* TREMFYA® ist indiziert: 1) für erwachsene Patienten mit mittelschwerer bis schwerer **Plaque-Psoriasis**, die für eine systemische Therapie in Frage kommen; 2) allein oder in Kombination mit MTX für die Behandlung der aktiven **Psoriasis-Arthritis** bei erwachsenen Patienten, wenn das Ansprechen auf eine vorherige nicht-biologische krankheitsmodifizierende antirheumatische (DMARD-)Therapie unzureichend gewesen ist oder nicht vertragen wurde.[1]

\# PASI 90: 84% (Wo 48; n=534) Non Responder Imputation (NRI)[2]; PASI 100: 52,7% (Wo 252; n=391) Treatment Failure Rules (TFR)[3]; Signifikante Überlegenheit vs. Placebo in Bezug auf ACR20 (64% vs. 33%, p<0,0001; NRI) nach 24 Wochen in der 8-Wochen-Dosierung (n=248) in bionaiven Patienten mit aktiver PsA.[4]

1. Aktuelle Fachinformation TREMFYA®. **2.** Reich K et al. Lancet. 2019;394(10201):831–839. **3.** Reich K et al. Br J Dermatol. 2021 Jun 9. doi: 10.1111/bjd.20568.
4. Mease P et al. The Lancet 2020; https://doi.org/10.1016/S0140-6736(20)30263-4 (Supplementary)

▼ Dieses Arzneimittel unterliegt einer zusätzlichen Überwachung. Daher ist es wichtig, jeden Verdacht auf Nebenwirkungen in Verbindung mit diesem Arzneimittel zu melden.

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JDDG Journal of the German Society of Dermat

Review

Submitted: 16.7.2020
Accepted: 28.1.2021
Conflict of interest
None.

DOI: 10.1111/ddg.14450

Figurate erythemas – update and diagnostic approach

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Summary

Figurate erythemas (FE) represent an etiopathophysiologically heterogeneous group of diseases defined by their characteristic annular erythematous skin lesions. Diagnosis is made primarily by clinical examination together with histological findings; often it is a diagnosis made by exclusion. While some authors discuss FE as clinical reaction pattern rather than distinct clinical entities, others identify four classic FE: erythema annulare centrifugum, erythema gyratum repens, erythema migrans and erythema marginatum. The differential diagnoses of FE are numerous and often challenging. We therefore present a potential diagnostic algorithm for FE that discriminates the differentials according to their temporal evolution and the clinical/histological phenotype of the various subtypes. Since some FE may present with an underlying malignancy, diligent clinicians are needed when dealing with those entities.

Introduction

The term figurate erythemas (FE) was first described by Fox in 1889 in the "Atlas of Rare Skin Diseases" [1]. Since then, multiple authors have tried to subdivide this disease cluster into different clinical entities based on varying morphological and etiopathophysiological findings, giving rise to a multitude of differential diagnoses in various textbooks (Table 1).

Nowadays, FE in a more restricted way form a heterogeneous group of diseases that may occur at any time throughout life, defined by annular, circinate, concentric, polycyclic or arciform erythematous lesions with a tendency to spread centrifugally. The patterns are non-scaling or scaling and usually start out as small raised erythematous spots, slowly expanding to a ring-shaped structure, while the center clears [2].

Like the clinical appearance, the etiology of FE is also heterogenous and has been linked to underlying conditions including infections, drugs, neoplasms and autoimmune diseases. However, in most cases the trigger remains elusive. While the exact pathophysiology of FE is unknown, an immune-mediated reaction to antigens of, for example, an infectious or neoplastic source is suspected. Some authors even regard FE as a defined clinical reaction pattern to specific stimuli rather than distinct clinical entities [2, 3].

There are four, so called "classic" FE: *(1)* erythema annulare centrifugum, *(2)* erythema gyratum repens, *(3)* erythema migrans and *(4)* erythema marginatum, each presenting with advancing erythematous circinate lesions, but separated by unique clinical and histopathological hallmarks. Since multiple cutaneous diseases can present with a figurated morphology, differential diagnoses of FE are numerous and challenging. In contrast to disease classifications according to molecular patterns [4], diagnosis of FE is made primarily clinically together with histological findings. Rios-Martin et al. stratified the histological pattern of FE according to the cellular infiltrate into four groups: lymphocytic, neutrophilic-eosinophilic, granulomatous and infiltrates containing plasma cells (Table 2) [5].

Besides a skin biopsy for dermatopathology, other investigations such as microbiology and serology may be necessary to exclude other causes of annular skin eruptions. Well established tools such as Wood's light, PAS staining and KOH test might be helpful to rule out a fungal infection. Thus, FE is often a diagnosis by exclusion [6].

