Linear IgA dermatosis presenting with erythema annulare centrifugum lesions: report of three cases in adults

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ABSTRACT
Linear IgA dermatosis presented with erythema annulare centrifugum lesions in three elderly women. Search for underlying malignancy revealed low-grade B-cell lymphoma in one case. In addition to subepidermal blistering, histology showed a typical mixed infiltrate of granulocytes and eosinophils and, occasionally, papillar microabsesses in one case. In the two other subjects, characteristic subepidermal lining with granulocytes was observed. Immunofluorescence studies confirmed the diagnosis, while autoantibodies characteristic for dermatitis herpetiformis were absent. To our knowledge this is the second report of adult linear IgA dermatosis in association with erythema annulare centrifugum lesions. Our observations concord with several other reports of figurate erythema associated with autoimmune blistering disease and other immune disorders. Common antibody-related immunological mechanisms indicate that the two distinct clinical pictures are probably stages of the same pathogenic entity.

Key words: bullous disease, erythema annulare centrifugum, linear IgA dermatosis

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Introduction
Linear IgA dermatosis is an acquired, autoimmune vesicobullous disease with subepidermal blister formation. Lesional and perilesional skin present linear IgA deposits at the dermoepidermal junction. Two clinical phenotypes have been reported, based on patient age: adult linear IgA dermatosis and childhood linear IgA dermatosis. Early appearance of linear IgA dermatosis, originally known as chronic bullous dermatosis of childhood, is seen in prepubertal, often pre-school children, but rarely in infancy. The disorder usually remits in 64% of subjects by the age of 6–8 years. The adult type of linear IgA dermatosis usually appears in subjects older than 40 years of age, with a slight female predisposition and a remission rate of 48%. The variable clinical picture makes diagnosis difficult: vesicular eruptions and bullae together with pruritus may also occur in bullous pemphigoid or dermatitis herpetiformis. As in bullous pemphigoid, adult linear IgA dermatosis can be accompanied by erythematous plaques, characterized by slow enlargement and migration. On the other hand, erythema annulare centrifugum is considered to be a clinical and morphological reaction pattern associated with diverse states of cutaneous hypersensitivity rather than a distinct disease entity. Induction and exacerbation of erythema annulare centrifugum mostly occur in association with malignancy and autoimmune diseases. Interestingly, autoimmune bullous diseases, such as pemphigus and bullous pemphigoid may initially manifest with erythema annulare centrifugum lesions that develop into typical bullae in the course of the disease. In this report, we describe three cases of linear IgA dermatosis in adults, all initially presenting with erythema annulare centrifugum lesions.

Case reports
Case 1
A 83-year-old woman had a 30-year history of a bullous disease diagnosed as dermatitis herpetiformis and continuously treated with dapsone (50 mg/d). Several attempts to discontinue medication were followed by a relapse of the blisters. Physical examination evidenced numerous annular, erythematous, non-ticky lesions 10–50 mm in diameter on the dorsal aspect of the hands, the upper right leg and knee. Eruptive firm-topped vesicles and some erosions were found behind...
the ears, on the neck, the submammary area and within some patches of annular erythema.

Histology of an annular erythematous lesion showed normal epidermis, a few eosinophils in the upper and middle dermis and a dense perivascular lymphohistiocytic infiltrate. Immuno-fluorescent studies of a blister revealed linear, smooth, homogeneous deposits of IgA and C3 in the basement membrane zone. The following parameters were within normal range: red blood cell and leucocyte count, haemoglobin, red cell count, serum protein electrophoresis, serum creatinine and urea, serum electrolytes, transaminases, alkaline phosphatase, glucose, triglycerides, thyroid hormone levels, carcinoembryonic antigen, antigliadin (IgG, IgA) antibodies, auto-IgA endomysium antibodies and urinalysis. Erythrocyte sedimentation rate was raised with 38/62 mmHg. Chest and breast X-rays, computed tomography and ultrasound scan of the abdomen, endoscopic examination of the colon and gynaecological examination were normal.

