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A case of tinea incognita and differential diagnosis of figurate erythema

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ABSTRACT

A patient with *tinea incognita* is presented together with a review of the literature of figurate erythema. Figurate lesions are emblematic for dermatology and perhaps the most picturesque efflorescences. The differential diagnosis can be broad and sometimes challenging. Many clinical entities with resembling primary and secondary efflorescences have to be considered as differentials and can be due to anti-infectious, paraneoplastic, allergic, autoimmune or other immune reactions.

1. Introduction

Few physicians can successfully master the clinical challenge of figurate erythema (FE). FE are non-scaling or scaling, usually non-pruritic, annular or arciform, erythematous eruptions that have a tendency to spread centrifugally within hours to days. Their colour can range from slight pink to deeply violaceous, and they are usually characterized histologically by a dense lymphohistiocytic infiltration surrounding superficial and deep dermal vessels. Usually, the papillary and reticular dermis are affected.

The etiology of FE is unknown but thought to be immune-related, most likely due to a hypersensitive immune reaction to antigens of infectious, drug-related, neoplastic or environmental origin. The FE group sensu stricto includes *erythema anulare centrifugum*, *erythema marginatum, erythema migrans* and *erythema gyratum repens*. The differential diagnosis (Fig. 1) can be broad and sometimes challenging, and include more than 30 conditions [1].

2. Case

A 40-year-old saleswoman with known atopic eczema of mild intensity presented with an itching, livid-erythematous patch in the left gluteal region, infiltrated at the edge with serum crusts that had slowly enlarged centrifugally during 7 months until it reached 10 × 7 cm in size (Fig. 1A) at the day of presentation (day 0). Furthermore, on the medial side of the right knee, the patient had noticed a round, 3 × 4 cm erythematous patch with small, grouped pustules at the edge since 6 month.

The patient reported very strong pruritus that had persisted for the whole period of 7 months when the lesion in the left gluteal region had first appeared. The patient had tried topical fusidic acid (day-48 until −39 and −15 until −5) as well as topical (clobetasol propionate) (day −38 until day −20) and systemic steroids (prednisone) (day −20 until day −15), which led to temporary improvement. However, a relapse occurred and lesions slowly enlarged centrifugally, even though the patient continued topical steroids. The patient did not take any other medication, but further medical history revealed a type I hypersensitivity to pollen and crustaceans.

An external histology (day −48) revealed perivascular lymphocytic-histiocytic and eosinophilic infiltrates in all dermal layers and in the superficial parts of the subcutis. In addition, the epidermis was somewhat hyperkeratotic, and some neutrophil granulocytes and small intracorneal serum deposits were detectable. PAS staining showed no fungal hyphae, and mycosis was thus not diagnosed. However, a bacterial swab of the lesion revealed *Staphylococcus aureus*.

Upon consultation at our clinic, we performed a review of the differential diagnosis of figurate erythema, looking for signs of infection, malignancy or other systemic diseases. A differential blood count revealed erythrocyte macrocytosis that was however considered unlikely to contribute to the skin condition. Signs of autoimmunity and systemic infection including ANA, anti-SS-A, anti-SS-B, anti-transglutaminase, anti-endomysia, anti-gliadin-IgA as well as HIV serology and fecal parasitology were inconspicuous. A chest x-ray and a sonography of the abdomen and lymph nodes only showed an enlarged right submandibular lymph node, but no signs of malignancy.

Topical steroids (clobetasol propionate) were paused and a biopsy with direct immunofluorescence was performed (day +2). Directly afterwards, the symptoms exacerbated, with the appearance of multiple

