



Eosinophilic dermatoses

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The classic eosinophilic dermatoses include eosinophilic cellulitis (Wells syndrome), granuloma faciale, eosinophilic fasciitis (Shulman syndrome) and eosinophilic folliculitis (Ofuji disease).

Summary

Eosinophilic dermatoses are a heterogeneous group of diseases, characterized by an eosinophil-rich infiltrate and/or degranulation of eosinophils. Blood eosinophilia may be an associated feature. Typical, albeit not specific histological findings include 'flame figures', which are caused by the accumulation of cationic proteins released by eosinophils and subsequent collagen denaturation.

"Classic" eosinophilic dermatoses include eosinophilic cellulitis (Wells syndrome), granuloma faciale, eosinophilic fasciitis (Shulman syndrome) and eosinophilic folliculitis (Ofuji disease). In addition, there is a multitude of skin diseases that present with varying degrees of eosinophilic infiltration. These include atopic dermatitis, bullous pemphigoid, urticaria, allergic contact dermatitis, prurigo nodularis, arthropod bite reaction, parasitic infections, and drug hypersensitivity. Even though these disorders share a common characteristic (tissue eosinophilia), they differ greatly in their clinical presentation.

Introduction

Four diseases constitute the group of "classic" eosinophilic skin diseases whose clinical and histological presentation is primarily characterized by the accumulation of eosinophils in tissue. The term 'classic eosinophilic dermatoses' is not based on expert consensus or used uniformly in the literature. We will use it in the present review to differentiate those skin diseases that are characterized by a prominent eosinophilic infiltrate. This is to say that the feature 'tissue eosinophilia' defines the clinical and histological picture and is not just a concomitant finding. A number of textbooks therefore address these diseases as a distinct group that includes:

- Eosinophilic cellulitis (Wells syndrome),
- Granuloma faciale,
- Eosinophilic fasciitis (Shulman syndrome),
- Eosinophilic folliculitis (Ofuji disease).

Blood eosinophilia may be an associated feature, but is not mandatory.

The eosinophilic infiltrates observed in these eosinophilic skin diseases are neither associated with parasitic infections/infestations nor with allergic disorders. There is currently no conclusive pathogenetic concept that could convincingly define the stimulus that results in tissue accumulation of eosinophils in these rare idiopathic disorders.

Maturation, migration and degranulation of eosinophils are subject to complex, cytokine-mediated regulation. At the same time, eosinophils interact with other cells of the immune system and with their direct environment by releasing cytokines and toxic proteins. Thus, eosinophils function not only as effector cells in inflammatory reactions but – as antigen-presenting cells – they are themselves able to initiate and modulate inflammatory reactions (Figure 1) [1].