Considering the heterogenous origin of FE, treatment varies significantly between the different entities. While some subtypes resolve on their own or with topical corticosteroids only, others do need systemic therapy, especially when an underlying causative disease is identified [2].

Table 1 Differential diagnoses of figurate erythema.

Infectious disease	Tinea corporis, impetigo, erythema migrans, secondary syphilis, tuberculoid leprosy
Autoimmune diseases	Bullous pemphigoid, linear IgA dermatosis, lupus erythematosus (esp. subacute cutaneous lupus erythematosus SCLE), Sjögren syndrome, lichen planus, pustular psoriasis (for example erythema annulare centrifugum-like psoriasis cum pustulatione), subcorneal pustulosis (Sneddon Wilkinson), pityriasis rubra pilaris, erythema dyschromicum perstans
Neoplastic diseases	Lymphoma, mycosis fungoides
Metabolic diseases	Necrolytic migratory erythema (glucagonoma syndrome)
Allergic (possibly) and miscellaneous diseases	Urticaria, urticarial vasculitis, annular erythema of infancy, eosinophilic annular erythema, purpura annularis teleangiectodes, erythema palpabile et arciforme, seborrheic dermatitis, erythema multiforme, sarcoidosis, elastosis perforans serpiginosa, erythema annulare centrifugum, erythema gyratum repens

This review focuses on the four classic FE and highlights a practical approach to the differential diagnosis of FE.

Erythema annulare centrifugum

The term erythema annulare centrifugum (EAC) was proposed by Darier in 1916, describing a persistent annular erythema [7]. Regarding the epidemiology, EAC can occur at any age with a peak incidence in the mid-adult life and an equal male to female ratio. Erythema annulare centrifugum is a classic FE in the sense that initial lesions appear as urticaria-like papules that spread centrifugally and enlarge up to greater than 6 cm in diameter, while developing central clearing with the progression of the disease (Figure 1) [8, 9]. The most common locations for EAC include the trunk and proximal extremities. Individual lesions usually last from several days to weeks and may resolve spontaneously while new lesions continue to appear, especially with a coexisting, underlying disease process [9].

Two different subtypes based on clinical and histological appearance have been described (Table 3) – superficial or deep EAC, also named as superficial gyrate or deep gyrate erythema. Characteristic for the superficial type is the so-called trailing scale, a fine scale at the inner margin of the advancing edge. It typically goes along with pruritus and occasionally vesicles can be seen at the outer margin. Histologically superficial EAC exhibits spongiosis, microvesiculation, focal parakeratosis and a superficial perivascular lymphohistiocytic infiltrate.

The deep EAC is usually non pruritic and presents with a firm "cord-like border" without scaling and is usually more indurated and elevated compared to the superficial type. This is represented by the histology showing no epidermal changes and a mononuclear infiltrate predominantly localized in the mid and lower dermis. Some authors define a third type of

Table 2 Histological patterns of FE (adapted from Rios-Martin et al. [5]).

Lymphocytic	Neutrophilic-Eosinophilic	Granulomatous	Plasma cell infiltration
Erythema annulare centrifugum	Erythema marginatum rheumaticum	Granuloma annulare	Secondary syphilis
Erythema gyratum repens	Annular psoriasis	Sarcoidosis	
Erythema migrans	Annular erythema of infancy/ eosinophilic annular erythema	Tuberculoid leprosy	
Necrolytic erythema	IgA pemphigus		
Cutaneous lupus erythematosus	Urticarial vasculitis		
Lymphoma			