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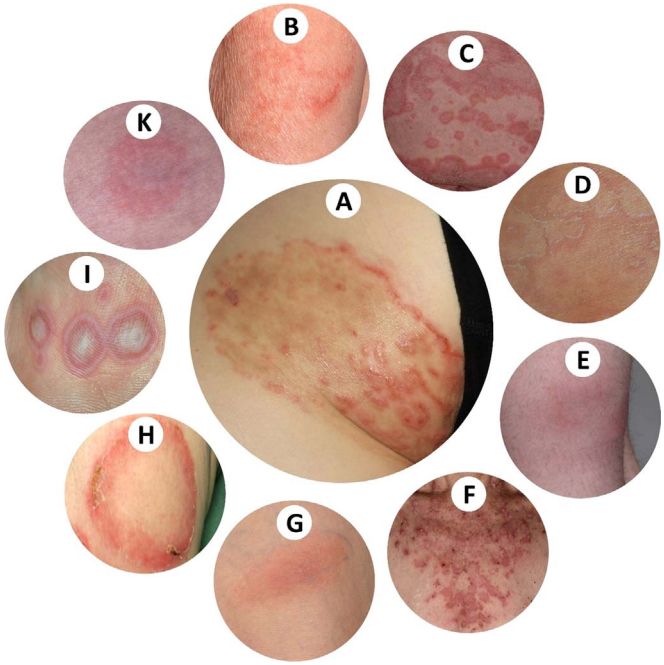

Fig. 1. Differentials and patients' lesion. A: Hyperergic mycosis at the left gluteal region in herein presented immunocompetent patient. B: Erythema annulare centrifugum (EAC). C: Erythema annulare. D: Erythema gyratum. E: Erythema nodosum. F: Rowell's Syndrome. G: Erythema chronicum migrans. H: Erythema necroticans migrans (courtesy of Oliver Wilde, Gilching, Germany). I: Erythema exsudativum multiforme. J: Annular Urticaria.

serous papules and blisters. In scales from the gluteal lesion, fungal hyphae were detected upon direct microscopic examination with 0.025% Congo red (in 5% SDS). On Sabouraud dextrose agar with gentamicin/chloramphenicol and Mycosel agar (both incubated at 25 °C) a dermatophyte was isolated which was identified as *Trichophyton rubrum* based on morphological criteria as previously described [2]. The diagnosis of tinea was confirmed histologically. We prescribed itraconazole 100 mg once a day in the morning for two weeks and complete healing of the lesions resulted.

3. Discussion

3.1. Approach to the differential diagnosis to figurate erythema

First, the temporal evolution of the erythema must be evaluated. Only few differentials of FE will produce transient lesions that persist for less than 24 h, namely urticaria, erythema marginatum induced by streptococcal infections, hereditary angioedema with erythema marginatum-like lesions, the genetic condition erythrokeratoderma variabilis and African trypanosomiasis. The rest of the figurate-like conditions consist of efflorescences that are stable over days to weeks.

Erythematous skin lesions persisting longer than 24 h can be differentiated according to their clinical appearance, situative context and histology. Allergic urticarial eruptions have deep lymphocytic infiltrates with eosinophils. Wells' syndrome is characterized by pruritic oedematous erythematous plaques, often annular or arciform with a greenish hue in the center and blood eosinophilia. Histology typically shows scattered eosinophils and flame figures. Urticarial vasculitis is defined by annular urticarial plaques that can have purpura and cause a burning sensation. The histology is leukocytoclastic vasculitis and it can be hypocomplementemic. Erythema migrans due to Borrelia also has aspects compatible with urticaria. Lymphohistiocytic infiltrates are found around superficial and deep vessels, and plasma cells and eosinophils can be present [3]. Erythema annulare centrifugum has slightly raised borders and perivascular lymphohistiocytic infiltrates upon histology. Lymphocytic infiltrates of Jessner (LIJ) and lupus erythematosus tumidus (LET) can both present with arciform urticarial plaques and block-like lymphocytic inflammatory infiltrates with (LET) or without (LIJ) mucin deposition. Rowell's syndrome, the association of LE and EEM, is characterized by annular, succulent or bullous lesions on the trunc, face and neck [4].

If the epidermis is not involved, but the border of the figurate erythematous lesion appears dense upon palpation, a granulomatous lesion should be considered. Granuloma annulare is the most common of these and its border is composed of multiple small papules. It occurs on hands, feet and extensor surfaces. A biopsy shows palisaded granulomas with central necrobiosis and increased mucin deposition. A variant is the elastolytic giant cell granuloma of Hanke that produces large annular plaques on sun-exposed skin with central atrophy and hypopigmentation. Histology demonstrates absence of elastic fibers in the center of the lesion and elastophagocytic giant cells in the periphery. Sarcoidosis can also produce annular plaques of brownish colour that are most often found on the face and are composed histologically of sarcoidal granulomas. Leprosy looks quite similar clinically and is usually characterized by hypoesthesia in the center of the lesion. Drug reactions can also produce annular granulomatous lesions, e.g. the interstitial granulomatous reaction that is most often due to antihypertensives or lipid-lowering agents but can also be associated with certain forms of autoimmune diseases. It is characterized by palisading granulomas surrounding small collagenous deposits [1].

