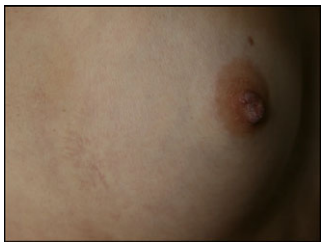

Figure 1 Hypopigmented patch lesion located on the right breast.

Figure 2 Right breast hypoplasia.

A 19-year-old woman was referred by a cardiopaediatrician for a macular lesion located on the right breast. She has been operated for atrial septal defect at the age of 16 by amplatzer septal occluder. Her parents had noticed during the postnatal period an erythematous patchy lesion located at the lateral part of the right breast. An echo Doppler investigation of the red plaque during the first year of life revealed fast-flow arterial vascularization compatible with IH. The parents reported that the lesion had grown for a few months and then spontaneously involuted within a few years. On examination, she had a 4 x 2.5 cm hypopigmented well-circumscribed patch with a few telangiectasias (Fig. 1). She had right breast hypoplasia compared to contralateral breast (Fig. 2). Physical examination revealed no other abnormalities.

We report a case of breast hypoplasia following a small IH on the ipsilateral breast. Only one case of a mixed IH of the breast that resulted in pronounced hypoplasia breast has been reported.[2]

As IH is sometimes associated with malformations, we here debate this link.

We raise the question of an analogy between some IH and some developmental defects such as Becker's naevus syndrome. Although Becker's naevus generally occurs as an isolated finding, several ipsilateral developmental abnormalities have been described, particularly breast hypoplasia.[3] The term *Becker's naevus syndrome* has been proposed to describe the association of a Becker's naevus with ipsilateral non-cutaneous abnormalities.[3]

Poland syndrome is a unilateral defect of pectoral muscle and ipsilateral syndactyly, with absence or hypoplasia of the breast and nipple, axillary hair loss and dermatoglyphic abnormalities. The association of congenital haemangioma with Poland syndrome has also been reported.[4] Our case is the second case of breast hypoplasia and IH reported; this could be a syndromic IH with breast malformation.

Conversely, Theiler *et al.*[2] believe that deep IH might interfere with normal breast gland development, even postnatally. Here, considering the small size of IH, we do not think that this could be a complication due to a deep IH of the breast bud.

Correction of atrial septal defects can be associated with the potential to affect unilateral breast development after a right anterolateral thoracotomy, which was not the case here.[5]

Theiler *et al.*[2] recommend to consider this potential complication in female infants with mixed or deep IH involving the breast and advocate consideration of systemic therapy to prevent this outcome.

As for Becker's naevus syndrome, we raise the question of a link between IH and secondary breast hypoplasia. We thus invite dermatologists and paediatricians to report such cases, in order to ascertain a potential relationship. If breast hypoplasia results from involvement of the underlying breast bud, treatment with oral propranolol could possibly prevent mammary hypoplasia.

No funding source supported the work.

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DOI: 10.1111/jdv.14158

A case of eosinophilic fasciitis associated with pyoderma gangrenosum

Editor

Eosinophilic fasciitis (EF) is a rare, systemic inflammatory disease that is characterized by symmetrical swelling and

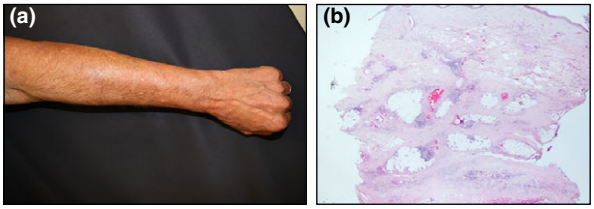

Figure 1 (a) Patient forearm displaying erythematous macules and patches with progressive swelling and tightening. (b) A wedge biopsy of the right forearm demonstrated sclerosis of the dermis, widening and sclerosis of the fat septae, thickened fascia, and a lymphoplasmacellular infiltrate with eosinophils consistent with eosinophilic fasciitis.

scleroderma-like indurations of the distal extremities and trunk, often accompanied by pain and eosinophilia. Rarely, muscle degeneration may occur. Histologically, EF is marked by thickened, fibrotic fascia and fascial inflammation with lymphocytes and eosinophils.[1,2] Herein, we present a previously unreported case of concurrent pyoderma gangrenosum (PG) and biopsy-proven EF successfully treated with rituximab.

