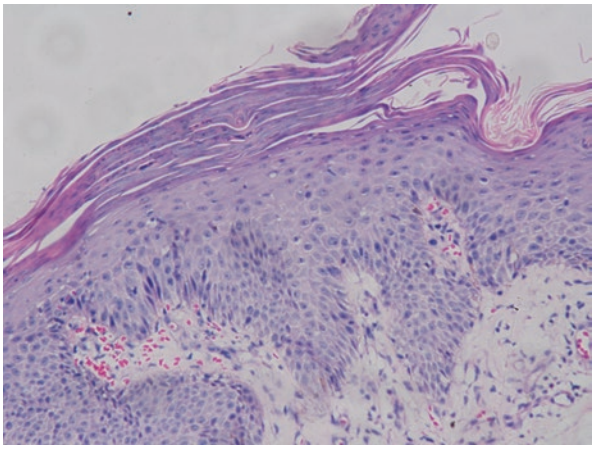

Fig. 8.2 hyperkeratosis, neutrophils within the stratum corneum, regular acanthosis and tortuous blood vessels in dermal papillae (HE×10)

corneum, regular acanthosis and tortuous blood vessels in dermal papillae. No spongiosis, eosinophils or atypical lymphocytes were observed in the slide (Fig. 8.2).

Diagnosis

Erythrodermic psoriasis

Discussion

Psoriasis is a common skin disorder that is associated with both a physical and psychological burden. Psoriasis is the most common underlying cutaneous disease known to cause erythroderma, responsible for approximately 23% of cases. Psoriasis is a multifarious disease without gender preference. Clinically, psoriasis can be divided into 5 subtypes: psoriasis vulgaris, which is characterized by circumscribed, erythematous, dry, scaling plaques; guttate psoriasis, which is characterized by scaly teardrop-shaped spots; inverse psoriasis that is usually found in folds of skin; pustular psoriasis, which can be either localized in the palms and soles (palmoplantar pustulosis) or generalized (generalized pustular psoriasis); and erythrodermic psoriasis, which is a rare but very serious complication of psoriasis and can result from any form of psoriasis [1]. Individuals with psoriasis are at an increased risk of developing other chronic and serious health diseases, including psoriatic arthritis, metabolic syndrome or components of the syndrome, cardiovascular disorders, and several other diseases.

Despite of infection, drugs, ultraviolet light and systemic disease, the frequent cause of erythrodermic psoriasis is the sudden withdrawal of plaque psoriasis treatment, including steroids, cyclosporin, and methotrexate. The general erythema covers more than 90% of body surface area and typical features of scales and plaques may or may not lost. Due to severe and extensive skin barrier defect, EP patients can present with systemic symptoms such as dehydration, fatigue, insomnia, weight changes, cachexia, and electrolyte abnormalities [2]. Inadequate treatment may lead to death.

Mycosis fungoides (MF) is the most frequent type of cutaneous T-cell lymphoma with long disease duration. Classically, It can be divided into 3 stage: patch, plaque and tumor stage. Erythrodermic MF was defined as erythroderma with confirmed histopathological features of MF and absence circulating Sezary cells, which is generally considered to be a type of MF progression. Erythroderma occurs as progression from plaque or patch MF, but it sometimes arises de novo. Pruritus is often prominent. Typical histology of mycosis fungoides showing infiltration of atypical lymphocytes in the superficial dermis with epidermotropism [3].

Atopic dermatitis (AD) is a chronic, inflammatory skin disease characterized by pruritus and a chronic course of exacerbations and remissions. It is associated with other atopic conditions, including food allergies, asthma, allergic rhinoconjunctivitis, eosinophilic esophagitis and eosinophilic gastroenteritis. It may be well controlled by standard treatment with anti-inflammatory medications, such as topical corticosteroids and topical calcineurin inhibitors, and possibly systemic medications, such as dupilumab, cyclosporine. Inadequate or sudden withdrawal of treatments for patients with AD have been suggested as factors associated with the development of erythroderma [4].

Drug eruptions are skin eruptions that are induced by drugs. Some severe cutaneous adverse drug reactions, including acute generalized exanthematous pustulosis (AGEP), Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN),

are another cause of erythroderma. AGEP is characterized by the rapid development of numerous sterile pustules in the epidermis accompanied with fever, leukocytosis and eosinophilia. SJS, SJS-TEN overlap and TEN are characterized by epidermal detachment. The skin detachment of SJS, SJS-TEN overlap and TEN is defined as less than 10%, 10–30% and 30% of body surface area, respectively. In addition, SJS/TEN often have mucocutaneous involvement, oral mucosa is more commonly involved than the ocular, genital or anal mucosa [5]. A thorough drug history, including prescribed and non-prescribed medication, is essential for diagnosis.

Based on the patient's medical history, clinical manifestation, and biopsy result, the diagnosis of Erythrodermic psoriasis was made.

The patient was treated with Secukinumab 300 mg once weekly for 5 times for induction and 300 mg once monthly for maintenance. In addition, topical moisture therapy was instructed.

Key Points

- Erythroderma is not a diagnosis but a clinical phenotype.
- Erythrodermic psoriasis is often secondary to sudden withdrawal of psoriasis treatment

References

1. Boehncke WH, Schön MP. Psoriasis. Lancet. 2015;386(9997):983–94.
2. Shao S, Wang G, Maverakis E, Gudjonsson JE. Targeted treatment for erythrodermic psoriasis: rationale and recent advances. Drugs. 2020;80(6):525–34.
3. Kamijo H, Sugaya M. Two distinct variants of mycosis fungoides (MF): Folliculotropic MF and erythrodermic MF. J Dermatol. 2019;46(12):1136–40.
4. Otsuka R, Tanaka A, Takahashi M, Saito R, et al. The relationship between the development of erythroderma in patients with atopic dermatitis and the avoidance of anti-inflammatory topical drugs. Allergol Int. 2021;70(3):376–8.
5. Chung WH, Wang CW, Dao RL. Severe cutaneous adverse drug reactions. J Dermatol. 2016;43(7):758–66.

Chapter 9
Chronic Erythematous and Desquamative Lesions

Özge Aşkın and Zekayi Kutlubay

Case

A 55-year-old male presented in the dermatology clinic with a two-month-history of rash, itching, burning, and crusting all over the body. The dermatologic examination of the patient revealed diffuse erythema (>90% of his body) and fine scaling including the face and the scalp. The scales were more prominent at the flexural areas and the posterior neck (Figs. 9.1, 9.2, and 9.3). Linear excoriation marks were present as well. The skin was dry, warm and indurated. There was no nail involvement or alopecia. No palpable lymphadenopathies were detected.

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

1. Psoriasis vulgaris
2. Allergic contact dermatitis
3. Exfoliative Dermatitis
4. Perforating collagenosis

The patient was hospitalized with the diagnosis of erythroderma for further investigation and treatment. This patient was admitted to our outpatient clinic two years ago with long-lasting multiple patches and plaques on the legs and thighs. In his histopathological examination, epidermal orthohyperkeratosis, acanthosis,

Ö. Aşkın · Z. Kutlubay (✉)
Department of Dermatology, Cerrahpaşa Medical Faculty, Istanbul University-Cerrahpaşa, Istanbul, Turkey

T. M. Lotti et al. (eds.), *Clinical Cases in Exfoliative Dermatitis*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08466-9_9

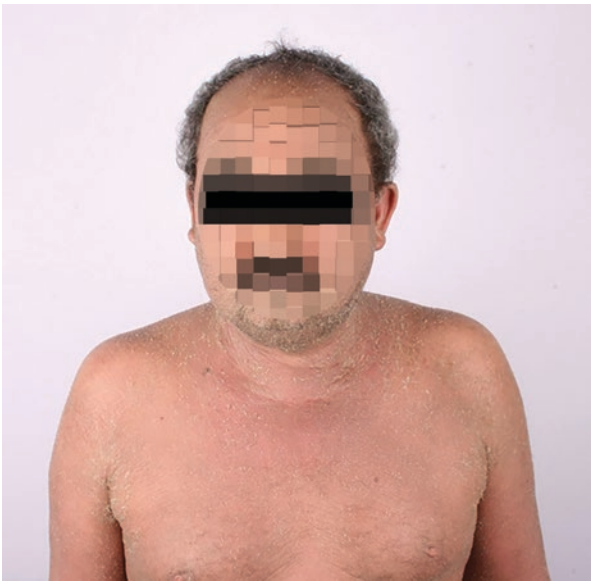

Fig. 9.1 Widespread erythema and exfoliation in upper chest

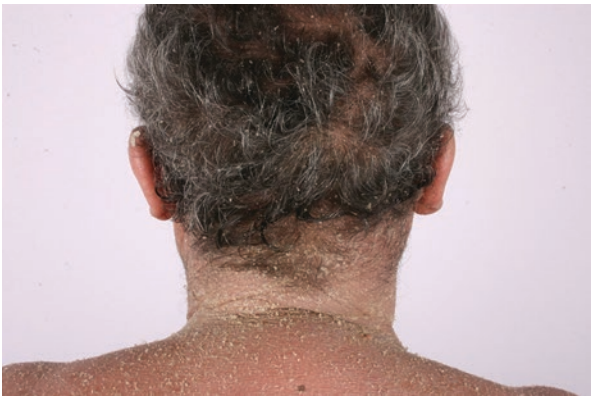

Fig. 9.2 Widespread exfoliation and dryness in neck and scalp area

spongiosis were defined. Few small lymphoid cells with irregular nuclei within the spongiotic areas were seen. Upper dermal vascular proliferation, lymphocytic and histiocytic proliferation similar to that of the epidermis, within the perivascular and interstitial areas, fibrosis were seen. Immunohistochemistry revealed that the infiltrating cells were CD3+, mostly CD2 and CD7+ as well. The CD 4 ratio was 4/1. With these findings, he was diagnosed as early stage of mycosis fungoides. He was treated with narrow band UV therapy and were followed by regular intervals. For the last six months he did not come to his control until he applied with exfoliative dermatitis.

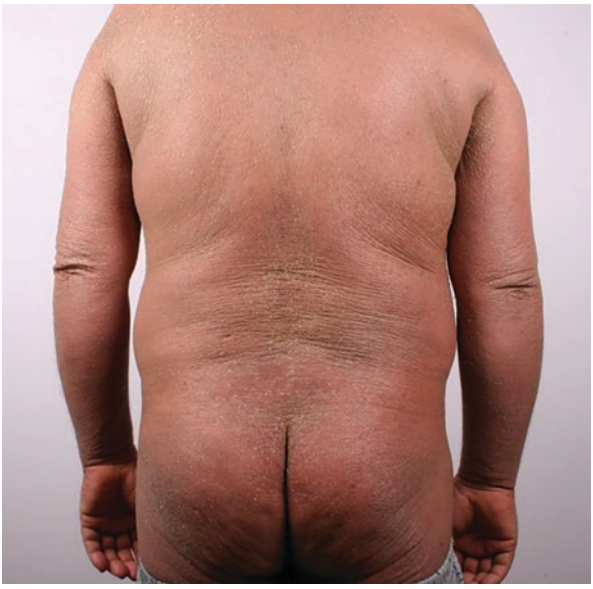

Fig. 9.3 Widespread erythema and exfoliation in back and gluteal region

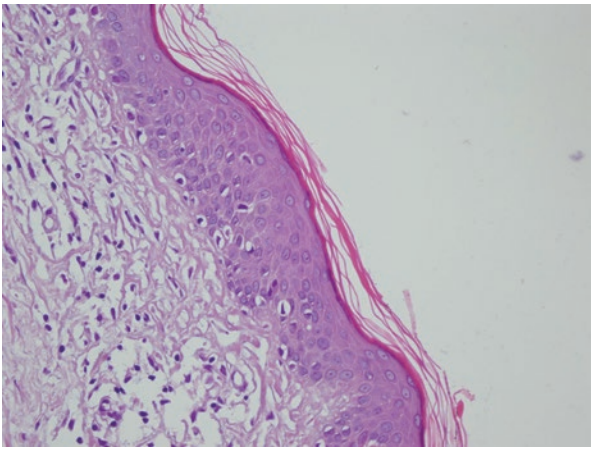

Fig. 9.4 Atypic lymphocytes with hyperchromatic nuclei with cytoplasmic halo showing epidermotropism within the epidermis (H&E, ×400)

Histopathology (Figs. 9.4 and 9.5)

1. Atypic lymphocytes with hyperchromatic nuclei with cytoplasmic halo showing epidermotropism within the epidermis (H&E, ×400)
2. Epidermal lymphocytes with CD4 positive staining (CD4, ×400)

There was no other drug use other than topical corticosteroids. There were no palpable lymphadenopathies but reactive femoral lymphadenopathies were seen in the USG examination. Hepatomegaly or splenomegaly were not detected. There

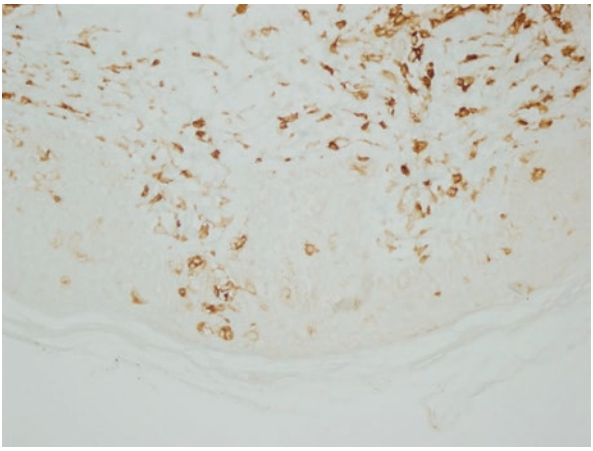

Fig. 9.5 Epidermal lymphocytes with CD4 positive staining (CD4, ×400)

were not Sezary cells on his peripheral blood smear. There was no systemic involvement so we initiated acitretin 25 mg/day with topical corticosteroid cream and emollient.

Diagnosis

Erythroderma due to Mycosis fungoides

Discussion

Erythroderma, or exfoliative dermatitis, is an inflammatory disorder that involves desquamation and erythema of more than 90% of the body surface area. It may be a result of many different causes such as previous dermatoses (psoriasis, eczema, atopic dermatitis, pityriasis rubra pilaris, and pemphigus foliaceous), drug reactions, malignancies (mycosis fungoides, Sézary syndrome, adult T cell leukemia/lymphoma), infections, and idiopathic disorders [1, 2].

Erythroderma is a rare condition but can affect all age groups from neonates to the elderly. Most published studies are retrospective and do not address overall incidence but it is usually more common in men over the age of 60. Excluding children, the average age of onset varies from 40 to 60 years; although it usually affects patients over 45 years of age [1, 3].

Regardless of the etiology, the clinical appearance of erythroderma is similar in all patients but the timing and the course of symptoms may depend on the primary skin disease or the triggering cause. The onset of symptoms is sudden and fast for drug-induced erythroderma, while primary skin disease may have a slower course.

Pruritus is observed in up to 90% of patients with erythroderma, and it is most severe in patients with atopic dermatitis or Sezary syndrome [3, 4].

Unique clinical features may suggest a specific diagnosis. Typical psoriasiform plaques or psoriatic nail changes may be evident for the psoriasis diagnose. Salmon-colored erythema, small areas of uninvolved skin known as islands of sparing, and keratoderma suggest pityriasis rubra pilaris in diagnosis. Heliotrope, poikiloderma, Gottron's papules, periungual telangiectasias, and muscle weakness may be evident in erythrodermic dermatomyositis [5].

This skin disease begins as patches of erythema that enlarge and coalesce to eventually affect most of the skin surface. It is associated with a scaling that typically appears 2–6 days after the onset of diffuse erythema. In acute form, scales may appear larger and crusted, where as in chronic phase they are smaller and drier with erosions and lichenification. Nails may also be involved [1].

Laboratory findings of erythrodermic patients may vary. Elevated erythrocyte sedimentation rate, leukocytosis, eosinophilia and anemia can be seen. Eosinophilia and elevated IgE may be found in patients with atopic dermatitis or drug reactions. Other findings include elevated uric acid and creatinine levels, reduced serum protein levels. Serum electrolytes may be imbalanced as the result of fluid loss. Liver and kidney function tests may be altered. Specific tests may be necessary to diagnose Sezary syndrome include Sezary cell count analysis. Antinuclear antibodies, extractable nuclear antigen, rheumatoid factor, anti-DNA antibodies and complement levels may be checked if the underlying connective tissue disease is suspected. Lymphadenopathy (neck, axillae, and groin) should be documented suggesting either a reactive lymphadenopathy or lymphoma. If lymphadenopathy is referred to lymphoma, referral should be made to related medical branch to investigate in more detail [1, 4, 6].

In erytrhodermic patients clinical and histopathological correlation may be difficult because the findings are usually nonspecific that include hyperkeratosis, acanthosis, spongiosis, and perivascular inflammatory infiltrate. Multiple biopsies can be necessary to enhance the histopathologic diagnoses and to be able to diagnose the underlying disease [1, 4].

The most significant systemic complications of erythroderma include fluid loss and electrolyte imbalance, hypoalbuminemia, thermoregulatory disregulation, cardiac failure, acute respiratory distress syndrome, and infection. Hospitalization may be necessary to stabilize the patient's condition and to pay attention to nutrition, fluid and electrolyte replacement. Any unnecessary medication should be avoided. Local skin care measures should be undertaken, such as emollients, wet dressings to crusted sites, topical corticosteroids. Sedative antihistaminics can reduce patient's pruritus and anxiety [1, 4, 7].

Psoriasis is the most common underlying cutaneous disease known to cause erythroderma. Systemic treatment of erythrodermic psoriasis includes methotrexate, acitretin, cyclosporine, and anti–tumor necrosis factor biologics. Systemic retinoids can also be used in the treatment of pityriasis rubra pilaris. Atopic dermatitis, contact allergic or irritant dermatitis, or seborrheic dermatitis may be treated with topical or/and systemic corticosteroids. In the treatment of severe atopic dermatitis,

cyclosporine, methotrexate, azathioprine, and mycophenolate mofetil may be the option in erythrodermic form. UV light, topical steroids, and retinoids were used to treat mild cutaneous T-cell lymphoma (CTCL) related erythroderma [7, 8].

Key Points

- Erythroderma can be caused by a variety of underlying dermatoses, infections, and systemic diseases. The prognosis of erythroderma varies depending on its cause.
- Erythroderma secondary to drug hypersensitivity is likely to clear rapidly with discontinuation of the drug. Erythroderma secondary to preexisting skin diseases, such as atopic dermatitis, contact dermatitis, or psoriasis, usually improves within several weeks to several months. Erythroderma secondary to cutaneous T cell lymphoma or other malignancy is generally persistent or recurrent.
- Patients with erythroderma require immediate attention as they may face a variety of medical complications.

References

1. Cuellar-Barboza A, Ocampo-Candiani J, Herz-Ruelas ME. A practical approach to the diagnosis and treatment of adult erythroderma. Actas Dermosifiliogr. 2018;109(9):777–90. https://doi.org/10.1016/j.ad.2018.05.011.
2. Askin O, Altunkalem RN, Uzuncakmak TK, Toplu FŞ, Engin B. Erythroderma: A clinicopathological study of 47 cases from 2018 to 2020. Dermatol Ther. 2020;26:e14342. https://doi.org/10.1111/dth.14342.
3. Inamadar AC, Ragunatha S. The rash that becomes an erythroderma. Clin Dermatol. 2019;37(2):88–98. https://doi.org/10.1016/j.clindermatol.2018.12.002.
4. Mistry N, Gupta A, Alavi A, Sibbald RG. A review of the diagnosis and management of erythroderma (generalized red skin). Adv Skin Wound Care. 2015;28(5):228–36.; Quiz 237–8. https://doi.org/10.1097/01.ASW.0000463573.40637.73.
5. Rothe MJ, Bialy TL, Grant-Kels JM. Erythroderma. Dermatol Clin. 2000;18(3):405–15. https://doi.org/10.1016/s0733-8635(05)70189-3.
6. César A, Cruz M, Mota A, Azevedo F. Erythroderma. A clinical and etiological study of 103 patients. J Dermatol Case Rep. 2016;10(1):1–9. https://doi.org/10.3315/jdcr.2016.1222.
7. Zhang P, Chen HX, Xing JJ, Jin Z, Hu F, Li TL, Zhou XY. Clinical analysis of 84 cases of erythrodermic psoriasis and 121 cases of other types of erythroderma from 2010–2015. J Huazhong Univ Sci Technolog Med Sci. 2017;37(4):563–7. https://doi.org/10.1007/s11596-017-1773-1.
8. Kamijo H, Sugaya M. Two distinct variants of mycosis fungoides (MF): folliculotropic MF and erythrodermic MF. J Dermatol. 2019;46(12):1136–40. https://doi.org/10.1111/1346-8138.15114.

Chapter 10
Desquamative Dermatitis in a Melanoma Patient

Uwe Wollina

A 52-year-old male patient presented with a generalized cutaneous rash that appeared first 8 weeks. More than 90% of the body surface were affected. There were eczematous lesions on the body except on palmoplantar skin were papulo-pustules developed. He reported about moderate itch. Outpatient treatment with topical corticosteroids had not been effective.

In November 2019, the patient had been treated for a frontal symptomatic tumor. Histopathology confirmed a melanoma metastasis of unknown origin. He was treated with PD-1 inhibitor nivolumab.

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

1. Acute generalized exanthematic pustulosis.
2. Late manifestation of atopic dermatitis.
3. Spongiform dermatitis due to nivolumab.
4. Pustular psoriasis.
5. COVID-19 associated rash.

Diagnosis PD-1 induced spongiform dermatitis.

On examination we observed an erythrodermic dermatitis with eczematous features on trunk and extremities, and papulo-pustules on palms and soles (Figs. 10.1, 10.2, and 10.3). His melanoma had spread to lymph nodes, adrenal gland and hepar.

BRAF-analysis revealed a wild-type. Therefore, combined PD-1 inhibitor therapy with nivolumab and immune therapy with ipilimumab was initiated after melanoma diagnosis. Due to drug-induced immune colitis, ipilimumab was

U. Wollina (✉)
Department of Dermatology and Allergology, Städtisches Klinikum Dresden, Academic Teaching Hospital of the Technical University of Dresden, Dresden, Germany
e-mail: Uwe.Wollina@klinikum-dresden.de

T. M. Lotti et al. (eds.), *Clinical Cases in Exfoliative Dermatitis*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08466-9_10

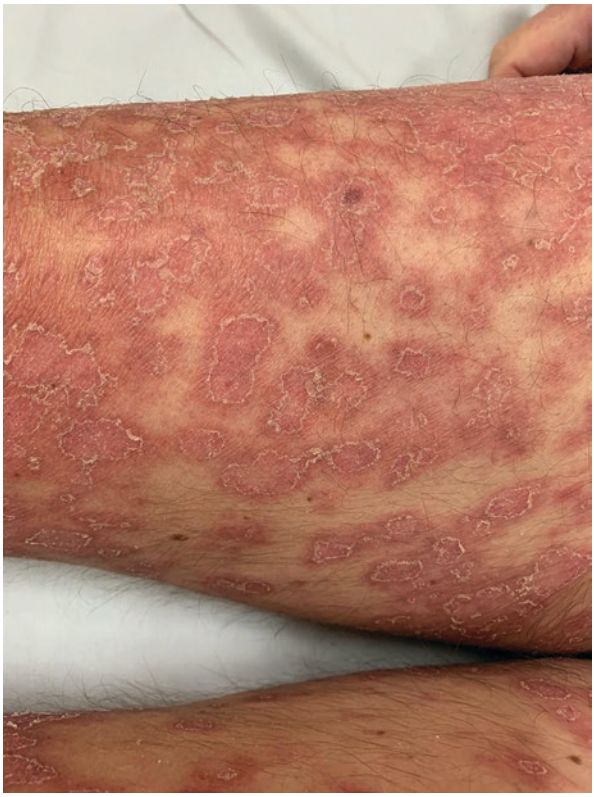

Fig. 10.1 Erythematous, eczematous lesions with marginal scaling

stopped. After corticoid therapy of the colitis, monotherapy with nivolumab could be continued in March and was ongoing, when the patient present with the skin rash. Due to arterial pulmonary embolism, he was treated with tinzaparin injections.

Laboratory investigations: Leucocytes 11.64 Gpt/l (normal range 3.8–11.0), erythrocytes 3.94 Tpt/l (4.6–6.2), hemoglobin 7.0 mmol/l (8.6–12.1), thrombocytes 428 Gpt/l (120–340), neutrophiles 9.4 GPt/l (1.8–7.6). Lactate dehydrogenase 3.00 μkat/l (2.25–3.75), blood sedimentation rate 50 mm/h (<20), C-reactive protein 20 mg/l (<5), S100 0.106 μg/l.

Skin biopsy: Epidermal spongiosis, mild acanthosis, hyper-orthokeratosis, single cell suprabasal keratinocyte necrosis. Minor inflammatory infiltrate in the papillary dermis and upper corium with lymphocytes and monocytes. Absence of eosinophiles, sparsely distributed mast cells.

He was treated with topical class III corticosteroids and oral levocetirizine. The dermatitis improved.

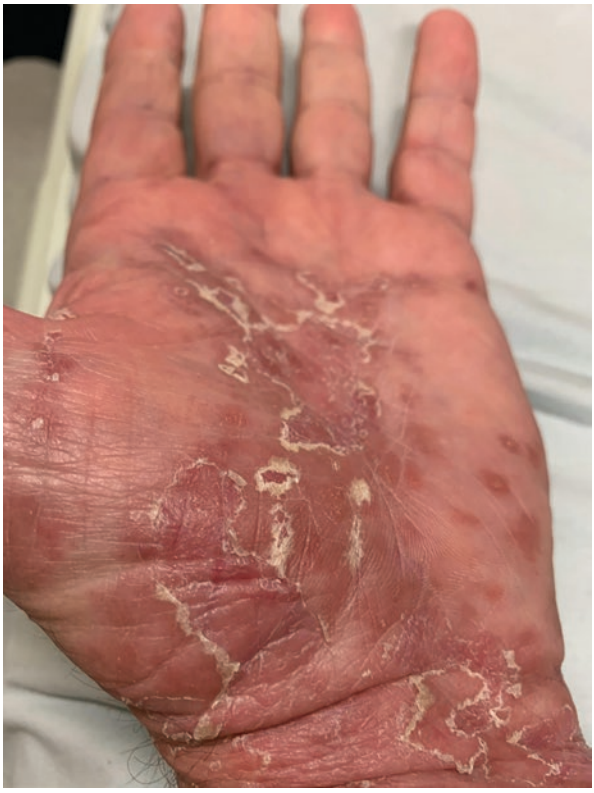

Fig. 10.2 Palmar remnants of a pustular rash

Discussion

Check point inhibitors against programmed cell death 1 Protein (PD1) and programmed cell death 1 ligand (PDL1) have become part of the therapeutic options in metastatic cutaneous melanoma and in adjuvant drug therapy in stage III melanoma.

Monoclonal antibodies to PD-1 include nivolumab and pembrolizumab, approved for melanoma among other tumor entities while monoclonal antibodies to PD-L1 include avelumab, atezolizumab, and durvalumab, used in Merkel cell carcinoma, lung cancer, and renal cell carcinoma [1].

There is a number of possible cutaneous adverse events that are associated with this type of treatment [2, 3] (Table 10.1). Most cutaneous adverse events occur during the first weeks of PD1-inhibitor therapy, some – like vitiligo – may occur weeks or months later. Early recognition and treatment are crucial for continuation of tumor treatment [2, 3].

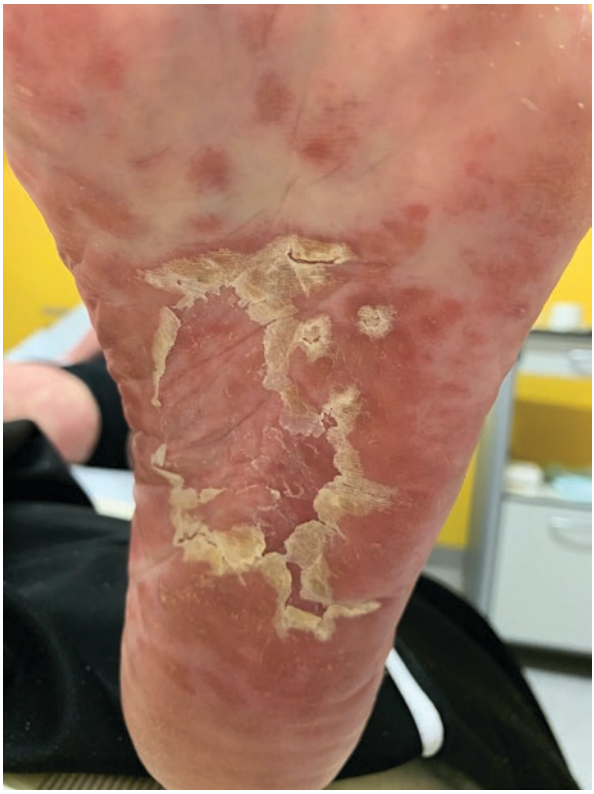

Fig. 10.3 Remnants of the pustular on the sole

Table 10.1 Cutaneous adverse events of check point inhibitor therapy in melanoma (Modified from [2, 4])

Skin disease	Remarks	Frequency
Lichenoid dermatitis		Up to 50%
Spongiotic dermatitis	Eczema-like	Up to 40%
Pruritus		13%
Immune Bullous disorders	Potentially life-threatening, BP-180 pemphigoid	1%
Maculopapular and morbilliform eruptions	DD: COVID-19; drug reactions; viral exanthemas	10–15%
Stevens-Johnson-syndrome/toxic epidermal necrolysis	Life threatening	<1%
Drug reaction with eosinophilia and systemic symptoms	Potentially life-threatening	Rare
Neutrophilic dermatoses	Can bear significant morbidity like pyoderma gangrenosum	Rare
Papulo-pustular dermatoses	Most common pustular psoriasis	Rare
Sarcoidosis	Systemic manifestations	Rare
Graft-versus-host disease	More common in hematologic Neoplasia	Very rare
Induction of autoimmune connective disorders	Like subacute cutaneous lupus erythematosus	Very rare
Vitiligo		≤1%

Key Points

- Targeted tumor therapy is associated with cutaneous adverse events in about half of the patients treated.
- Check point inhibitors can cause potentially life-threatening cutaneous adverse events.
- Early diagnosis and treatment of cutaneous side effects is of importance for effective antineoplastic therapy.
- Non-life threating cutaneous side effects may indicate a better response to check point inhibitor therapy.

