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Figurate erythema in a patient with bullous pemphigoid and *Toxocara* infection

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Abstract

Figurate erythema can appear in a wide spectrum of dermatological diseases. Rarely, it can present as an atypical manifestation of bullous pemphigoid. Among eosinophilic dermatoses, figurate erythema may appear in Wells syndrome, which has been occasionally reported in association with *Toxocara* infection. We present the case of an older female patient diagnosed with bullous pemphigoid, who presented with an unusual combination of blisters and figurate erythema outside the area of blister formation. In addition, high blood eosinophilia associated with lymph node and bone marrow eosinophilia was diagnosed and was causally related to *Toxocara canis* infection. The patient was treated with dapsone for bullous pemphigoid and with albendazole for toxocariosis, with complete regression of all skin lesions and blood eosinophilia. This paper discusses the possible etiopathogenesis of figurate erythema in our patient and summarizes previous clinical and histological findings in bullous pemphigoid and eosinophilic dermatoses presenting with figurate erythema lesions.

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Introduction

Figurate erythema (FE) includes various and etiologically unrelated dermatological diseases presenting with annular or polycyclic erythematous lesions with peripheral spread. Although its pathogenesis has not been completely elucidated, FE may represent a hypersensitivity reaction to various infections, infestations, drugs, and foods, but can also develop in the background of malignancies and in connective tissue diseases (1). Diagnosis of FE is made clinically, but finding the underlying disease responsible for FE may prove difficult.

In rare instances, FE has been observed as an atypical manifestation of bullous pemphigoid (BP) (2). FE may also appear in eosinophilic dermatosis (ED), especially in Wells syndrome (WS) (3, 4). Both conditions were considered as differential diagnoses in the patient presented, diagnosed concomitantly with BP and *Toxocara* infestation.

Case report

A 75-year-old woman first presented with bullous eruptions on the extremities and mild mucosal lesions of the oral cavity. A diagnosis of bullous pemphigoid was confirmed by direct immunofluorescence. Temporary regression of skin and mucosal lesions was achieved with systemic tetracyclines.

Several months later, bullous lesions reappeared and, in addition, numerous annular erythemas developed on the trunk and extremities (Fig. 1). Except for a new finding of enlarged axillary and inguinal lymph nodes, there were no symptoms of other organ involvement. High blood eosinophilia was first registered at that time (36.3%). A skin biopsy performed from the annular lesions revealed a superficial perivascular and interstitial infiltrate of lymphocytes and numerous eosinophils scattered throughout the papillary dermis and upper part of the reticular dermis. Slight eosinophilic spongiosis was present focally and there were also solitary eosinophils in the subcutis (Fig. 2).

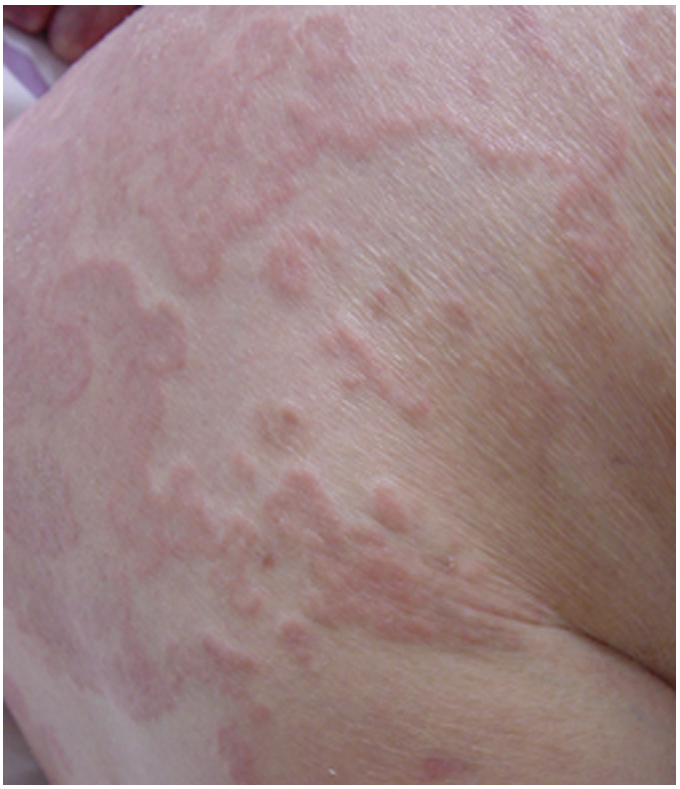

Figure 1 | Annular erythemas on the trunk and leg.