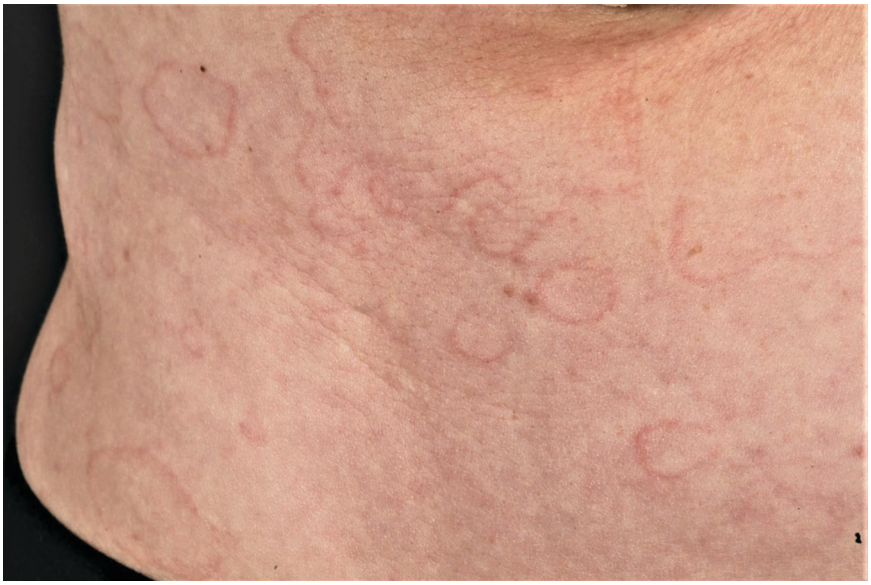

Figure 1 Clinical picture of erythema annulare centrifugum, (50 y/f, archives of Dept. of Dermatology and Allergology, Biederstein, TUM).

EAC as the clinical and histological collision of the superficial and deep gyrate erythema, which is named mixed type [10, 11].

While the pathogenesis of EAC is unknown, like most FE, it has been associated with a myriad of possible etiologies. From the infectious category, fungal diseases, especially dermatophytes, have been linked to EAC, while there are also reports of bacterial and viral diseases as causative factors. Furthermore, immunologic diseases such as Crohn's disease and certain drugs have been implicated in the onset of EAC [8].

There is also a connection between EAC and an underlying malignancy, with some authors classifying EAC as a facultative cutaneous paraneoplastic syndrome. Confirmed cases of paraneoplastic EAC are also specified by the acronym PEACE (paraneoplastic erythema annulare centrifugum eruption), which is most commonly associated with lymphoproliferative malignancies, especially leukemia and lymphoma. Paraneoplastic erythema annulare centrifugum eruption appears more often in women and typically precedes the diagnosis of the underlying malignancy. While skin lesions often resolve with the remission of the neoplasm, the reappearance of EAC in these cases might indicate a tumor relapse. In their review of 2012 Chodkiewicz et al. identified 40 patients with malignancy associated EAC with 62.5 % of lymphoproliferative and 37.5 % of solid tumor origin. They proposed that the underlying malignant condition leads to the formation of cytokines or antigens, stimulating the development of cutaneous eruptions like EAC [12–16].

Table 3 EAC subtypes.

	Superficial EAC	Deep EAC
Synonym	Superficial gyrate erythema	Deep gyrate erythema
Clinical characteristics	Trailing scale, pruritus	"cord-like border", non-scaling, non-pruritic
Histological characteristics	Spongiosis, parakeratosis, superficial perivascular lymphohistiocytic infiltrate	No epidermal changes, mononuclear infiltrate at the mid and lower dermis

However, in most EAC cases no causative trigger can be detected, resulting in a label of idiopathic EAC. Nevertheless, if the etiology remains unclear, we suggest age-appropriate tumor screening according to national guidelines. When there is clinical suspicion of PEACE, for example fever, weight loss or night sweat a symptom-based evaluation of malignancy should be performed.

The treatment of EAC depends on whether a causative underlying condition can be identified or not. If EAC is associated with an underling disease, it will usually clear once the triggering process has been treated properly. For idiopathic cases management is focused on associated symptoms such as pruritus and the resolution of the cutaneous lesions. There are no prospective, randomized controlled trials evaluating the efficacy of the various treatment methods in EAC (Table 4). Treatment options attempted in EAC include topical and systemic steroids, topical calcineurin inhibitors, topical vitamin D analogues and oral erythromycin, metronidazole and fluconazole [17–19]. Additionally, one case report

Table 4 EAC treatment options.

Topical	Systemic
Glucocorticoids	Glucocorticoids
Calcineurin inhibitors	Erythromycin
Vitamin D analogues	Metronidazole
	Fluconazole
	Azithromycin

has shown efficacy of etanercept in the treatment of reluctant EAC [20]. Recently Sardana et al. reported a remarkable response to oral azithromycin 250 mg once daily in eight out of ten EAC patients during an open trial [21]. Subanalysis revealed an earlier response in the superficial type compared to the deep type EAC patients. Interestingly, although thorough examinations have been carried out in all patients, the etiology of EAC has not been identified in a single case. The mechanism behind the clinical efficacy was attributed to the anti-inflammatory effect of low dose azithromycin [8].