A previously healthy, 66-years-old man presented with 1 month of asymptomatic, scattered, erythematous macules and patches on his trunk, which progressed to swelling and tightening of the extremities without associated telangiectasias, Raynaud's phenomenon, acrosclerosis or capillary nail fold abnormalities (Fig. 1). A wedge biopsy of the right forearm demonstrated sclerosis of the dermis, widening and sclerosis of the fat septae, thickened fascia, and a lymphoplasmacellular infiltrate with eosinophils consistent with EF. Imaging and a rheumatologic workup were unremarkable. Prednisone 60 mg daily and 30 treatments of ultraviolet A-1 phototherapy (50 J/cm^2) were attempted without improvement.

One year following the onset of the initial eruption, the patient developed bilateral shin ulcers. Venous and arterial studies and wound cultures were unremarkable. Debridement performed by podiatry resulted in significant worsening (Fig. 2a). Based on the ulcers' significant pathergy and negative infectious workup, the patient was diagnosed with PG.

Subsequent treatments included oral methotrexate 20 mg weekly combined with prednisone 30 mg daily, followed by two cycles of intravenous immunoglobulin (2 g/kg over 5 days monthly), and finally cyclosporine 200 mg daily (2.3 mg/kg/day), none of which resulted in substantial clinical improvement. Eventually, two cycles of rituximab (each consisting of two 1 g infusions 14 days apart), in combination with methotrexate 20 mg weekly, prednisone 40 mg daily, and wound care resulted in stabilization and moderate improvement. Prednisone was tapered to 10 mg and methotrexate reduced to 10 mg weekly with continued wound healing and improvement in skin tightness (Fig. 2b).

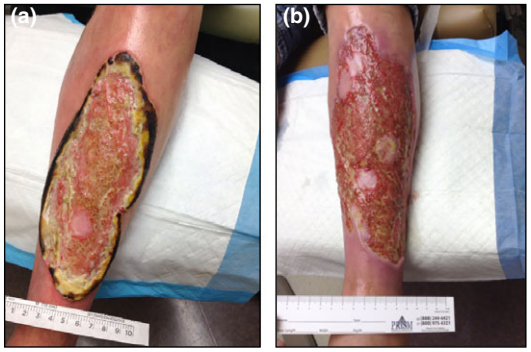

Figure 2 Patient's leg ulcer (a) leg ulcer following surgical debridement, demonstrating significant necrotic tissue as well as a violaceous, tense border. (b) Leg ulcer following two cycles of rituximab and continued methotrexate, demonstrating interval improvement and stabilization, with notable granulation tissue present.

Eosinophilic fasciitis is a rare inflammatory disorder of the skin that has been associated with several autoinflammatory syndromes and malignancies. Chronic leg ulcerations may develop as vasculitic lesions associated with overlapping scleroderma or morphea-like changes. In this case, however, the ulcerations were most consistent with PG. The association of EF and PG has not previously been reported, although awareness in patients with EF is critical as debridement of PG can result in significant morbidity.

Given the rarity of EF, no well-powered prospective studies exist to guide management. Reported treatments include mycophenolate mofetil, hydroxychloroquine, tumour necrosis factor-α inhibitors, rituximab, colchicine, extracorporeal photopheresis, cyclosporine, intravenous immunoglobulins and azathioprine. One study of 69 patients with EF observed better outcomes using a combination of methotrexate and corticosteroids.[3] In this case, the progression of EF and PG did not remit until rituximab was started.

The use of rituximab in PG has been described in a patient with overlap of granulomatosis with polyangiitis.[4] Additionally, the senior authors (BR and HWL) have another patient with extensive recalcitrant EF who improved upon initiation of rituximab. Thus, rituximab was chosen as a next-line therapeutic agent in this patient.

Our patient's successful response to rituximab raises several questions regarding the underlying immunopathology of the two disorders. The exact immunologic mechanism of EF is unclear, and the role of B cells in PG and EF has yet to be elucidated, although both conditions have been described in the setting of underlying B-cell malignancy. [5,6] Herein, we presented a previously unreported case of concurrent EF and PG successfully treated with rituximab. While the pathogenic process underlying the association between EF and PG is unknown, it is important to appreciate the widening spectrum of these two diseases.