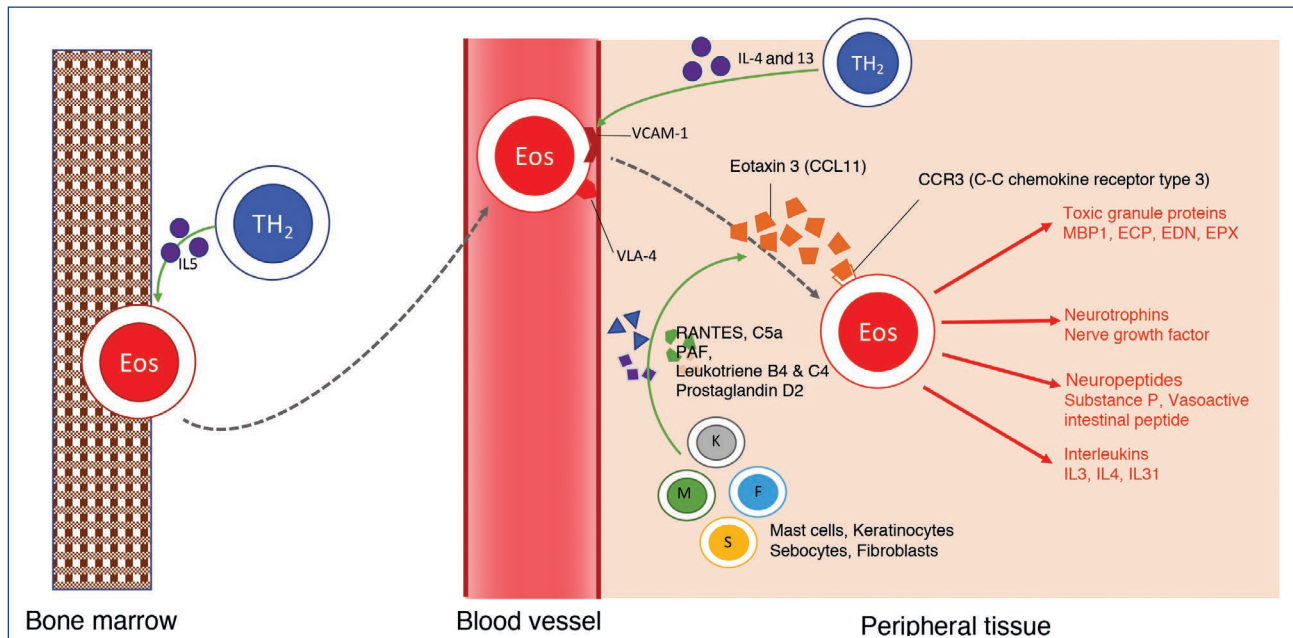


Figure 1 Cytokine-mediated effects on maturation, migration and degranulation of eosinophils.

Abbr.: Eos, eosinophils; TH₂, type 2 helper T cells; IL, interleukin; VCAM, vascular cell adhesion molecule; VLA, very late antigen; CCR, chemotactic cytokines receptor; PAF, platelet-activating factor; RANTES, regulated on activation, normal T cell expressed and secreted; C5a, complement factor 5a; MBP, major basic protein; ECP, eosinophilic cationic protein; EDN, eosinophil-derived neurotoxin; EPX, eosinophil peroxidase.

Regulation of eosinophil maturation and migration

The maturation of eosinophils occurs in the bone marrow and takes approximately five days. It is mediated through interleukin (IL)-5 released by activated T lymphocytes (TH₂). Subsequently, the eosinophils are discharged into the bloodstream where they circulate for roughly one day before migrating into tissue.

IL-4, IL-5 and IL-13 lead to tissue infiltration of eosinophils.

CC stands for chemotactic cytokines, a group of cytokines that attract cells. Cells bind to the ligand (CCL) via their CC receptor (CCR). Eotaxin 3 is the alternative designation for chemotaxin CCL11, which is involved in eosinophil migration into tissue.

Secretion of IL-4 and IL-13 results in increased expression of VCAM-1 (vascular cell adhesion molecule 1) in the endothelium [2]. Adhesion to the vessel wall is subsequently mediated by the adhesion molecule *very late antigen 4* (VLA-4), which is expressed by eosinophils (Figure 1) [3].

At the same time, chemokines such as eotaxin 3 (CCL11, CC-chemokine ligand-11) stimulate the migration of eosinophils, which bind to eotaxin 3 via their C-C motif chemokine receptor 3 (CCR3).

Apart from eotaxin 3, there are a number of other mediators that have a chemotactic effect on eosinophils. These include RANTES (regulated on activation, normal T cell expressed and secreted), complement factor 5 (C5a), lipid mediators such as platelet-activating factor (PAF), leukotriene (LT) B₄, LT C₄ and prostaglandin (PG) D₂. These are secreted by various different cell types, including mast cells, keratinocytes, sebocytes and fibroblasts [4]. Novel treatment approaches for eosinophil-associated diseases are based on inhibiting the aforementioned processes [5].

Eosinophils as effector cells

It has been known for a long time that eosinophils contain cationic proteins. Apart from these toxic proteins, eosinophils possess a large number of other mediators

Table 1 Important mediators released by eosinophils.

Group	Designation
(Toxic) granule proteins	Major basic protein 1 (MBP1)
	Eosinophilic cationic protein (ECP)
	Eosinophil-derived neurotoxin (EDN)
	Eosinophil peroxidase (EPX/EPO)
Neurotrophins	Nerve growth factor (NGF)
Neuropeptides	Substance P
	Vasoactive intestinal peptide (VIP)
Interleukins	IL-3, IL-4, IL-31

that play a key role not only in immune regulation, but also in mediating symptoms such as pruritus (Figure 1, Table 1).

Histology of eosinophils

Due to their eponymous characteristics, eosinophils are readily detectable on hematoxylin-eosin-stained sections. The chemical reaction between the cationic proteins and the acidic eosin not only results in the staining of intracellular granules but also of any granules bound to collagen fibers following degranulation (bright red). Extracellular granules also give rise to thickening of collagen fibers. This histological pattern is referred to as 'flame figures' (Figure 2) [6]. However, such a pattern is not specific for any dermatosis but simply indicates collagen denaturation caused by the toxic proteins contained in the eosinophilic granules. This degranulation and associated toxicity to the surrounding tissue is part of the physiological effect of eosinophils, for instance, in the defense against parasites. The same mechanism plays a pathophysiological role in eosinophil-associated disorders.