With admission of the patient to our wards, treatment was discontinued for 2 weeks. During this time disseminated annular erythematous lesions with marginal vesiculation appeared. After confirmation of the diagnosis, treatment with prednisolone (60 mg/d) and dapsone (50 mg/d) was reintroduced. With clearing of the lesions prednisolone was slowly tapered to 5 mg/d, but dapsone was continued at 50 mg/d with continuous remission of lesions.

Case 2
A 68-year-old woman, with a history of carcinoma of the cervix 10 years before, initially noted annular erythema and tenderness on her neck, subsequently on the upper trunk and lastly all over her body. In the course of the disease pruritus and vesication developed.

Physical examination showed annular, serpiginous or ring-shaped, slowly migrating erythematous papules and plaques involving the neck, trunk and limbs. Blisters and erosions were found within the erythematous lesions (fig. 1). Direct immuno-fluorescent studies of perilesional skin showed linear, homogeneous deposits of IgA in the basement membrane zone (fig. 1, insert). Circulating IgA antibodies against the basement membrane zone were positive with oesophagus substrate. Histological examination of perilesional skin showed a characteristic subepidermal lining with granulocytes (fig. 2). Antigliadin and antiendomysium antibodies were negative. Chest computed tomography revealed a 4 × 6 cm process at the left hilus, and widening of the superior mediastinum. Histological examination of a biopsy (taken by bronchoscopy) of the hilar tumour revealed low-grade B-cell lymphoma.

The patient was treated with dapsone 2 × 50 mg/d, resulting in considerable improvement of the skin disease. The B-cell lymphoma was treated with chemotherapy and radiation.

Case 3
A 74-year-old woman first presented with pruritic papules and vesicles within annular erythematous plaques. The eruption initially involved the hands and feet and then spread over the
entire body surface during the following few weeks. The patient reported general weakness and weight loss over the previous 5 months. Overall physical examination was normal. Histological and direct and indirect immunofluorescent studies supported diagnosis of linear IgA dermatosis. Antigliadin and antientomysium antibodies were negative. Chest and breast X-rays, ultrasound scan of the abdomen, endoscopic examination of the colon and gynaecological examination were normal. After treatment with dapsone (50 mg/d) and, initially, prednisolone (20 mg/d) the skin lesions showed rapid improvement.

Discussion

The three patients described here presented with erythema annulare centrifugum lesions as an initial manifestation of linear IgA dermatosis. Histological examination typically showed subepidermal bullae formation with mixed neutrophilic and eosinophilic infiltrate in the dermal papillae and, in certain areas, characteristic subepidermal lining with granulocytes. Figurate erythema accompanying bullous dermatosis has been reported in 11 cases of bullous pemphigoid and/or pemphigus vulgaris; additional reports described polycyclic erythema in association with linear IgA dermatosis in one case of the adult type and three cases of the childhood type (Table 1). Both figurate erythema and linear IgA dermatosis have been reported in association with malignancy. In our second patient clinical investigation revealed a low-grade B-cell lymphoma located in the lungs, but no signs of underlying malignancy were found in the other two patients.

Erythema annulare centrifugum lesions may develop several months before malignancy. In linear IgA dermatosis the clear association with malignancy remains controversial. For figurate erythema and figurate erythema associated with bullous diseases, immunoglobulin and/or complement deposits have been reported in the basement membrane zone, suggesting a comparable immunological pathogenesis. Erythema annulare centrifugum has also been reported with manifestation of autoimmune disorders, such as lupus erythematosus, CREST syndrome and polyglandular autoimmune disease. The existence of similar antibody-related autoimmune mechanisms reflects that the two clinically diverse features may represent stages of the same pathogenic entity, starting with occurrence of serpiginous or ring-shaped macular erythema before the development of blistering eruptions. However, it remains to be

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explained why autoimmune bullous diseases can present as erythema annulare centrifugum. Concerning therapy, we point out that two of our patients (1 and 3) improved rapidly with dapsone associated with corticosteroids.

In summary, our observations support previous reports that figurate erythema can represent an initial manifestation of bullous disease. In particular, we report, for the second time, that two of our patients (1 and 3) improved rapidly with dapsone associated with corticosteroids.

References