Erythema gyratum repens

Erythema gyratum repens (EGR) is a rare and clinically characteristic FE with a strong association to malignancy. Erythema gyratum repens was first described in 1952 by Gammel in a patient nine months before the appearance of breast cancer [22]. Epidemiologically, EGR mainly affects Caucasians, with a male to female ratio of 2 : 1 and an average age of onset at 63 years. Clinically, EGR is characterized by rapidly migrating (about 1 cm/day), concentric erythematous, pruritic bands with a typical "knotty-cypress wood-grained" configuration and scaling edges (Figure 2). Additional findings include palmoplantar keratoderma, hypereosinophilia and acquired ichthyosis. Erythema gyratum repens usually involves large areas of the body and appears on the trunk and extremities while sparing the hands, feet and face. Diagnosis is based upon the characteristic clinical morphology. Although histopathology is non-specific, exhibiting focal parakeratosis, spongiosis and a superficial perivascular lymphocytic infiltrate with islands of eosinophils, it is used to rule out other possible FE [23–26].

Since its first description, EGR has been linked to a variety of different malignancies, most frequently including bronchial (32 %), esophageal (8 %) and breast (6 %) cancer [23]. Similar to the first published case of Gammel, skin lesions typically precede the occurrence of neoplasia by four to nine months. In the past, EGR has therefore been considered to be an obligatory paraneoplastic cutaneous skin disease, although an underlying neoplasm could only be detected in

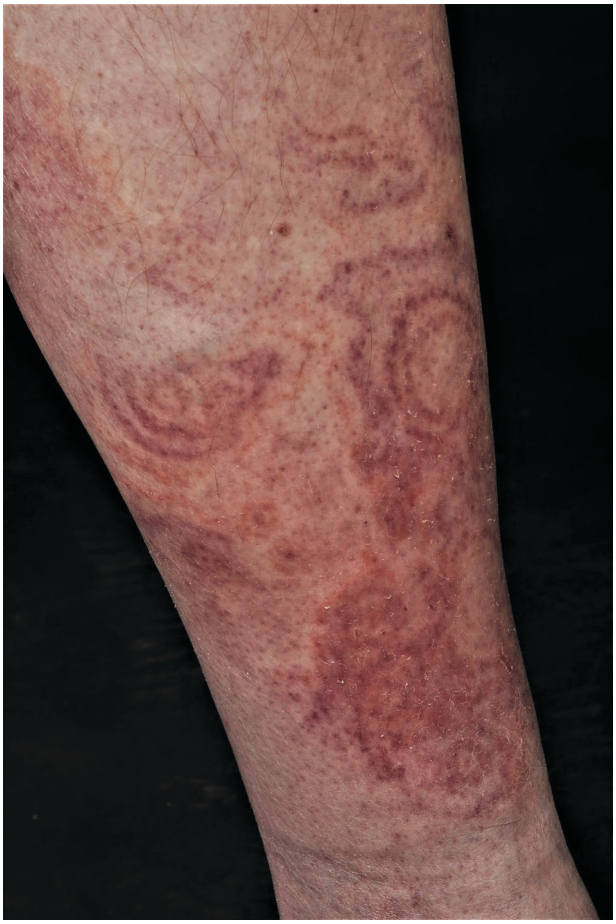

Figure 2 Clinical picture of erythema gyratum repens (57 y/m, archives of Dept. of Dermatology and Allergology, Biederstein, TUM).

82 % of the cases [23]. A more recent review by Rongioletti et al. identified 83 cases of EGR with only 70 % presenting with an underlying malignancy. The non-paraneoplastic cases of this cohort were either idiopathic (32 %) or associated with an underlying skin disease (52 %), an autoimmune disease (8 %), a systemic infection (4 %) or with drug intake (4 %) [27]. Interestingly, there a several reports in the literature describing the transition of pityriasis rubra pilaris (PRP) [28] and psoriasis to EGR, with none of these cases showing evidence for malignancy. For PRP patients EGR eruptions might be a sign for impending remission [29–31]. The various possible etiological factors of EGR are listed in Table 5 [24, 25]. In summary, EGR should not always be considered as an obligate paraneoplastic syndrome and clinicians need to be alert for other possible causes. However, all patients should undergo age-based cancer screening together with symptom-based malignancy evaluations as indicated, since a prompt identification of paraneoplastic EGR is essential to decrease morbidity and mortality [23, 24, 27].

Table 5 Etiological entities including underlying malignancies in EGR [23, 27, 49, 50].