Papulosquamous figurate erythematous lesions reveal additional epidermal involvement histologically. Tinea corporis is defined by annular plaques with a sharply defined, scaly border, facultative pustules at the edge of the lesion [5], and dermatophytes in the stratum corneum. Central clearing and peripheral enhancement causes annular or arcuate lesions, furthermore the fusion of the lesions can result in gyrate patterns [6]. The most frequent pathogen of dermatomycoses worldwide is *Trichophyton rubrum* [7]. Tinea corporis is by far the most common dermatosis within the list of differentials of FE, perhaps apart from psoriasis, and should be sought and excluded first. Erythema annulare centrifugum (EAC) lesions are sterile but can be triggered by fungal infections such as tinea pedis. EAC is not a specific clinicopathological entity; it rather represents a clinical reaction pattern of unidentified etiology. It is assumed that the EAC is a general term for many different clinical-histological reaction patterns. It initially presents with an erythematous patch or urticarial papules, which spread centrifugally. It often shows a trailing scale that corresponds to focal parakeratosis and spongiosis in histology. Due to centrifugal migration, confluence of single lesions and central clearing, EAC can have an annular and arciform appearance. This effect makes EAC the emblematic representative of figurate erythema [8]. Erythema gyratum repens is a rare paraneoplasia that looks like EAC painted on the skin with broad strokes in a wood-grain pattern. It also has a moving edge that wanders about one cm per day [9]. Resolving pityriasis rubra pilaris resembles erythema gyratum repens and its histology typically shows checkerboard-like ortho- and parakeratosis. Erythrokeratoderma variabilis and some bullous conditions are important differentials as well. Because pityriasis rosea can also produce annular scaly plaques and is relatively common, it should be considered as well. It is commonly located on the posterior trunk, partly in a Christmas-tree distribution and starts with a comparatively large herald plaque. Lichen planus produces a central brownish hyperpigmentation and can have mucosal involvement. The main histological finding is a band-like lymphocytic infiltrate at dermal-epidermal junction and hypergranulosis. Annular lupus erythematosus (LE), characterized by photosensitivity also shows interface dermatitis. Discoid LE favours the face, the subacute-cutanous LE the upper extremities and the upper trunk. Seborrheic dermatitis stays within the seborrheic areas and is less well demarcated than psoriasis, which shows annular scaly plaques with slow expansion and sharp edges. In the histology of psoriasis, neutrophil infiltrates in epidermis and parakeratosis are typically observed. Ichthyosis linearis

circumflexa in Netherton syndrome is associated with atopic diathesis, highly elevated serum IgE and its erythematous plaques are bordered by double-edged scales [1].

If the lesions are covered by scales of variable severity, the figurate erythematous lesion could be annular lichenoid dermatitis of youth, whose clinical features include red-brownish annular plaques with central hypopigmentation, and, histologically, a lichenoid infiltrate. Secondary syphilis looks clinically alike and is accompanied by flu-like symptoms. Mycosis fungoides in the patch and plaque stage can also have annular erythematous plaques. The histology is quite characteristic in typical cases with chain-like infiltrates of atypical lymphocytes ("indian file"), plasma cells and eosinophils in the dermis as well as epidermotropism of lymphocytes.

Pustular lesions can be differentiated based on clinical features and histology. Pustular psoriasis can have an annular pattern and is characterized by fast-growing erythematous borders with pustules. The histology reveals neutrophilic infiltrates and pustules. IgA pemphigus shows pustules in a circinate pattern. The histology is comparable to pustular psoriasis with additional intercellular epidermal IgA deposition. Ofuji's disease, the eosinophilic pustular folliculitis is defined by grouped follicular pustules arranged in annular configuration [10].