Flame figures are the result of eosinophil degranulation. They are not specific for any disease.

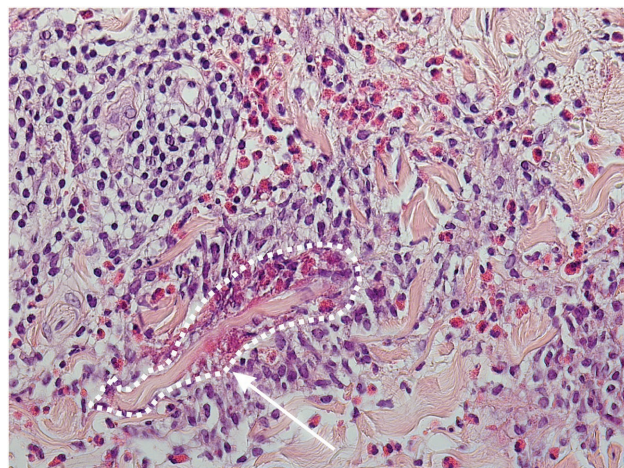


Figure 2 Histology showing 'flame figures' (hematoxylin-eosin stain, original magnification x 400).

Classification of eosinophilic dermatoses

There is a multitude of diseases associated with a detectable increase in eosinophils in the skin. Disorders that show an increased number of eosinophils on histology include parasitic infections or infestations, arthropod bite reactions, allergic contact dermatitis and atopic dermatitis, urticaria, prurigo nodularis, bullous dermatoses such as bullous pemphigoid or dermatitis herpetiformis (Dühring's disease). In addition, blood and tissue eosinophilia may also be observed in patients with eosinophilic granulomatosis with polyangiitis (formerly Churg-Strauss vasculitis), hypereosinophilic syndrome, eosinophilic leukemia, and drug reaction with eosinophilia and systemic symptoms (DRESS; hypersensitivity syndrome) as well as lymphoma (e.g., Hodgkin's lymphoma) and mastocytosis.

Strictly speaking, the "classic" eosinophilic dermatoses include eosinophilic cellulitis (Wells syndrome), granuloma faciale, eosinophilic fasciitis (Shulman syndrome) and eosinophilic folliculitis (Ofuji disease). These will be discussed in detail in the following paragraphs.

Wells syndrome

Wells syndrome was first described by George Wells in 1971 as "granulomatous dermatitis with eosinophilia". The term "eosinophilic cellulitis" was established at a later point in time. While its exact pathogenesis is unknown, Wells syndrome is considered to be a histological reaction pattern. Various possible triggers have been reported, including drugs such as penicillin or infliximab, solid and hematological malignancies, arthropod bites, vaccinations, varicella, and parvovirus infections.

Clinical features

Wells syndrome most commonly presents with large, markedly inflamed, infiltrated plaques associated with a burning sensation and/or pruritus (Figure 3). Recurrences are not uncommon. Overall, clinical manifestations may be highly varied. The diagnostic criteria proposed by Heelan et al. in 2013 include the following variants as major criteria: plaque-like, urticaria-like, papulovesicular, bullous, papulonodular, granuloma annulare-like and fixed drug eruption-like [7].

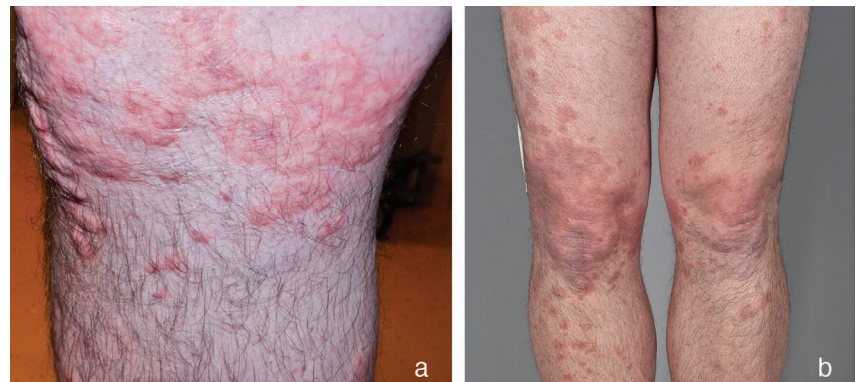


Figure 3 Eosinophilic cellulitis (Wells syndrome) on the thigh showing an urticaria-like appearance (a). Clinical presentation twelve days later showing atrophic, in some cases granuloma-annulare-like plaques (b).