Eric L. Maranda had full access to all of the data in the study and takes responsibility for the integrity of the data and the

accuracy of the data analysis. Maranda, Sheinin, Brys, Rubin and Lim involved in study concept and design. Maranda, Sheinin, Brys, Rubin and Lim involved in acquisition, analysis and interpretation of data. Maranda involved in drafting of the manuscript. Maranda, Sheinin, Brys, Rubin, Lim involved in critical revision of the manuscript for important intellectual content. None of the author involved in statistical analysis. No funding was obtained. Maranda, Sheinin and Brys involved in administrative, technical or material support. Lim involved in study supervision.

Informed consent was provided by the patient discussed in the manuscript.

No funds were received for the design and conduct of the study, collection, management, analysis and interpretation of data, preparation, review or approval of the manuscript or in the decision to submit the manuscript for publication.

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DOI: 10.1111/jdv.14148

ACE inhibitors may interfere with omalizumab in chronic spontaneous urticaria

Editor

The extrinsic pathway of coagulation cascade is activated in chronic spontaneous urticaria (CSU), and such activation parallels disease severity.[1] D-dimer levels are elevated in cases resistant to antihistamines[2] and/or cyclosporine.[3] Omalizumab is highly effective in most patients with severe, antihistamine-resistant CSU. Two cases of severe CSU in which ACE inhibitor was associated with the loss of response to omalizumab are reported.

A 47-year-old woman suffered from severe CSU unresponsive to cetirizine 40 mg/day for 3 months. Oral prednisone 25 mg induced only a temporary remission. Thyroid autoantibodies and elevated D-dimer (3929 ng/mL; normal < 500) were detected at baseline. Three days after the first administration of omalizumab 300 mg, a dramatic improvement occurred and 2 weeks later D-dimer was 785 ng/mL, and urticaria became easily controlled with cetirizine 10 mg/day. Treatment efficacy increased after the second dose, and D-dimer further decreased to 419 ng/mL. The benefit persisted until 4 weeks after the third dose when a relapse occurred, and D-dimer plasma levels increased to 688 ng/mL. Urticaria worsened dramatically after the fourth dose and D-dimer rose to 2269 ng/mL. In order to exclude possible cofactors, the ACE inhibitor that had been taken for >1 year due to hypertension was stopped. After few days, the patient improved dramatically and urticaria became again easily controlled by cetirizine 10 mg/day (Fig. 1a). Four months after this semi-remission, state persisted.

A 65-year-old man with a history of urticaria/angioedema after taking chemically unrelated NSAIDs had severe

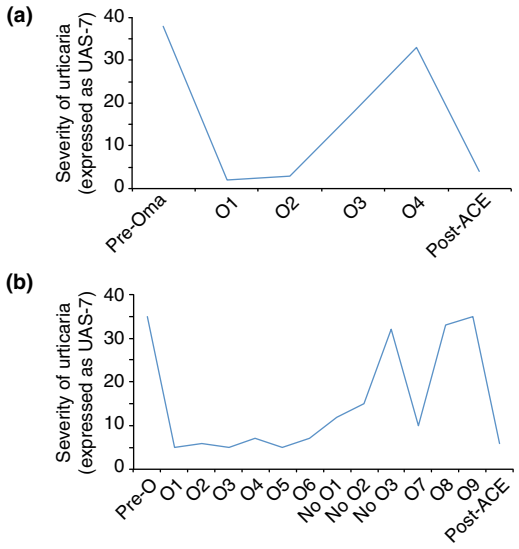

Figure 1 Clinical evolution in patient 1 (a) and patient 2 (b) before and during omalizumab treatment and after ACE inhibitor withdrawal. On the *y*-axis severity of urticaria expressed as UAS-7 is shown. On the *x*-axis: Pre-O = basal UAS-7 before omalizumab treatment; O1-O9 = months under omalizumab; No O1-No O3 = months without omalizumab therapy. Post-ACE = after ACE inhibitor withdrawal.