Acquired bullous dermatosis associated with IgA multiple myeloma

Sir,

Several skin disorders have been described in patients with monoclonal gammapathies.[1] Only two cases of acquired bullous dermatosis associated with immunoglobulin A (IgA) multiple myeloma have been reported in the literature, for which no target antigen has been identified.

We report the association of IgA λ multiple myeloma with cutaneous vasculitis and bullous dermatosis characterized by subepidermal deposits of IgA λ specific for a 120 kDa epidermal antigen. An 87-year-old woman developed in 2007, a pruriginous bullous eruption on the legs, trunk, hands, face, and scalp, with no mucosal involvement. The skin biopsy showed a subepidermal blister associated with an infiltrate of neutrophils and eosinophils. Immunoblot analysis on epidermal extracts detected several IgA bands. Serum immunoelectrophoresis revealed IgA λ paraprotein (30.2 g/L) and bone marrow aspiration showed 37% of atypical plasma cells. Magnetic resonance imaging of the rachis found several lytic lesions of the vertebrae. Stage III IgA multiple myeloma was diagnosed and treated with melphalan, prednisone, and thalidomide for 6 months. Complete remission was achieved after three cycles, with rapid resolution of the skin lesions. After 32 months of remission, in May 2010, a relapse of bullous skin lesions was observed on the abdomen, face, and limbs [Figure 1], whereas serum immunoelectrophoresis was normal. Palpable purpura without bullae was present on the legs. A skin biopsy on the abdomen showed a subepidermal blister with upper dermal neutrophilic infiltrate and leukocytoclastic vasculitis of the small vessels [Figure 2]. Direct immunofluorescence (DIF) revealed thick subepidermal deposits of IgA λ, and no IgG, IgA, or C3 deposits in the vessel wall [Figure 3].

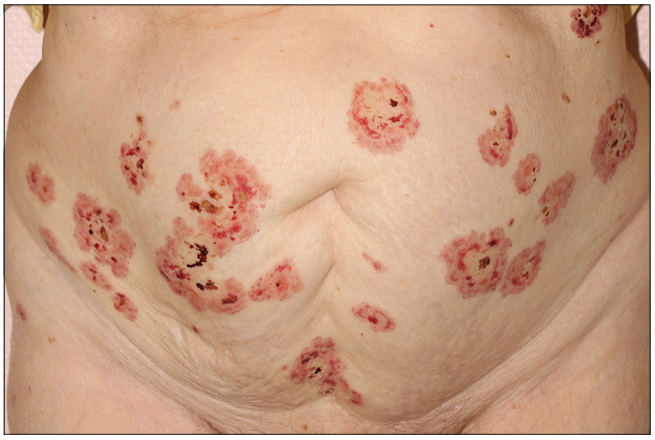

Figure 1: Round or annular bullous and erosive cutaneous lesions on the abdomen

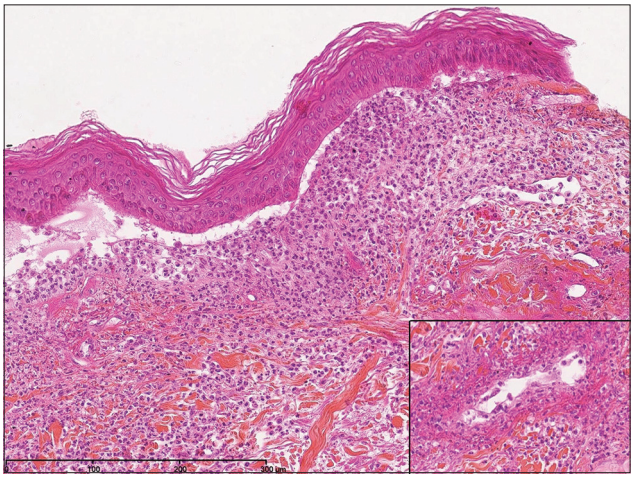

Figure 2: Subepidermal blister with numerous neutrophils in the papillary dermis. Inset: Dermal vasculitis with fibrinoid necrosis and neutrophil infiltrate (H and E; ×200, inset: ×400)