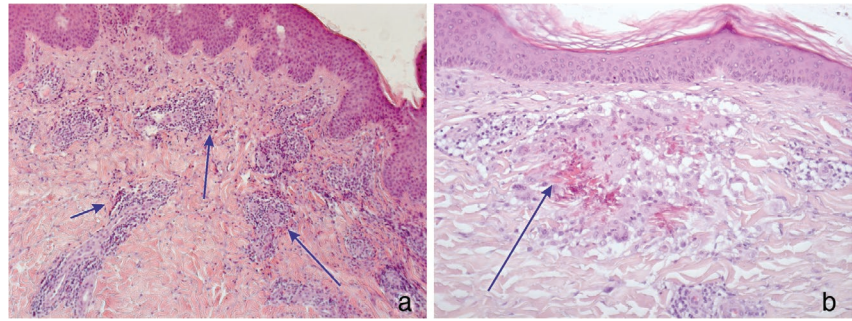


Figure 4 Histology of eosinophilic cellulitis (Wells syndrome): early lesion showing a dense eosinophilic infiltrate (arrows) (hematoxylin-eosin stain [HE], original magnification $\times 50$) (a). Fourteen days later: typical ‘flame figures’ (arrow) surrounded by granulomatous inflammation (HE, $\times 200$) (b).

Wells syndrome typically presents with large, markedly inflamed plaques associated with a burning sensation and/or pruritus.

On a pathophysiologic level, the aforementioned variability in clinical findings may be readily explained by the varying degree of eosinophilic infiltration, respectively eosinophil degranulation. Thus, infiltration with only mild degranulation will result in a plaque-like appearance. On the other hand, a greater release of mediators and toxic granules will result in urticarial, vesicular or even bullous lesions, caused by the resultant vasodilation and additional tissue damage. The clinical (and histological) presentation in the same patient thus frequently changes over time (“life of lesions”) [8].

Histology

Though characteristic, flame figures are not specific for Wells syndrome.

Initial findings frequently consist of a nonspecific, superficial and deep lymphocytic and eosinophilic dermal infiltrate. Edema, especially in the papillary dermis, may also be observed; hence, an arthropod bite reaction may also be considered in the histological differential diagnosis (Figure 4a). The typical flame figures develop over the course of 1–3 weeks. While they persist, predominantly perivascular histiocytic granulomas with multinucleated giant cells may subsequently occur (Figure 4b).

Treatment

Topical or systemic corticosteroids are useful in the initial treatment of Wells syndrome.

Räbßler et al. have systematically reviewed the various treatment options available [9]. In their summary, they recommend initial treatment with topical and/or systemic corticosteroids. Although there is no dosing regimen that is clearly better than any other, the best results have been achieved with an initial dose of 2 mg/kg over a period of 1–2 weeks, followed by a taper over 2–3 weeks. If corticosteroids are not sufficiently effective or long-term treatment is required, an attempt can be made with dapsone and cyclosporine A as well as antihistamines. There have also been reports (some of them individual case reports) on the use of azathioprine, tetracyclines, (hydroxy)-chloroquine, tacrolimus, colchicine and other drugs [10]. A recent publication reported on the successful use of mepolizumab (anti-IL-5 antibody).

Granuloma faciale (GF, Granuloma faciale)

Granuloma faciale was first described in 1945 by Wigley and designated as “eosinophilic granuloma of the skin”. While the term “granuloma faciale” is



Figure 5 Granuloma faciale: raised plaque on the forehead with a rubbery consistence.

predominantly used in English-language publications, the term “granuloma eosinophilicum faciei” is still used in German-speaking countries.

Clinical features

Important differential diagnoses of granuloma faciale include sarcoidosis, lupus vulgaris, chronic discoid lupus erythematosus, persistent arthropod bite reaction, rosacea, and deep trichophytosis.

Granuloma faciale usually presents with brownish-reddish plaques or nodules that are markedly raised and have a rubbery consistence; the lesions typically occur on the face and measure 1–2 cm in diameter (Figure 5). The diagnosis should be confirmed by histology to rule out differential diagnoses such as sarcoidosis, lupus erythematosus tumidus, persistent arthropod bite reaction, rosacea, leishmaniasis, B-cell lymphoma as well as deep trichophytosis, lupus vulgaris or erythema elevatum diutinum.