References

1. Yan Y, Zhang L, Zuo Y, Qian H, Liu C. Immune checkpoint blockade in cancer immunotherapy: mechanisms, clinical outcomes, and safety profiles of PD-1/PD-L1 inhibitors. Arch Immunol Ther Exp. 2020;68(6):36.
2. Coleman EL, Olamiju B, Leventhal JS. The life-threatening eruptions of immune checkpoint inhibitor therapy. Clin Dermatol. 2020;38(1):94–104.
3. Muntyanu A, Netchiporouk E, Gerstein W, Gniadecki R, Litvinov IV. Cutaneous immune-related adverse events (irAEs) to immune checkpoint inhibitors: A dermatology perspective on management. J Cutan Med Surg. 2021;25(1):59–76.
4. Min Lee CK, Li S, Tran DC, Zhu GA, Kim J, Kwong BY, Chang ALS. Characterization of dermatitis after PD-1/PD-L1 inhibitor therapy and association with multiple oncologic outcomes: A retrospective case-control study. J Am Acad Dermatol. 2018;79(6):1047–52.

Chapter 11
Eczema-like Dermatosis with Perlèche and Glossitis

Uwe Wollina

A 50-year-old female Caucasian patient was referred to the department of dermatology and allergology because of a treatment-resistant disseminated eczematous dermatosis (Fig. 11.1). She also presented with perlèche and mild glossitis. Pruritis was temporary and not sleep-disturbing.

Treatment with topical corticosteroids class II for more than 4 weeks had not resulted in any improvement. She suffered from diabetes mellitus type II, glaucoma, peripheral artery disease, leg ulcers, pancreatitis (partial resection), and acute decompensation of liver cirrhosis with ascites.

Based upon History and Clinical Appearance, What Is Your Diagnosis?

1. Acrodermatitis enteropathica.
2. Biotinase deficiency.
3. Atypical psoriasis.
4. Acrodermatitis-like dermatitis.
5. Pellagra.

On examination we observed a wide-spread erythematous eczematous dermatitis of the trunk, anogenital region, and the extremities with a purpuric note. Neck and face and palmoplantar skin were spared. She presented perlèche and mild glossitis.

Her medical history was positive for alcohol dependency.

U. Wollina (✉)
Department of Dermatology & Allergology, Städtisches Klinikum, Academic Teaching Hospital of the Technical University of Dresden, Dresden, Germany
e-mail: Uwe.Wollina@klinikum-dresden.de

T. M. Lotti et al. (eds.), *Clinical Cases in Exfoliative Dermatitis*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08466-9_11

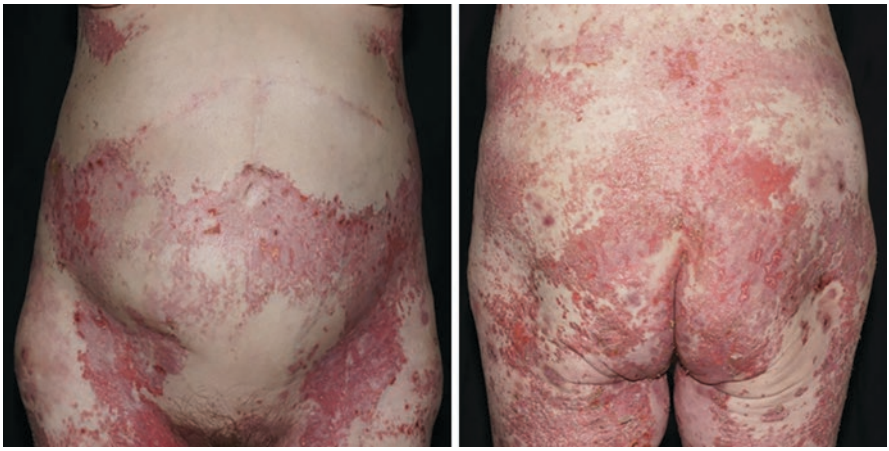

Fig. 11.1 Eczematous dermatitis with marginal scaling and purpuric note

Laboratory investigations: Erythrocyte count 3.09 Tpt/L (normal range: 4.2–5.2), hemoglobin 6.40 mmol/L (7.4–10.7), leukocytes 16.73 Gpt/L (3.8–11.0), Quick test 59.4% (70–130), creatinine 132.5 μmol/L (< 88), alkaline phosphatase 2.96 μkat/L (0.54–1.70), C-reactive protein 136.7 mg/L (< 5), urine glucose >1000 mg/dL (< 50), hepatitis A IgA antibodies 8.91 g/L (0.70–4.00), hepatitis B and C antibodies negative, hepatitis Bs antigen negative. Zinc 4 μmol/L (10.7–23.0).

Treatment: We started with topical betamethasone ointment which resulted in a marked improvement within 2 weeks. Zinc supplementation was planned but the general situation of the patient deteriorated dramatically, and she died due to an acute hepato-renal syndrome.

Discussion

Zinc is an essential trace element, indispensable for health. When zinc is ingested orally, not more than 66% is absorbed in the small intestine. The human body does not have a special zinc store, but muscles and bones contain about 90% of all zinc in the body. In circulation zinc is bound to albumins, α2 globulin, transferrin and amino acids. Intracellular zinc homeostasis is controlled by 14 different zinc importers which control zinc influx into the cytosol and 10 zinc exporters [1].

Inherited genetic variants in *SLC39A4*—the gene coding for the ZIP4 transporter—lead to acrodermatitis enteropathica, a rare zinc deficiency presenting at or after birth [2]. Acquired zinc deficiency has been reported in patients with end-stage renal disease, chronic inflammatory bowel disorders, hepatic disorders, anorexia, bulimia, after bariatric surgery, and prolonged parenteral nutrition [3].

Insufficient zinc supply by nutrition and/or gastrointestinal absorption is known as type I zinc deficiency, while extensive zinc loss by a variety of different disorders is classified type II.

Alcohol-dependency is commonly associated with zinc deficiency. The etiology is complex and involves poor zinc uptake, increased excretion, internal redistribution and altered zinc transporters.

Low zinc serum levels are associated with increased C-reactive protein, aspartate aminotransferase/alanine aminotransferase ratio, and decreased albumin levels. Low zinc-levels are contributing to progression of alcoholic liver disease [4].

Diagnosis of acquired zinc deficiency (type II) is mainly based on medical history and clinical features of eczematous dermatitis with involvement of periorifical and intertriginous skin, alopecia, nail changes, cheilitis and glossitis, and impaired wound healing. Serum or plasma zinc concentrations are less reliable, since a clinical zinc deficiency may occur with normal values. Zinc-dependent enzymes such as alkaline phosphatase may be reduced—useful as a surrogate marker.

Treatment of choice is oral elemental zinc at a dose of 0.5–1 mg/kg/day and optimization of the underlying pathology, whenever possible [5].

References

1. Kambe T, Tsuji T, Hashimoto A, Itsumura N. The physiological, biochemical, and molecular roles of zinc transporters in zinc homeostasis and metabolism. Physiol Rev. 2015;95(3):749–84.
2. Hoch E, Levy M, Hershfinkel M, Sekler I. Elucidating the H^+ coupled Zn^{2+} transport mechanism of ZIP4; implications in acrodermatitis enteropathica. Int J Mol Sci. 2020;21(3):734.
3. Di Baise M, Tarleton SM. Hair, nails, and skin: differentiating cutaneous manifestations of micronutrient deficiency. Nutr Clin Pract. 2019;34(4):490–503.
4. Vatsalya V, Kong M, Cave MC, Liu N, Schwandt ML, George DT, Ramchandani VA, McClain CJ. Association of serum zinc with markers of liver injury in very heavy drinking alcohol-dependent patients. J Nutr Biochem. 2018;59:49–55.
5. Glutsch V, Hamm H, Goebeler M. Zinc and skin: an update. J Dtsch Dermatol Ges. 2019;17(6):589–96.

Chapter 12
Erythema Exsudativum Multiforme as a First Symptom of a SARS-CoV-2 Infection

Klaus Fritz, George-Sorin Tiplica, and Carmen Salavastru

Case Report

A 54 year old man came for a consultation because of erythematous maculopapular eruptions on the back of hands and arms showing the typical clinical signs of Erythema in circles and central small blister respectively erythema (Fig. 12.1). The lesions started 2 days before, no herpes infection or symptoms that could be related to any other virus infections were reported, except some fatigue, increased body temperature of 38.6 °C and some itch within the lesions. There was no mucosal involvement, no medication was reported, the blood count showed normal leucocytes, histological examination was refused.

The day after this consultation the patient was tested positive for COVID 19. During the next 2 weeks, the skin lesions slowly disappeared using a Betamethason valerat cream twice a day, while other symptoms of COVID 19 remained moderate. The patient was not referred to a hospital, he improved at home in quarantine with a medication of acetylsalicylic acid 1 g/day. Retrospectively the skin lesions started to appear about 1 week after being infected and before serious symptoms occurred.

K. Fritz (✉)
Dermatologys and Laser Center, Landau, Germany

"Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania
e-mail: drklausfritz@drklausfritz.com

G.-S. Tiplica · C. Salavastru
"Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

"Colentina" Clinical Hospital, Bucharest, Romania

T. M. Lotti et al. (eds.), *Clinical Cases in Exfoliative Dermatitis*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08466-9_12

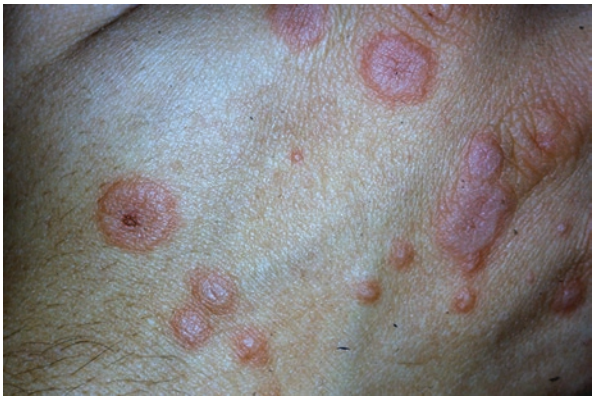

Fig. 12.1 54 year old man with erythematous maculopapular eruptions in circles and central small blister on the back of hands and arms showing as typical clinical signs of Erythema Exsudativum multiforme in early COVID 19 infection

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

1. Fixed drug eruption
2. Erythema elevatum et diutinum
3. Erythema Exsudativum multiforme
4. Sweet Syndrome

Diagnosis

Erythema Exsudativum multiforme.

Discussion

Only very few cases of Erythema Exsudativum multiforme have been reported following or during COVID 19 infection. Erythema multiforme is a dermatologic entity that can occur as a minor or major type. The minor type shows typical clinical lesions and appears frequently associated with viral infections or following medications and can be stimulated by sun light. Target lesions are a typical manifestation, can be itchy, tend to appear in light exposed areas such as arms and hands preferably at the age of 30–60 years. These symptoms probably are caused by immune complexes in the skin. Histological findings are apoptotic individual keratinocytes and perivascular lymphocytic infiltrate in the papillary dermis and along the dermo-epidermal junction.

During the COVID 19 pandemic, increasingly skin disorders were observed. "The incidence of dermatological findings in patients with COVID 19 has been

reported between 0.2% and 29% in the literature" [1]. Among them Erythema Exsudativum multiforme was rarely reported in COVID 19 infected patients, most skin lesions during COVID 19 infection presented as chilblain-like (40.1%), maculopapular (23.1%) and vesicular lesions (10.1%), urticaria (21.8%), livedoid/necrotic lesions (2.3%), and other non-classified skin lesions (19.8%) [2, 3].

Symptoms of the skin start in 50% before systemic symptoms and 50% during the infection and medication, which means that those starting under medication could be caused by the treatment instead the virus [4].

Dermatological manifestations associated with SARS-CoV-2 infection mostly show chilblain-like, urticarial and acro-papular eruption, purpuric/petechial and livedoid lesions, varicella-like, papulo-vesicular and morbilliform rashes or others which can be considered as adverse reactions to drugs for the treatment of COVID 19 [5].

Most lesions show "microvascular and endothelial cell injury, perivascular lymphocytic infiltrate, thrombosis, extremely dilated vessels and prominent deposits of C5b-9". 63.2% of cutaneous manifestations happened within 10 days, 21.1% in 10–20 days and 15.8% were 20 days after the time the patient presented with COVID 19 main symptoms and no correlation between skin rash type, onset day and COVID 19 severity was found [6].

The actual prevalence of the infection cannot be accurately determined. During the pandemic skin lesion were not always documented because of the lack of routine dermatology and those patients who presented themselves in dermatology practices and clinics with symptoms, were not always tested for COVID 19 infection in the beginning, because most of the skin findings were well known as disorders of various other reasons that seemed to be more likely than COVID 19, respectively many were not aware of the fact, that COVID 19 may manifest first in skin lesions in 14.77% of the patients and many more might experience skin findings during the course of the infection later. In average symptoms occurred after 9.92 days (range: 1–30). The receptor of SARS-CoV-2, ACE2, was found to be expressed mainly on keratinocytes [7].

Erythema Exsudativum multiforme minor was rarely reported [8], among them two small children of 2 and 6 years with Kawasaki Syndrome [9] one as a skin reaction to hydrochinon given for COVID 19 therapy [10, 11].

Questions arise, if dermatological symptoms signal any information on the COVID 19 infection. Some authors postulate, that skin lesions were associated with progressively increasing disease severity [2]. So far there are no studies yet, that prove a relation between viral load and type, onset or severity of a skin rashes nor if they have any impact on the prognosis, the severity of pneumonia or the treatment.

It is interesting, that there are almost no case reports, respectively studies, showing if pre-existing chronic inflammatory diseases such as psoriasis or atopic dermatitis is altered in any way. Probably the cutaneous manifestations of SARS-CoV-2 infection are the result of an aberrant immune response [5].

According to Recalcati et al. [12] the skin manifestations of COVID 19 patients are similar to other skin diseases caused by viral infection.

Erythema multiforme (EM) is linked to infectious agents in 90% of the cases, while drug-associated EM is reported in less than 10% of cases. Herpes simplex virus (HSV) and *Mycoplasma pneumoniae* are the main agents, but other viruses have been reported, such as Adenovirus, Coxsackie, Parvovirus B19 [13].

References

1. Gül Ü. COVID-19 and dermatology. Turk J Med Sci. 2020;50:1751–9.
2. Galván Casas C, Català A, Carretero Hernández G, et al. Classification of the cutaneous manifestations of COVID-19: a rapid prospective nationwide consensus study in Spain with 375 cases. Br J Dermatol. 2020;183:71–7. https://doi.org/10.1111/bjd.19163.
3. Kubanov AA, Deryabin DG. Skin manifestations in COVID-19 provide a clue for disease's pathophysiology understanding. J Eur Acad Dermatol Venereol. 2021;35(1):e3–4. https://doi.org/10.1111/jdv.16902.
4. Öksüm SE, Baran KB, Aslaner H, Çinar SL, Kartal D, Benli AR, Borlu M. Cutaneous symptoms of patients diagnosed with COVID-19 in one province: a cross-sectional survey. J Eur Acad Dermatol Venereol. 2021;35(2):e105–6. https://doi.org/10.1111/jdv.16904.
5. Gisondi P, Piaserico S, Bordin C, Alaibac M, Girolomoni G, Naldi L. Cutaneous manifestations of SARS-CoV-2 infection: a clinical update. J Eur Acad Dermatol Venereol. 2020;34:2499–504.
6. Zheng Y, Gong Z, Chen J, Lin Y, Liu Y. Inflammation and vascular injury as the basis of COVID-19 skin changes: preliminary analysis of 23 patients from the literature. Clin Cosmet Investig Dermatol. 2021;14:1–7. https://doi.org/10.2147/CCID.S278833.
7. Zhao Q, Fang X, Pang Z, Zhang B, Liu H, Zhang F. COVID-19 and cutaneous manifestations: a systematic review. J Eur Acad Dermatol Venereol. 2020;34:2505–10. https://doi.org/10.1111/jdv.16778.
8. Janah H, Zinebi A, Elbenaye J. Atypical erythema multiforme palmar plaques lesions due to Sars-Cov-2. J Eur Acad Dermatol Venereol. 2020;34:e346–432.
9. Labé P, Ly A, Si CN, Nasser M, Chapelon-Fromont E, Ben Saïd P, Mahé E. Erythema multiforme and Kawasaki disease associated with COVID-19 infection in children. J Eur Acad Dermatol Venereol. 2020;34:e532–652. https://doi.org/10.1111/jdv.16666.
10. Robustelli Test E, Vezzoli P, Carugno A, Raponi F, Gianatti A, Rongioletti F, Sena P. Acute generalized exanthematous pustulosis with erythema multiforme-like lesions induced by Hydroxychloroquine in a woman with coronavirus disease 2019 (COVID-19). J Eur Acad Dermatol Venereol. 2020;34:e433–531.
11. Sánchez-Velázquez A, Falkenhain D, Rivera DR. Eritema multiforme en contexto de infección por SARS-Coronavirus-2. Med Clin (Barc). 2020;155:141.
12. Recalcati S. Cutaneous manifestations in COVID-19: a first perspective. J Eur Acad Dermatol Venereol. 2020;34:e212–3.
13. Jimenez-Cauhe JJ, Ortega-Quijano D, Carretero-Barrio I, Suarez-Valle A, Saceda-Corralo D, Moreno-Garcia Del Real D, Fernandez-Nieto D. Erythema multiforme-like eruption in patients with COVID-19 infection: clinical and histological findings. Clin Exp Dermatol. 2020;45(7):892–5.

Chapter 13
Exfoliative Dermatitis After a Long-Distance Drive

Stamatios Gregoriou, Ileana-Afroditi Kleidona, Eleftheria Christofidou, and Dimitrios Rigopoulos

A 57-year-old male presented to our department with disperse pruritic exfoliative dermatitis for the last 20 days. On clinical examination he presented diffuse, erythematous patches with fine desquamation on the trunk, arms and thighs (Figs. 13.1 and 13.2). Lesions on the palms were more demarcated, coalescing to cover the entire volar aspect of both hands and wrists. Fissures and hyperkeratosis suggested a more chronic course for the palm lesions (Fig. 13.3).

He worked as a car mechanic and his past medical history included high blood pressure managed with the same antihypertensives for years, a history of allergic rhinitis but without symptoms for the last 7 years, and a single parental atopic history, but no personal history of atopic dermatitis. He reported chronic hand dermatitis for the last 5 years. He had been previously treated, for his hand eczema, with topical corticosteroids, acitretin 0.5 mg/kg that resulted in mild improvement with periods of remission and recurrent exacerbations, and alitretinoin 30 mg/day that achieved disease control for 3 years, but was discontinued after increase in plasma cholesterol and triglyceride levels. He did not report uptake of any new medication for the last 6 months, including dietary supplements or vitamins. Interestingly, he reported aggravation of his hand eczema and appearance of the lesions on the trunk, arms and thighs after driving his car to his birthplace, for 7 h, for an Easter vacation.

Complete blood count and routine biochemistry including total IgE were within normal limits.

A biopsy specimen from the thigh lesions revealed epidermal edema with spongiosis and acanthosis. An inflammatory infiltrate in the dermis predominately containing lymphocytes was observed (Fig. 13.4).

S. Gregoriou (✉) · I.-A. Kleidona · E. Christofidou · D. Rigopoulos
1st Department of Dermatology-Venereology, Andreas Sygros Hospital, National and Kapodistrian University of Athens, Athens, Greece

T. M. Lotti et al. (eds.), *Clinical Cases in Exfoliative Dermatitis*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08466-9_13

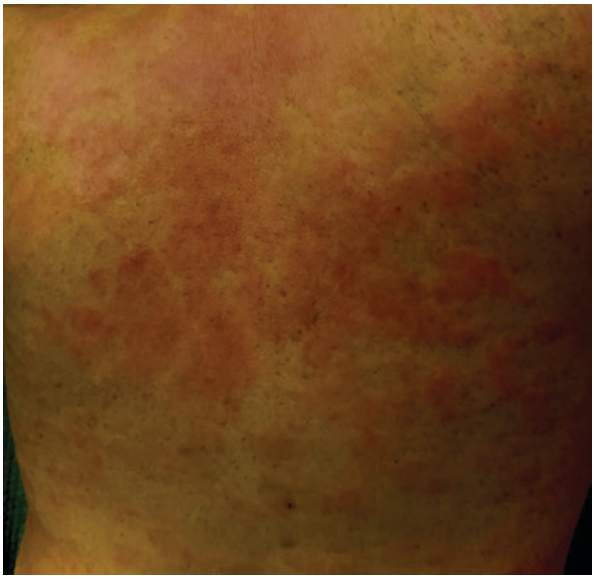

Fig. 13.1 Erythematous pruritic patches with desquamation on the patient's back

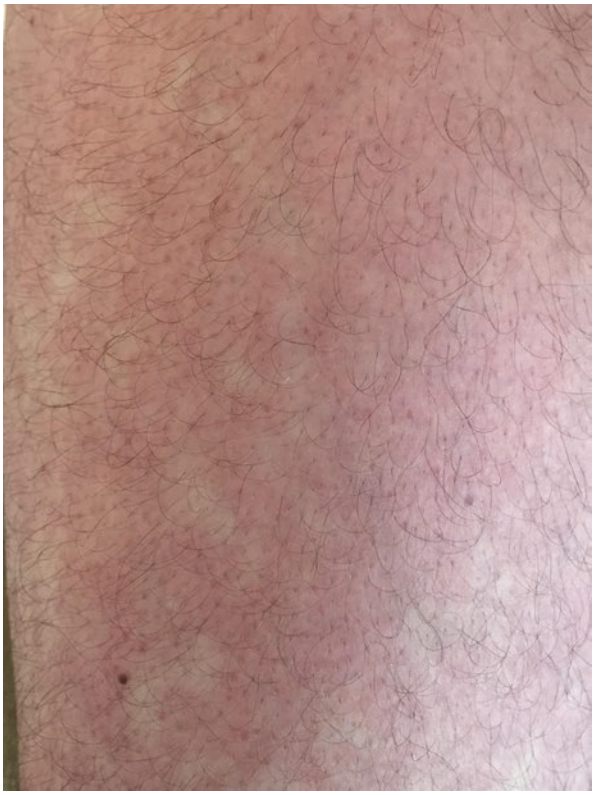

Fig. 13.2 Erythematous pruritic patches on the patient's thigh

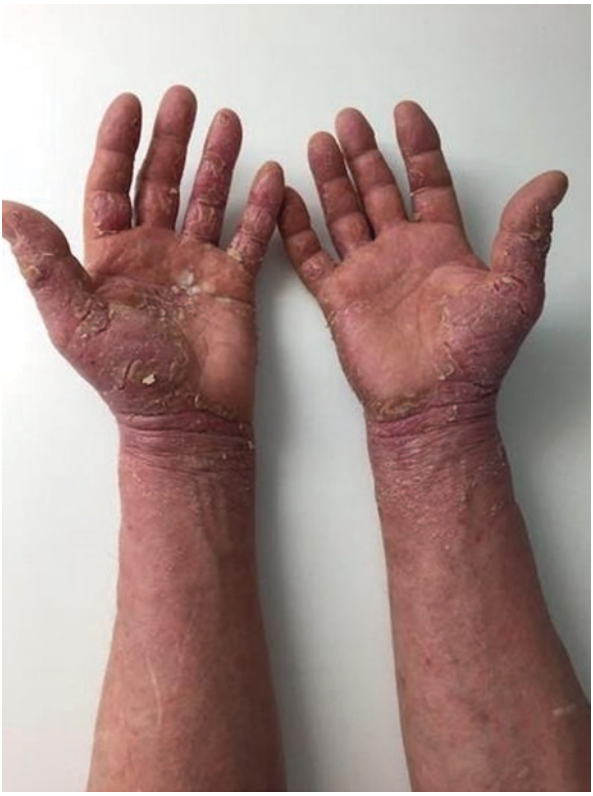

Fig. 13.3 Erythematous coalescing plaques with hyperkeratosis and fissures on the patient's palms

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

1. Contact dermatitis
2. Cutaneous lymphoma
3. Atopic dermatitis
4. Drug reaction
5. Psoriasis

Diagnosis

Exfoliative Dermatitis Due to Allergic Contact Dermatitis

A diagnosis of dermatitis was made based on the clinical and histological data. The patient was prescribed prednisolone 0.5 mg/kg with tapering after control of the dermatitis, levocetirizine 5 mg/day and topical mometasone furoate cream

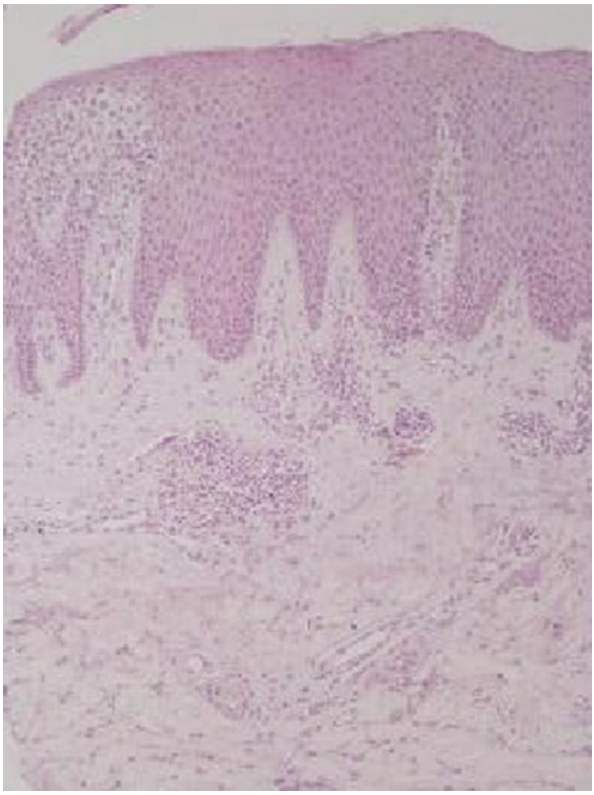

Fig. 13.4 Histopathology revealed epidermal edema with spongiosis, acanthosis and a lymphocytic infiltrate in the dermis. H+E ×80

application once daily. Complete resolution of the trunk and leg lesions and improvement of the hand lesions was observed after 4 weeks.

The patient underwent patch testing 4 weeks after discontinuation of the treatment. Seven millimetre ribbon of the patch test preparation (equivalent to 20 mg) was placed in 8-mm Finn Chambers® on Scanpor tape (SmartPractice, Pheonix, AZ, USA), immediately applied on patients' upper back to prevent evaporation, and left under occlusion for 48 h. Patch test reactions were read on days 2 (D2) and 3 (D3), according to the International Contact Dermatitis Research Group (ICDRG) and the European Society of Contact Dermatitis (ESCD) criteria. The patient was tested with the European Baseline Series of allergens and an extended metal compounds and lubricants series (allergEAZE; SmartPractice, Calgary, Alberta, Canada). When reading was performed at 72 h, positive reactions to rubber components were observed (Table 13.1).

A diagnosis of exfoliative dermatitis secondary to allergic contact dermatitis to rubber additives was made. The exfoliative widespread dermatitis developed after prolonged contact with the rubber surface of the steering wheel of his car, during the 7-h journey to his home town. The patient was counselled about protective measures: avoidance of rubber material including rubber in overalls and footwear, wearing protective gloves when working and driving and implementing a non-rubber steering wheel cover.