No bullae formation was present. Direct immunofluorescence demonstrated linear deposits of IgG and C3 (Fig. 3) and, in addition, granular deposits of IgM along the epidermal basement membrane. The histological features, taking into consideration the immunofluorescence findings, were consistent with pre-bullous BP. Aspiration biopsy of the enlarged lymph node revealed reactive lymphadenitis with marked eosinophilia. A bone marrow biopsy showed marked eosinophilia; however, the histological criteria for hypereosinophilic syndrome (HES) were lacking, and there were no features present to suggest malignancy. Tests showed elevated IgE

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(1014 IU/ml) and a high titre of antibodies to *Toxocara canis* with the ELISA test. Additional examinations showed no signs of systemic involvement or malignancies.

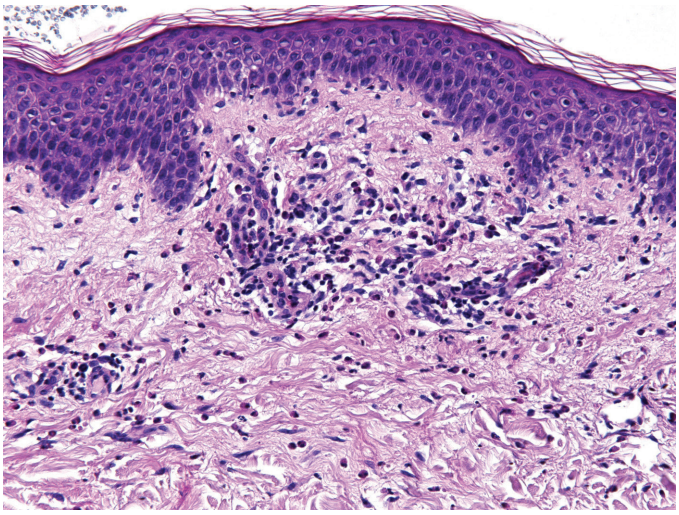

Figure 2 | Pre-bullous pemphigoid. Mild spongiosis of the epidermis, associated with numerous eosinophilic granulocytes in the dermis. Hematoxylin & eosin staining.

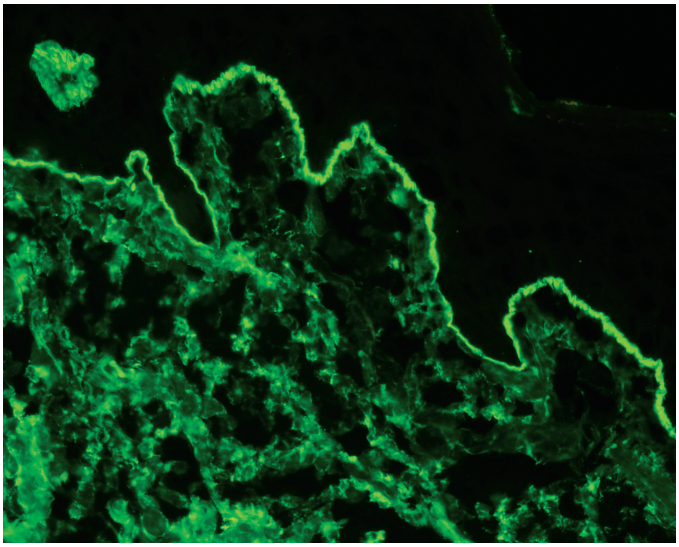

Figure 3 | Immunofluorescence microscopy shows linear deposits of IgG along the epidermal basement membrane.

Treatment with tetracyclines was discontinued and dapsone was introduced in a 100 mg daily dose. Regression of the bullous lesions and FE, as well as blood eosinophilia, was observed within a few weeks. Thereafter, the patient received albendazole 400 mg orally twice daily for 5 days. Complete regression of blood eosinophilia and of all skin lesions followed in 1 month. The level of IgE antibodies normalized in 3 months and the titre of *Toxocara canis* antibodies decreased slowly.

After 2 years of follow-up, dapsone was discontinued due to sustained complete remission. Within a few months, a reappearance of annular erythema was noticed, accompanied with only mild blood eosinophilia (7.1%). Histopathology showed similar findings as in the previous biopsy, but eosinophilic infiltrate was only present along the dermoepidermal junction. Treatment with dapsone was reintroduced. Two years later, the patient is still being treated with a low maintenance dose of dapsone (50 mg 2 days per week), without signs of BP exacerbation or the presence of malignant disease.