Histology

Histology shows a dense mixed-cell infiltrate with a grenz zone. This German term (meaning ‘border zone’) is also used in English. It describes an inflammatory dermal infiltrate that extends into the papillary dermis but is separated from the epidermis by a narrow zone (that contains no inflammatory cells) (Figure 6a).

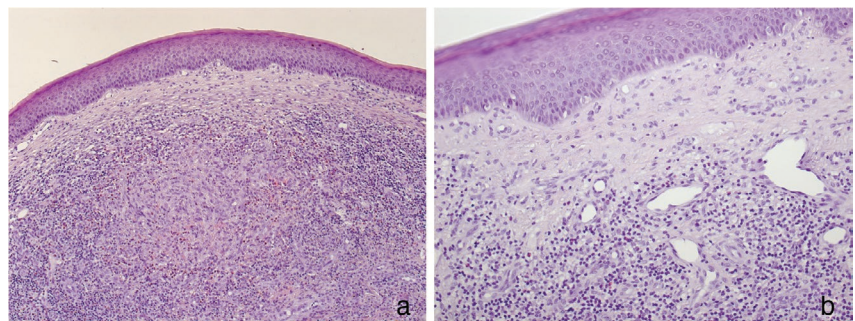


Figure 6 Histology of granuloma faciale: dense eosinophil-rich inflammatory infiltrates underneath a ‘grenz zone’ (hematoxylin-eosin stain [HE], original magnification x 50) (a). Close-up: eosinophil-rich inflammatory infiltrate with a ‘grenz zone’ and telangiectases (HE, x 200) (b).

Even though it was responsible for the original designation (granuloma eosinophilicum faciei) and is a typical finding, not every case of GF presents with an eosinophilic infiltrate. The term “granuloma faciale” should therefore be preferred. In their study of 66 cases, Ortonne et al. proposed further criteria that are diagnostically suggestive of GF. In addition to the grenz zone, other typical histological findings in GF include neutrophilic infiltration, telangiectases (Figure 6b) and vascular changes; occasionally, there are also perivascular deposits of IgG, IgA, IgM, C3c and C1q [11, 12].

Treatment

Treatment is often less than satisfactory. Topical calcineurin inhibitors, intralesional corticosteroids and dapsone should preferably be used.

Treatment of granuloma faciale is frequently challenging. A recently published systematic review by Lindhaus et al. compared various topical and systemic treatment options [13]. Even though topical/intralesional corticosteroids appear to be the most frequently employed treatment, they are insufficiently effective in 42 % of all cases. By comparison, topical application of the calcineurin inhibitor tacrolimus is significantly more effective and potentially associated with fewer adverse effects than local corticosteroid treatment, which often requires prolonged treatment [13].

In studies, dapsone proved to be effective in a certain percentage of cases. While there have also been reports on the efficacy of various laser systems and cryotherapy, both modalities showed varying degrees of success.

Eosinophilic fasciitis (Shulman syndrome)

Eosinophilic fasciitis is clinically similar to morphea, as it is also associated with subcutaneous sclerosis. Its cause is unknown but a certain percentage of patients report a history of local mechanical trauma or overexertion. Given the probability – albeit low (5–10 % of cases) – of an association with (predominantly hematological) neoplasms, an appropriate diagnostic workup (at least blood tests) should be performed [14, 15].

A hematological neoplasm should be ruled out in patients with Shulman syndrome.

Unlike morphea, the pathogenesis seems to be associated with a dominance of CD8-positive vis-à-vis CD4-positive cells; likewise, the percentage of Th17 cells appears to be higher. While this might have therapeutic implications, there are as yet no studies in this regard [16].

Clinical features

In many cases, eosinophilic fasciitis (EF) presents with acute onset of erythematous, edematous plaques with a “peau d’orange” appearance (Figure 7). In addition, patients often show a negative groove sign (depression along the course of superficial veins) caused by the fixation of veins to (deep) connective tissue. This prevents the veins from moving freely as the tissue expands due to edema. Unlike systemic sclerosis, EF is characterized by the absence of Raynaud’s phenomenon. Not uncommonly do patients develop with myalgia and/or arthralgia in addition to the skin lesions. Blood tests frequently show eosinophilia and elevated inflammatory markers (ESR, CRP).