Malignancies	Lung cancer, esophageal cancer, breast cancer, stomach cancer, lymphoma, genitourinary cancer
Chronic inflammatory skin disease	Pityriasis rubra pilaris, psoriasis, ichthyosis, hypereosinophilic syndrome
Idiopathic	
Autoimmune disease	CREST syndrome, rheumatoid arthritis
Systemic infection	Tuberculosis, *Helicobacter pylori*
Drugs	Azathioprine, interferon

While the exact pathophysiology of EGR remains unknown, three immunologic mechanisms have been postulated: *(1)* Induction of autoantibodies by the tumor that cross-react with the basement membrane of the epidermis. This is supported by the presence of immune deposits in the sublamina densa seen in direct immunofluorescence. *(2)* Production of polypeptides by the tumor that bind to skin antigens that subsequently turn immunogenic. *(3)* Deposition of tumor induced antigen-antibody complexes at the cutaneous basement membrane [23, 32].

Management of EGR should aim primarily at the recognition and treatment of the underlying malignancy, since most cases experience full remission of the cutaneous lesions including the often-debilitating pruritus after resolution of the associated neoplasm. For the treatment of non-paraneoplastic cases and the symptomatic treatment of paraneoplastic EGR various therapies have been described, including steroids, azathioprine and retinoids. Unfortunately, these therapies are often ineffective [23].

Erythema migrans

Erythema migrans (EM) represents a classic FE with a distinctive etiology. It is the skin manifestation of early Lyme disease, caused by an infection with *Borrelia (B.) burgdorferi*, which is transmitted by tick bites in endemic areas. It was first described clinically by Afzelius in 1909 as an annular erythema developing after tick bites, before being connected to *B. burgdorferi* spirochetes in the 1980s by Burgdorfer [33].

Lyme borreliosis is separated into three stages: *(1)* early localized disease; *(2)* early disseminated disease and *(3)* chronic disease, with EM being the characteristic clinical feature of early disease. Typical EM is characterized by an erythematous annular rash with centrifugal extension developing three to 30 days after and at the same site of a previous tick bite. A targetoid lesion may develop through clearing in or around the center during expansion of EM (Figure 3). Another feature of typical solitary EM is illustrated by a visible puncture site in the center of the erythema. Expansion of cutaneous lesions can last for several weeks and individual lesions can reach up to 70 cm of diameter, until spontaneously disappearing after a median of four weeks. To separate EM from other diseases (in particular localized inflammatory reactions to tick bites) and to increase diagnostic specificity, the minimum diameter of skin lesions should exceed 5 cm.

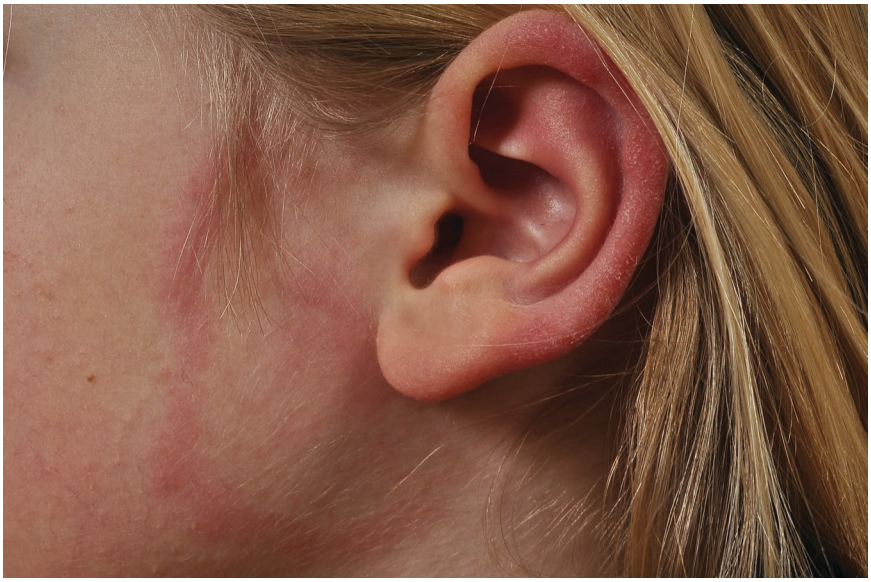

Figure 3 Clinical picture of erythema migrans (5 y/f, archives of Dept. Of Dermatology and Allergology, Biederstein, TUM).

Most commonly EM appears on the trunk, groin, axilla or the popliteal fossa. While most of EM lesions are asymptomatic some patients experience mild pruritus, pain or transient numbness or tingling [34, 35].

According to the guidelines of the German Dermatological Society from 2017, atypical EM skin lesions can present with a variable morphology also including non-migrating, centrally vesicular, hemorrhagic, infiltrated instead of macular or persisting EM over four weeks which is referred to as erythema chronicum migrans (ECM) [34]. Central clearing is more likely to appear in long-standing lesions, making it a typical morphological pattern for ECM.