Table 13.1 Results of the patch tests

	Allergen	Concentration	Reaction
Standard European series	Thiuram mix	Pet 1%	++
	Myroxylon pereira (Peru balsam)	Pet 25%	+
	Mercapto mix	Pet 2%	+
	Black Rubber mix	Pet 0.1%	+
	Ethylenediamine	Pet 1%	+
	Mercaptobenzothiazole	Pet 2%	+
	Wool alcohols	Pet 30%	+
	Thiomersal	Pet 0.1%	+
Extended series	Amerchol L101	Pet 50%	+
	1,2-Benzisothiazol-3(2H)-one, sodium salt	Pet 0.1%	+

Discussion

Exfoliative dermatitis or erythroderma is a generalised manifestation of pre-existing conditions elicited by various triggers. A recent study reveals that, most common causes in adults are underlying dermatitis (20.7%), psoriasis (16.8%), Sézary syndrome (12.3%), drug reactions (12.3%), atopic dermatitis (8.7%) and mycosis fungoides (5.5%) [1]. For the eczematous reactions group, few studies report atopic dermatitis, contact dermatitis, seborrheic dermatitis and chronic actinic dermatitis as etiologic factors [2–4]. However, in some cases no specific aetiology is identified and they are described as "idiopathic". The pathways involved in the pathogenesis of erythroderma remain to be elucidated [5]. Typically, it is preceded by localised skin disease followed by secondary generalization and 2–6 days later by exfoliation [6].

Allergic contact dermatitis (ACD), is a cutaneous response to a chemical (allergen) and requires prior sensitization of the individual. Typically, erythematous patches or plaques with vesicles and scales are observed. The skin lesions are predominately localised to the site of contact. Nevertheless, patchy or diffuse distribution may be observed depending on the responsible substance [7].

Herein, we illustrate a case of exfoliative dermatitis on a background of allergic contact dermatitis to rubber substances. Prolonged contact of the patient's hands with the steering wheel, resulted in dispersed erythematous patches with desquamation. Allergic and irritant contact dermatitis often have similar clinical pictures and may coexist. Patch testing is the gold standard procedure for identifying the causative allergen in ACD. Potential sources of sensitization in the occupational setting of the patient include car tires, hoses, gaskets that seal fluid leakage from pipes and shields for electrical components. Even though, one could expect metal sensitization in a car mechanic that was not the case in the patient presented. Factors that could influence the development and severity of ACD include the nature of the allergen (e.g. solubility, lipophilicity), frequency of contact, dose of allergen, anatomic site involved, individual's susceptibility factors (e.g. compromised skin barrier). Likely, in our case all the factors described above contributed to the progression and evolution of the

allergic cutaneous reaction to exfoliative dermatitis. Similarly, a case of steering wheel and gearstick dermatitis due to chromate was recently reported [8].

Rubber compounds have been reported to be common causes of occupational contact allergies, in particular in the healthcare sector [9]. Rubber manufacturing implicates the intervention of various compounding ingredients such as vulcanisation agents, vulcanising accelerators, antidegradants, plasticisers and softeners.

Thiuram mix contains four substances, which are used as chemical accelerators to speed up the manufacturing of rubber products (Tetramethylthiuram monosulfide, Disulfiram, Tetramethylthiuram disulfide, Dipentamethylenethiuram disulfide). They are also used as pesticides and fungicides. Since the widespread use of natural rubber latex gloves, there has been an increasing incidence of thiuram allergy. These substances are found in several products such as animal repellents, household, occupational sources, clothing, cosmetics, recreational objects. Car mechanics may handle rubber products at work such as tubes, utility gloves, rubber bands, plugs, adhesives and gloves [10, 11].

Myroxylon pereirae (Peru balsam) is an aromatic liquid originating from the tree *Myroxylon balsamum* found in Central America. It contains a mixture of substances, predominately cinnamic acid, cinnamyl cinnamate, benzyl benzoate, benzoic acid, nerolidol, farnesol and eugenol. It has aromatic, fixative, antiseptic, antiparasitic and antifungal properties. Therefore, it is used in perfumes and toiletries as a fragrance and in food for its flavouring properties. Also, medicinal and dental products may contain Balsam of Peru. In mechanics, contact allergy may occur through cleaning products, car air fresheners and deodorizers [12].

Mercapto mix includes three substances (N-Cycloxylbenzothiazyl-sulfenamide, Dibenzohiazyl disulfide, Morpholinylmeraptobenzothiazole) which are accelerators of rubber vulcanisation process. They are widely used as components of rubber products and can be found in shoes, gloves, tires, tubing, hoses, condoms, adhesives and cleansing products. Most of these products are involved in a mechanic's work activities [13].

Black Rubber mix contains a mixture of three allergens [N-dimethyl-1, C-butyl-N-phenyl-p-phenylenediamine (DMBPPD) 0.25%, Diphenyl-p-phenylenediamine 0.25%, N-isopropyl-N-phenyl-p-phenylenediamine (IPPD) 0.1%]. Pure rubber is vulnerable to oxidation when exposed to air, leading to loss of its physical properties. These are antidegradation agents which turn the rubber mixture black and were developed to prevent damage to the molecules from oxidation and effect of ozone. Commonly, they are found in belts, aprons, cables, masks, tires, car steering wheel, wire insulation. Clearly, auto mechanics may be sensitised through contact with any of the above substances in their work environment [14].

Ethylenediamine dihydrochloride is a chemical with stabilizing properties found in topical antibiotic or steroid creams, antihistamines, insecticides, lubricants, waxes, solvents, dye-assist compounds, electroplating and other industrial products. Because of its features, it is also used in the rubber industry. Many individuals become sensitized to ethylenediamine through the use of topical preparations but cases of occupational dermatitis following contact in industry have been reported. In particular, mechanics may handle ethylenediamine containing products such as

coolant oils, coatings, electrophoretic gels, fuel additives, corrosion inhibitors, waxes and lubricants [15, 16].

Mercaptobenzothiazole (MBT) is a rubber accelerator due to its sulfur containing properties. It is found in shoes, undergarments, clothing, gloves, toys, medical devices, tires, tubes. It is also used in antifreeze products, detergents, cutting oils, greases, adhesives which together with rubber products may be involved in the development of contact allergy in a mechanic occupational setting [17].

Wool alcohols are the principal component of lanolin, an emollient and emulsifier. They can be found in pharmaceutical products, cosmetics, shoe and furniture polish formulations, leather, ink and papers. In mechanic occupations, these may be responsible allergens for dermatitis through contact with cutting fluids, lubricants and rust preventers [18].

Thiomersal is an organic mercury-containing substance with antiseptic and antifungal properties. Despite the debates on the clinical significance of positive patch-tests, thiomersal remains a frequent contact allergen. It is used as a preservative in some vaccines, cosmetics, ophthalmic solutions and tattoo inks. At work, a mechanic may be sensitized through fluorescent dyes used in metal industry [19].

Amerchol L101 is a trade name of products containing lanolin. It is found in cosmetics, pharmaceuticals, topical drugs, furniture polish, leather, paper, inks, textiles, furs, cutting oils, and waxes. In a mechanic occupational setting it is encountered in metal corrosion preventing products.

1,2-Benzisothiazolin-3-one (BIT) (CAS no. 2634-33-5) is a biocide and fungicide that is widely used in paint and varnishes, but also in household cleaning products such as laundry detergents, and in agriculture pesticide formulations. In a mechanic occupational setting it is encountered indirectly in car cleaning products.

Timely recognition of occupational ACD is essential to avoid diagnostic delay, warranty good quality of life and prevent economic consequences due to loss of work time, healthcare visits and medical treatments. Once causative allergens have been identified, it is imperative to counsel the patients. Further information and support may be obtained from information sheets, websites and programs developed to enhance appropriate behaviour. Examples are the American Contact Dermatitis Society website and the Contact Allergen Management Program (CAMP) [20, 21].

In conclusion, our case emphasises that allergic contact dermatitis can may progress to disperse exfoliative dermatitis. Further, underscores the importance of patch testing in order to guide correct diagnosis in contact dermatitis. Subsequently, patient's education has a central role in disease management and prevention of complications.

Key Points

- Allergic contact dermatitis should be included in the differentials of exfoliative dermatitis.
- Patch tests are the gold standard in the diagnosis of allergic contact dermatitis.
- Counselling and allergen avoidance are the hallmarks to disease remission in ACD.

References

1. Miyashiro D, Sanches JA. Erythroderma: a prospective study of 309 patients followed for 12 years in a tertiary center. Sci Rep. 2020;10(1):9774.
2. Yuan X-Y, Guo J-Y, Dang Y-P, Qiao L, Liu W. Erythroderma: a clinical-etiological study of 82 cases. Eur J Dermatol. 2010;20(3):373–7.
3. Li J, Zheng H-Y. Erythroderma: a clinical and prognostic study. Dermatology. 2012;225(2):154–62.
4. Sehgal VN, Srivastava G. Exfoliative dermatitis. A prospective study of 80 patients. Dermatologica. 1986;173(6):278–84.
5. Kanthraj GR, Srinivas CR, Devi PU, Ganasoundari A, Shenoi SD, Deshmukh RP, et al. Quantitative estimation and recommendations for supplementation of protein lost through scaling in exfoliative dermatitis. Int J Dermatol. 1999;38(2):91–5.
6. Khaled A, Sellami A, Fazaa B, Kharfi M, Zeglaoui F, Kamoun MR. Acquired erythroderma in adults: a clinical and prognostic study. J Eur Acad Dermatol Venereol. 2010;24(7):781–8.
7. Bologna JL, Schaffer JV, Cerroni L. Allergic contact dermatitis. In: Dermatology. 4th ed. Amsterdam: Elsevier; 2018. p. 242–61.
8. Tewari A, Khan I, Ostlere L. Steering wheel and gearstick dermatitis caused by chromate. Contact Dermatitis. 2019;81(4):322–3.
9. Hamnerius N, Svedman C, Bergendorff O, Björk J, Bruze M, Engfeldt M, et al. Hand eczema and occupational contact allergies in healthcare workers with a focus on rubber additives. Contact Dermatitis. 2018;79(3):149–56.
10. Uter W, Werfel T, Lepoittevin J-P, White IR. Contact allergy—emerging allergens and public health impact. Int J Environ Res Public Health. 2020;17(7):2404.
11. Pak VM, Watkins M, Green-McKenzie J. What is the role of thiurams in allergy to natural rubber latex products? J Occup Environ Med. 2012;54(5):649–50.
12. de Groot AC. Myroxylon pereirae resin (balsam of Peru)—a critical review of the literature and assessment of the significance of positive patch test reactions and the usefulness of restrictive diets. Contact Dermatitis. 2019;80(6):335–53.
13. Adams AK, Warshaw EM. Allergic contact dermatitis from mercapto compounds. Dermatitis. 2006;17(2):56–70.
14. Uter W, Werfel T, White IR, Johansen JD. Contact allergy: a review of current problems from a clinical perspective. Int J Environ Res Public Health. 2018;15(6):1108.
15. Iammatteo M, Akenroye A, Jariwala S, Lee B, Schairer D, Rosenstreich D. Severe contact dermatitis due to ethylenediamine dihydrochloride in nystatin cream. J Allergy Clin Immunol Pract. 2017;5(5):1448–50.
16. Chieregato C, Vincenzi C, Guerra L, Farina P. Occupational allergic contact dermatitis due to ethylenediamine dihydrochloride and cresyl glycidyl ether in epoxy resin systems. Contact Dermatitis. 1994;30(2):120.
17. Warshaw EM, Gupta R, DeKoven JG, Maibach HI, Taylor JS, Fransway AF, et al. Patch testing of mercaptobenzothiazole and mercapto mix: the North American Contact Dermatitis Group Experience, 1994–2016. Dermatitis. 2021;32(4):232–44.
18. Knijp J, Bruynzeel DP, Rustemeyer T. Diagnosing lanolin contact allergy with lanolin alcohol and Amerchol L101. Contact Dermatitis. 2019;80(5):298–303.
19. Freiman A, Al-Layali A, Sasseville D. Patch testing with thimerosal in a Canadian center: an 11-year experience. Am J Contact Dermat. 2003;14(3):138–43.
20. CAMP [Internet]. [cited 2021 Jan 23]. Available from: http://www.acdscamp.org/
21. American Contact Dermatitis Society (ACDS) [Internet]. [cited 2021 Jan 23]. Available from: https://www.contactderm.org/

Chapter 14
Exfoliative Dermatitis Associated with Hair Abnormalities

Sorina Dănescu, Corina Baican, Cristian Păpară, Paula Anca Iluț, Alexandru Tătaru, and Adrian Baican

A 56-year-old female patient with a history of erythroderma since infancy, presented for generalized xerosis, diffuse erythema and hair abnormalities.

What Is Your Diagnosis?

1. Atopic dermatitis.
2. Allergic contact dermatitis.
3. Netherton's syndrome.
4. Ichthyosis vulgaris.
5. Wiskott–Aldrich syndrome.

Diagnosis

Netherton's syndrome.

On dermatological examination we observed xerosis, diffuse erythema and scaling of the trunk, arms and legs, and serpiginous, erythematous plaques with double-edged peripheral scale on the arms. In addition, we found sparse, lusterless and brittle hair on the scalp, and loss of the outer part of the eyebrow (Fig. 14.1).

None of the family members reported any dermatological problems.

Laboratory blood tests revealed eosinophilia and elevated IgE serum levels.

S. Dănescu (✉) · C. Baican · C. Păpară · P. A. Iluț · A. Tătaru · A. Baican
Department of Dermatology, Iuliu Hațieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania

T. M. Lotti et al. (eds.), *Clinical Cases in Exfoliative Dermatitis*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08466-9_14

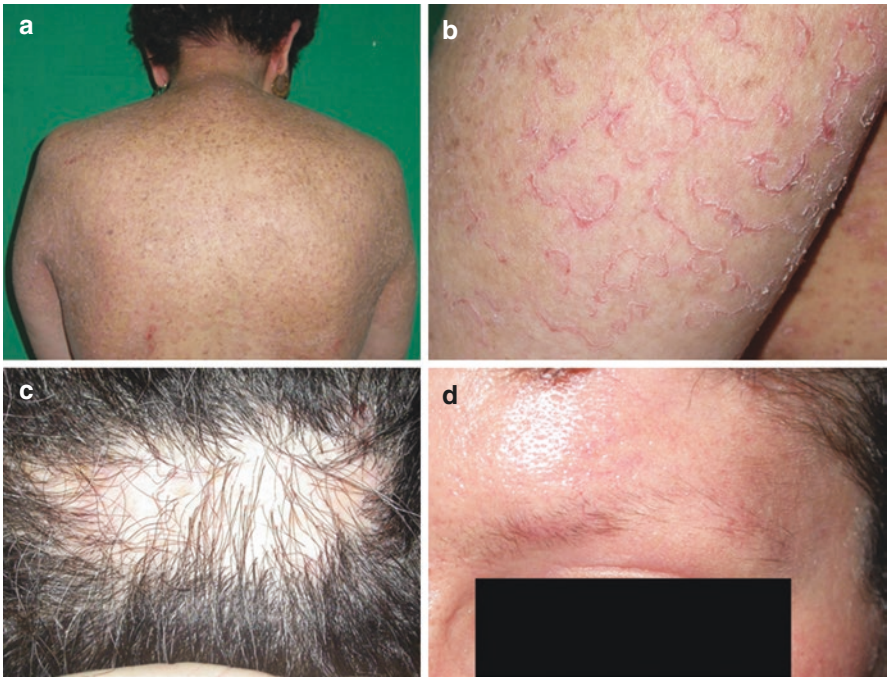

Fig. 14.1 Clinical features: (**a**) generalized xerosis with diffuse erythema and scaling; (**b**) serpiginous, erythematous plaques with double-edged peripheral scale; (**c**) sparse, lusterless and brittle hair on the scalp; (**d**) loss of the outer part of the eyebrow

Fig. 14.2 Optical microscopy analysis of the hair (×100)

Optical microscopy analysis of the hair follicle revealed trichorrhexis invaginata or "bamboo hair" (Fig. 14.2).

She was treated with oral antihistamines, topical corticosteroids and emollients without any clinical improvement, but with persistence of the lesions and with recurrent episodes of exacerbation.

Discussion

Netherton's syndrome is a recessive autosomal disorder caused by germline mutations in SPINK5 gene, the latter playing an important role in normal skin scaling and barrier function [1]. Netherton's syndrome is characterized by the triad of congenital ichthyosiform erythroderma/ichthyosis linearis circumflexa, trichorrhexis invaginata ("bamboo hair") and atopic diathesis [2].

The onset is usually after birth, with generalized erythroderma and desquamation. Later, manifestations of atopy and hair shaft abnormalities appear.

Ichthyosis linearis circumflexa presents as distinctive circular scaly lesions with thickened scaling borders characterized by a slowly changing pattern.

Most of the patients have a sparse, abnormal hair, which is short, lusterless and brittle. Older patients may lose eyebrows and eyelashes. The hair follicle alterations (trichorrhexis invaginata or "bamboo hair"), especially of the eyebrows, represents the most characteristic finding in Netherton's syndrome. This is due to the invagination of the distal portion of the hair shaft into the proximal portion [3].

Atopic manifestations include atopic dermatitis, asthma, allergic rhinitis, urticaria, angioedema, blood hyper-eosinophilia, and elevated IgE serum levels [4].

Histological examination shows epidermal acanthosis, parakeratosis, hyper- and agranulosis, and the papillary dermis contains dilated vessels and a mild perivascular lymphocyte infiltrate. Genetic analysis identifies mutations in the SPINK5 gene [1].

The treatment is symptomatic, with topical corticosteroids, calcineurin inhibitors, emollients, and PUVA treatment. Other therapies include oral acitretin, intravenous immunoglobulin and infliximab, whereas kallikrein inhibitors represent a novel potential therapy [4, 5].

Key Points

- Netherton's syndrome is a genetic disorder characterized by the triad of congenital ichthyosiform erythroderma/ichthyosis linearis circumflexa, trichorrhexis invaginata ("bamboo hair") and atopic diathesis.
- Trichorrhexis invaginata of scalp hair and eyebrows is pathognomonic for Netherton's syndrome.
- Netherton's syndrome is usually misdiagnosed with atopic dermatitis, it is marked by a chronic evolution, and currently there is no cure for it.

References

1. Flora A, Smith A. Netherton's syndrome: a case of two male siblings diagnosed in adulthood. Case Rep Dermatol. 2020;12:64–9.
2. Saleem H, Shahid M, Shahbaz A, et al. Netherton syndrome: a case report and review of literature. Cureus. 2018;10(7):e3070.

3. Bittencourt MJS, Mendes AD, Moure ERD, Deprá MM, Pies OTC, Mello ALP. Trichoscopy as a diagnostic tool in trichorrhexis invaginata and Netherton syndrome. An Bras Dermatol. 2015;90(1):114–6.
4. Leung AKC, Barankin B, Leong KF. An 8-year-old child with delayed diagnosis of Netherton syndrome. Case Rep Pediatr. 2018;2018:9434916.
5. Tan X, Soualmia F, Furio L, Renard JF, Kempen I, Qin L, et al. Toward the first class of suicide inhibitors of kallikreins involved in skin diseases. J Med Chem. 2015;58(2):598–612.

Chapter 15
Face Dermatitis After Sun Exposure of a 48 Year Old Woman

Olga Olisova, N. P. Teplyuk, A. A. Lepekhova, E. V. Grekova, and V. Varshavsky

A 48-year-old woman presented to our Department with the progressive lesions involving the nose, cheeks, and forehead developed 6 months ago after insolation (Fig. 15.1). On examination, the patient presented with irregular pink-yellow patches with sharp borders and small serous crusts.

Histopathological examination revealed acantholysis at the granular level and edema at the basal layer (Fig. 15.2).

Direct immunofluorescence (DIF) showed C3 and IgG deposition at the cell surface of epidermal keratinocytes (Fig. 15.3a, b). ELISA showed circulating IgG-autoantibodies to desmoglein 1.

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

Impetigo
Rosacea
Erythematosus
Seborrheic Dermatitis

O. Olisova · N. P. Teplyuk · A. A. Lepekhova (✉) · E. V. Grekova
Department of Dermatology and Venereology, Sechenov University, Moscow, Russia

V. Varshavsky
Department of Pathological Anatomy, Sechenov University, Moscow, Russia

T. M. Lotti et al. (eds.), *Clinical Cases in Exfoliative Dermatitis*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08466-9_15

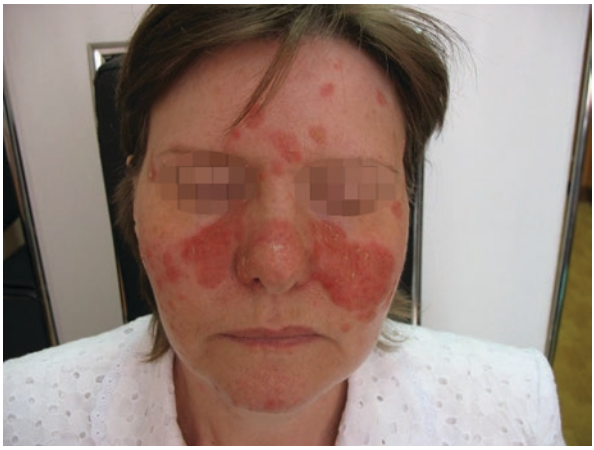

Fig. 15.1 Irregular pink-yellow patches with sharp borders and small serous crusts on the nose, cheeks, and forehead

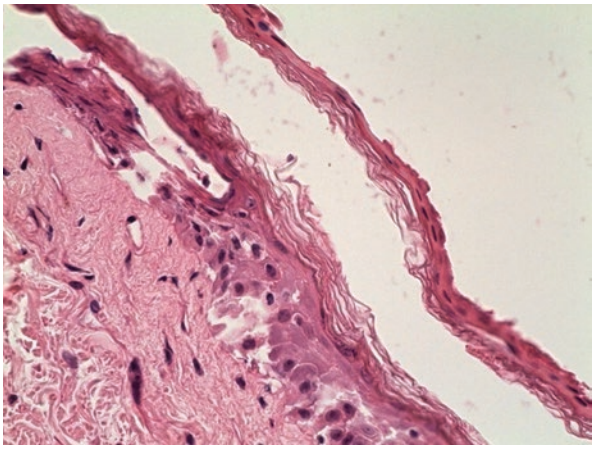

Fig. 15.2 Histology. Acantholysis at the granular level and edema at the basal layer

Diagnosis

Pemphigus erythematosus.

Discussion

Pemphigus erythematosus (PE) is a minor subtype of pemphigus foliaceus (PF) and a life-threatening autoimmune bullous disease characterized by the development of plaques, erythema, superficial erosions, and crusts impregnated with serous exudate (serous crusts) on the open areas (face, scalp, chest, or upper back) [1]. In pemphigus the mortality rate is approximately 5–15%. According to desmoglein compensation theory, the mucosal lesions, large flaccid and small tense blisters are

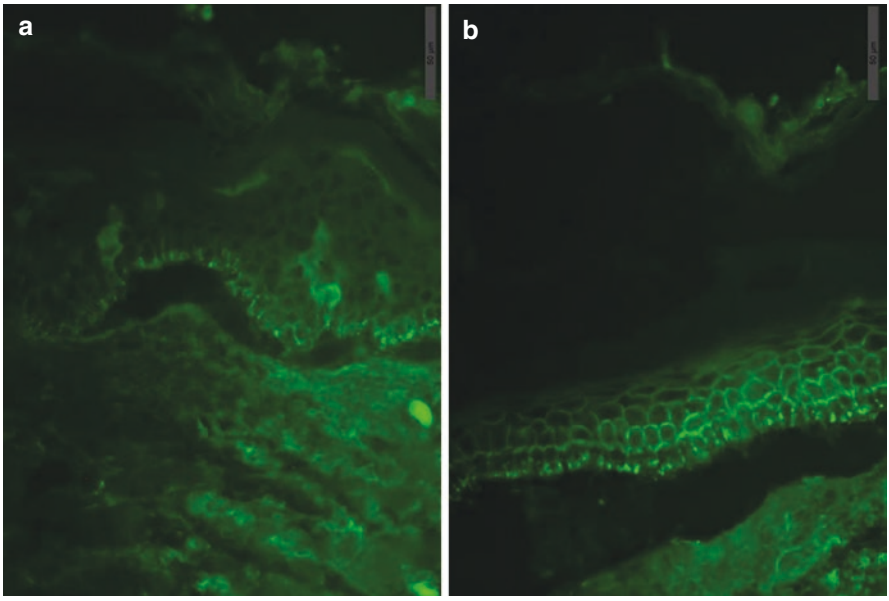

Fig. 15.3 Direct immunofluorescence (DIF) showing (**a**) C3 and (**b**) IgG deposition at the cell surface of epidermal keratinocytes

not common for pemphigus foliaceus as the acantholysis occurs at the granular layer [2].

Systemic corticosteroids (CS) remain the first-line therapy for pemphigus. Introduction of CS decreased the mortality rate from 75% to 30% [3]. However, high doses of CS sometimes cannot produce adequate symptoms control. Thus, CS resistant patients should be treated with the adjuvant therapy (cyclophosphamide, azathioprine, methotrexate, mycophenolate mofetil, cyclosporine, high-dose intravenous immunoglobulins, and rituximab). The initial clinical evaluation of pemphigus should be confirmed histologically and also by direct immunofluorescence (DIF) examination of a perilesional skin and "serological detection of autoantibodies against epithelial cell surface by indirect immunofluorescence (IIF) and/or enzyme-linked immunosorbent assay (ELISA Dsg1)" [4].

Erythematotelangiectatic rosacea is a chronic inflammatory skin disease with facial eruption (cheeks and nose) characterized by bright erythema with telangiectasia and dryness, with or without scaling. Patients may have associated symptoms like stinging, burning, itching. Rosacea can be triggered by the sun exposure, spicy food, alcohol, and infestation by Demodex folliculorum. Follicular scales with increased Demodex folliculorum colonization were also observed in patients with erythematotelangiectatic rosacea [5]. It is important to perform a Demodex density test to confirm the diagnosis [6]. Histopathology in erythematotelangiectatic rosacea is nonspecific, showing enlarged, dilated capillaries and venules, spongiosis, edema, and varying degrees of perivascular lymphocytic inflammation in the upper

dermis [7]. Usually, these patients should avoid topic preparations containing alcohol, formaldehyde, menthol, camphor, or sodium lauryl sulfate, and use of products with sun protection factor (SPF) 30 and higher. The topical treatment includes brimonidine, ivermectin, metronidazole, and azelaic acid (not in cases with telangiectasia). In severe and\or treatment-resistant rosacea, combination topical and systemic therapy (low-dose isotretinoin, doxycycline, or tetracycline) is necessary [8].

Cutaneous Lupus Erythematosus (CLE), a chronic autoimmune disease primarily affecting skin and mucosal tissue, is typically classified into three main subtypes: acute (ACLE), subacute (SCLE), and chronic (CCLE) [9]. CLE is often triggered by ultraviolet exposure. ACLE presents with erythematous patches called butterfly rash, classically crossing both cheeks but sparing the nasolabial folds. It does not leave any atrophy or dyspigmentation. However, ACLE is considered a criterion for the diagnosis of Systemic Lupus Erythematosus (SLE). SCLE typically presents as papulosquamous lesions and/or annular plaques with central clearing and raised erythematous scaly edges. It can leave dyspigmentation but no atrophy. The most common form of CLE is discoid LE (DLE). It is a cutaneous form of LE and only 1–5% of widespread cases may progress to SLE. DLE presents as erythematous scaling patches with sharp boards and central atrophy. Scrapping of the scales is usually painful because of follicular hyperkeratosis, and their undersurface looks like the "lady's heel". Histopathological findings include hyperkeratosis with follicular plugs, epidermal atrophy, vacuolar degeneration of basal keratinocytes in epidermis, and tight perivascular and periadnexal lymphocytic infiltrate, telangiectasis, edema, actinic elastosis, and mucin deposits between collagen strands in dermis. DIF may show immunoglobulins G and C3 deposition at dermoepidermal junction (DEJ) in cutaneous LE and even non-involved skin of sun-protected areas in systemic LE (lupus band test) [10]. The most commonly prescribed are antimalarial drugs, followed by calcineurin inhibitors, mycophenolate mofetil, methotrexate, and systemic steroids.

Seborrheic Dermatitis (SD) is a chronic inflammatory skin disease presenting with symmetrical pink-yellow moist patches and plaques particularly on the face, and other areas rich in sebaceous glands. Rash can be present with firm greasy scales and sharp borders. *Malassezia* spp. can also play a role in the SD pathogenesis. Thus, in some several cases it is necessary to make swab for microscopy, culture, and sensitivities. The dermatopathology is non-specific, but the epidermis usually shows acanthosis, focal spongiosis, and focal parakeratosis. The surface of derma shows a superficial lymphocyte perivascular infiltrate and even leukocytoclasis in severe SD. Some authors use the term "Shoulder parakeratosis" when describing scale-crust accumulation around the infundibular ostia. DIF and IIF are negative. Conventional therapy includes antifungals, keratolytics, antipruritics, and anti-inflammatory drugs (calcineurin inhibitors). First-line therapy includes antifungal drugs [11].

Key Points

- Pemphigus erythematosus is a minor subtype of pemphigus foliaceus.
- Pemphigus erythematosus is a life-threatening autoimmune bullous disease, with 5–15% mortality.
- The initial evaluation of pemphigus includes clinical and histological features, direct immunofluorescence (DIF) examination of a perilesional skin, and "serological detection of autoantibodies against epithelial cell surface by indirect immunofluorescence (IIF) and/or enzyme-linked immunosorbent assay (ELISA Dsg1)".
- Systemic corticosteroids are the major drugs for Pemphigus erythematosus treatment.
- Adjuvant therapy includes cyclophosphamide, azathioprine, methotrexate, mycophenolate mofetil, cyclosporine, high-dose intravenous immunoglobulins, and rituximab.