The inflammatory stage is followed by a phase predominantly characterized by sclerosis of the affected areas. As it may be difficult to differentiate EF from morphea on clinical grounds – especially from rare (5 % of all cases) subtypes with fascial and muscle involvement – the diagnosis of eosinophilic fasciitis should be confirmed by a deep biopsy that includes subcutis, fascia and muscle. Ultrasound, magnetic resonance imaging (MRI) or PET/CT may also be useful, not only to establish the diagnosis of fasciitis but also to determine the best site for biopsy.



Figure 7 Shulman syndrome: erythematous, partly sclerotic plaque on the forearm.

Histology

Histology of EF is characterized by a thickened fascia surrounded by lymphocytes and eosinophils (Figure 8). Plasma cells and macrophages may also be observed. In longstanding disease or following treatment initiation, the eosinophils may also be absent. Concomitant myositis is a common finding [17]. In addition, there is thickening of dermal collagen fibers.

Treatment

Magnetic resonance imaging prior to treatment and over the course of the disease may be useful in assessing treatment success in patients with EF. Intravenous administration of gadolinium-based contrast agents allows for the detection of perifascial inflammation due to signal enhancement.

Treatment of EF should be based on a combination of systemic corticosteroids (0.5–2 mg/kg) and methotrexate (MTX; 15–25 mg/week). Data from retrospective studies suggest that this combination is superior to systemic corticosteroids alone [14]. In a small non-controlled prospective trial, an MTX dose of 4 mg/kg once a month with subsequent folic acid supplementation proved to be effective [18]. There are also case reports on the use of infliximab, rituximab, tocilizumab, sirolimus, azathioprine, sulfasalazine, cyclophosphamide, cyclosporine A and intravenous immunoglobulins.

A negative groove sign may point to the diagnosis of Shulman syndrome.

The combination of MTX and corticosteroids is superior to corticosteroids alone.

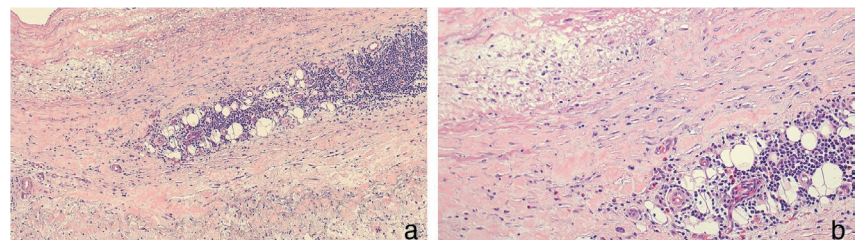


Figure 8 Histology of Shulman syndrome: eosinophil-rich inflammatory infiltrate around the fascia (hematoxylin-eosin stain, original magnification x 100 (a), x 200 (b)).



Figure 9 Eosinophilic folliculitis (Ofuji disease) presenting with papulopustules on the upper thorax.

Eosinophilic pustular folliculitis (EPF; Ofuji disease)

In 1970, Ofuji was the first to describe eosinophilic pustular folliculitis, clinically characterized by sterile papulopustules, with histological evidence of a perifollicular, predominantly eosinophilic infiltrate.

Clinical features

In the initial publication, Ofuji described erythematous plaques with prominent peripheral papulopustules on the trunk, face and extremities, characterized by slow centrifugal growth (Figure 9) [19]. There is spontaneous resolution with persistent hyperpigmentation.

Apart from this ‘classic’ form of EPF, there is another variant observed in immunosuppressed individuals (e.g., HIV infection). Compared to classic EPF, immunosuppression-associated EPF is frequently characterized by significant pruritus. Another variant is infantile EPF, which, unlike classic EPF, also affects the scalp. In 2016, Nomura et al. proposed a classification of EPF subtypes [20], adding another entity: episodic eosinophilic dermatosis of the face.

However, the question must be asked whether the aforementioned EPF variants (classic, immunosuppression-associated, infantile, episodic) are indeed well-defined, distinct entities. In addition, it should be reviewed whether it really makes sense to take a clinically and histologically well-defined skin disease – such as EPF – and include it in a disease group by adding a number of clinically and histologically different disorders, and then to divide this group once more into “different subtypes” [21].

In general, the differential diagnosis of inflammatory follicular lesions should include acne vulgaris, steroid acne, trichophytosis and other forms of folliculitis.

Histology

Ofuji described infundibular spongiosis with eosinophils, in some cases even microabscess formation in the infundibular epithelium (Figure 10). Using this relatively precise description as a basis, particularly as regards the location of the

Not every folliculitis with histological evidence of eosinophilia is consistent with the original description of EPF.