During stage two of Lyme disease, secondary EM lesions may develop at other body areas through spreading of *B. burgdorferi* from the initial tick bite site via the blood. This is seen in around 20–25 % of the patients and referred to as multilocular EM (MEM). Single cases with up to 100 EM have been described. Multilocular EM are usually smaller in diameter, symptomless, often symmetrical and lack the typical puncture site. Other indicators for hematogenous dissemination are flu-like symptoms such as fatigue, headache, arthralgias, myalgias and fever as well as lymphadenopathy, which can accompany both primary and secondary EM lesions. However, European patients are less likely to experience systemic symptoms compared to US patients, since *B. afzelii*, the major strain of Lyme disease in Europe, exhibits a lower virulence [34, 36].

The correlate of the centrifugal expansion is the migration of the spirochetes, spreading outwards from the inoculation site, which leads to a growth rate of 20 cm^2/day for early EM lesions. The following erythema is the correlate of a triggered immune response by macrophages and lymphocytes in response to Borrelia organisms. The histologic features of EM are often non-specific and manifest with superficial and deep lymphoid infiltrates accompanied with few eosinophils and plasma cells. In some cases, EM might even present with focal interface dermatitis, as demonstrated in a recent study by Tekin et al. [37, 38].

Concerning the diagnosis of EM, three settings need to be addressed according to the German guidelines [34]:

1. If a clinical typical solitary EM lesion is present, no further laboratory diagnostic confirmation is necessary.
2. Suspicion of solitary atypical EM needs to be clarified through a serological test. If the test is negative and clinical suspicion remains, direct pathogen detection via culture or molecular-biological (PCR) methods from skin biopsy material (near the inflamed edge) shall be used for diagnostic clarification.
3. In the presence of MEM: cf. *(2)*.

Treatment recommendations for Lyme disease have been published in numerous European and American guidelines with doxycycline and amoxicillin being the antibiotics of choice. According to the German guidelines, Doxycycline 100 mg bid should be used as a first-line treatment of EM (solitary: 10–14 days; MEM: 14–21 days). Besides amoxicillin, alternative antibiotics include cefuroxime and azithromycin. In case of a disseminated infection (MEM), up to 10 % of the patients might experience a possible Jarisch-Herxheimer reaction presenting with a flare up of erythema and flu-like symptoms within 24 hours of taking the antibiotics. While systemic steroids are not necessary, this condition can be treated with NSAIDs [34].

Erythema marginatum

Erythema marginatum, also named erythema marginatum rheumaticum (EMR), is a migratory annular and polycyclic erythematous eruption and the cutaneous manifestation of acute rheumatic fever (RF). Rheumatic fever is an autoimmune, systemic inflammatory disease characterized by an abnormal response to an infection with group A β-hemolytic streptococci (usually pharyngitis) in genetically susceptible individuals. Besides EMR (< 6 %), patients with RF develop carditis (50–78 %), arthritis (35–88 %), chorea (2–19 %) and subcutaneous nodules (< 1–13 %). Rheumatic fever is primarily a disease of developing countries with an annual incidence of > 100/100,000 [39].

With a latency of usually 2–5 weeks after initial manifestation of streptococcal infection, lesions of EMR appear as erythematous, peripherally spreading, non-scaling macules which can develop to patches or plaques. Lesions are typically fluctuant, migrating, fading and reappearing within hours. Erythema marginatum rheumaticum is usually asymptomatic and favors the proximal extremities, the trunk and axillae with sparing of the face as well as the palms and soles. It can persist intermittently for weeks to months, while being primarily associated with the active phase of RF. There is a strong correlation between EMR and the manifestation of carditis. Erythema marginatum rheumaticum is more frequent in children and very rare in adults [40].

According to the Jones criteria, diagnosis of RF can be established by evidence of group A streptococcal infection (either culture/rapid antigen test via swap or serological) accompanied by either two major (carditis, polyarthritis, chorea, EMR, subcutaneous nodules) or one major and two minor criteria (fever, arthralgias, elevated ESR, elevated CRP, prolonged PR interval on an ECG). Histologically, EMR exhibits a perivascular infiltrate composed predominantly of neutrophils. Although the exact pathogenesis of EMR is unknown, it is suspected that antigenic mimicry between streptococci and human skin epitopes plays an important role [39, 41].

Erythema marginatum rheumaticum usually resolves spontaneously and is unaltered by treatment of the underlying

RF. Treatment of RF consists of anti-streptococcal (penicillin) therapy and in case of cardiac involvement also anti-inflammatory (glucocorticosteroids) therapy [39].

Besides these four classic representatives of FE, rare forms of FE include the palpable arciform migratory erythema with similarities to urticarial vasculitis [42] and the annular erythema of infancy [43] also called eosinophilic annular erythema [44].