References

1. Joly P, Horvath B, Patsatsi A, Uzun S, Bech R, Beissert S, Caux F. Updated S2K guidelines on the management of pemphigus vulgaris and foliaceus initiated by the European academy of dermatology and venereology (EADV). J Eur Acad Dermatol Venereol. 2020;34(9):1900–13.
2. Amagai M. Pemphigus as a paradigm of autoimmunity and cell adhesion. Keio J Med. 2002;51(3):133–9.
3. Bystryn JC. Adjuvant therapy of pemphigus. Arch Dermatol. 1984;120(7):941–51.
4. Joly P, Horvath B, Patsatsi A, Uzun S, Bech R, Beissert S, et al. Updated S2K guidelines on the management of pemphigus vulgaris and foliaceus initiated by the European academy of dermatology and venereology (EADV). J Eur Acad Dermatol Venereol. 2020;34(9):1900–13.
5. Forton FM. The pathogenic role of demodex mites in rosacea: a potential therapeutic target already in erythematotelangiectatic rosacea? Dermatol Ther. 2020;10:1–25.
6. Forton F, De Maertelaer V. Rosacea and demodicosis: little-known diagnostic signs and symptoms. Acta Derm Venereol. 2019;99(1–2):47–52.
7. Cribier B. Rosacea under the microscope: characteristic histological findings. J Eur Acad Dermatol Venereol. 2013;27(11):1336–43.
8. Reinholz M, Tietze JK, Kilian K, Schaller M, Schöfer H, Lehmann P, et al. Rosacea–S1 guideline. J Dtsch Dermatol Ges. 2013;11(8):768–80.
9. Garelli CJ, Refat MA, Nanaware PP, Ramirez-Ortiz ZG, Rashighi M, Richmond JM. Current insights in cutaneous lupus erythematosus immunopathogenesis. Front Immunol. 2020;11:1353.
10. Kempf W, Hantschke M, Kutzner H, Burgdorf WHC. Dermatopathology. Dresden: Steinkopff Verlag; 2008. p. 66–8.
11. Tucker D, Masood S. Seborrheic dermatitis. In: StatPearls [Internet]. StatPearls Publishing; 2019.

Chapter 16
Facial-Sparse Exfoliative Dermatitis: A Hint for Crusted Scabies?

Windy Keumala Budianti and Sandra Widaty

A 54-year-old male with a complaint of thick scaly skin on the trunk, arms, and legs since 3 weeks before admission. Initially there was severe pruritus on the hands and feet then it extended to the stomach and all over the body, except face. Visual analog scale for itch 7–8, prominent at night. There is no history of applying other topical medications. Four months earlier the patient also complained of intense itch and pustular lesion, then was given 2 × 32 mg of methylprednisolone, desloratadine, and moisturizer by a dermatologist who diagnosed with pustular psoriasis. It got better, but when the drug was stopped, the itching got worse so methylprednisolone was increased again, until the last 3 days before admission. There is no previous history of other skin diseases. History of generalized pruritus with night aggravation was present in both of the patient's children.

On physical examination, there was erythema throughout the body, accompanied by thick dusty white scales (Figs. 16.1, 16.2, and 16.3). The face looks very clean, without a single lesion (Fig. 16.1). Subungual hyperkeratosis and thick white-yellowish scales on finger was found (Fig. 16.4).

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

1. Generalized pustular psoriasis
2. Psoriasis erythroderma

W. K. Budianti (✉) · S. Widaty
Department of Dermatology and Venereology, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia

Dr Cipto Mangunkusumo Hospital, Jakarta, Indonesia

Indonesian Society of Dermatology and Venereology, Jakarta, Indonesia
e-mail: windy.keumala07@ui.ac.id

T. M. Lotti et al. (eds.), *Clinical Cases in Exfoliative Dermatitis*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08466-9_16

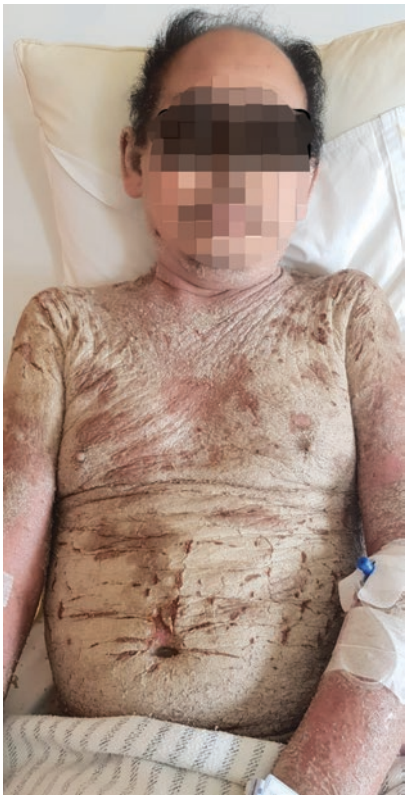

Fig. 16.1 Grossly and exfoliative dusty thickened skin, but facial-sparse

3. Pemphigus foliaceus
4. Atopic dermatitis
5. Crusted scabies

Laboratory findings showed anemia leukocytosis, high count of total eosinophil (1450), hyper-IgE (2192), and hypoalbuminemia. Dermoscopy examination revealed multiple delta wing jet (Fig. 16.5) and microscopic examination with 10% potassium hydroxide examination showed *Sarcoptes scabiei* (Fig. 16.6) so the diagnosis was crusted scabies.

Discussion

Clinical manifestations, investigations, and prompt response to treatment confirmed that the cause for erythroderma in our patient was crusted scabies. Furthermore, the outbreak of scabies in the family members. Clinical diagnosis may be guided by the yellow-to-brown crusts with "piled up sand" appearance affecting the dorsal aspect of nails, fingers, and hands. This thick crust appears in divided segments by deep

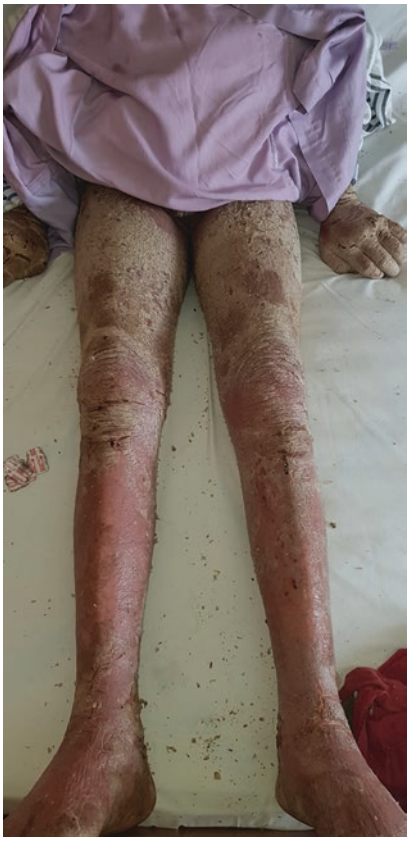

Fig. 16.2 Thick dusty white scale on erythematous skin

fissures with an erythematous background that we describe as resembling a "rocky surface" [1]. A very clean face but grossly thickened skin with large hyperkeratotic warty crusts, gave a hint to the diagnosis that erythroderma was caused by crusted scabies, not generalized pustular psoriasis or other diagnosis. We also found thick deposits of debris accumulate beneath the nails. The palms and soles show deep fissuring of the crusts.

Crusted scabies should always be suspected in any crusted lesion in acquired immune deficiency patients. It can mimic various conditions such as psoriasis, eczema, seborrheic dermatitis, pemphigus foliaceus, Darier disease, pityriasis rubra pilaris, lichen planus, and cutaneous lymphoma. Diagnosis is confirmed using microscopic evidence of mites or eggs, from skin scrapings or on the basis of evidence of mites obtained by dermoscope [2].

The risk factor is generally attributable to immunosuppression either iatrogenic or caused by immunocompromised conditions such as HIV infection, lymphoma, and malnutrition. The current common treatment options are permethrin 5% topical, benzyl benzoate 10%/25% topical, and crotamiton 5%/10% topical with oral ivermectin [3]. As crusted scabies [4], the patient was given topical permethrin for 7

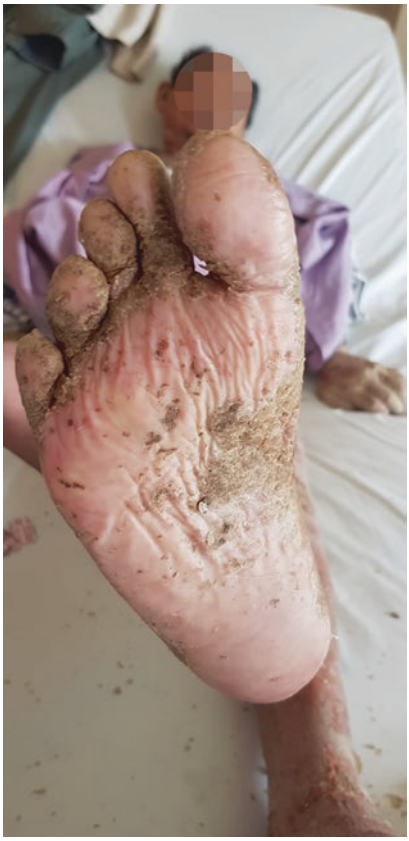

Fig. 16.3 Thick scales with fissures on feet

Fig. 16.4 Thick white-yellowish scales on finger and subungual hyperkeratosis

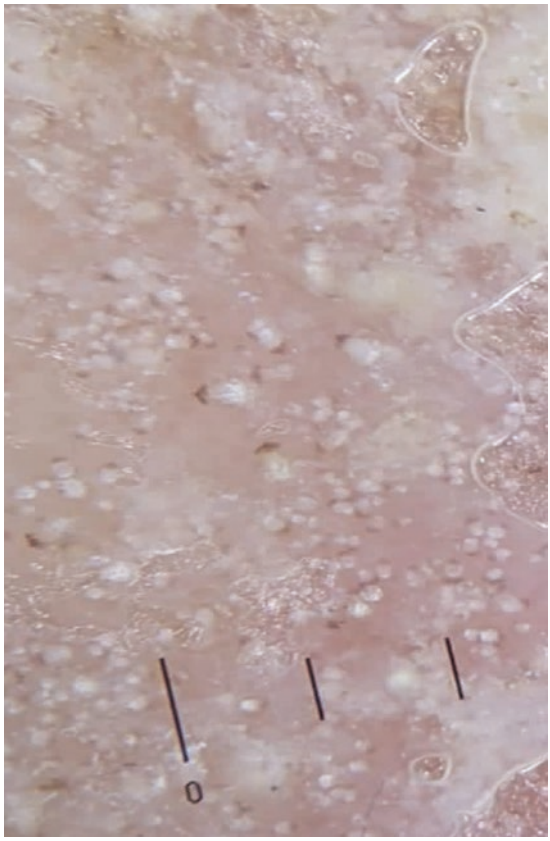

Fig. 16.5 Delta wing jet sign on dermoscopy examination

consecutive days, because systemic ivermectin is not available in our country. After 1 week of therapy, patients showed significant improvement.

Key Point

- Crusted scabies should be considered in an immunocompromised patient presenting with exfoliative dermatitis.

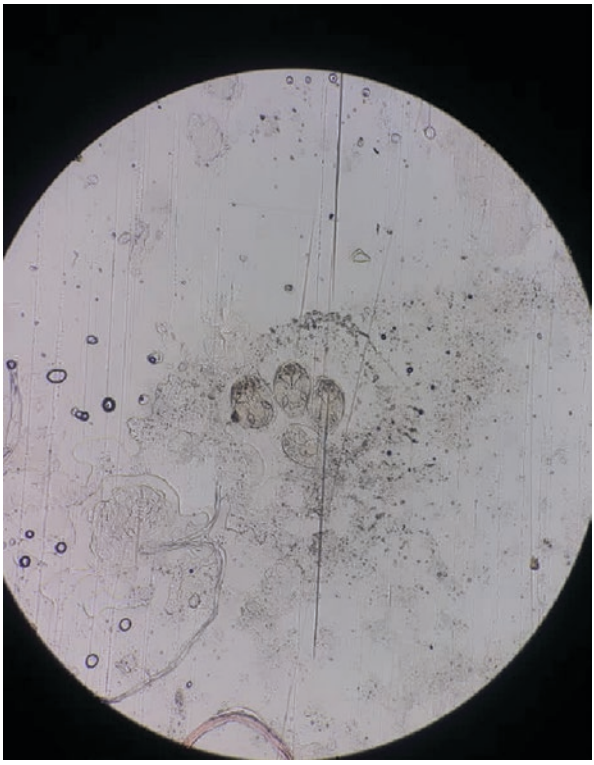

Fig. 16.6 *Sarcoptes scabiei* on microscopic examination

References

1. Cuellar-Barboza A, Cardenas-de la Garza JA, García-Lozano JA, Martinez-Moreno A, Jaramillo-Moreno G, Ocampo-Candiani J. A case of hyperkeratotic crusted scabies. PLoS Negl Trop Dis. 2020;14(3):e0007918.
2. Kulkarni S, Shah H, Patel B, Bhuptan N. Crusted scabies: presenting as erythroderma in a human immunodeficiency virus-seropositive patient. Indian J Sex Transm Dis AIDS. 2016;37(1):72–4.
3. Dressler C, Rosumeck S, Sunderkötter C, Werner RN, Nast A. The treatment of scabies. Dtsch Arztebl Int. 2016;113(45):757–62. https://doi.org/10.3238/arztebl.2016.0757.
4. Wheat CM, Burkhart CN, Burkhart CG, Cohen BA. Scabies, other mites and pediculosis. In: Kang S, et al., editors. Fitzpatrick's dermatology. New York: MacGrawHill; 2019. p. 3274–82.

Chapter 17
Herniated Sac-like Erythematous Lesions on the Trunk with Punctiform Desquamation

Torello M. Lotti, Uwe Wollina, and Umit Tursen

Case Presentation

A 59 year old man was referred from the immunologist to our Institute for more than 30 erythematous herniated sac-like lesions on the trunk (Fig. 17.1) with diameter from 0.3 to 2.7 cm, presented 2 months before after 3 weeks of urticorial-like lesions. There was light erythema, punctiform scaling around the lesions and no pruritus. The subject was in good health. Underlying pathologies including inflammatory, auto-immune, metabolic and neoplastic ones were not shown by the investigations carried out. The skin biopsy taken for histology showed focal loss of elastic fibers, narrowed collagen fibers and no inflammatory infiltrate.

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

- Leprosy
- Amyloidosis
- Morphea

T. M. Lotti (✉)
Department of Science of Communication, Marconi University, Rome, Roma, Italy
e-mail: professor@torellolotti.it

U. Wollina
Department of Dermatologie & Allergologie, Städtisches Klinikum Dresden, Dresden, Germany
e-mail: Uwe.Wollina@klinikum-dresden.de

U. Tursen
Department of Dermatology, Mersin University, School of Medicine, Mersin, Turkey

T. M. Lotti et al. (eds.), *Clinical Cases in Exfoliative Dermatitis*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08466-9_17

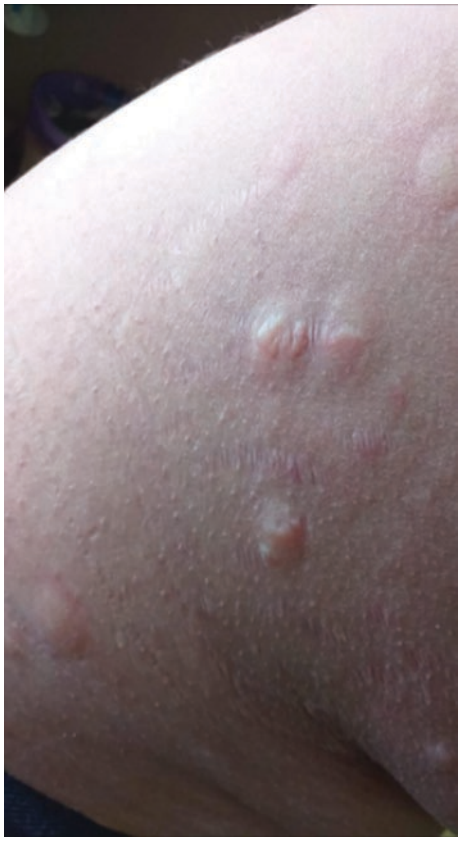

Fig. 17.1 Erythematous herniated sac-like lesions on the trunk

- Lichen sclerosus et atrophicus
- Primary anetoderma, inflammatory type (Jadassohn-Pellizzari)
- Primary non inflammatory anetoderma (Schweninger-Buzzi)
- Elastosis Perforans serpiginosa

Diagnosis

Primary anetoderma, inflammatory type (Jadassohn-Pellizzari)

Discussion [1–4]

Anetoderma (A) is an uncommon condition belonging to the so-called "acquired connective tissue disorders", characterized by flaccid-herniated-elevated-depressed skin areas with focal loss of elastic fibers. A is divided into the primary form

Table 17.1 Primary and secondary anetoderma: clinical presentation

Anetodermas type	
Primary anetoderma	Jadassohn-Pellizzari (preceding inflammatory lesions) Schweninger-Buzzi (no preceding inflammatory lesions)
Secondary anetoderma	• Infectious diseases (Lyme disease, syphilis, HIV, Leprosy, Varicella, Tuberculosis) • Inflammatory disorders (granuloma annulare, Sweet syndrome, Stevens-Johnson syndrome, folliculitis, Lymphocytoma cutis, sarcoidosis) • Drug induced (penicillamine, penicillin) Metabolic disorders (Wilson's disease). • Tumor associated (Reed syndrome, pilomatricoma, cutaneous lymphomas, xanthogranuloma) • Autoimmune (Lupus erythematosus, Anti phospholipid syndrome)

(Jadassohn-Pellizzari type), with preceding cutaneous inflammatory lesions, and Schweninger-Buzzi type with no preceding skin inflammatory lesions. The primary forms of A occur when there is no underlying associated disease with unknown pathogenesis. The Italian author who first described this form was Celso Pellizzari of Florence (Italy) who directed in the years 1906–1920 in Florence the same University Dermatology Institute directed by the first author of this chapter in 2005–2010 (Torello Lotti).

A secondary form of anetoderma is well known, associated to Infective, Inflammatory, Autoimmune and deposition-tumoral conditions (Table 17.1).

Treatment is mandatory in the secondary anetoderma according to the associated-underlying disease. The primary forms are not consistently responding to systemic or localized therapeutic approaches including hydroxychloroquine, penicillin, dapsone, vitamin E. Surgical excision of selected lesions may give good results according to patients' and doctors' opinion.

Key Points

- Anetoderma is a rare skin condition occurring with flaccid-herniated lesions on the skin, always histologically characterized by the focal loss of elastic fibers.
- Primary anetoderma can be of inflammatory type (Jadassohn-Pellizzari) or non inflammatory type (Schweninger-Buzzi). Treatments are apparently useless.
- The Italian Author who first described inflammatory anetoderma (Celso Pellizzari) directed in the years 1906–1920 in Florence the same University Dermatology Institute directed by the first author of this chapter in 2005–2010 (Torello Lotti).
- Secondary anetoderma may be related to infectious, inflammatory and autoimmune diseases which need specific treatments. Secondary anetoderma can be drug induced and tumor-associated.

References

1. Venencie PY, Winkelmann RK, Moore BA. Anetoderma. Clinical findings, associations, and long-term follow-up evaluations. Arch Dermatol. 1984;120(8):1032–9.
2. Fabbri P, Lotti T, Panconesi E. A case of Pellizzari-Jadassohn anetoderma. Clinical and immunopathologic study. G Ital Dermatol Venereol. 1985;120(5):333–7.
3. Casigliani R, Difonzo EM, Ganucci Cancellieri GA, Lotti T. A case of Schweninger-Buzzi anetoderma. G Ital Dermatol Venereol. 1988;123(3):83–5.
4. Wollina U, Mühle D, Lotti T, Vojvodic A. Anetoderma Schweninger-Buzzi: two case reports. Open Access Maced J Med Sci. 2019;7(18):3093–5.

Chapter 18
Homeless Man with Thick Scales on the Skin

Mariana Karwan, Piotr Brzeziński, Justyna Słomka, Aleksandra Kitowska, and Katarzyna Borowska

A 46-year-old man was admitted to the Department of Dermatology as a matter of urgency.

The patient came to the nursing home (alcohol abuse history).

Departments from a history of treatment with Methotrexate several times. In May 2020, he was hospitalized to implement biological treatment due to changes in the X-ray of the lungs, treatment was not implemented and the patient was referred for further diagnostics at the Pulmonology Clinic. On admission lesions covered over 80% of the body surface area. It was 75% covered with thick scales with the largest build-up of feet. The scales gave an unpleasant, rancid swing (rotten odor). Itching and a burning sensation within the skin lesions were reported (Fig. 18.1a–c).

The patient complained of chronic spinal and shoulder joints pain with a feeling of stiffness in the joints of the fingers.

Changes within the nails as a nail plate thickening and onychogryphosis were observed.

Laboratory evaluation was significant for leukocytosis (11,380/μL), renal function parameters were abnormal (Creatinine 0.38 mg/dL, eGFR144) and C-reactive protein was elevated (48 mg/dL).

M. Karwan · J. Słomka · A. Kitowska
Department of Dermatology, Provincial Specialist Hospital in Slupsk, Ustka, Poland

P. Brzeziński (✉)
Department of Dermatology, Provincial Specialist Hospital in Slupsk, Ustka, Poland

Institute of Biology and Environmental Protection, Pomeranian Academy, Slupsk, Poland

K. Borowska
Department of Histology and Embryology with Experimental Cytology Unit, Medical University of Lublin, Lublin, Poland

T. M. Lotti et al. (eds.), *Clinical Cases in Exfoliative Dermatitis*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08466-9_18

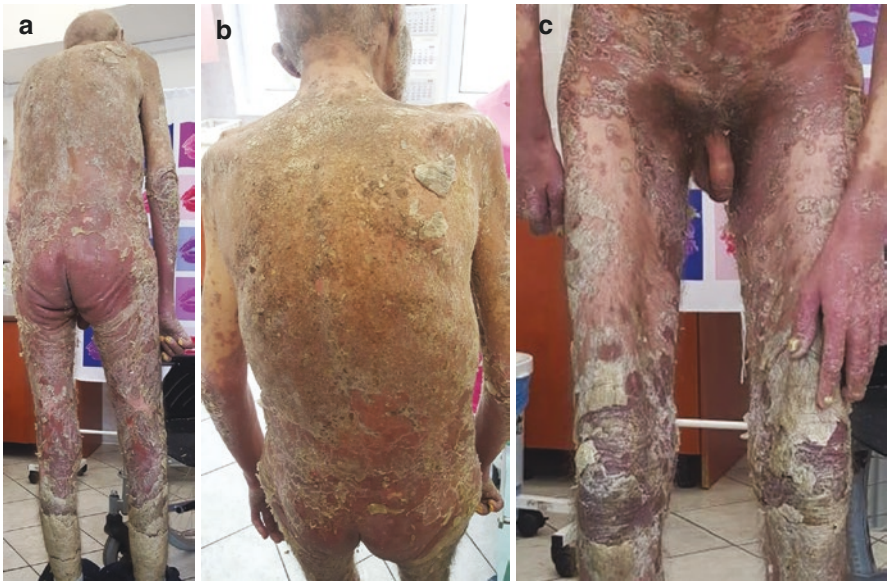

Fig. 18.1 (**a–c**) Skin lesions with scales all over the body

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

1. Nummular Dermatitis (Nummular Eczema)
2. Erythrodermic psoriasis
3. Scabies in homeless (Norwegian scabies)
4. Secondary syphilis
5. Mycosis fungoides
6. Tinea corporis

Histopathology confirmed of diagnosis (Fig. 18.2a–c).

Diagnosis

Erythrodermic psoriasis.

During the hospitalization in the ward general treatment (Vit C 300 mg, Folic acid 5 mg, Clexane 0.4J, Ciprofloxacin 500 mg, and topical treatment (5% salicylic ointment, salicylic oil, steroid liniment, dermocosmetics) were introduced.

The treatment resulted in reduction of joint ailments and improvement of skin lesions in the form of scales removal and reduction of inflammation.

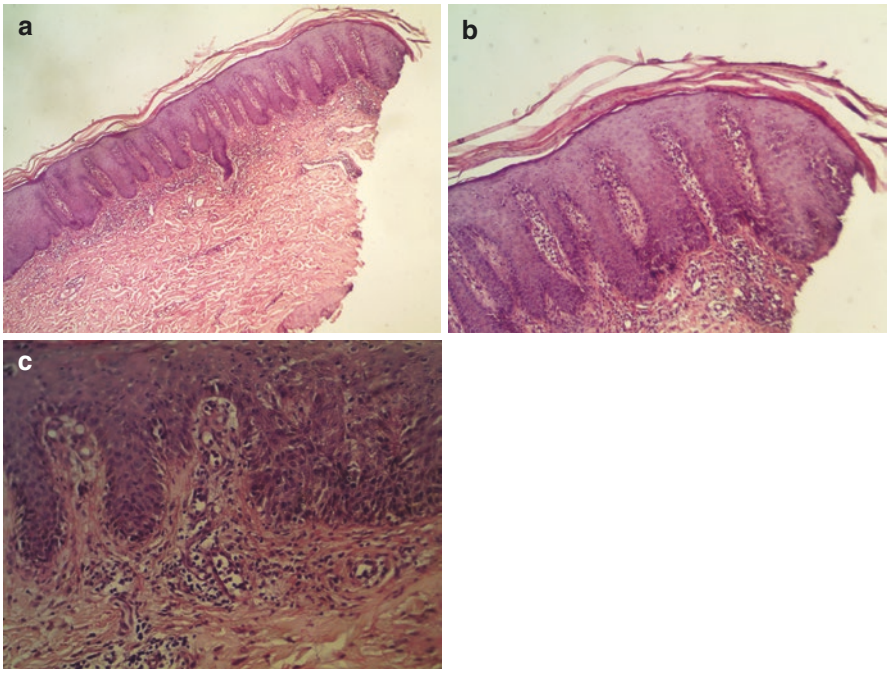

Fig. 18.2 (**a**–**c**) Epidermal hyperplasia, confluent parakeratosis, loss of granular layer and dilated capillaries with thinned suprapapillary plate and prominent papillomatosis (HE ×200)

Discussion

Erythroderma is a dermatological clinical syndrome of generalized erythema and scaling, due to various etiologies. Although the causes may be diverse, most cases of erythroderma have a preexisting skin disease. Patients with previously normal skin often have drug-induced erythroderma or malignancy. Indeed, its early diagnosis allows a fast and adequate care thus improving the prognosis of these entities [1].

The most common cause of erythroderma is erythrodermic psoriasis (responsible for about 25% of all cases). Erythrodermic psoriasis estimated prevalence among psoriatic vulgaris patients ranging from 1.0% to 2.25% [2]. This disease presents with generalized cutaneous findings such as erythema, edema, pruritus, psoriatic plaques, hair loss, and exudative lesions palmoplantar or/and diffuse desquamation. Nail changes are very common. In described case changes as nail plate thickening and onychogryphosis were observed. In order to confirm a diagnosis of erythrodermic psoriasis, clinicians must rule out other plausible causes of erythroderma for example drug eruptions, atopic dermatitis, pityriasis rubra pilaris, contact dermatitis, immunobullous disorders and Sezary syndrome. In addition, patients can have systemic symptoms including fever, chills, lymphadenopathy. Laboratory results may show protein and fluid loss, leukocytosis, elevated C-reactive protein (CRP), hydroelectrolytic abnormalities, anemia and rarely abnormal liver function tests [3].

Various severe complications have been reported for example shock and acute renal failure due to skin fluid loss, acute respiratory distress syndrome and sepsis from skin pathogens (*Staphylococcus aureus*). Laboratory evaluation in described case are significant for leukocytosis. CRP was elevated. Renal function parameters were abnormal. The histologic analysis demonstrates an epidermal perivascular infiltrate of lymphocytes, dilated capillaries, and hyperkeratosis. Additional histological features include some features of classical psoriasis vulgaris including parakeratosis, acanthosis, spongiosis, Munro micro-abscesses, and apoptotic keratinocytes [4]. A epidemiological study in patients with erythrodermic psoriasis revealed a positive history of psoriasis in 78% of cases, a need for systemic therapy in 55% of cases, clinical improvement in 69.4% of cases, disease recurrence in 15% of cases [5]. Erythrodermic psoriasis is more common in men. The male-to-female ratio is 3:1 and an average age is 53.7 years [5]. (Our patient is 46-year old man). The condition presents clinical findings, which include a generalized inflammatory erythema involving at least 75% of the body surface area. Many authors suggest that there must be generalized inflammatory erythema at least 75% of the body surface area. Other authors argue that at least 90% of the body surface area must be affected. Erythrodermic psoriasis can be categorized into two general clinical two subtypes. The first type of erythrodermic psoriasis is relatively stable and prognosis is good. This type is characterized by the presence of psoriatic plaques with gradual additional development of a generalized erythroderma. The second type, which is more commonly seen in the setting of psoriatic arthritis, is often characterized by rapid whole body erythema. This type of disease course is relatively unstable and is more likely to be associated with systemic symptoms and mentioned above abnormal laboratory values [6].