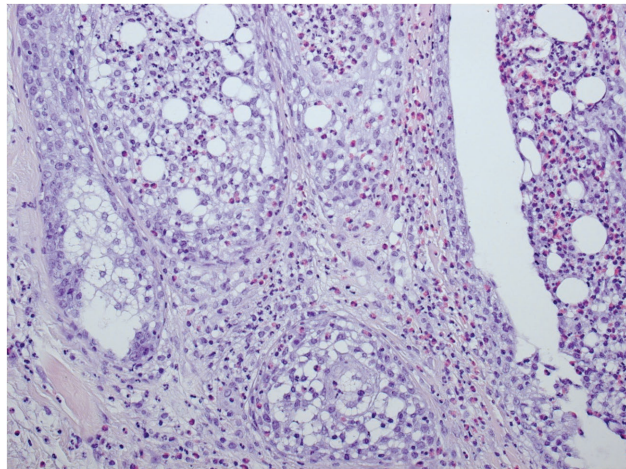


Figure 10 Histology of eosinophilic folliculitis (Ofuji disease): eosinophil-rich, follicular inflammatory infiltrate (hematoxylin-eosin stain, original magnification x 400).

eosinophils, the question needs to be asked whether all EPF cases subsequently reported are indeed consistent with the original description, or whether these cases actually described various other diseases associated with a follicular eosinophilic infiltrate. In their review of many cases purported to be EPF, Ziemer et al. found that diagnoses such as erythema toxicum neonatorum, arthropod bites, or scabies were more likely to be the cause of the follicular eosinophilic infiltrate [21].

Treatment

Many authors consider indomethacin to be the treatment of choice for ‘classic’ EPF as described by Ofuji. Both systemic and topical formulations may be considered [20]. Second-line alternatives include UV therapy, cyclosporine A, dapsone, topical tacrolimus or doxycycline.

Conclusion

Not only are eosinophils effector cells (degranulation) involved in the final pathway of antiparasitic or allergic processes, they also play a key role in immunoregulation. This explains why they may be histologically detected in a multitude of other, non-parasitic and non-allergic dermatoses. Eosinophils also play an important part in the causation/mediation of pruritus.

Eosinophils mediate their effects through a myriad of – frequently toxic – proteins. The interaction between these proteins and extracellular collagen may result in a typical histological pattern referred to as flame figures.

Wells syndrome, Shulman syndrome, eosinophilic folliculitis (Ofuji disease), and granuloma faciale are characterized by particularly prominent eosinophilic infiltration and – frequently – by a distinctive clinical presentation. Neither the cause nor the pathogenesis of these diseases is as yet well understood and should be further investigated in the future.

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Lernerfolgskontrolle

1. Welcher der nachfolgend genannten Stoffe zählt **nicht** zu den typischen von eosinophilen Granulozyten freigesetzten Stoffen?

- a) major basic protein 1 (MBP)
- b) nerval growth factor (NGF)
- c) Substanz P
- d) IL-3 und IL-4
- e) Myeloperoxidase

2. Welche Aussage zu Zytokinen ist korrekt?

- a) Zytokine sind eine Untergruppe der Chemokine.
- b) Zu den wesentlichen Zytokinen, die Eosinophilen-Chemotaxis, Proliferation und Differenzierung steuern, zählen IL-19 und IL-20.
- c) Mepolizumab ist ein Antikörper gegen IL-5.
- d) Dupilumab ist ein Antikörper gegen die Alpha-Untereinheit von IL-4 und IL-13.
- e) Interleukine sind natürlich vorkommende Steroidhormone.

3. Zu den „klassischen“ eosinophile Dermatosen zählt **nicht**:

- a) Wells-Syndrom
- b) atopische Dermatitis
- c) Granuloma faciale
- d) Shulman-Syndrom
- e) eosinophile Follikulitis Ofuji

4. Welche Aussage zu *flame figures* bei eosinophilen Dermatosen ist korrekt?

- a) Der Begriff beschreibt klinisch flammende Ausläufer von Erythemen entlang der Lymphbahnen.
- b) *Flame figures* sind ein spezifisches Zeichen der eosinophilen Zellulitis (Wells-Syndrom).
- c) *Flame figures* entstehen durch die Denaturierung von Kollagen durch kationische Proteine.
- d) *Flame figures* sind in HE-Färbung nicht sichtbar und erfordern eine Kongo-Rot-Färbung.

- e) *Flame figures* beschreiben die „flammenartige“ Anordnung von eosinophilen Granulozyten in der Epidermis mit breitem basalem Infiltrat und apikaler Verjüngung.