Approach to the differential diagnosis of FE

As in the case presented here, dealing with FE is challenging since a myriad of other dermatoses can also present with a figurative pattern. Therefore, clinicians are in need of a diagnostic algorithm for addressing those dermatoses. Maul et al. recently proposed an approach to the differential diagnosis of FE (Figure 4) [6]: In a first step, lesions should be evaluated with regard to their temporal evolution, since only a few annular presenting dermatoses persist for less than 24 hours. Besides EM as a representative of the classic FE, this group includes urticaria, serum sickness-like reaction, EM-like lesions of hereditary angioedema and erythrokeratodermia variabilis.

Differentials of FE lasting longer than 24 hours should be discriminated according to their clinical phenotype and the histology. This heterogenous group includes urticarial lesions (EM, EAC deep type, LE tumidus, Wells' syndrome, etc.), granulomatous lesions (granuloma annulare, sarcoidosis, etc.), papulosquamous lesions (EAC superficial type, EGR, pityriasis rosea, PRP, tinea, etc.), lesions with variable presence of scale (annular lichenoid dermatitis, secondary syphilis, etc.), pustular lesions (IgA pemphigus, pustular psoriasis [45]), erosive/vesiculobullous lesions (erythema multiforme group, necrolytic migratory erythema, etc.), purpuric lesions (purpura annularis telangiectoides) and perforating lesions (Elastosis perforans serpiginosa).