Key Points

- Erythrodermic psoriasis is a rare and severe variant of psoriasis vulgaris, with an estimated prevalence of 1–2.25% among psoriatic patients.
- The condition presents with distinct histopathologic and clinical findings, which include a generalized inflammatory erythema involving at least 75% of the body surface area.
- The management of Erythrodermic psoriasis begins with a comprehensive assessment of the patient's presentation and often requires multidisciplinary supportive measures.

References

1. Aqil N, Nassiri A, Baybay H, Douhi Z, Elloudi S, Mernissi FZ. Erythroderma: a clinical and etiological study of 92 patients. Our Dermatol Online. 2019;10(1):1–6.
2. Boyd AS, Menter A. Erythrodermic psoriasis. Precipitating factors, course, and prognosis in 50 patients. J Am Acad Dermatol. 1989;21(5 pt 1):985–91.

3. Evans AV, Parker JC, Russell-Jones R. Erythrodermic psoriasis precipitated by radiologic contrast media. J Am Acad Dermatol. 2002;46(6):960–1.
4. Zhang F, Li H, Zhou Y, Gu Y, Wang L. Caveolin-1 expression in different types of psoriatic lesions: analysis of 66 cases. Indian J Dermatol. 2014;59(3):225–9.
5. Hawilo A, Zaraa I, Benmously R, et al. Erythrodermie psoriasique: profil epidemio-clinique et therapeutique a propos de 60 cas. [Erythrodermic psoriasis: epidemiological clinical and therapeutic features about 60 cases]. Tunis Med. 2011;89(11):841–7.
6. Alsamarai AM, Alobaidi AHA. Psoriasis is a systemic disease: A proposed approach for inflammation scale calculation. Our Dermatol Online. 2021;12(4):381–6.

Chapter 19
Itching Exfoliating Plaques on Lower Legs

Uwe Wollina

A 48-year-old woman presented with mildly itching erythematous plaques on the lower legs that developed about 6 months ago. She had no medical history of skin diseases or atopic disorders. The lesions did not respond to class I corticosteroids (Fig. 19.1).

Based upon History and Clinical Appearance, What Is Your Diagnosis?

1. Verrucous lichen planus.
2. Nummular eczema.
3. Ringworm.
4. Impetigo contagiosa.
5. Squamous cell carcinoma.

Diagnosis

Nummular eczema.

On examination, we observed erythematous plaques covered with scales. Excoriations were missing. The pruritus was described as mild. A diagnostic skin biopsy was taken. The histopathologic examination revealed perivascular and

U. Wollina (✉)
Department of Dermatology & Allergology, Städtisches Klinikum Dresden, Academic Teaching Hospital of the Technical University Dresden, Dresden, Germany
e-mail: Uwe.Wollina@klinikum-dresden.de

T. M. Lotti et al. (eds.), *Clinical Cases in Exfoliative Dermatitis*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08466-9_19

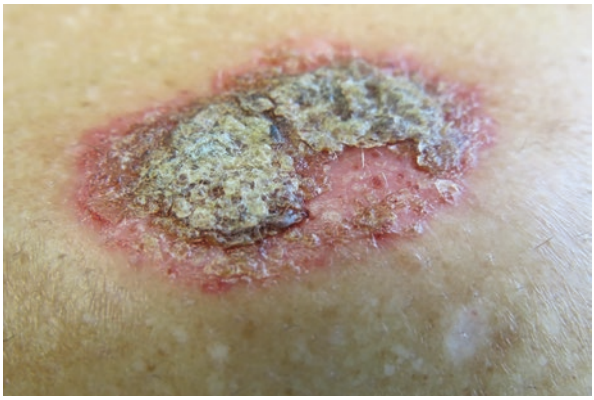

Fig. 19.1 Erythematous plaque with scales on the lower leg

interstitial inflammatory infiltrates composed of eosinophils and some mast cells. Erythrocyte extravasates were observed. The epidermis was acanthotic with a mild spongiosis and infiltration granulocytes. Mycotic elements were missing.

Diagnosis

Nummular eczema.

Discussion

Nummular eczema (also known as microbial eczema) is characterized by sharply defined, coin-shaped, erythematous plaques. Predilections sites are the lower and upper extremities. Typically, these lesions are intensively itching, which was not the case in the present patient.

Nummular eczema is often associated to dry skin. Nummular eczema is part of the spectrum of atopic dermatitis although elevated IgE levels are not mandatory [1].

Diagnosis is made clinically. A mycosis should be excluded by KOH test from skin scrapings. To exclude contact dermatitis, patch testing should be considered. Contact allergies are not uncommon in patients with nummular eczema [2]. Biopsy is rarely necessary. In the present case, we wanted to exclude a squamous cell carcinoma, since the lesions were not as pruritic as in most other cases.

Regular skin care and high or ultra-high potency topical corticosteroids are the treatment of choice. Dupilumab has been investigated for recalcitrant cases with success [3]. Here were removed the scales with a microfiber wound pad (Prontosan® Debridement Pad; B. Braun Melsungen AG, Melsungen, Germany). Afterwards, the lesions were treated topically with betamethasone plus fusidic acid ointment (Fucidine®Creme, Leo Pharma GmbH, Neu-Isenburg, Germany) under occlusion

for 1 week, without occlusion for another 10 days. A complete remission was achieved.

Key Points

- Nummular eczema is a subtype of atopic dermatitis.
- The typical lesions are intensively itching, coin-shaped erythematous plaques.
- Lower limbs are mostly involved.
- Contact allergies are not uncommon among patients with nummular eczema.

References

1. Silverberg NB. Typical and atypical clinical appearance of atopic dermatitis. Clin Dermatol. 2017;35(4):354–9.
2. Jiamton S, Tangjaturonrusamee C, Kulthanan K. Clinical features and aggravating factors in nummular eczema in Thais. Asian Pac J Allergy Immunol. 2013;31(1):36–42.
3. Patruno C, Stingeni L, Hansel K, Ferrucci SM, Tavecchio S, Fabbrocini G, Nisticò SP, Foti C, De Prezzo S, Napolitano M. Effectiveness of dupilumab for the treatment of nummular eczema phenotype of atopic dermatitis in adults. Dermatol Ther. 2020;33(3):e13290.

Chapter 20
Multiple Scaling Erythematous Lesions in the Gluteal Region

Filippo Viviani, Alba Guglielmo, Diego Abbenante, Alessandro Pileri, and Federico Bardazzi

Case Presentation

A 46-year-old woman presented with multiple itching, erythematous lesions in the right gluteal region that had slowly enlarged centrifugally during the previous 6 months. These lesions had been treated with multiple courses of topical steroids, without improvement. She reported a history of hypertension, Hashimoto's disease and, during childhood, a diagnosis of atopic dermatitis. In addition, recent general laboratory investigations were negative. At physical examination, we observed several scaling, erythematous patches on a hyperpigmented background, about 11–12 cm in diameter, in the right gluteal region. No other lesions were found (Fig. 20.1).

Based upon the History and Clinical Appearance, What Is Your Diagnosis?

1. Drug eruption
2. Tinea incognito
3. Psoriasis
4. Eczema

F. Viviani · A. Guglielmo · D. Abbenante · A. Pileri (✉) · F. Bardazzi
Dermatology - IRCCS Policlinico di Sant'Orsola Department of Experimental, Diagnostic and Specialty Medicine (DIMES), Alma Mater Studiorum, University of Bologna, Bologna, Italy
e-mail: filippo.viviani3@studio.unibo.it; diego.abbenante@studio.unibo.it; alessandro.pileri2@unibo.it; federico.bardazzi@aosp.bo.it

T. M. Lotti et al. (eds.), *Clinical Cases in Exfoliative Dermatitis*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08466-9_20

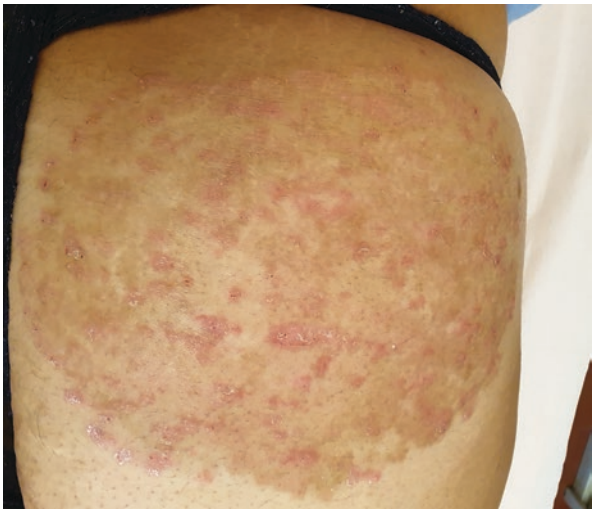

Fig. 20.1 Multiple scaling, erythematous patches in the gluteal region

Diagnosis

Tinea incognito (Fig. 20.2).

Discussion

Direct microscopy of skin scraping samples revealed the presence of several septate hyphae, indicating the diagnosis of tinea incognito caused by dermatophytes. The patient was treated with oral terbinafine 250 mg once a day for 4 weeks combined with topical imidazole, achieving complete remission. Tinea incognito is a variant of dermatophytic superficial skin infection with an atypical clinical presentation due to an erroneous treatment with topical or systemic corticosteroids, as well as topical calcineurin inhibitors. The incidence of this condition is rising as a result of the increasing use (and abuse) of immunosuppressive drugs and self-prescribed topical therapies [1]. On the other hand, prolonged use of topical glucocorticoids for chronic inflammatory dermatoses may inhibit the ability of the host to eliminate the infection, also contributing to a higher incidence of this condition [2]. Therefore, tinea incognito should be taken into account when assessing any chronic, erythematous, scaly lesion, which is unresponsive to topical steroids [3]. Differential diagnosis may depend on the affected area, but the main differentials include: various types of eczema, psoriasis, intertrigo, subacute cutaneous lupus erythematosus, drug eruption and Sweet's neutrophilic dermatosis [4]. A direct mycological examination of skin scrapings and fungal culture, in association with a periodic acid-Schiff stain

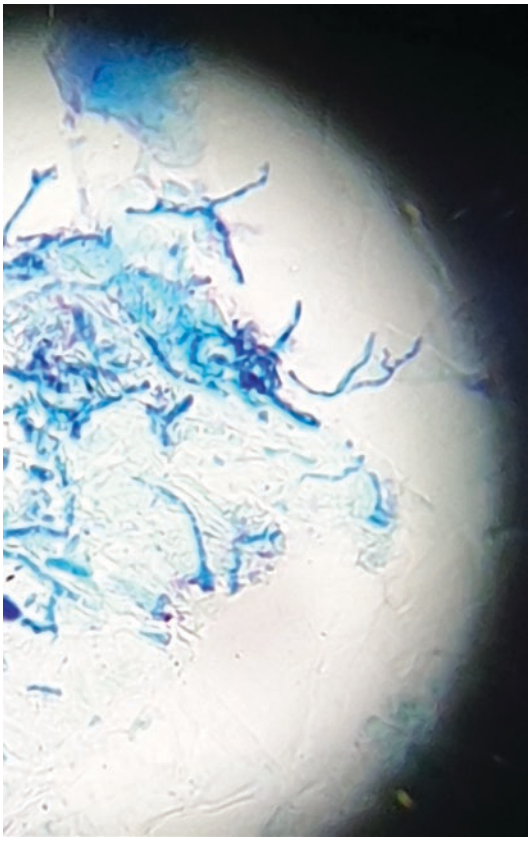

Fig. 20.2 Direct microscopy: septate hyphae

on a skin biopsy, can guide the differentiation between these skin diseases and tinea incognito [5]. Furthermore, real-time polymerase chain reaction (PCR) techniques could represent a major improvement in both speed of diagnosis and sensitivity, compared with traditional methods [6].

Key Points

- Tinea incognito should be considered when assessing any chronic, erythematous, scaly lesion, unresponsive to topical steroids.
- The clinical appearance is atypical and could imitate many skin affections: eczema, psoriasis, intertrigo, subacute cutaneous lupus erythematosus, drug eruption and Sweet's neutrophilic dermatosis.
- Real-time polymerase chain reaction (PCR) techniques could represent a major improvement in the diagnostic process, although direct mycological examination of skin scrapings is often sufficient to make a diagnosis.

References

1. Froidefond M, Dudouet P, Ranque S, Cassir N. Tinea incognito: Primum non nocere. Int J Infect Dis. 2021;103:597–8. https://doi.org/10.1016/j.ijid.2020.11.136.
2. Kalekhan FM, Asfiya A, Shenoy MM, Vishal B, Pinto M, Hegde SP. Role of Tinea unguium and other factors in chronic and recurrent dermatophytosis: a case control study. Indian Dermatol Online J. 2020;11(5):747–52. https://doi.org/10.4103/idoj.IDOJ_515_19.
3. Arenas R, Moreno-Coutiño G, Vera L, Welsh O. Tinea incognito. Clin Dermatol. 2010;28(2):137–9. https://doi.org/10.1016/j.clindermatol.2009.12.011.
4. Dhaher S. Tinea incognito: clinical perspectives of a new imitator. Dermatol Rep. 2020;12(1):8323. https://doi.org/10.4081/dr.2020.8323.
5. Maul J-T, et al. A case of tinea incognita and differential diagnosis of figurate erythema. Med Mycol Case Rep. 2017;18:8–11.
6. Đorđević Betetto L, Žgavec B, Bergant Suhodolčan A. Psoriasis-like tinea incognita: a case report and literature review. Acta Dermatovenerol Alp Pannonica Adriat. 2020;29(1):43–5. https://doi.org/10.15570/actaapa.2020.10.

Chapter 21
Mysterious Skin Lesions

Elena Sergeevna Snarskaya, Olga Yuryevna Olisova, and Kseniia Dmitrievna Vasileva

Short Clinical Story of the Patient

A 48-year-old patient considers herself to be ill for several years, when for no apparent reason she noticed the occurrence of small yellowish nodules on the skin of the neck, armpits and elbow folds, accompanied by moderate itching. Gradually, the nodules merged with each other to form diffuse plaques. She did not go to doctors, did not receive any treatment. Family members did not have similar symptoms. During the last year, she noticed a decrease in the visual acuity when visiting an ophthalmologist, during the examination of the fundus of the eye, angioid streaks were diagnosed in the area of Bruch's membrane, and in the central zone there were atrophic changes. There was absence of signs of an active subretinal neovascular membrane in the macular zone, it was decided to monitor this patient. Also, the ophthalmologist, having noticed pathological changes on the skin, sent the patient for a consultation to the V. A. Rakhmanov Clinic of Skin and Venereal Diseases.

St. localis The clinical picture is represented by whitish-yellowish papules, sometimes merging into diffuse plaques with a linear pattern of location, on the background of thickened, flabby skin of yellow and brown colour, which is noticeably sagging and easily folds (Figs. 21.1 and 21.2).

During the histological analysis, pathomorphological changes in the structures of the dermis have been found mainly in the middle and lower parts, where there is an uneven location and loss of normal structures of elastic fibers, they are thickened, fragmented in the form of lumps and peculiarly twisting structures. In the papillary layer, the amount of elastic fibers is reduced (Fig. 21.3).

E. S. Snarskaya (✉) · O. Y. Olisova · K. D. Vasileva
V. A. Rakhmanov Department of Skin and Venereal Diseases, I.M. Sechenov First Moscow State Medical University, Sechenov University, Moscow, Russia

T. M. Lotti et al. (eds.), *Clinical Cases in Exfoliative Dermatitis*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08466-9_21

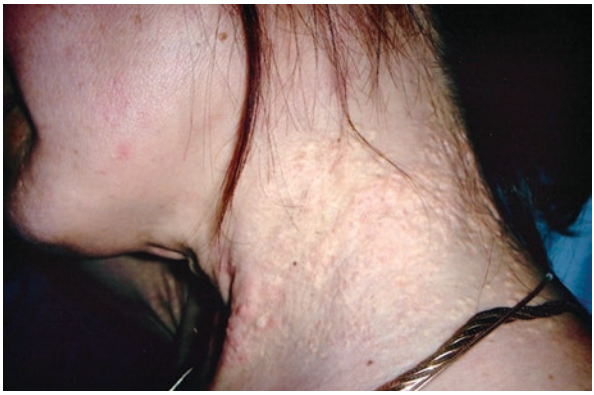

Fig. 21.1 Yellow nodules, laxity in the neck

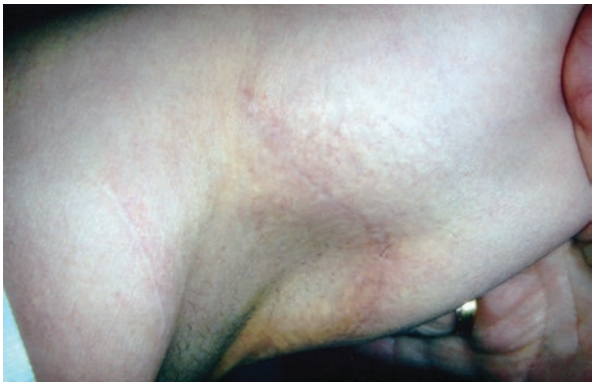

Fig. 21.2 Pseudoxanthoma elasticum in the armpits

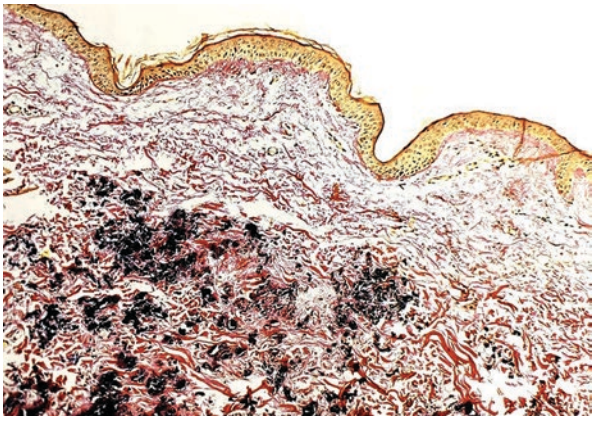

Fig. 21.3 Pathomorphology of Gronblad-Strandberg syndrome. Staining with picrofuchsin and fuchsin. Magnification ×120. Epidermis with signs of weak atrophy, in the dermis—foci of degeneration of elastic fibers throughout the depth. Perifocal excess collagen formation

Taking into account the data of the anamnesis (including angioid streaks in the area of Bruch's membrane), the clinical and histological picture, the diagnosis is Gronblad-Strandberg Syndrome. The patient was registered with a general

practitioner, the ophthalmologist and the dermatovenerologist. It is also necessary to observe by a cardiologist, because the disease is characterized by a violation of the formation of elastic fibers in the cardiovascular system. The patient is advised to avoid taking non-steroidal anti-inflammatory drugs and antiplatelet drugs because of the increased risk of the gastrointestinal bleeding, excessive physical activity due to the risk of retinal haemorrhage. When a subretinal neovascular membrane appears, it is necessary to use intravitreal administration of VEGF inhibitors and focal laser coagulation of the subretinal neovascular membrane. As far as skin occurrences are concerned: surgery for esthetic reasons is not recommended as there are no life-threatening symptoms.

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

List of three possible clinical diagnoses:

- Intense solar elastosis (actinic elastosis)
- Increased skin laxity due to the deficiency of vitamin K-dependent clotting factor
- Ehlers-Danlos syndrome

Diagnosis

Gronbland-Strandberg Syndrome.

Discussion

Pseudoxanthoma elasticum (PXE, Gronblad-Strandberg syndrome) is a genetic metabolic disease with autosomal recessive inheritance caused by mutations in the ABCC6 gene on the 16 chromosome. The lack of functional protein ABCC6 leads to ectopic mineralization, which is more evident in the elastic tissues of the skin, eyes and blood vessels. The clinical prevalence of PXE is estimated at 1 in 100,000 to 1 in 25,000 of the general population, with a slight predominance of women [1–4]. Main features: skin lesion—100% (skin is senile and sagging), retinal involvement—100% (Bruch's membrane calcification, subretinal neovascularization with bleeding can lead to blindness), vascular lesion—60% (lameness, minor strokes, angina pectoris, myocardial infarction), gastrointestinal bleeding—10% (more often in the upper sections) [1].

It has been described recently that the deficiency of inorganic pyrophosphate (PPi, calcification inhibitor) may be the main cause of ectopic calcification in this

disease and in other genetic disorders associated with ENPP1 or CD73 mutations. PPi inhibits crystallization and the growth of crystalline calcium phosphate phases such as hydroxyapatite. The joint activity of ABCC6 (expressed in hepatocytes and proximal tubule cells) and NPP1 (in arteries and capillaries) generates AMP in addition to PPi. AMP is rapidly converted to adenosine by CD73, which inhibits tissue nonspecific alkaline enzyme (TNAP). TNAP breaks PPi to form inorganic phosphate and promotes the deposition of hydroxyapatite in ectopic tissues. Thus, ABCC6, NPP1, and CD73 increase systemic PPi synthesis and decrease endogenous degradation of PPi through TNAP inhibition. An increased prevalence of kidney stones has also been reported recently in patients with PXE [5, 6].

Modern data indicate that TGF-β is an important mediator of vascular calcification. In addition to binding to its receptor, TGF-β modulates the activity of the ABCC6 promoter [7].

Nowadays there is no specific treatment or prophylactic therapy for patients with PXE. Bisphosphonates such as etidronic acid seem to be promising for preventing cardiovascular calcifications, and intraocular injections of anti-vascular endothelial growth factor (VEGF) limit neoangiogenesis [5].

Solar elastosis and pseudoxanthoma elasticum show an abnormal elastic tissue, but in solar elastosis this material is located in the upper 1/3 of the dermis and is present as dense masses rather than individually altered fibers. Also, these dense masses always show negative coloration for calcium.

Increased skin laxity due to the deficiency of ***vitamin K-dependent clotting factor*** is an autosomal recessive disorder caused by mutations in the GGCX or VKORC gene.

In ***Ehlers-Danlos syndrome*** the ABCC6 genetic mutation is absent, and there are also certain clinical features (joint hypermobility, increased fragility of blood vessels, flat feet, etc.)

Key Points

- The clinical prevalence of PXE is estimated at 1 in 100,000 to 1 in 25,000 of the general population, with a slight predominance of women.
- Main features of PXE are skin lesions, retinal involvement, vascular lesions and gastrointestinal bleeding
- It is important to conduct medical genetic consultation in order to confirm the diagnosis and exclude other pathologies (solar elastosis, sickle cell anemia, Ehlers-Danlos syndrome, etc.)

References

1. Terry SF, Uitto J. Pseudoxanthoma elasticum. In: GeneReviews®. Seattle, WA: University of Washington; 2020. https://www.ncbi.nlm.nih.gov/books/NBK1113/. Accessed 13 Dec 2020.
2. Germain DP. Pseudoxanthoma elasticum. Orphanet J Rare Dis. 2017;12(1):85.
3. Panagou E, Ratynska M, Heelan K. Pseudoxanthoma elasticum-like papillary dermal elastolysis: a case report and review of literature. Int J Dermatol. 2019;58(1):93–7.

4. Tsang SH, Sharma T. Inborn errors of metabolism: pseudoxanthoma elasticum. Adv Exp Med Biol. 2018;1085:187–9.
5. Letavernier E, Bouderlique E, Zaworski J, Martin L, Daudon M. Pseudoxanthoma elasticum, kidney stones and pyrophosphate: from a rare disease to urolithiasis and vascular calcifications. Int J Mol Sci. 2019;20(24):6353. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6940945/. Accessed 13 Dec 2020.
6. Li Q, van de Wetering K, Uitto J. Pseudoxanthoma Elasticum as a Paradigm of Heritable Ectopic Mineralization Disorders. Am J Pathol. 2019;189(2):216–25.
7. Van Gils M, Nollet L, Verly E, Deianova N, Vanakker OM. Cellular signaling in pseudoxanthoma elasticum: an update. Cell Signal. 2019;55:119–29.

Chapter 22
Palmoplantar Pustular Rash in a 41-Year-Old Woman

Lyudmila M. Smirnova, Ekaterina V. Orlova, and Gaiane A. Gabrielian

A 41-year-old woman patient with a history of psoriasis occurring for 30 years but without a family history of such condition and diagnosed with rheumatoid arthritis went to the dermatology department for received biologic therapies due to his unsatisfaction with the efficacy of the traditional treatment. We administered 400 mg certolizumab pegol (it is a PEGylated Fab′ fragment of a humanized tumour necrosis factor α (TNF-α) inhibitor monoclonal antibody) subcutaneously once every 4 weeks. However, we was observed palmoplantar pustular rash at Week 20 of treatment (Figs. 22.1 and 22.2).

The histology of a skin biopsy from the affected areas: parakeratosis, acanthosis, neutrophils in stratum corneum and a dermal infiltrate of lymphocytes.

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

- Pustular bacterid (Andrews)
- Cutaneous adverse reactions
- Hand eczema
- Paradoxical psoriasis

Diagnosis

Paradoxical psoriasis.

L. M. Smirnova · E. V. Orlova · G. A. Gabrielian (✉)
Department of Dermatology and Venereology, Sechenov University, Moscow, Russia

T. M. Lotti et al. (eds.), *Clinical Cases in Exfoliative Dermatitis*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08466-9_22

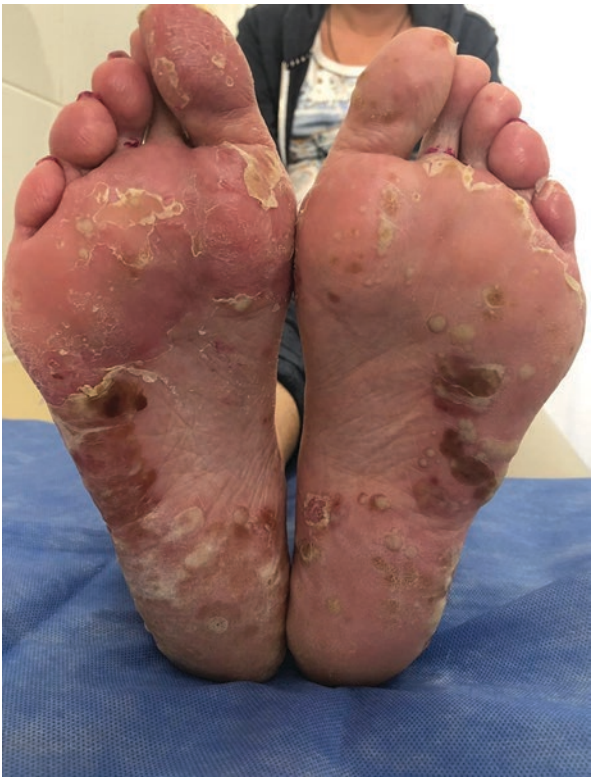

Fig. 22.1 Sterile pustules with erythema, hyperkeratosis, and scaling on the soles

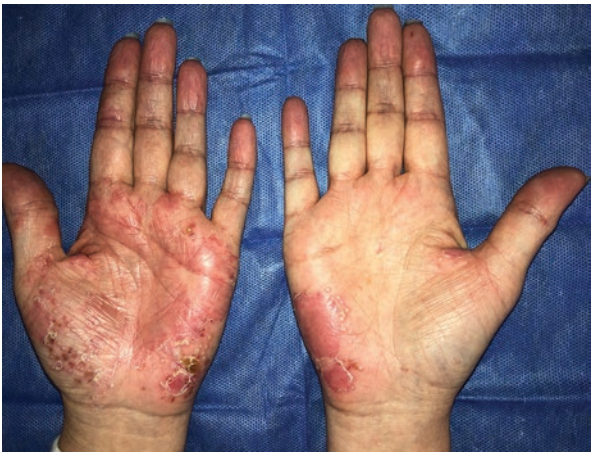

Fig. 22.2 Multiple pustules studded on the palmar surface of the hands with an areas of erythematous desquamative changes

Discussions

It is established that anti-TNF-α agents can cause a *paradoxical psoriasis* (PP) which are defined as the occurrence under TNF-α inhibitors therapy of a pathological condition that usually responds to this class of drug. Thus, TNF-α inhibitors can worsen the course of a previous disease (for example, exacerbation of psoriasis or psoriatic arthritis (PsA) in the treatment of TNF-α inhibitors). PP is observed in about 2–5% of patients treated with anti-TNF-α drugs, with a slight predilection for women. The time between the onset of PP and the introduction of the treatment can range from a few days to several months. The most frequently reported clinical presentations of PP are palmoplantar pustular eruption, plaque-type and guttate psoriasis, and nail and scalp involvement have also been described. Paradoxical psoriasis (PP) occurring under TNF-α inhibitors therapy may be induced or exacerbated by biological agents without identified predisposing factors. However, in half of the patients who were prescribed another TNF-α inhibitor, a relapse of skin changes was observed, which also speaks in favor of a class effect of TNF-α blocking agents rather than a drug-specific adverse event [1–3].