5. Welche Aussage trifft zum Wells-Syndrom **nicht** zu?

- a) Das klinische Bild kann vielgestaltig (plaqueartig, urtikariell, papulovesikulös, bullös, papulonodulär, Granuloma-anulare-artig, fixes-toxisches-Arzneimittel-artig) imponieren.
- b) Histologisch findet man oft sogenannte *flame-figures*.
- c) Der quälende Juckreiz ist im Wesentlichen durch die Degranulation von neutrophilen Granulozyten verursacht.
- d) Therapeutisch ist initial die systemische Steroidtherapie sinnvoll.
- e) Bezüglich der Therapie sind auch Erfolge unter Anwendung von Azathioprin, Tetracyclinen, Chloroquin und Tacrolimus beschrieben.

6. Das Granuloma eosinophilicum faciei (Syn.: Granuloma faciale) ...

- a) zeigt klassisch Blasen, Pusteln und Urtikae.
- b) zeigt histologisch typischerweise eine Grenzzone, das heißt ein dermales Entzündungsinfiltrat, welches kurz vor der Epidermis endet.
- c) bildet sich auch ohne Therapie typischerweise innerhalb von 8–12 Wochen komplett zurück.
- d) ist meist mit einer ausgeprägten Allgemeinsymptomatik im Sinne von Fieber und Abgeschlagenheit verbunden.
- e) ist bei Frauen deutlich häufiger als bei Männern zu finden.

7. Welche Aussage zur Therapie des Granuloma eosinophilicum faciei ist korrekt?

- a) Es benötigt selten eine Therapie, da es meist selbst limitierend innerhalb von Wochen abklingt.

- b) Lokale Steroide sind in der Therapie kontraindiziert.
- c) Topische Calcineurininhibitoren sind in der Lokalthherapie wirkungslos.
- d) In der Therapie wird häufig ein Ansprechen auf eine Therapie mit Antimykotika wie Terbinafin beobachtet.
- e) Dapson kann erfolgreich in der Therapie des Granuloma faciale eingesetzt werden.

8. Welche Aussage zum Shulman Syndrom ist **falsch**?

- a) Aufgrund der Assoziation eines Teiles der Fälle mit hämatologischen Tumoren ist eine diesbezügliche Diagnostik empfohlen.
- b) Die typische Klinik beschreibt ödematöse Plaques mit orangenschalen-artiger Oberfläche.
- c) Blutsenkungsgeschwindigkeit (BSG) und C-reaktives-Protein (CRP) sind nur ausnahmsweise erhöht.
- d) Im Gegensatz zur progressiv systemischen Sklerose sind antinukleäre Antikörper (ANA) und extrahierbare nukleäre Antikörper (ENA) meist negativ.
- e) Therapeutisch ist ein Erfolg unter einer kombinierten Therapie von Prednisolon mit Methotrexat häufiger zu beobachten als unter Prednisolon allein.

9. Welche Aussage zur eosinophilen pustulösen Follikulitis ist **falsch**?

- a) Klinisch imponieren juckende Papulopusteln, die zu Plaques mit randständigen Pusteln konfluieren können.
- b) Prädispositionsstellen sind Gesicht, Stamm und Extremitäten.
- c) Histologisch sieht man klassisch eosinophile infundibuläre Mikroabszesse.
- d) Häufig ist eine Abheilung unter Hinterlassung einer Hypopigmentierung zu beobachten.
- e) Ursächlich ist eine Follikel-bezogene Infektion mit Mikrokokken.

10. Welche Aussage zur eosinophilen pustulösen Follikulitis (EPF) ist korrekt?

- a) Durch die Degranulation toxischer Substanzen durch die Eosinophilen und deren Wirkung auf Nervenfasern ist die Anästhesie der betroffenen Areale sehr typisch.
- b) Nicht selten entstehen pralle Blasen an den betroffenen Hautarealen.
- c) Die Therapie mit Indometacin ist oft erfolgreich.
- d) Die Wirkung von Indometacin beruht auf der Blockade des Substanz-P-Rezeptors.
- e) In mehreren Studien konnte Adalimumab die EPF rasch und nachhaltig bessern.

Liebe Leserinnen und Leser,
der Einsendeschluss an die DDA für
diese Ausgabe ist der 13. Dezember 2019.
Die richtige Lösung zum Thema
„Extragenitale kutane War-
zen – Klinik, Diagnose und The-
rapie“ in Heft 6 (Juni 2019) ist:
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