Discussion

An unusual coincidence of BP and *Toxocara canis* infestation was found in this case, both of which have rarely been associated with the development of FE.

BP usually affects elderly patients. In addition to the typical presentation with blisters, it may also present in many atypical variants (5). Interestingly, manifestation of BP with FE has been reported only sporadically (2, 6–9). In some patients, an association with a malignant disease was observed, such as with colonic carcinoma (2), carcinoma of the bronchus (6), and metastatic spread of carcinoma (7). In BP in general, the majority of studies have failed to demonstrate a significant association with malignancies (5, 10, 11). In a study by Hadi et al., malignant disease was found in nine of the 50 patients, a rate comparable to that of age-matched controls. However, in three of the nine patients, BP presented with FE (12). On the basis of these observations, BP with FE may be regarded as a paraneoplastic phenomenon, especially in cases that are resistant to conventional immunosuppressive therapy. In our patient, as in some of the previous reports (8, 9), association with malignant disease was not found.

Because of concomitant systemic eosinophilia, interpretation of the histological picture was more challenging in our patient. Eosinophilic infiltrate in the upper dermis could fit with BP. In non-bullous variants of BP, eosinophils are also often seen in the dermis (5). In the elderly, BP should be considered in a case of eosinophilic dermatitis and urticarial lesions (3). In BP with FE, epidermal spongiosis with eosinophilic infiltrate was also observed (2, 9).

On the other hand, similar histological findings as in pre-bullous BP can also be observed in WS, eosinophilic annual erythema (EAE), and hypereosinophilic dermatitis (HED) (3, 4, 13–15). In adults, EAE was first suggested by Kahofer et al. for annular skin lesions associated with cutaneous eosinophilia (13). Recently, it has been recognized as a special subtype in the spectrum of WS (14). The classic histological appearance with characteristic flame figures was only found in long-standing lesions, with eosinophilic infiltrate extended into the subcutis. However, direct immunofluorescent examination has shown negative or non-specific findings in WS (4, 15), EAE (13, 14), and HED (16, 17). Linear deposits of IgG and C3 along the epidermal basement membrane were decisive for the diagnosis of BP in our patient. Therefore, FE may be considered an atypical manifestation of BP in the case presented. The course of the disease, with reappearance of FE after discontinuation of dapsone treatment, also speaks in favor of BP.

Mild peripheral blood eosinophilia may be present in 50% of patients with BP (11). However, high blood eosinophilia, eosinophilic lymphadenitis, and bone marrow eosinophilia are unusual for BP. The possibility of concomitant ED was also considered as a reactive response to *Toxocara canis* infestation. The criteria for HES (3, 4) were not fulfilled in our patient because systemic symptoms were absent and eosinophilia was not idiopathic. WS has previously been reported in a possible relationship to *Toxocara* infestation, also associated with bone marrow eosinophilia (15). Blood eosinophilia may accompany at least 50% of patients with WS and EAE (4, 14). Data on eosinophilic lymphadenitis and bone marrow eosinophilia in association with ED are lacking in the literature. We could find only one report of HED with associated eosinophilic lymphadenitis (18). The spectrum of dermatologic features in toxocariasis is also not well defined. Generalized

pruritus, prurigo, and urticarial and papular eruptions have been most commonly observed (19).

Because direct immunofluorescence examination was consistent with BP in our patient, *Toxocara* infection could be interpreted as an accidental finding and unimportant in relationship to FE. Considering the findings of all examinations, however, an overlap of BP and probable initial WS might be possible. WS lacks specific clinical, histological, and immunohistological characteristics, and therefore we can only assume that cutaneous eosinophilia might have been induced by both conditions.

Dapsone may be a good treatment option in BP as well as in WS (3, 4, 14). It probably also had a good influence on the cutaneous and extracutaneous eosinophilia in our patient. On the other hand, the decline in the *Toxocara* titre and levels of IgE may be viewed as the result of albendazole treatment.

If the known reasons for eosinophilia are excluded, ED is usually considered to be idiopathic and treated with immunosuppressive drugs. However, when the cause of WS was identified and effectively treated, the disease regressed (14). Examinations for *Toxocara* with more sensitive serological tests were not performed in many of the previously published cases of WS, EAE, and HED.