Biopsy samples of anti-TNF-α agents induced paradoxical psoriasis are histologically identical to those of patients with idiopathic psoriasis (in contrast to the histology seen in patients with psoriasis induced by other medications), implying that the mechanism of action of the two processes is similar or identical. Though, classical psoriasis is a T-cell mediated autoimmune disease driven by TNF, characterised by T-cells memory, and a relapsing disease course. In contrast, paradoxical psoriasis is caused by the absence of TNF and represents an ongoing type I interferon-driven innate inflammation that fails to elicit T-cell autoimmunity and lacks memory T cell-mediated relapses. TNF-α, IL-17 and IFN-α are the main cytokines that contribute to the development of psoriatic lesions. TNF-α inhibits the activity of plasmacytoid dendritic cells (pDC), which are key producers of IFN-α. During anti-TNF-α treatment, there is an unopposed IFN-α production by pDC. In parallel, IFN-α leads to the expression of chemokines such as CXCR3 on T cells, favouring T cell homing to the skin. IFN-α also stimulates and activates T cells to produce TNF-α and IL-17, sustaining inflammatory mechanisms for psoriasis lesions [1, 3–5]. Given the above, the diagnosis of paradoxical psoriasis is beyond doubt.

Pustular bacterid Andrew (PbA) is characterized by sterile pustules with a red halo but not scaly erythema on the trunk and extremities accompanied with intermittent fever up. The disease seems to be induced by upper respiratory infection, especially streptococcal infection (anti-streptolysin O (ASO) titer is often elevated at the onset of the disease). It is possible to differentiate by typical clinical manifestations as follows: coincidence with an infection, no personal or family history of psoriasis, isolated sterile pustules and no lesions of psoriasis vulgaris, good response to antibiotics, and a short course. Additionally, the typical pustules in PbA are observed on the palms, soles, and the dorsal surface of the hands and feet, while those in (PP) are on the palm or sole, but not on the dorsal surface of the hand or

foot. Clinicians should consider this diagnosis in patients who present with these clinical manifestations and further case accumulation will contribute to the better understanding of the disease [6].

Cutaneous adverse reactions to drugs are common and encompass a variety of mild to severe and life-threatening reactions. Acute generalized exanthematous pustulosis (AGEP) represents a severe, usually drug-related skin reaction characterized by acute formation of sterile pustules on an erythematous background, fever and neutrophilia. Although many causative factors leading to AGEP have been described, it is, in over 90% of cases, associated with the ingestion of drugs. Aminopenicillins, pristinamycin, sulphonamides, quinolones, hydroxychloroquine, terbinafine and diltiazem are the most frequent causative drugs. AGEP develop an acute rash with pinhead-sized pustules on an erythematous oedematous base, predominantly in the large pleats (axillary folds, inguinal folds). This eruption typically begins with an abrupt onset, appearing within 24 h to 4 days after initiation of medication. The most common symptoms are burning and pruritus. The eruption generally regresses in 10 days. Typically, the biopsy shows spongiform subcorneal and/or intraepithelial pustules, an oedematous papillary dermis and perivascular infiltrates with neutrophils and some eosinophils [7].

Hand eczema may sometimes be difficult to distinguish from pustular palmoplantar psoriasis. A careful medical history, including family history and previous skin conditions, should be taken, and a clinical examination, looking for other psoriasis symptoms, should be performed. Biopsies may add information, although differentiation here is also challenging. Sometimes, it may be necessary to follow the development of the lesion to differentiate here.

Key Points

- Paradoxical psoriasis (PP) occurring under TNF-α inhibitors therapy may be induced or exacerbated by biological agents without identified predisposing factors. PP is observed in about 2–5% of patients treated with anti-TNF-α drugs.
- The most frequently reported clinical presentations of PP are palmoplantar pustular eruption, plaque-type and guttate psoriasis, and nail and scalp involvement have also been described
- TNF normally inhibits PDC maturation from hematopoietic progenitors as well as IFN production, and the inhibition of TNF may allow unlimited and unregulated production of IFN by PDCs
- Plasmacytoid dendritic cells (PDCs) and their production of interferon—(IFN) appear to be the key factors in psoriasis induction in patients with paradoxical psoriasis
- Biopsy samples of anti-TNF-α agents induced paradoxical psoriasis are histologically identical to those of patients with idiopathic psoriasis
- Investigation of the pathogenesis of paradoxical psoriasis not only is helpful to guide clinicians to better manage patients, but also may contribute to the discovery of new therapeutic targets in the future

References

1. Toussirot E, Aubin F. Paradoxical reactions under TNF-α blocking agents and other biological agents given for chronic immune-mediated diseases: an analytical and comprehensive overview. RMD Open. 2016;2(2):e000239. https://doi.org/10.1136/rmdopen-2015-000239.
2. Brown G, et al. Tumor necrosis factor-alpha inhibitor-induced psoriasis: systematic review of clinical features, histopathological findings, and management experience. J Am Acad Dermatol. 2017;76:334–41.
3. Puig L. Paradoxical reactions: anti-tumor necrosis factor alpha agents, ustekinumab, secukinumab, ixekizumab, and others. Curr Probl Derm. 2018;53:49–63.
4. Mylonas A, Conrad C. Psoriasis: classical vs. paradoxical. The Yin-Yang of TNF and type I interferon. Front Immunol. 2018;9:2746.
5. Conrad C, Di Domizio J, Mylonas A, Belkhodja C, Demaria O, Navarini AA, Lapointe AK, French LE, Vernez M, Gilliet M. TNF blockade induces a dysregulated type I interferon response without autoimmunity in paradoxical psoriasis. Nat Commun. 2018;9(1):25. https://doi.org/10.1038/s41467-017-02466-4.
6. Kamiya K, Ohtsuki M. Acute generalized pustular bacterid. J Gen Fam Med. 2018;19(1):32–3. https://doi.org/10.1002/jgf2.141.
7. Feldmeyer L, Heidemeyer K, Yawalkar N. Acute generalized exanthematous pustulosis: pathogenesis, genetic background, clinical variants and therapy. Int J Mol Sci. 2016;17:1214. https://doi.org/10.3390/ijms17081214.

Chapter 23
Recurrent Erythroderma in a 56-Year-Old Female

Alexandra-Irina Butacu and George-Sorin Tiplica

Case Presentation

A 56-year-old female with no significant pathological personal history, presented to the Dermatological Department for the recurrence of an erythematous, scaly eruption, which involved more than 90% of the skin, evolving for 6 months.

The lesions consisted of erythematous plaques, covered by thick white scales on the face and extremities (Figs. 23.1 and 23.2) and by fine silver scales on the trunk and proximal regions of the limbs (Figs. 23.3 and 23.4), in association with erosions and hemorrhagic crusts.

Regarding symptomatology and history of the lesions, the patient stated a persistent burning, stinging sensation of the lesions in association with pruritus, and the initial appearance of the eruption 6 months prior, with one or two episodes per month, without identifying any triggering factors. Clinical examination did not identify any lymphadenopathy. Local treatment was applied, using low potency topical steroids and emollients, with minimal improvement.

The patient denied intake of any drugs prior to the appearance of lesions, any photosensitivity or any systemic symptoms.

A complete blood panel was conducted, including a complete blood count, which identified eosinophilia (15.80%) and testing the liver and renal function which were within normal limits. Urine analysis did not detect any pathological changes. No autoimmune markers were identified, including antinuclear antibodies, antithyroperoxidase antibodies, cANCA, pANCA or the complement and its fractions (C3, C4).

A.-I. Butacu (✉) · G.-S. Tiplica
2nd Department of Dermatology, Colentina Clinical Hospital, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

T. M. Lotti et al. (eds.), *Clinical Cases in Exfoliative Dermatitis*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08466-9_23

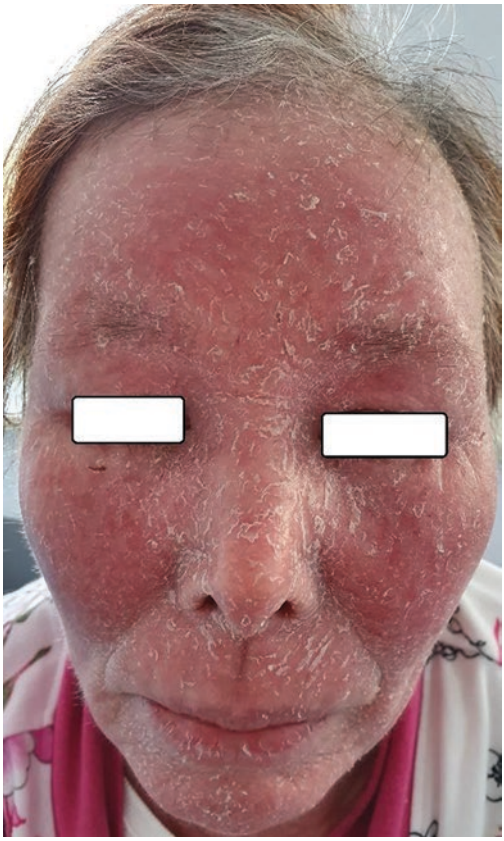

Fig. 23.1 Erythematous, scaly eruption of the face in a 56-year-old female

Immunoglobulin E presented a high titer of 861.00 IU/mL and inflammation markers were present, with elevated levels of the erythrocyte sedimentation rate. Immunoglobulins A, M, G were within normal limits.

The coproparasitological test did not identify any parasites, mucous, blood or purulent discharge.

A bone marrow cytology was also performed and did not detect and pathological changes.

A chest X-ray did not identify any pathological changes.

Two punch biopsies were performed, followed by histopathological examination, both identifying irregular acanthosis, agranulosis, spongiosis, minimal lymphocyte exocytosis and a minimal inflammatory infiltrate in the papillary dermis consisting of lymphocytes, histocytes, eosinophils and melanophages. No atypical lymphocytes were observed, nor the presence of mitoses.

Furthermore, immunohistochemical studies were performed and identified CD3+, CD2+, CD5+, CD7+, CD4+, CD8+, CD25+, CD20+, CD30+ lymphocytes in the inflammatory infiltrate with a Ki67 index of 10%.

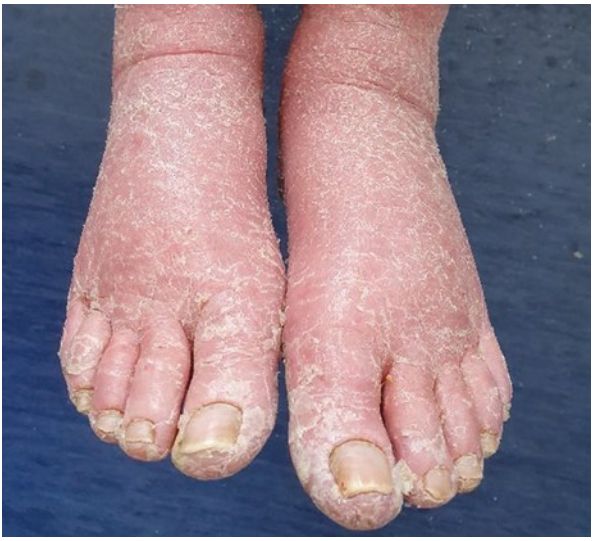

Fig. 23.2 Erythematous, pruritic plaques covered by thick white scales involving both feet

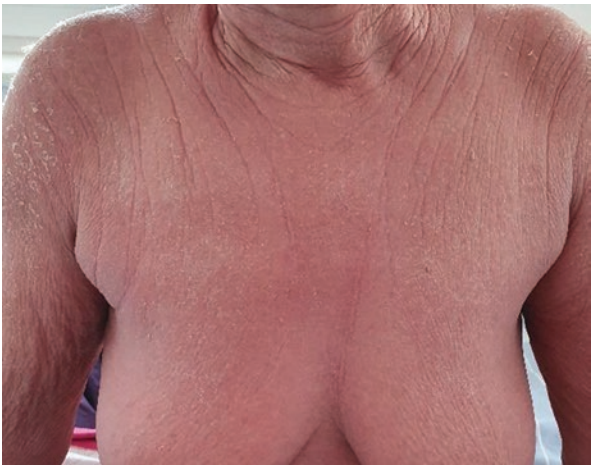

Fig. 23.3 Discrete erythematous plaques covered by fine silver scales located in the trunk

Therapy was initiated and included oral antihistamines and systemic steroids with favorable evolution and the patient was referred to the Allergology Department.

What Is Your Diagnosis?

Allergic contact dermatitis
- Drug-induced hypersensitivity syndrome
- Mycosis fungoides
- Actinic reticuloid

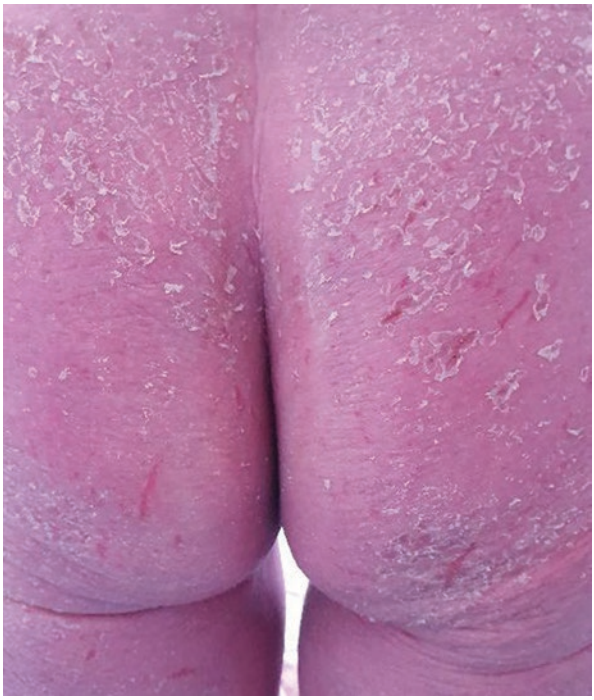

Fig. 23.4 Erythematous, scaly plaques on the buttocks associated with erosions

Diagnosis

Allergic contact dermatitis.

Discussion

Allergic contact dermatitis represents an allergic reaction caused through a delayed-type hypersensitivity response (type 4) by small molecules called haptens (less than 500 Da), in contact with a previously sensitized person's skin and accounts for approximately 20% of contact dermatoses [1]. In contrast to irritant contact dermatitis, clinical findings appear after the second contact with the incriminated agent, usually after 48–72 h and the lesions are disseminated throughout the body. The most frequently encountered allergic agents include plants (such as the poison ivy and poison oak), metals and jewelry (especially nickel), rubber, fragrances and flavorings in different cosmetic or food and drinks, hair dyes or tattoo ink or adhe-

sives such as glues [2]. Clinical findings include pruritic, erythematous, scaly eruptions that may lead to erythroderma in severe cases. Management of allergic contact dermatitis includes identifying the triggering factor through patch testing and avoiding the specific agents as well use of topical or systemic antihistamines and steroids [1].

Drug-induced hypersensitivity syndrome was excluded by the fact that the patient denied any associated morbidities and use of any drugs in the last year and by the absence of systemic findings. Drug-induced hypersensitivity syndrome represents a drug eruption (frequently caused by abacavir, dapsone, nevirapine) which seems to be characterized by a close relation to the reactivation of certain herpes viruses (especially type 6) [3] and which associates eosinophilia and systemic findings including fever, cutaneous eruptions and multiorgan failure [4].

Mycosis fungoides represents the most frequent T-cell cutaneous lymphoma, encompassing more than 50% of all primary cutaneous lymphomas and is characterized by three stages of evolution: macules, plaques and tumors. Erythroderma may be associated with mycosis fungoides *de novo* or in patients with a history of mycosis fungoides and is characterized by the presence of well-demarcated plaques. Diagnosis of mycosis fungoides is establish by histopathological examination, immunohistochemical studies and PCR [5]. Additionally, Sezary syndrome is a particular type of T-cell lymphomas characterized by the triad: erythroderma, generalized lymphadenopathy and circulating malignant T cells [6].

Actinic reticuloid also called chronic actinic dermatitis represents a rare and severe photodermatitis which usually affects elderly males and is characterized by the appearance of cutaneous plaques similar to those identified in mycosis fungoides and other T-cell lymphomas. Management of actinic reticuloid is focused on avoiding sun exposure and applying broad spectrum sunscreens [7].

Key Points

- Allergic contact dermatitis represents a delayed-type hypersensitivity response to small molecules called haptens in contact with a previously sensitized person's skin.
- The most frequently encountered allergic agents include plants, metals, jewelry, rubber, fragrances and flavorings in different cosmetic or food and drinks, hair dyes or tattoo ink or adhesives.
- Clinical findings include pruritic, erythematous, scaly eruptions that may lead to erythroderma in severe cases.
- Management of allergic contact dermatitis includes identifying and avoiding the triggering agents and use of topical or systemic antihistamines and steroids.

References

1. Murphy PB, Atwater AR, Mueller M. Allergic contact dermatitis. In: StatPearls. Treasure Island, FL: StatPearls Publishing; 2020.
2. Fonacier LS, Sher JM. Allergic contact dermatitis. Ann Allergy Asthma Immunol. 2014;113(1):9–12. https://doi.org/10.1016/j.anai.2014.03.018.
3. Watanabe H. Recent advances in drug-induced hypersensitivity syndrome/drug reaction with eosinophilia and systemic symptoms. J Immunol Res. 2018;2018:5163129.
4. M'rad MB, Leclerc-Mercier S, Blanche P, Franck N, Rozenberg F, Fulla Y, Guesmi M, Rollot F, Dehoux M, Guillevin L, Moachon L. Drug-induced hypersensitivity syndrome: clinical and biologic disease patterns in 24 patients. Medicine (Baltimore). 2009;88(3):131–40.
5. Zinzani PL, Ferreri AJ, Cerroni L. Mycosis fungoides. Crit Rev Oncol Hematol. 2008;65(2):172–82. https://doi.org/10.1016/j.critrevonc.2007.08.004.
6. Foss FM, Girardi M. Mycosis fungoides and Sezary syndrome. Hematol Oncol Clin North Am. 2017;31(2):297–315.
7. Zak-Prelich M, Schwartz RA. Actinic reticuloid. Int J Dermatol. 1999;38(5):335–42.

Chapter 24
Recurrent Erythroderma in the Course of Pityriasis Rubra Pilaris in a 41-Year-old Female

I. G. A. A. Elis Indira, Nyoman Suryawati, and Roslina Horo

A 41 years old female patient was referred from the Emergency Ward to the Dermatology Department in Sanglah General Hospital, Denpasar, Bali, with suspect seborrheic dermatitis. The patient presented with generalized erythema, itching and dryness of skin for the last 2 weeks.

Erythema, dryness and scaling started from the scalp and face and slowly involved the trunk and limbs. The skin was very dry and itchy thus made movement difficult. There was also discoloration of the finger and toe nails. She also experienced the same condition 3 months ago (Figs. 24.1, 24.2, and 24.3).

Based Upon History and Clinical Appearance, What Is Your Diagnosis?

1. Recurrent erythroderma due to pityriasis rubra pilaris
2. Recurrent erythroderma due to seborrheic dermatitis
3. Recurrent erythroderma due to cutaneous T-Cell Lymphoma

From physical examination we observed there was generalized erythema and scaling that involved more than 90% of the total body surface area with an orangish tinge. The skin was severely dry and it formed an ichthyosiform scale. Ectropion was seen on both eyes and eclabium on the lips. Moreover, there was multiple erosion all over the body. The patient's movements were restricted. Respiratory and

I. G. A. A. E. Indira (✉) · N. Suryawati · R. Horo
Department of Dermatology and Venereology, Faculty of Medicine, Sanglah General Hospital, Universitas Udayana, Denpasar, Bali, Indonesia

Indonesian Society of Dermatology and Venereology, Jakarta, Indonesia
e-mail: elisindira@unud.ac.id; suryawati@unud.ac.id

T. M. Lotti et al. (eds.), *Clinical Cases in Exfoliative Dermatitis*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08466-9_24

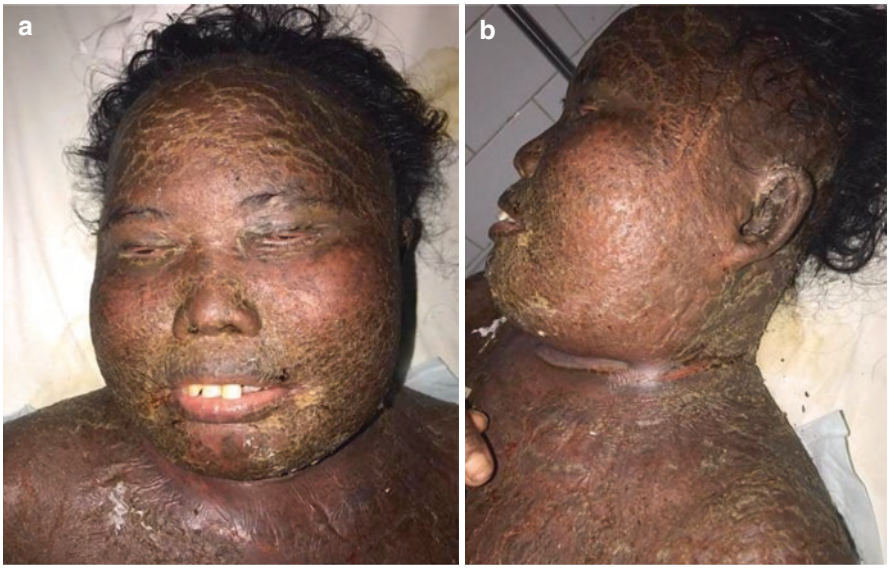

Fig. 24.1 (**a**, **b**) There was an ichthyosiform thick scale on the scalp, face and body that led to ectropion in the area of both eyelids, eclabium, crumpled ears and erosion on the neck

cardiovascular systems were within normal limits. Nails were thickened and became yellowish in colour with whitish longitudinal bands. Subungual hyperkeratosis was also found. Palms and soles also showed hyperkeratotic.

Laboratory investigations The PRP most commonly associated with HIV infection but our patient's HIV serology test was negative. Skin biopsy taken from the arm showed a checkerboard appearance that is a specific pattern of PRP.

Treatment The patient was given methylprednisolone 8 mg every 12 h orally in addition to methotrexate as the immunosuppressant to treat the PRP. The other treatment was a supportive care to improve the general conditions of the patient and symptomatic treatment. After 7 days of treatment the condition was significantly improved, the scales became thinner and the texture of the skin became smoother.

Discussion

Pityriasis rubra pilaris (PRP) is a rare erythemato-squamous disorder of unknown etiology. It is characterized by prominent scaling, perifollicular redness and follicular plugging. It may cause recurrent erythrodermic and palmo-plantar hyperkeratosis [1].

There are five subtypes of PRP which are described by Griffith. Type I PRP is the classic adult variant which affects 55% of adult patients [2]. The most

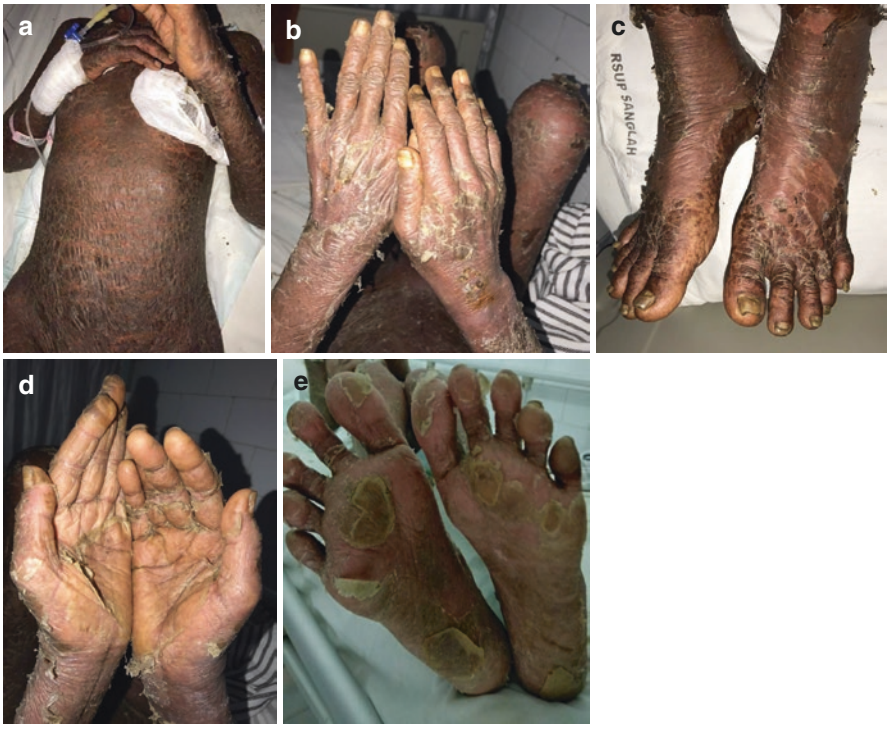

Fig. 24.2 (**a–e**) There was an ichthyosiform thick scale on all over the body and discoloration of finger and toe nails

distinguishing features are classic red-orange papules and plaques with islands of sparing, perifollicular keratotic papules, and waxy palmoplantar keratoderma [3]. In this patient, the clinical symptoms are associated with type-1 classical adult form, but due to erythroderma, some of these features either clinical and histopathology can't be seen clearly.

The PRP is often associated with HIV infection [4]. From laboratory investigation, the patient's HIV serology test was negative. Then a skin biopsy taken from the arm after the episode of erythroderma is being improved showed a checkerboard appearance that is a specific pattern of PRP.

The treatment of PRP is challenging. There were no specific guidelines to treat PRP. Most studies recommend combination therapy with topical for symptomatic management and systemic therapy aimed at reducing inflammation [5].

In this case the patient responded very well with treatment of methylprednisolone and methotrexate. Supportive and symptomatic care as an adjuvant also speed up the recovery process. After only 7 days of treatment the skin appearance was very much improved. However, long term observation is still needed to prevent the recurrence erythroderma and the side effect of the medications [6].

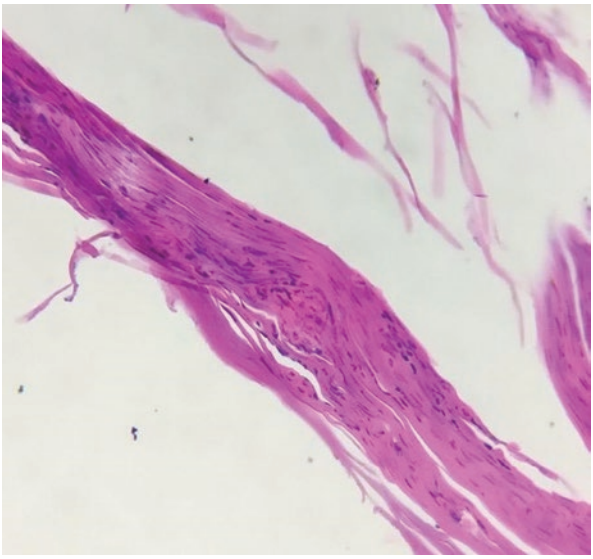

Fig. 24.3 There was checkerboard pattern on skin biopsy that classic to PRP

Key Points

- Pityriasis rubra pilaris (PRP) is a rare erythemato-squamous disorder of unknown etiology. It is characterized by prominent scaling, perifollicular redness and follicular plugging. It may cause recurrent erythrodermic and palmo-plantar hyperkeratosis.
- There are five subtypes of PRP which are described by Griffith. Type I PRP is the classic adult variant which affects 55% of adult patients.
- The treatment of PRP is challenging. There were no specific guidelines to treat PRP. Most studies recommend combination therapy with topical for symptomatic management and systemic therapy aimed at reducing inflammation.

References

1. Eastham AB, Tkachenko EY, Femia AN, Pappas-Taffer LK, Rosenbach M, Joyce CJ, Liu S, Vleugels RA. Pityriasis rubra pilaris: a study evaluating patient quality of life in 2 populations. J Am Acad Dermatol. 2019;81(2):638–40.
2. Griffiths WAD. Pityriasis rubra pilaris. Clin Exp Dermatol. 1980;5:105–12.
3. Miralles ES, Nunez M, De Las Heras ME, et al. Pityriasis rubra pilaris and human immunodeficiency virus infection. Br J Dermatol. 1995;133:990–3.
4. Klein A, Landthaler M, Karrer S. Pityriasis rubra pilaris: a review of diagnosis and treatment. Am J Clin Dermatol. 2010;11:157–70.
5. Ross NA, Chung HJ, Li Q, Andrews JP, Keller MS, Uitto J. Epidemiologic, clinicopathologic, diagnostic, and management challenges of pityriasis rubra pilaris: a case series of 100 patients. JAMA Dermatol. 2016;152(6):670–5.
6. Moretta G, De Luca E, Di Stefani A. Management of refractory pityriasis rubra pilaris: challenges and solutions. Clin Cosmet Investig Dermatol. 2017;10:451–7.

Chapter 25
Refractory Erythemato-Squamous Eruption of Facial Skin

Alin Laurentiu Tatu, Florin Ciprian Bujoreanu, Diana Sabina Radaschin, and Lawrence Chukwudi Nwabudike

Short History of the Patient

We present the case of a 46-year-old male patient, Fitzpatrick III phototype, known with primary immune deficiency, who undergoes regular intravenous treatment with normal human immunoglobulin. The patient's medical history was remarkable for primary immune deficiency, the presence of cervical spondylosis, mixed dyslipidemia and primary arterial hypertension, but he had no prior history of any dermatological complaints.

The patient is given regularly, monthly, a liquid intravenous immunoglobulin preparation of highly purified immunoglobulin G (Panzyga—Pfizer®) used in the treatment of patients with primary immune deficiency (PID) and secondary immune deficiency (SID).