Another differential diagnosis of figurate erythema are erosive and vesiculo-bullous lesions such as erythema multiforme (EM) or more severe forms such as Stevens-Johnson syndrome. Necrotic keratinocytes and inflammation are demonstrated in histology. Less common is the necrotic migratory erythema, which is associated with liver or gastrointestinal disorders and clinically shows erosions and crusting mirrored by histologic findings of erosions and edema. Bullous pemphigoid has tense blisters and pruritic annular urticarial plaques with typical IgG and C3 deposits in the basal membrane zone (BMZ). Linear IgA bullous dermatosis is clinically comparable but shows linear deposits of IgA in the BMZ instead. Epidermolysis bullosa simplex, Dowling-Meara subtype has a mutation in the genes encoding keratin 5 or 14 and produces a generalized distribution of herpetiform or figurate groups of blisters. Annular epidermolytic ichthyosis is characterized by superficial peeling and scaling at the border of annular erythematous plaques [11].

Purpura annularis teleangiectoides Majocchi produces petechiae and telangiectasia in annular shape and is located mainly on the legs. In histology, perivascular infiltrations of lymphocytes and extravasated erythrocytes are present. A leukocytoclastic vasculitis with annular, erythematous to purpuric, oedematous plaques is known as acute haemorrhagic edema of infancy. Lastly, perforating dermatoses can also look like figurate erythema, namely *elastosis perforans serpiginosa* with transepidermal elimination of elastic fibers.

3.2. Differential diagnosis in our patient with figurate erythema

Applying the presented strategy for the differential diagnosis of figurate erythema to the presented case, we had observed long-standing (> 24 h), slowly enlarging, roundish plaques with epidermal involvement and sharply defined, scaly border, as well as dried pustules. A tumor screen was negative. The lesions were in region with little sun-exposure. No blisters or purpura were present. Taken together, the likely diagnosis was The number of patients with fungal infections is substantial and growing; at least 5–10% of dermatological consultations worldwide involve this disease [7]. However, the majority of those infections are local, most notably affecting the nails. Persistent or chronically recurrent tinea corporis due to *Trichophyton rubrum* in immunocompetent patients on the contrary is rare and often misdiagnosed. The reason of misdiagnosis include but are not limited to the few subtle differences in the clinical presentations of tinea corporis and FE (for example erythema annulare). While tinea corporis classically presents itself as an annular erythematous plaque with a raised edge, erythema annulare is typically characterized by one or several indurated, erythematous or violaceous annular plaques on the extremities. The subtlety of the differences in clinical presentation represent a challenge for clinicians who rarely see such cutaneous disorders.

As a result, misdiagnosis can occur in any primary outpatient setting, which is why it is important to re-evaluate patients with chronic annular skin lesions on a regular basis and, if in doubt, refer them to a specialised center (university clinic). A biopsy and a mycological examination of skin scrapings including a direct microscopic examination, e.g. a potassium hydroxide (KOH) mount, and a fungal culture can help in most cases to distinguish between FE (for example erythema annulare) and tinea corporis. However, both the microscopic examination and the fungal culture can be false-negative., due to i) sampling errors, i.e. the specimen does not contain the fungus or insufficient amount of specimen, ii) non-adequate handling, transport and storage of specimen, iii) prior anti-fungal therapy, iv) unexperienced staff or v) limited sensitivity of the method itself. Based on several studies, the sensitivity of a KOH mount and culture has been estimated to be in the range of 60–85% and 40–60%, respectively [12–14]. It is therefore recommended to repeat mycological examinations when results initially are negative and a fungal infection cannot be ruled out.

If misdiagnosed and treated with steroids (which unfortunately happened to our patient, too), tinea corporis may change its clinical presentation and become a tinea incognita because topical steroids often supress local immune responses. We consider our patient immunocompetent, based on her detailed medical history, our investigation of the infiltrating cells, as well as the differential blood count that did not reveal any anomalies. However, the changes in the local immune response in patients with tinea corporis undergoing topical steroid therapy certainly deserve further investigation.

In conclusion, a thorough review of the presented case led to the diagnosis of tinea corporis, which had been missed initially. This case illustrates that a thorough review of the differential diagnoses of FE, critical evaluation of the prior diagnosis, and repeated investigations (analysis of scales for tinea and skin biopsy) is valuable in establishing the correct diagnosis of FE.

Conflict of interest

There are no conflicts of interests.

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