Anti-laminin γ1 pemphigoid associated with ulcerative colitis and psoriasis vulgaris showing autoantibodies to laminin γ1, type XVII collagen and laminin-332

Anti-laminin γ1 pemphigoid is a novel autoimmune subepidermal bullous disease characterized by the presence of circulating immunoglobulin (Ig) G autoantibodies to laminin γ1, a common constituent at various basement membrane zones (BMZs). Although an association between various subepidermal blistering diseases and inflammatory bowel disease (IBD) has been reported, there have been no previous reports on an association between anti-laminin γ1 pemphigoid and IBD. Here, we demonstrate a case of anti-laminin γ1 pemphigoid associated with ulcerative colitis (UC), in whom circulating autoantibodies against laminin γ1, laminin-332 and the C-terminus of type XVII collagen (BP180) were detected.

A 65-year-old Japanese man was referred to our hospital for worsening widespread tense blisters with pruritus over the entire body. He had previously been diagnosed with psoriasis vulgaris and UC. The symptoms of UC, namely fever, bloody stool and abdominal pain, had recently worsened, with the subsequent appearance of blisters. Clinical examination revealed prominent oedematous erythema, tense blisters and erosions with a few scattered milia on the entire body (figure 1A). No mucosal involvement was observed. Histopathology of a lesional skin biopsy specimen demonstrated subepidermal blisters with infiltration of eosinophils and neutrophils at the dermoeidermal junction and in the papillary dermis (figure 1B). Direct immunofluorescence (IF) of the lesional skin showed linear deposition of IgG and complement component 3 at the epidermal BMZ (figure 1C). Indirect IF detected circulating IgG autoantibodies, which bound to both the epidermal and dermal sides of 1M sodium chloride-split normal human skin at titre 1:20 (figure 1D). Enzyme-linked immunosorbent assay using recombinant protein of the NC16a domain of type XVII collagen showed a negative result. To determine the target antigen of the patient autoantibodies, immunoblotting (IB) analyses were performed as previously described [1–3]. The results showed the presence of three distinct circulating IgG autoantibodies against laminin γ1, the C-terminus of type XVII collagen and the α3 and γ2 subunits of laminin-332 (figures 1E-G). After initial treatment with oral prednisolone 1 mg/kg/day, the skin lesions rapidly healed with milium formation. When prednisolone was tapered to 0.4 mg/kg/day, tense blisters reappeared. Additional administration of mizoribine 2 mg/kg/day ameliorated the skin lesions, and thereafter prednisolone was gradually...

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tapered to 0.15 mg/kg/day. Prednisolone 0.15 mg/kg/day and mizoribine 2 mg/kg/day controlled the bullae and erosions well.

While anti-laminin γ1 pemphigoid reacts with laminin γ1, autoantibodies to the C-terminus of type XVII collagen and laminin-332 are detected in anti-BP180-type and anti-laminin-332-type, respectively, of mucous membrane pemphigoid (MMP). Although both of these MMP autoantibodies were detected in the IB assays, the present case showed no mucosal involvement. In addition, the tense blisters and urticarial skin lesions resembling bullous pemphigoid, rapid response to systemic treatments, co-existence of psoriasis vulgaris, and non-scarring resolution of skin lesions were consistent with the characteristics of pemphigoid, rapid response to systemic treatments, co-existence of psoriasis vulgaris, and non-scarring resolution of skin lesions were consistent with the characteristics of anti-laminin γ1 pemphigoid [4]. Altogether, these findings indicated that the diagnosis of anti-laminin γ1 pemphigoid was appropriate in this case.

The current classification of autoimmune blistering diseases based on targeted antigens may be relatively inappropriate in some cases, as in the present case in which several autoantigens were detected. This issue is likely to occur more frequently because of the increasingly concomitant use of various sensitive techniques. Appropriate diagnosis should be determined not only from the results of serological analysis but also from clinical features.

It has been reported that approximately 30–50% of anti-laminin γ1 pemphigoid cases are associated with psoriasis vulgaris [4–6]. Our patient had concurrent psoriasis vulgaris and UC with anti-laminin γ1 pemphigoid. Furthermore, blister formation occurred in conjunction with worsening of the UC symptoms. Concurrence of IBD and subepidermal bullous dermatosis, including linear IgA bullous dermatitis, pemphigoid group and epidermolysis bullosa acquista, has been reported [7]. However, to our knowledge, there are no previous reports describing concurrent anti-laminin γ1 pemphigoid and UC. Several major laminin trimers containing the laminin γ1 subunit exist in the intestinal BMZ [8]. IBD results from a breakdown of the epithelial layer and exposure of the components of the BMZ to the immune system. Accordingly, we speculate that laminin γ1 was first processed by intestinal inflammation in the present case. The laminin γ1 fragments may promote the production of anti-laminin γ1 autoantibodies, resulting in BMZ separation in the skin.


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Osteomalacia induced by a phosphaturic mesenchymal tumor secreting fibroblast growth factor 23

Tumor-induced osteomalacia (TIO) is a rare paraneoplastic condition characterised by the presence of a tumor, hypophosphatemia caused by renal phosphate wasting and low serum concentration of 1,25-dihydroxyvitamin D (1,25(OH)2D), with clinical and histological evidence of osteomalacia [1–4]. Hypophosphatemia subsequently causes muscle weakness, bone pain and multiple fractures [1]. Most cases of TIO are associated with mesenchymal tumors secreting fibroblast growth factor 23 (FGF23) [1], which was recently identified as an important factor involved in the development of hypophosphatemic rickets and osteomalacia. We report a case of TIO with a subcutaneous tumor. Interestingly, the osteomalacia dramatically improved after resection of the tumor.

A 28-year-old Japanese man presented with a 5-year history of pain in the lower back and right knee, which gradually worsened over time. Bone mineral density (BMD) was 0.649 g/cm2. Serum chemistry showed low phosphate (1.7 mg/dl) and intact parathormone (13.4 pg/mL), increased alkaline phosphatase (599 U/L), and decreased reabsorption of phosphatase. The level of 1,25-(OH)2D3 was within the normal range (45.8 pg/mL). FGF23 was elevated in the peripheral blood (1340 pg/mL). From these results, tumor-induced osteomalacia was suggested, but the tumor could not be localized. An F-18 fluorideoxyglucose positron emission tomography/computed tomography (PET/CT) test showed no remarkable changes. Venous blood samplings for FGF23 were performed from both right and left dorsal, femoral and median veins, and a significantly higher level of FDF23 (9900 pg/mL) was detected from the left dorsal vein than from the other veins, sug-

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