A. L. Tatu · F. C. Bujoreanu (✉) · D. S. Radaschin
Multidisciplinary Integrated Center of Dermatological Research Center, MICDIR, Dunarea de Jos University of Galati, Galati, Romania

Dermatology, Clinical Department, Faculty of Medicine and Pharmacy, "Dunărea de Jos" University, Galati, Romania

L. C. Nwabudike
Multidisciplinary Integrated Center of Dermatological Research Center, MICDIR, Dunarea de Jos University of Galati, Galati, Romania

N. Paulescu Institute, Bucharest, Romania

T. M. Lotti et al. (eds.), *Clinical Cases in Exfoliative Dermatitis*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08466-9_25

The patient reports 6 months ago the onset of an eruption consisting of nonpruriginous erythematosquamous superficial patches and plaques with a yellow, branny and greasy scale localized on the face, affecting the forehead, supraciliary aspects, nasolabial folds, with extension to both cheeks. The patient denied any previous episodes, and no other changes were detected on dermatological examination (Fig. 25.1).

In the first stage, the patient was administered various dermatocosmetic products, without significant clinical improvement of the skin lesions. Subsequently, topical antifungals and an antifungal in combination with a corticosteroid were administered, along with oral antifungals, with a favorable evolution of cutaneous lesions, with diminished scales.

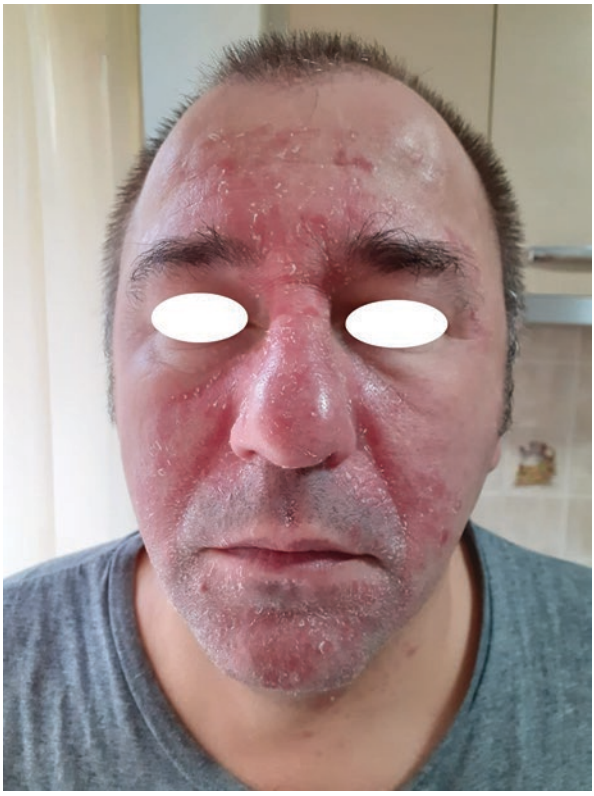

Fig. 25.1 Erythematosquamous eruption, with thick adherent scale, affecting the forehead, supraciliary regions, and nasolabial folds

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

Psoriasis
- Rosacea
- Contact dermatitis
- Seborrheic dermatitis
- Drug-induced photosensitivity

Diagnosis

Seborrheic dermatitis (Fig. 25.2).

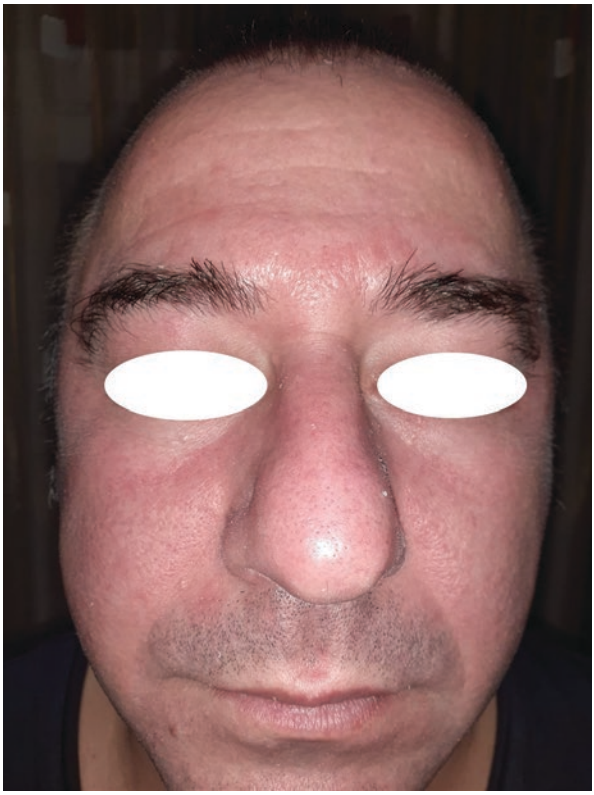

Fig. 25.2 Complete clearance of the dermatosis after appropriate treatment

Discussion

Seborrheic dermatitis (SD) is a chronic recurrent erythemato-squamous condition that affects seborrheic areas causing, erythema, flaking and pruritus. Etiology is multifactorial and the role of Malassezia sp. remains controversial [1].

We present one case of seborrheic dermatitis, which has been resistant to the continuous therapy over 1 year and showed the excess proliferation and overgrowth of Malassezia sp.

Seborrheic dermatitis is characterized by desquamation and inflammation in areas with a rich supply of sebaceous glands, usually the scalp, face and upper trunk. It is a common disease, and the prevalence ranges from 2% to 5% of general population in different studies. It is more common in males than in females. The disease usually begins during puberty and is more frequent around 40 years of age. The prevalence of seborrheic dermatitis is higher in HIV-positive individuals and the condition tends to be more intense and refractory to treatment in these patients [2]

The typical eruption is characterized by red scaly lesions predominantly located on the face, scalp and upper trunk, with distribution on eyebrows, nasolabial folds, cheeks, ears, presternal and interscapular regions, groins and axillae. The course of seborrheic dermatitis tends to be chronic with recurrent flares. Mental stress and dry air or seasonal variations are observed to exacerbate the rash [3].

There are many theories that suggests Malassezia furfur playing an important role in seborrheic dermatitis. The increased incidence of seborrheic dermatitis in patients with immunosuppressive disorders. We presented one case of seborrheic dermatitis, which has been resistant to the continuous therapy over 1 year and showed the excess proliferation of Malassezia sp.

Seborrheic dermatitis is regarded as a very common chronic and relapsing inflammatory skin disorder whose pathophysiology is poorly understood. Aberrant host immune activity or failure to clear skin microbes may bypass the initial epidermal or sebaceous abnormalities [4].

Mild corticosteroids are effective in treating seborrheic dermatitis, however the disease recurs often within a few days. Antifungal therapy is effective in the treatment of seborrheic dermatitis because it reduces the number of yeasts and the recurrences are less frequent compared when using only topical corticosteroids [5].

Key Points

- Seborrheic dermatitis is considered a very common chronic and relapsing inflammatory skin disorder whose pathophysiology is poorly understood.
- The diagnosis is a clinical and it is based on the location and aspect of the lesions. The skin changes are thought to result from an inflammatory response to a common skin organism, Malassezia yeast
- Its classification is controversial in the spectrum of cutaneous diseases, having being classified as a form of dermatitis, a fungal disease, or an inflammatory disease, closely related with psoriasis.

References

1. Ruiz-Arriaga LF, Arenas R, Vega-Sánchez DC, Asz-Sigall D, Martínez-Velazco MA. Seborrheic dermatitis: three novel trichoscopic signs and its correlation to *Malassezia* sp. colonization. Skin Appendage Disord. 2019;5(5):288–92.
2. Sampaio AL, Mameri AC, Vargas TJ, Ramos-e-Silva M, Nunes AP, Carneiro SC. Seborrheic dermatitis. An Bras Dermatol. 2011;86(6):1061–71; quiz 1072–4. English, Portuguese.
3. Clark GW, Pope SM, Jaboori KA. Diagnosis and treatment of seborrheic dermatitis. Am Fam Physician. 2015;91(3):185–90.
4. Wikramanayake TC, Borda LJ, Miteva M, Paus R. Seborrheic dermatitis-looking beyond Malassezia. Exp Dermatol. 2019;28(9):991–1001.
5. Faergemann J. Management of seborrheic dermatitis and pityriasis versicolor. Am J Clin Dermatol. 2000;1(2):75–80.

Chapter 26
Sub-Erythroderma in a 52 Year Old Man

O. Yu Olisova, N. P. Teplyuk, O. V. Grabovskaya, and Ekaterina Grekova

A 52-year-old man with no significant medical history presented to the Dermatology Clinic with erythroderma and no associated symptoms (Fig. 26.1).

The onset had been 1 month before when he noted plaques on his trunk with no obvious trigger factor. Over the next 2 months, the patient developed erythroderma which prompted the use of topical steroids without any effect. Physical examination revealed erythroderma with a yellowish tinge and white dry scales on the skin surface with areas of normal skin on his chest ("islands of sparing"). The skin of the palms and soles was dry and hyperkeratotic with an orange hue; the nails were thickened and turned yellow–brown (Fig. 26.2). Histopathological examination revealed hyperkeratosis, horizontal and vertical pattern of changing ortho- and parakeratosis, irregular acanthosis, a confluent granular layer and perivascular lymphocytic dermal infiltrate without exocytosis or microabscesses (Fig. 26.3).

Patient consent for the publication has been obtained.

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

Mycosis fungoides, erythrodermic form
- Psoriasis
- Drug-induced erythroderma
- Pityriasis rubra pilaris

O. Y. Olisova · N. P. Teplyuk · O. V. Grabovskaya · E. Grekova (✉)
Department of Dermatology and Venereology, Sechenov University, Moscow, Russia

T. M. Lotti et al. (eds.), *Clinical Cases in Exfoliative Dermatitis*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08466-9_26

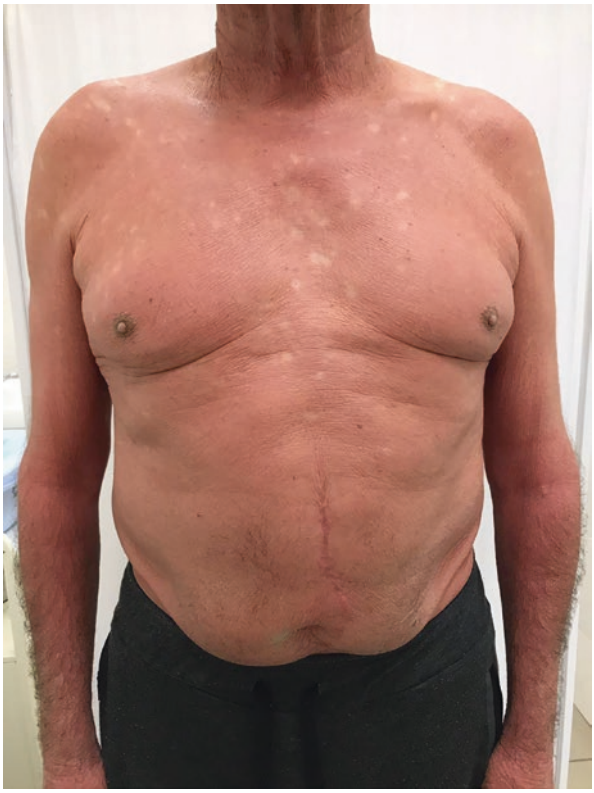

Fig. 26.1 Clinical findings. Generalized erythroderma with areas of normal skin on his chest ("islands of sparing")

Diagnosis

Pityriasis rubra pilaris, classical adult type I.

Discussions

Classical adult pityriasis rubra pilaris (PRP) is a rare chronic papulosquamous disorder characterized by follicular hyperkeratotic papules followed by orange-red erythroderma with "islands of sparing" and palmoplantar keratoderma with an orange hue [1]. Ectropion may be observed. Histologically, it is characterized by hyperkeratosis, alternating ortho- and parakeratosis oriented in vertical and horizontal directions ("checkerboard pattern"), irregular acanthosis, follicular plugging, perivascular lymphocytic infiltration of the dermis and absence of exocytosis, neutrophils or microabscesses in the epidermis [2]. Systemic treatment includes oral immunosuppressants (methotrexate) and retinoids (acitretin). TNF-antagonists (infliximab, etanercept, adalimumab) may be used as monotherapy or in combination with oral immunosuppressants or retinoids.

Fig. 26.2 Clinical findings. Dry and hyperkeratotic skin of palms with an orange hue

In severe cases of *psoriasis*, generalization of the dermatosis is observed with the formation of erythroderma and no "islands of sparing" because typical papules and plaques may appear on visually healthy skin. While the face may be involved, ectropion does not develop. The skin of the palms and soles is dry and hyperkeratotic but without a yellowish tinge. Oil drop changes, onycholysis or nail pitting are often present. However, erythrodermic psoriasis is more common in patients with a history of psoriasis. Histopathological examination reveals hyper- and parakeratosis in the epidermis, collections of neutrophils in tiny unicellular pustules (Kogoj pustule) and larger confluent abscesses (Munro's microabscesses and occasional apoptotic keratinocytes) in both spinous and cornified layers; focal loss of granular layer; acanthosis with elongated rete ridges (psoriasiform acanthosis). In the elongated dermal papillae, there are ectatic capillaries and superficial lymphocytic perivascular infiltrate with neutrophils. Systemic treatment of erythrodermic psoriasis includes methotrexate, retinoids (acitretin), cyclosporine, anti–tumor necrosis factor biologics (etanercept, adalimumab, and infliximab) [3], IL-12/23 inhibitors (ustekinumab) and a humanized IgG4 monoclonal antibody that inhibits IL-17A (ixekizumab) [4, 5]. Phototherapy is employed when acute erythrodermic psoriasis becomes more stable to avoid aggravation and reduce the risk of koebnerization.

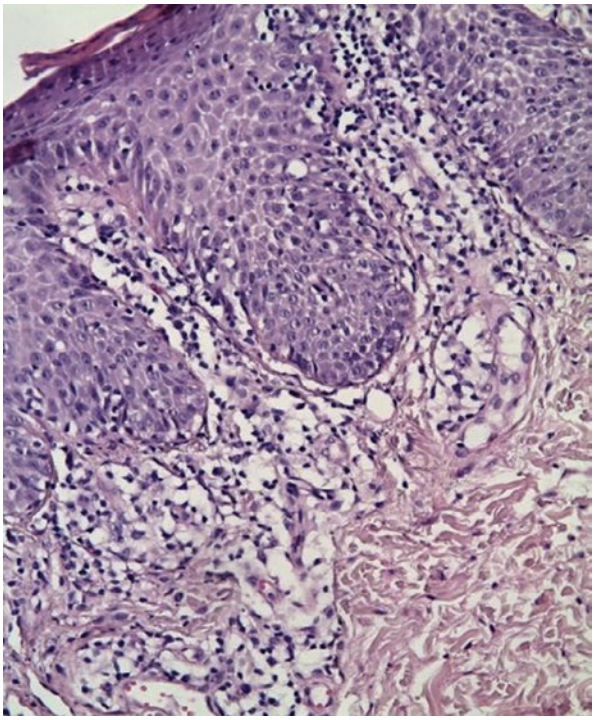

Fig. 26.3 Morphology results. HE ×200: Photomicrograph reveals hyperkeratosis, horizontal and vertical pattern of changing ortho- and parakeratosis, irregular acanthosis

Mycosis fungoides is the most common subtype of cutaneous T-cell lymphomas (CTCL) accounting for approximately 65–85% of all CTCLs. It is characterized by proliferation and accumulation of malignant monoclonal T-lymphocytes or natural killer cells in the skin, which may also subsequently involve lymph nodes, internal organs and bone marrow [6]. Patients with erythrodermic form develop erythroderma without areas of unaffected skin (or "islands of sparing"), severe itching, palmoplantar hyperkeratosis without a yellowish tinge and lymphadenopathy. Histopathological examination reveals epidermotropic infiltrates of medium-sized lymphocytes with mildly atypical to hyperconvoluted cerebriform nuclei. The diagnosis of MF is made based on clinical manifestation, histopathological examination, immunohistochemical tests (tumor cells have the phenotype of CD3+, CD4+, CD45RO+ and CD8− T-cells) and molecular diagnostics (T-cell receptor γ-chain rearrangement on PCR) [7].

Drugs such as antimicrobials, antihypertensives, antiarrhythmics, antiepileptics, gastrointestinal drugs and other agents may induce erythroderma [8]. *Drug-induced erythroderma* which is characterized by additional manifestations such as facial swelling, fever, peripheral eosinophilia, hepatitis, myocarditis and allergic interstitial nephritis is referred to as DRESS-syndrome (drug reaction with eosinophilia and systemic symptoms) [9]. The clinical and histopathologic features of drug-induced erythroderma are nonspecific. Histopathological examination in

DRESS-syndrome shows foci of interface dermatitis involving cutaneous adnexae, with eosinophils only observed in 20% of cases and neutrophils in 42% of cases. It may have two or three patterns characteristic of different diseases such as eczematous (40%), interface dermatitis (74%), acute generalized exanthematic pustulosis-like (20%) and erythema multiforme-like (24%) [10]. When compared with other forms of erythroderma, the onset of erythroderma secondary to medication is typically more sudden, rapidly progressing, and the resolution is often quicker. The management of drug-induced erythroderma depends on the extent of skin lesions, mucosal involvement and comorbidities. In early stages, systemic agents such as oral steroids and pulse intravenous solumedrol therapy are effective.

Key Points

- *Classical adult pityriasis rubra pilaris (PRP)* is a rare chronic papulosquamous disorder.
- It is characterized by follicular hyperkeratotic papules followed by orange-red erythroderma with "islands of sparing" and palmoplantar keratoderma with an orange hue.
- Ectropion may be observed.
- Histologically, it is characterized by hyperkeratosis, alternating ortho- and parakeratosis oriented in vertical and horizontal directions ("checkerboard pattern").

References

1. Petrof G, Almaani N, Archer CB, Griffiths WAD, Smith CH. A systematic review of the literature on the treatment of pityriasis rubra pilaris type 1 with TNF-antagonists. J Eur Acad Dermatol Venereol. 2013;27(1):e131–5.
2. Danis J, Göblös A, Gál B, Sulák A, Farkas K, Török D, Bata-Csörgö Z. Nuclear factor κB activation in a Type V pityriasis rubra pilaris patient harboring multiple CARD14 variants. Front Immunol. 2018;9:1564.
3. Buggiani G, D'Erme AM, Krysenka A, Pescitelli L, Lotti T, Prignano F. Efficacy of ustekinumab in sub-erythrodermic psoriasis: when TNF-blockers fail. Dermatol Ther. 2012;25(3):283–5.
4. Carrasquillo OY, Pabón-Cartagena G, Falto-Aizpurua LA, Santiago-Vázquez M, Cancel-Artau KJ, Arias-Berrios G, et al. Treatment of erythrodermic psoriasis with biologics: a systematic review. J Am Acad Dermatol. 2020;83(1):151–8.
5. Craig S, Warren RB. Ixekizumab for the treatment of psoriasis: up-to-date. Expert Opin Biol Ther. 2020;20(6):549–57.
6. Argnani L, Broccoli A, Zinzani PL. Cutaneous T-cell lymphomas: focusing on novel agents in relapsed and refractory disease. Cancer Treat Rev. 2017;61:61–9.
7. Willemze R, Jaffe ES, Burg G, Cerroni L, Berti E, Swerdlow SH, Grange F. WHO - EORTC classification for cutaneous lymphomas. Blood. 2005;105:3768–85.
8. Mistry N, Gupta A, Alavi A, Sibbald RG. A review of the diagnosis and management of erythroderma (generalized red skin). Adv Skin Wound Care. 2015;28(5):228–36.

9. Wolfson AR, Zhou L, Li Y, Phadke NA, Chow OA, Blumenthal KG. Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome identified in the electronic health record allergy module. J Allergy Clin Immunol Pract. 2019;7(2):633–40.
10. Ortonne N, Valeyrie-Allanore L, Bastuji-Garin S, Wechsler J, de Feraudy S, Duong TA, et al. Histopathology of drug rash with eosinophilia and systemic symptoms syndrome: a morphological and phenotypical study. Br J Dermatol. 2015;173(1):50–8.

Chapter 27
Sudden Appearance of Widespread Desquamation and Hypoacusia in a 49-Year-Old Man

César Bimbi, Georgia Kyriakou, Manuela Boleira, Raquel Ferreira Queiroz de Melo, and Antonio Carlos Bastos Gomes

Case Report

A 49-year-old male with a personal history of arterial hypertension presented with acute and widespread erythema as well as severe scaling of the skin accompanied by intense pruritus. He reported that the amount of scales was so large that they accumulated on the floor of his house and he had to sweep constantly (Fig. 27.1). The eruption had first appeared on the scalp and soon involved the face as well. Within a few days, the rash spread cephalocaudally and coalesced to finally affect more than 90% of the body surface (Figs. 27.2, 27.3, and 27.4). Physical examination additionally revealed conjunctival erythema and both upper and lower eyelid oedema. The patient was afebrile without palpable lymphadenopathy, but reported a burning sensation in the eyes along with a slow and progressive hear loss. The latter was reported to present simultaneously with the rash and was accompanied by ear pain and episodes of vertigo.

Routine laboratory studies were unremarkable with the exception of a mild elevation of lipid levels. HIV tests were repeatedly negative. The complaint of hypoacusia was assessed by an otorhinolaryngologist who concluded that there was moderate

C. Bimbi (✉) · A. C. B. Gomes
Dermatologia Integrada Moinhos Clinic, Porto Alegre, Brazil
e-mail: cbimbi@terra.com.br

G. Kyriakou
Department of Dermatology, University General Hospital of Patras, Patras, Greece

M. Boleira
Dermatology at Policlinica Geral do Rio de Janeiro, Rio de Janeiro, Brazil

R. F. Q. de Melo
Dermatology Resident at Clinical Hospital of Federal University of Minas Gerais, Belo Horizonte, Brazil

T. M. Lotti et al. (eds.), *Clinical Cases in Exfoliative Dermatitis*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08466-9_27

Fig. 27.1 A large amount of scales was produced daily and the patient had to sweep his house's floor constantly

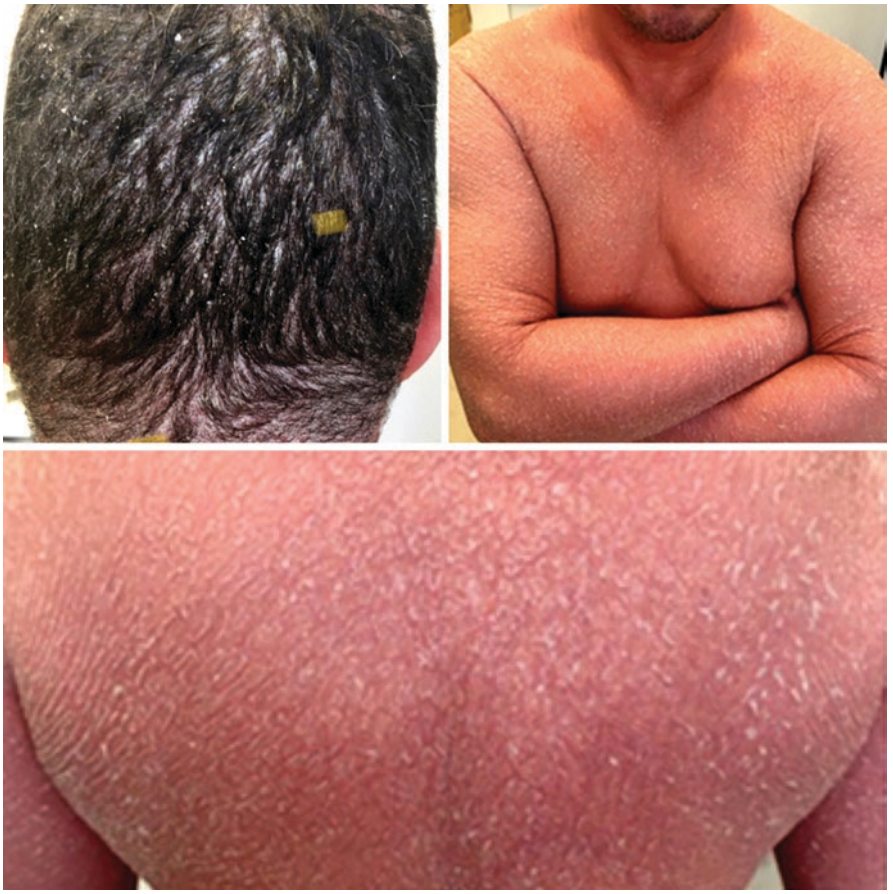

Fig. 27.2 Diffuse thick scaling on the scalp over red, thickened skin. Exfoliative dermatitis with an erythematous base and severe powdery scaling. The lesions affected more than 90% of the skin surface in the form of red-orange plaques that had expanded quickly to involve the entire body

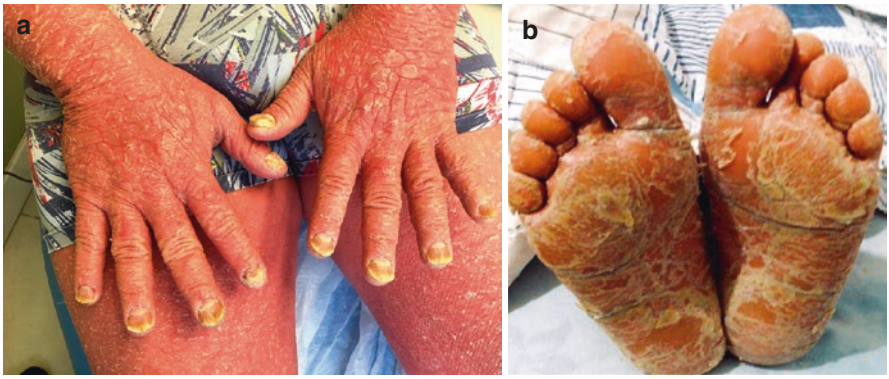

Fig. 27.3 (**a**) Both the palmar and the dorsal surface of the hands presented with skin thickening, prominent yellowish hyperkeratosis and scaling as well as subungual hyperkeratosis on the fingernails. (**b**) Soles grossly thickened with waxy keratoderma

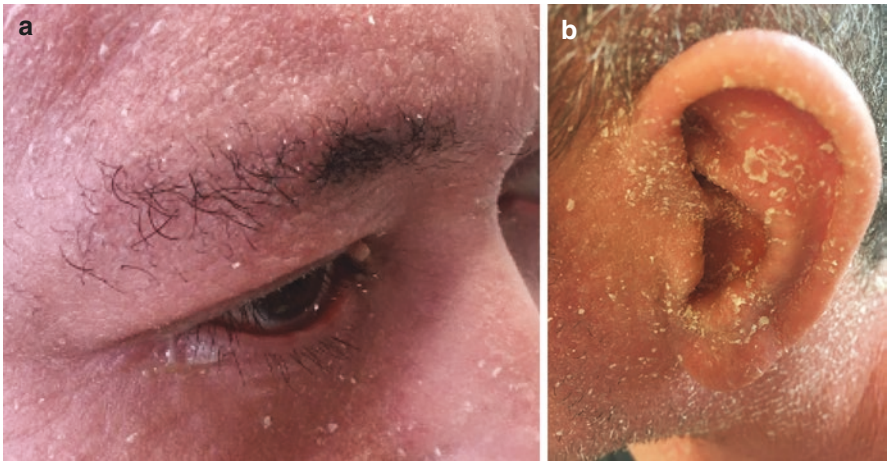

Fig. 27.4 (**a**) Tightly adherent scales accumulating on the eyelashes and eyebrows. (**b**) External ear involvement

to severe degree mixed-type hear loss (sensorineural and conductive) in both ears. The sensorineural component could be explained by the existence of systemic arterial hypertension and also the fact that, during his 2 years military service, he did rifle, pistol and machine gun shooting exercises, hence he was diagnosed with noise-induced hearing loss (NIHL), which is hearing impairment resulting from exposure to loud sound. Interestingly, the conductive component was attributed to the accumulation of layered skin into the external auditory canals. Otoscopy showed that both ears were filled with flaking in the external auditory canals preventing visualization of tympanic membranes. Keratin plugs had formed and blocked the passage of sound to tympanic membranes, and from there to the middle and internal ears.

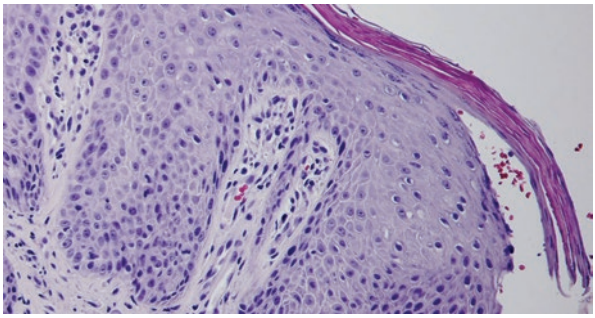

Fig. 27.5 Histopathological examination showed acanthosis, thinning of the granular layer and slight psoriasiform hyperplasia of the epidermis, with pallor of the keratinocytes of the stratum corneum and parakeratotic foci alternating with orthokeratosis. The hyperkeratosis tracked down the infundibular ostia forming follicular plugs (Hematoxylin and eosin stain, 200×)

A skin biopsy was obtained and demonstrated acanthosis, diffuse compact hyperkeratosis and focal parakeratosis (Fig. 27.5).