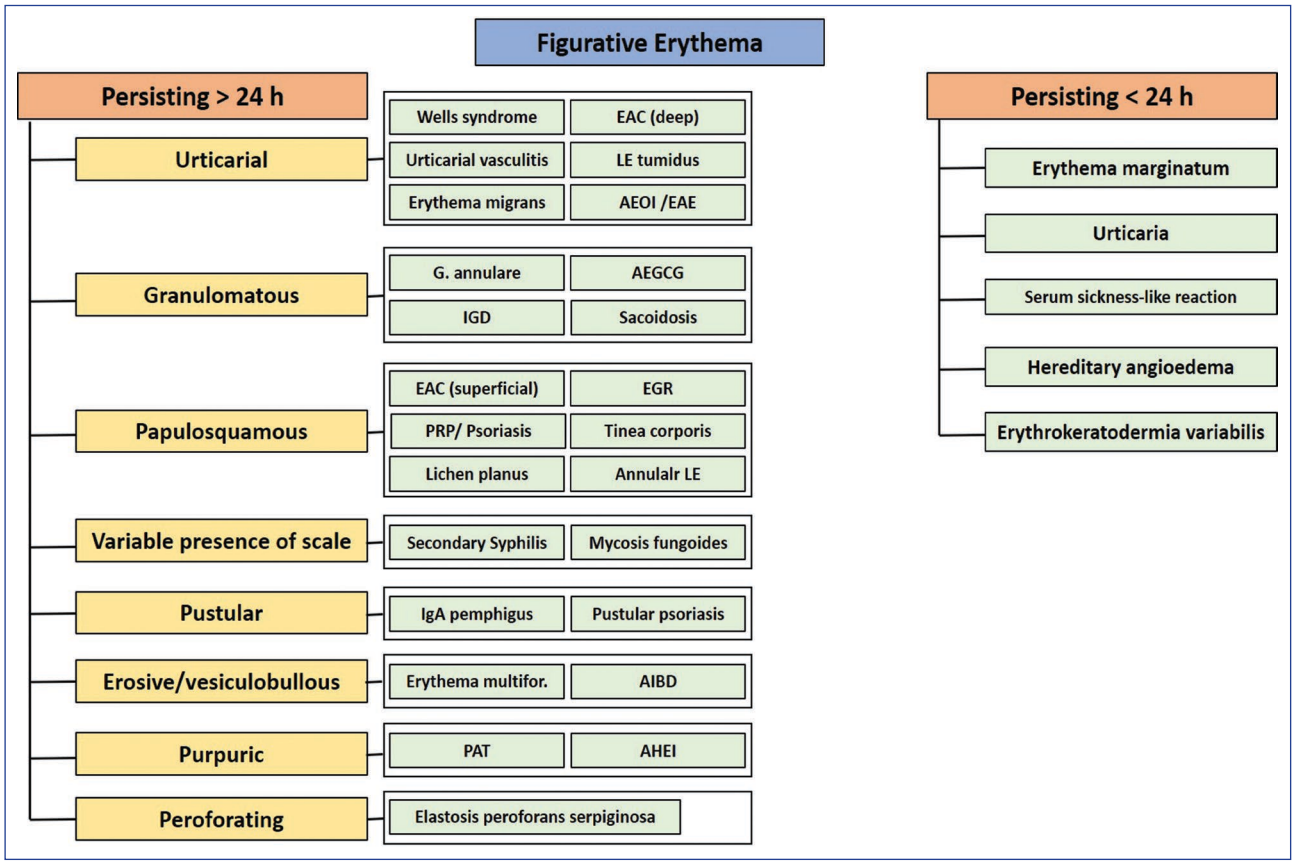

Figure 4 Approach to the differential diagnosis of FE. *Abbr.:* AEGCG, annular elastolytic giant cell granuloma; AHEI, acute hemorrhagic edema of infancy; AIBD, autoimmune bullous dermatoses; AEOI, annular erythema of infancy; EAC, erythema annulare centrifugum; EAC, eosinophilic annular erythema; EGR, erythema gyratum repens; IGD, interstitial granulomatous dermatitis; LE, lupus erythematosus; PAT, purpura annularis teleangiectodes; PRP, pityriasis rubra pilaris).

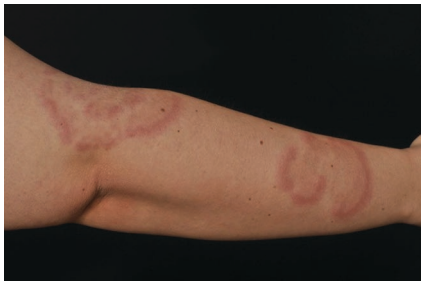

Figure 5 Multiple, disseminated, annular, urticarial, non-scaling, erythematous, figurated plaques on the proximal extremities (24 y/f, archives of Dept. of Dermatology and Allergology, Biederstein, TUM).

Case report

As an example for use with the proposed algorithm, we present a special case from our outpatient department. A 24-year-old woman presented to our hospital with a three-month history of a pruritic rash resistant to topical steroids. Prior dermatological history as well as family history was unremarkable.

On examination our patient was in a good clinical condition showing multiple, disseminated, annular, urticarial, non-scaling, erythematous, figurated plaques on neck, trunk and proximal extremities (Figure 5). Mucosal tissue was unaffected. Pruritus was seven out of 10 on a numeric rating scale. The Dermatology Life Quality Index (DLQI) on admission was 21.

By applying this presented diagnostic algorithm on our patient, we could limit the differentials to the group of persisting urticarial eruptions (Figure 4). To further narrow the diagnosis down we performed a skin biopsy of a representative lesion showing a perivascular and interstitial infiltrate consisting of numerous eosinophils and lymphocytes. Mucin in the upper corium was revealed via alcian-blue stain. Flame figures or granuloma formation were absent and there was no sign of vasculitis. Blood testing including screening parameters for autoimmune disease and sarcoidosis was without pathological finding. There was no peripheral eosinophilia. Due to our findings the diagnosis of eosinophilic annular erythema (EAE) was made and a therapy with 50 mg of oral dapsone once daily was started. Additionally, the treatment with topical steroids was continued. Due to an initially poor treatment response, we consequently escalated the dose of dapsone to 100 mg alternating with 150 mg every other day. After a few weeks, a significant reduction of the erythematous lesions and pruritus was observed.

With this case, we demonstrated the complexity of diagnosis and treatment of this heterogeneous group of skin diseases. In our case, the diagnosis of EAE could be made via typical clinical presentation and skin biopsy. Eosinophilic annular erythema is a rare entity of figurated erythema of unknown etiology and was originally described in children, where it was initially named annular erythema of infancy [46]. It is characterized by recurrent annular skin lesions with tissue eosinophilia, typically resistant to various treatments. There is still controversy whether EAE should be considered as a distinct clinical entity or as subtype of Wells' syndrome. In contrary to Wells' syndrome, histological findings in EAE typically exclude flame figures or granulomatous formations and there is an absence of blood eosinophilia [47]. Treatment approaches encompass antimalarials such as hydroxychloroquine, systemic and topical steroids, UVB and dapsone. Additionally, there is one report of effective treatment of recalcitrant EAE with dupilumab [48].

Conclusions

There is a great clinical variability of FE, but together with histology and laboratory investigations a logical algorithm can be applied allowing correct diagnosis. Therapy consists – apart from elimination or treatment of causative factors – in anti-inflammatory or antimicrobial strategies. By identifying the immune response patterns [4] associated with FE, and through the introduction of biologics into dermatology, it may be possible to target specific cytokines involved in severe cases of FE.

Acknowledgements

Open access funding enabled and organized by Projekt DEAL.

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