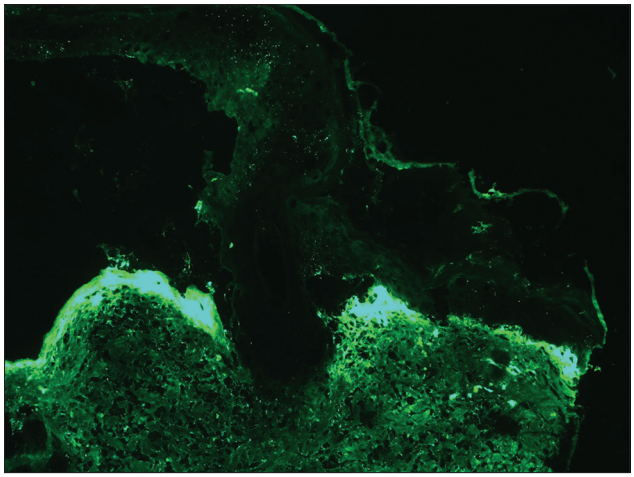

Figure 3: Direct immunofluorescence with fluorescein isothiocyanate-conjugated anti-IgA antibody showing thick subepidermal deposits (immunofluorescence staining, ×200)

Treatment with dapsone 100 mg/day and topical steroids during 5 months was ineffective. In September 2010, a 36.7 g/L seric IgA λ paraprotein was detected. Immunoblot on normal epidermal extracts detected a 120 kDa target with IgA. Indirect immunofluorescence on monkey and rat esophagus was negative, as well as BP180 enzyme-linked immunosorbent assay. The patient was started on cyclophosphamide (500 mg oral weekly), prednisone (100 mg oral each other day), and thalidomide (50 mg oral daily). Skin lesions initially healed but the tolerance of the chemotherapy was bad, and the patient ultimately died of severe systemic infection.

Multiple myeloma has been associated with a variety of specific and nonspecific skin manifestations.[1] Multiple myeloma, and especially IgA-myeloma, has been associated with neutrophilic dermatoses, that is, Sweet's syndrome, pyoderma gangrenosum, erythema elevatum diutinum, eccrine neutrophilic hidradenitis, and Sneddon-Wilkinson subcorneal pustulosis. IgA pemphigus and Henoch-Schönlein purpura (IgA-mediated leukocytoclastic vasculitis) have also been reported in association with IgA-myeloma.

In this case, a peculiar IgA-mediated acquired bullous eruption revealed IgA multiple myeloma, and the recurrence of the skin lesions predicted the relapse of the myeloma. The recurrence of the bullous lesions was associated with leukocytoclastic vasculitis. The vasculitis may have been secondary to intense neutrophils infiltration as is seen in some cases of Sweet's syndrome. Bullous lesions in the context of cancer may have risen hypotheses such as bullous Sweet syndrome or paraneoplastic pemphigus that have been ruled out by DIF and histopathology.

Only two other cases of acquired bullous dermatosis associated with IgA multiple myeloma have been reported in the literature.[2,3] The three cases shared some features: The eruption appeared before the diagnosis of paraproteinemia; the skin biopsy showed subepidermal bullae with a predominantly neutrophilic infiltrate; and DIF showed thick subepidermal IgA deposits in the upper dermis.

Acquired bullous disorders with other paraproteins than IgA have been reported, in association with IgG multiple myeloma, or with IgM gammopathy.[4] Bullous lesions are supposed to be induced by the monoclonal paraproteins, acting as autoantibodies. We report for the first time a 120 kDa epidermal protein as the specific target of the IgA paraprotein. This protein probably corresponds to the 120 kDa linear IgA dermatosis antigen (LAD-1), an autoantigen target in linear IgA bullous dermatosis (LAD).[5] The subepidermal blister with neutrophils accumulating in the papillary dermis in our case was reminiscent of LAD. However, DIF was peculiar, with thick IgA λ deposits in the papillary dermis, suggesting a specific paraneoplastic blistering disease due to IgA paraprotein and not LAD *stricto sensu*.

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