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

1. Erythrodermic psoriasis
2. Pityriasis rubra pilaris
3. Sézary syndrome
4. Darier disease

Diagnosis

Pityriasis rubra pilaris.

Discussion

Pityriasis rubra pilaris (PRP) is a rare, chronic cutaneous disorder of unknown etiology characterized by orange-red desquamation patches and constant inflammation and shedding of the skin. The name Pityriasis—from the Greek

πίτυρον meaning "bran" (scales-like flour), rubra-from the Latin *rubra* meaning "red" (skin erythema) and pilaris-from the Latin *pilus* meaning "hair" (intensification of epidermal formation in the outflow of hair) is simply descriptive. Histopathological findings are not uniform and vary greatly. Although PRP has a sporadic occurrence in most cases, familial forms have also been described. To date, the exact aetiology and pathogenesis of PRP are still unknown, but bacterial infection and trauma on a predisposed genetic background have postulated as triggering factors [1].

Clinical features include follicular hyperkeratotic papules converging into widespread salmon-colored plaques with lichenification. Often, islands of uninvolved skin which are called "nappes claires", are present in between these plaques. Perifollicular erythema and palmoplantar hyperkeratosis are also characteristic clinical findings [2]. PRP can either be generalized, extending throughout large areas of the body or the even the entire skin, or localized, with a predilection for the elbows, knees, hands, feet and ankles. In these cases PRP may be misdiagnosed as plaque psoriasis [1, 3].

The incidence and prevalence of PRP are not accurately known, but are estimated at 1 in 5000 new dermatological patients. It occurs in individuals of all racial backgrounds and seems to affect both sexes equally. PRP peaks in the first and fifth decades and can be classified as juvenile or adult type. In 1980, Griffiths classified PRP into five subtypes based on age of onset, clinical features, and prognosis. More recently, an HIV-associated form has been added to this classification system by Miralles et al. [4–6].

The case presented here is the classic adult (type I) form which usually resolves spontaneously after a few years course and is the most common type responsible for 50% of all PRP cases. Nevertheless, this case presents some clinical manifestations of PRP not yet reported in the medical literature including the sudden loss of hearing and blepharitis-like symptoms such as itchy watery eyes. Both symptoms were related to the presence of scales on the external ear and the periorbital area.

Establishing treatment guidelines for PRP is confounded by its rarity, as well as its natural tendency towards spontaneous resolution. However, a proposal for a treatment algorithm based on small case series and case reports has been published recently, and suggests the use of medium to high potency topical corticosteroids, calcineurin inhibitors, keratolytics, emollients, Vitamin D derivatives and retinoids in localized forms. In severe generalized forms, systemic retinoids are recommended additionally as a first-line systemic therapy, followed by methotrexate, cyclosporine, or azathioprine as second-line treatment options. The use of biologics should also be considered in refractory cases [1, 7]. In our case, the use of topical corticosteroids and calcipotriol did not show any therapeutic effect, however, the patient responded satisfactorily to treatment with acitretin along with topical emollients application.

Key Points

- Pityriasis rubra pilaris represents an uncommon chronic papulosquamous inflammatory dermatosis presenting with cutaneous salmon-colored erythema with islands of sparing and abundant desquamation.
- The etiology remains unclear but a few documented severe cases were associated with viral or bacterial infection, while anecdotal reports suggest that autoimmune diseases and malignancy can also trigger PRP.
- Although a large number of exfoliative diseases have been reported, only one report of the otologic manifestations of keratosis follicularis was identified in the medical literature [8]. It is safe to assume, however, that there may be more patients suffering from otologic symptoms that have not been identified as related to the underlying cutaneous dermopathy.
- The symptoms are due to skin debris accumulation inside the auditory canal and are not limited to hypoacusia but also include feelings of otalgia, blocked ear sensation, tinnitus, vertigo and autophony, which is hearing one's own amplified voice when speaking.
- In this report, we highlight the importance of inspection of the auditory canal in patients with exfoliative skin disorders. In these cases, routine debridement of the keratotic debris from the external ear can lead to quick improvement of the auditory symptoms, however recurrence may occur.

References

1. Roenneberg S, Biedermann T. Pityriasis rubra pilaris: algorithms for diagnosis and treatment. J Eur Acad Dermatol Venereol. 2018;32(6):889–98. https://doi.org/10.1111/jdv.14761. PMID: 29247481.
2. Eastham AB. Pityriasis rubra pilaris. JAMA Dermatol. 2019;155(3):404. https://doi.org/10.1001/jamadermatol.2018.5030. PMID: 30725099.
3. Gemmeke A, Schönlebe J, Koch A, Wollina U. Pityriasis rubra pilaris--a retrospective single center analysis over eight years. J Dtsch Dermatol Ges. 2010;8(6):439–44. https://doi.org/10.1111/j.1610-0387.2010.07338.x. PMID: 20202046.
4. Griffiths WA. Pityriasis rubra pilaris. Clin Exp Dermatol. 1980;5(1):105–12. https://doi.org/10.1111/j.1365-2230.1980.tb01676.x. PMID: 7398119.
5. Wang D, Chong VC, Chong WS, Oon HH. A review on pityriasis rubra pilaris. Am J Clin Dermatol. 2018;19(3):377–90. https://doi.org/10.1007/s40257-017-0338-1. PMID: 29302927.
6. Miralles ES, Núñez M, De Las Heras ME, Pérez B, Moreno R, Ledo A. Pityriasis rubra pilaris and human immunodeficiency virus infection. Br J Dermatol. 1995;133(6):990–3. https://doi.org/10.1111/j.1365-2133.1995.tb06939.x. PMID: 8547057.
7. Kamarachev J, Grozdev I, Darlenski R, Tsankov N. Pityriasis rubra pilaris as a systemic disease. Clin Dermatol. 2019;37(6):657–62. https://doi.org/10.1016/j.clindermatol.2019.07.030. PMID: 31864444.
8. Pickard RE, Mandy SH. The ear in keratosis follicularis (Darier's disease). Arch Otolaryngol. 1971;94(2):162–4. https://doi.org/10.1001/archotol.1971.00770070398014. PMID: 5556274.

Chapter 28
Surprising Cause of Erythroderma in an Adult Patient

Eda Gökalp, Gizem Filazi Kök, Yasemin Yuyucu Karabulut, and Ümit Türsen

A 54-year-old male patient presented to the dermatology clinic complaining of itching. Dermatological examination showed eczematous lesions all over the body. Also, the erythematous background was detected (Fig. 28.1). These erythematous lesions were involved more than 90% of the body's surface area, therefore the existence of erythroderma was thought. When evaluated laboratory data, there was eosinophilia and increased IgE level in peripheral blood.

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

1. Psoriasis
2. Contact Dermatitis
3. Atopic Dermatitis

Biopsies were taken from the arm, leg, and trunk to highlight the pathology. Histopathologic examination revealed hyperkeratosis, parakeratosis and loss of granular layer in the epidermis. Accompanied eosinophil leukocytes a mixed type of inflammatory cell infiltration was observed in perivascular and periadnexial areas in the dermis (Fig. 28.2). Psoriasiform changes were also noted in arm and leg localisations. Although the presence of psoriasiform changes, intense eosinophil

E. Gökalp · Y. Y. Karabulut
Department of Pathology, Mersin University School of Medicine, Mersin, Turkey

G. F. Kök · Ü. Türsen (✉)
Department of Dermatology, Mersin University School of Medicine, Mersin, Turkey

T. M. Lotti et al. (eds.), *Clinical Cases in Exfoliative Dermatitis*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08466-9_28

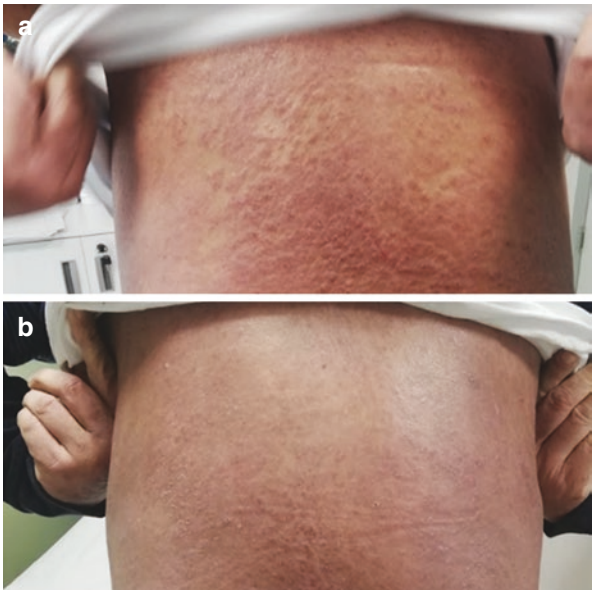

Fig. 28.1 (**a**) Eczematous lesions in the erythrodermic ground. (**b**) Lesions were regressed after steroid treatment

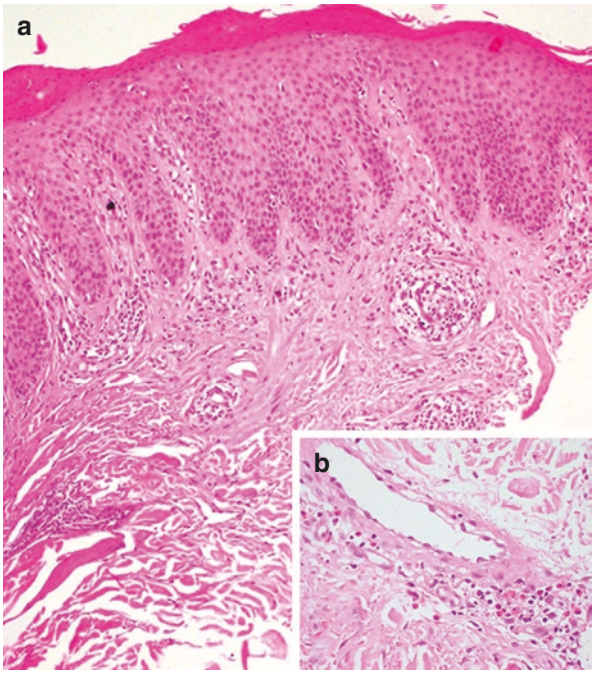

Fig. 28.2 (**a**) Hyperkeratosis, parakeratosis and loss of granular layer in the epidermis (H&E ×100). (**b**) Accompanied eosinophil leukocytes a mixed type of inflammatory cell infiltration in the perivascular area (H&E ×400)

leukocytes suggest eczematous dermatitis. With these clinical and histopathological findings steroid treatment was applied. By the treatment, lesions were regressed dramatically.

Diagnosis

Atopic Dermatitis.

Discussion

Erythroderma, or exfoliative dermatitis is a common pathology and diagnosis of the underlying disease is a challenge. Despite laboratory improvements, many cases remain idiopathic. Several skin disorders may culminate with erythroderma: exacerbation of previous dermatoses (e.g., psoriasis, eczema, atopic dermatitis, pityriasis rubra pilaris, pemphigus foliaceous), drug eruption, and cutaneous lymphomas (mycosis fungoides, Sézary syndrome, adult T-cell leukemia/lymphoma). The challenge in these patients is represented by the identification of the etiological agents or conditions, which is relevant in clinical management and prognosis. Despite extensive investigation, some patients are classified as idiopathic erythroderma [1, 2].

Atopic dermatitis is a chronic, pruritic, inflammatory dermatosis [1]. Disease generally begins in infants. In infants distribution of the lesions prefer flexor surfaces of the limbs. Whereas, extensor surfaces preferred in adults. Males and females are equally affected.

The cause of atopic dermatitis is not known, but some genetic, environmental and immunologic factors can play a role in pathogenesis.

The most common symptoms of atopic dermatitis are pruritus, xerosis, lichenifications. Other symptoms can change according to age, ethnicity, and pathogenesis. Erythroderma isn't a common symptom of atopic dermatitis.

In a prospective study in which 309 erythrodermic patients were evaluated, it was revealed that atopic dermatitis is the cause of erythroderma in 8.7% of the patients [2]. In this study, an important characteristic of the atopic dermatitis group is the younger age at diagnosis. Atopic dermatitis should be kept in mind in cases of erythroderma especially, developing at early ages [2, 3].

In a different study that 97 patients were evaluated with erythroderma, atopic dermatitis was detected in 13.4% of the patients [4].

Especially psoriasis and contact dermatitis are entities that can be confused with atopic dermatitis.

In our case, the existence of eosinophilia and intense eosinophil leukocytes observed in biopsy helped us to exclude psoriasis, with the distribution pattern of lesions.

Although erythroderma is a rare symptom of atopic dermatitis, it should be considered in erythrodermic patients. As in our case, it is important to correlate clinical and laboratory data with a histopathological examination in determining the etiology of erythroderma.

Key Points

- Atopic dermatitis should be kept in mind in erythrodermic children and young adults.
- Clinicopathological correlation is important to determine the etiology of erythroderma.

References

1. Eichenfield LF, Tom WL, Chamlin SL, et al. Guidelines of care for the management of atopic dermatitis: section 1. Diagnosis and assessment of atopic dermatitis. J Am Acad Dermatol. 2014;70:338–51.
2. Miyashiro D, Sanches JA. Erythroderma: a prospective study of 309 patients followed for 12 years in a tertiary center. Sci Rep. 2020;10(1):9774.
3. Sarkar R, Sharma RC, Koranne RV, Sardana K. Erythroderma in children: a clinico-etiological study. J Dermatol. 1999;26:507–11.
4. Akhyani M, Ghodsi ZS, Toosi S, et al. Erythroderma: a clinical study of 97 cases. BMC Dermatol. 2005;9:5.

Chapter 29
The Greatest Psoriasis Copycat

César Bimbi, Georgia Kyriakou, Antonio Carlos Bastos Gomes, and Raquel Ferreira Queiroz de Melo

Case Report

Keywords Exfoliative dermatitis, Adult T-cell leukaemia/lymphoma, Human T-cell lymphotropic virus, Psoriasis-like lesions

A 41-year-old woman presented with widespread erythema and thick, hyperkeratotic lesions evolving for 1 year without improvement. The lesions affected the knees, pelvic girdle, and feet and were being treated as psoriasis (Fig. 29.1). Vesicles were all over skin areas not covered by the plaques (Fig. 29.2). The general health state was good except for these skin lesions. HIV tests were already done, all negative.

She had already been discharged from previous pathologies: cervical ganglion tuberculosis and hepatitis C.

Seven months after cure of crusted lesions, her general health worsened. Laboratory investigation showed anemia, leukocytosis with atypical cells, hypercalcemia and elevated lactate dehydrogenase. The symptoms were fever, fatigue, night sweating, malaise, weight loss, enlarged lymph nodes, and bruised skin and was admitted to the Hematology Unit. Samples were positive for anti-HTLV-1 antibodies (ELISA, PCR). Investigation with bone-marrow biopsy specimen, computed tomography scan showing intra-abdominal lymphadenopathies led to diagnosis of Adult T-cell leukemia/lymphoma (ATL) associated with HTLV-1 infection.

C. Bimbi (✉) · A. C. B. Gomes
Dermatologia Integrada Moinhos Clinic, Porto Alegre, Brazil

G. Kyriakou
Department of Dermatology, University General Hospital of Patras, Patras, Greece

R. F. Q. de Melo
Dermatology Resident at Clinical Hospital of Federal University of Minas Gerais, Belo Horizonte, Brazil

T. M. Lotti et al. (eds.), *Clinical Cases in Exfoliative Dermatitis*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08466-9_29

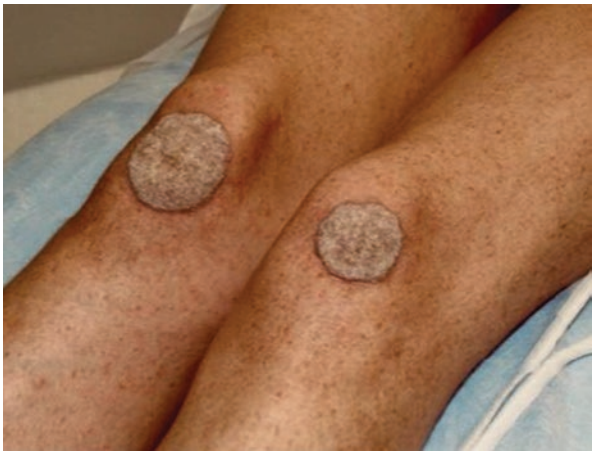

Fig. 29.1 hyperkeratotic, sharp-edged, psoriasis-like lesions affecting the knees and disseminated vesicles all over skin areas not covered by the plaques

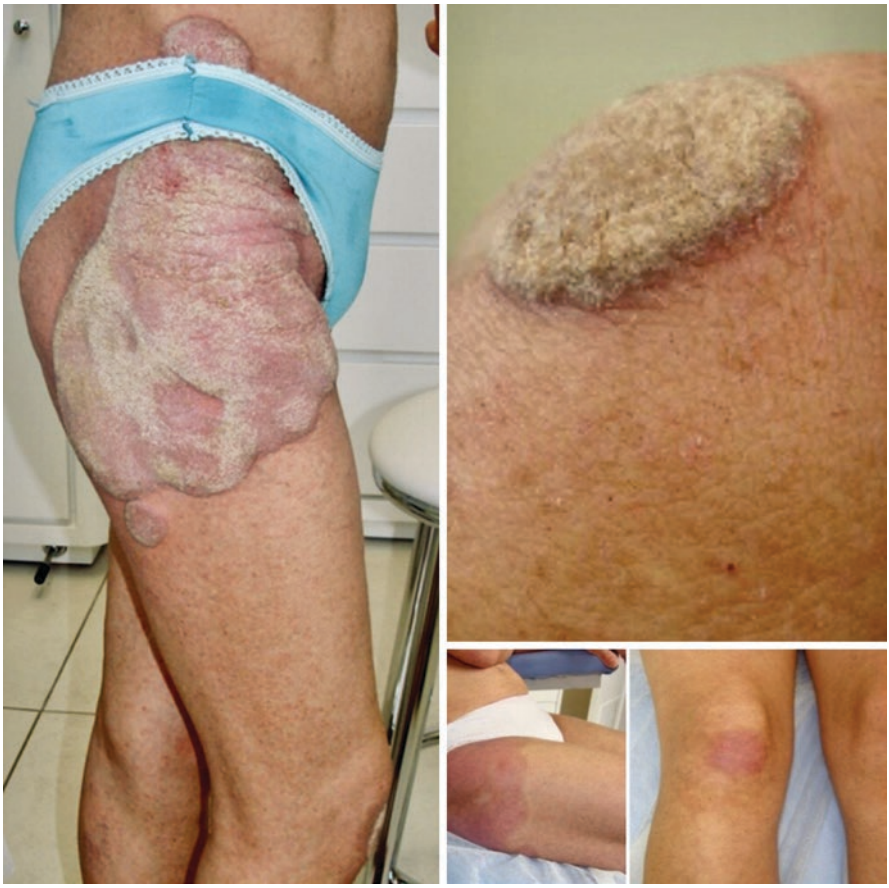

Fig. 29.2 Hyperkeratotic psoriasis-like lesions affecting the knees, pelvic girdle. Vesicles were all over skin areas not covered by the plaques. Treatment cleared skin lesions rapidly

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

1. Tuberculosis verrucosa
2. Crusted (Norwegian) scabies
3. Pityriasis rubra pilaris,
4. Ofuji's papuloerythroderma
5. Dapsone Hypersensitivity Syndrome

Diagnosis

Crusted (Norwegian) scabies.

Discussion

Crusted scabies is not conventional scabies. It is a rare variant of Sarcoptes infestation and occurs in patients with neurological disorders, age, reduced mobility, impaired immunological function and autoimmune diseases. Residency in a nursing home is considered a major risk factors in our patients. CS is one of the least frequent causes of erythroderma and is also considered "an infestation more than skin deep" [1] in the sense that this is one of those clinical cases that often represents the tip of the iceberg for the patient's health demanding deep investigation.

The patient was infected by human T-cell lymphotropic virus type 1 (HTLV-1) which is a silent infection affecting 20 million people worldwide, mostly in Brazil, Japan, Africa and the Caribbean. This case describes the link between three conditions—crusted scabies, HTLV-1 virus and adult T-cell leukaemia [2, 3]. In a study in French Guiana, an HTLV-1 endemic area, four of six HTLV-1 seropositive patients had concomitant ATL when CS was diagnosed, or developed ATL a few months later, suggesting that the occurrence of CS in these patients is a sign of ATL-related immunosuppression [4] or a prediagnostic sign of ATL [5].

A skin biopsy revealed *Sarcoptes scabiei* mites in burrows in the stratum corneum, but even microscopic examination of scales showing large number of adult Sarcoptes, also its eggs and the so-called scybala (black football-shaped masses which are scabies feces) are the simplest way to confirm diagnosis. Treatment cleared skin lesions rapidly with oral ivermectin along with topical application of 5% permethrin lotion.

Key Points

- Crusted (Norwegian) scabies is a rare variant of Sarcoptes scabiei infestation and occurs in patients with neurological disorders, reduced mobility, impaired immunological function such malignancies and autoimmune diseases.
- Residency in a nursing home is considered a major risk factor for crusted scabies.
- Occurrence of crusted scabies in endemic HTLV areas may be a sign of ATL-related immunosuppression or a prediagnostic sign of ATL
- Microscopic examination of scales are the simple diagnostic method to detect Sarcoptes presence.
- We emphasize the need to investigate systemic associations that are almost always present in cases of crusted scabies [6]. This variant has shown an increasing incidence in recent years due to the increase in cases of Alzheimer disease, use of immunosuppressive medications, in addition to HIV and HTLV [7], transplanted, neurological and cognitive disorders.

References

1. Chandler DJ, Fuller LC. A review of scabies: an infestation more than skin deep. Dermatology. 2019;235(2):79–90.
2. Brites C, Weyll M, Pedroso C, Badaro R. Severe and Norwegian scabies are strongly associated with retroviral (HIV-1/HTLV-1) infection in Bahia, Brazil. AIDS. 2002;16:1292–3.
3. Romanelli LC, Caramelli P, Proietti AB. [Human T cell lymphotropic virus (HTLV-1): when to suspect infection?]. Rev Assoc Med Bras (1992). 2010;56:340–7.
4. del Giudice P, Sainte Marie D, Gerard Y, Couppie P, Pradinaud R. Is crusted (Norwegian) scabies a marker of adult T cell leukemia/lymphoma in human T lymphotropic virus type I-seropositive patients? J Infect Dis. 1997;176:1090–2.
5. McLaughlin-Drubin ME, Munger K. Viruses associated with human cancer. Biochim Biophys Acta. 2008;1782:127–50.
6. Esau D. Viral causes of lymphoma: the history of epstein-barr virus and human T-lymphotropic virus 1. Virology. 2017;8:1178122X17731772.
7. Rho HM, Poiesz B, Ruscetti FW, Gallo RC. Characterization of the reverse transcriptase from a new retrovirus (HTLV) produced by a human cutaneous T-cell lymphoma cell line. Virology. 1981;112:355–60.

Chapter 30
Yellowish Erythematous Desquamative Lesion in a Middle Aged Man

Torello M. Lotti and Olga Olisova

A 51 years-old Caucasian man has been referred to our Institute for the first time 3 years ago for progressive itching diffuse and plane erythematous yellowish discoloration of the skin of the trunk and neck (Figs. 30.1 and 30.2). A tiny desquamation was evident at the center of the lesions. Blood tests were all normal or negative according to our laboratory while in the past serum protein electrophoresis had shown the presence of an immunoglobulin M lambda Monoclonal component with negative Bence-Jones urine protein. The serum protein electrophoresis repeatedly showed a normal profile after the initial detection of the IgM lambda monoclonal peak.

Repeated computed tomography never showed any skeletal alterations. The bone marrow contained a normal cellular population.

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

1. Diffuse plane normolipaemic xanthomatosis
2. Generalized eruptive histiocytosis
3. Non-X histiocytosis
4. Histiocytosis of mononuclear phagocytes other than Langerhans cells
5. Multicentric reticulohistiocytosis
6. Letterer-Siwe disease

T. M. Lotti (✉)
Science of Communication, Marconi University, Rome, Roma, Italy
e-mail: professor@torellolotti.it

O. Olisova
Department of Dermatology & Venereology, Sechenov University, Moscow, Russia

T. M. Lotti et al. (eds.), *Clinical Cases in Exfoliative Dermatitis*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08466-9_30

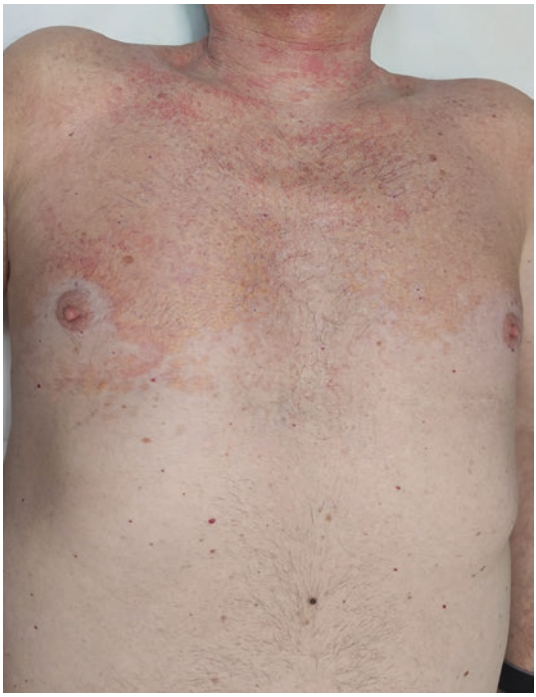

Fig. 30.1 Plane erythematous yellowish discoloration of the skin of the trunk and neck

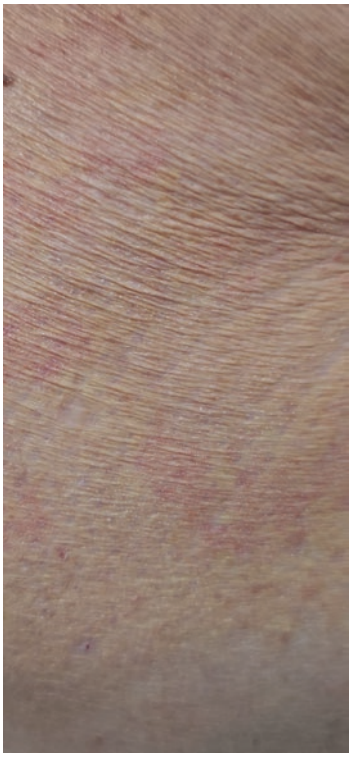

Fig. 30.2 Higher magnification of Plane erythematous yellowish discoloration of the skin of the trunk and neck

Diagnosis

Diffuse plane normolipaemic xanthomatosis.

Skin biopsy showed aggregates of foamy macrophages in the upper and medium dermis.

Plasma cells and limited zones of necrobiosis with cholesterol clefts were evident. Touton giant cells were not visible.

Discussion [1–5]

Diffuse plane normolipaemic xanthomatosis (DPNX) is a rare acquired dermatosis characterized by yellow-orange-erythematous plaques usually symmetrically distributed. DPNX is in fact a type of non-Langerhans histiocytosis due to the deposition of cholesterol and lipids in the skin in subjects who may have normal levels of blood cholesterol and no underlying disorders. Oral manifestations have been described including verruciform and plane xanthomas. DPNX is often associated with lymphoproliferative malignancies, multiple myeloma and hepatitis C and monoclonal gammopathies. Aggregation of foamy histiocytes in the superficial and medium dermis is always evident. Patients should be kept under surveillance for many years for the appearance of other associated diseases.

Key Points

- Diffuse plane normolipaemic xanthomatosis is a rare form of acquired non-Langerhans histiocytosis showing as yellowish plaques of the skin and of the oral mucosa. Multicentric reticulohistiocytosis should be excluded always.
- Deposition of cholesterol between the collagen fibers is evident in the upper and medium dermis with aggregates of foamy histiocytes.
- Underlying monoclonal gammopathies, multiple myeloma, hepatitis C and other lymphoproliferative malignancies should be always suspected, keeping the affected subjects under surveillance.

References

1. Cota C, Pellacani G, Lora V, Brancorsini D. Diffuse (generalized) plane xanthoma misdiagnosed as carotenoderma: usefulness of reflectance confocal microscopy. Am J Dermatopathol. 2020;42(12):e167–9.
2. Souza MCC, Martins PHT, Vivian A, Luzzatto L. Diffuse normolipemic plane xanthoma and hepatitis C: chance? An Bras Dermatol. 2020;95(2):261–2.

3. Gupta M, Sharma R, Gulati A, Gupta A. Diffuse normolipemic plane xanthoma with underlying photosensitive dermatoses. BMJ Case Rep. 2019;12(11):e230720.
4. Morsink LM, Nijhof IS. Diffuse plane normolipaemic xanthomatosis as a manifestation of monoclonal gammopathy. Br J Haematol. 2019;187(4):411.
5. Lotti T, Santucci M, Casigliani R, Fabbri P, Bondi R, Panconesi E. Multicentric reticulohistiocytosis. Report of three cases with the evaluation of tissue proteinase activity. Am J Dermatopathol. 1988;10(6):497–504.

Index

T. M. Lotti et al. (eds.), *Clinical Cases in Exfoliative Dermatitis*, Clinical Cases in Dermatology, https://doi.org/10.1007/978-3-031-08466-9