To summarize, the spectrum of differential diagnoses in FE is broad. Correlation between the anamnestic data, clinical picture, histology, direct immunofluorescence, and additional examinations is needed to establish the causative disease. In rare cases of BP presentation with FE, an underlying malignancy should be considered. In ED, all known causes of eosinophilia that might be more easily treated should be excluded before starting treatment with systemic immunosuppressive drugs. A *Toxocara* ELISA test, together with IgE, may be recommended among other routine examinations in ED.

References

1. España A. Figurate erythemas. In: Bolognia JL, Jorizzo JL, Schaffer JV, eds. Dermatology. 3rd ed. Philadelphia: Elsevier Saunders; 2012. p. 307-17.
2. Gilmour E, Bhushan M, Griffiths CEM. Figurate erythema with bullous pemphigoid: a true paraneoplastic phenomenon? Clin Exp Dermatol. 1999;24:446-8.
3. Stetson CL, Leiferman KM. Eosinophilic dermatoses. In: Bolognia JL, Jorizzo JL, Schaffer JV, eds. Dermatology. 3rd ed. Philadelphia: Elsevier Saunders; 2012. p. 411-21.
4. Simon JC. Diseases with eosinophilia. In: Burgdorf WHC, Plewig G, Wolff HH, Landthaler M, eds. Braun Falco's dermatology. 3rd ed. Heidelberg: Springer; 2009. p. 564-9.
5. Zillikens D. Autoimmune bullous diseases. In: Burgdorf WHC, Plewig G, Wolff HH, Landthaler M, eds. Braun Falco's dermatology. 3rd ed. Heidelberg: Springer; 2009:652-6.
6. Graham-Brown RAC. Bullous pemphigoid with figurate erythema associated with carcinoma of the bronchus. Br J Dermatol. 1987;117:385-8.
7. Saikia NK, MacKie RM, McQueen A. A case of bullous pemphigoid and figurate erythema in association with metastatic spread of carcinoma. Br J Dermatol. 1973;88:331-4.
8. Breathnach SM, Wilkinson JD, Black MM. Erythema gyratum repens-like figurate eruption in bullous pemphigoid. Clin Exp Dermatol. 1982;7:401-6.
9. Mussani F, Siddha S, Rosen CF. Figurate erythema: an unusual presentation of the nonbullous phase of bullous pemphigoid. J Cutan Med Surg. 2012;16:61-3.
10. Venning VA, Wojnarowska F. The association of bullous pemphigoid and malignant disease: a case control study. Br J Dermatol. 1990;123:439-45.
11. Bernard P, Borradori L. Pemphigoid group. In: Bolognia JL, Jorizzo JL, Schaffer JV, eds. Dermatology. 3rd ed. Philadelphia: Elsevier Saunders; 2012. p. 475-81.
12. Hadi SM, Barnetson RS, Gawkrodger DJ, Saxena U, Bird P, Merrett TG. Clinical, histological and immunological studies in 50 patients with bullous pemphigoid. Dermatologica. 1988;176:6-17.
13. Kahofer P, Grabmaier E, Aberer E. Treatment of eosinophilic annular erythema with chloroquine. Acta Derm Venereol. 2000;80:70-1.
14. El-Khalawany M, Al-Mutairi N, Sultan M, Shaaban D. Eosinophilic annular erythema is a peculiar subtype in the spectrum of Wells syndrome: a multicentre long-term follow-up study. J Eur Acad Dermatol. 2013;27:973-9.
15. Hurni MA, Gerbig AW, Braathen LR, Hunziker T. Toxocariasis and Wells' syndrome: a causal relationship? Dermatology. 1997;195:325-8.
16. Kemmler N, Peitsch WK, Glorer E, Goerdt S. Hypereosinophile dermatitis. Ein verkanntes Krankheitsbild? Hautarzt. 2005;56:1060-7.
17. Miljković J, Bartenjev I. Hypereosinophilic dermatitis-like erythema annulare centrifugum in a patient with chronic lymphocytic leukaemia. J Eur Acad Dermatol Venereol. 2005:19:228-31.
18. Kaufmann S, Altmeyer P. Rezidivieriendes Angioödem mit eosinophiler Dermatitis – Minusvariante des Hypereosinophiliesyndroms. Hautarzt. 1987;38:206-9.
19. Humbert P, Niezborala M, Salembier R, Aubin F, Piarroux R, Buchet S, Barale T. Skin manifestations associated with toxocariasis: a case-control study. Dermatology. 2000;201:230-4.