

BULLOUS PYODERMA GANGRENOSUM IN PATIENTS WITH ULCERATIVE COLITIS AND MULTIPLE MYELOMA

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Sir,

Bullous pyoderma gangrenosum (PG) is a rare subtype of PG, which frequently involves extremities. We herein report two cases of bullous PG in association with other systemic diseases, such as hematological malignancy and inflammatory bowel disease.

Case 1

A 52-year-old man suffered from stomachache, diarrhea, and bloody stools for some months, and was diagnosed with ulcerative colitis (UC) by colonoscopy examination. Biopsy specimens showed inflammatory cell infiltration in the mucosal epithelium. Almost simultaneously, he developed bullous lesions on the lower legs. Physical examination showed rounded, edematous bloody bullous lesions on the bilateral shin (Fig. 1). Laboratory examination showed increased levels of C-reactive protein (CRP; 3.12 mg/dl) and erythrocyte sedimentation rate (53 mm/h), and white blood cell counts (8900/mm³) with 70% neutrophils. Histological examination showed subepidermal bulla and neutrophil and mononuclear cell infiltration in the mid- to lower dermis. After admission, systemic prednisolone (30 mg/day) was administered for intestinal lesions, which also improved skin lesions.

Case 2

A 76-year-old man was suffering from multiple myeloma for 8 years. He had been treated with chemotherapies (ranimustine, vincristine, melphalan, dexamethasone), which however could not lead to remission induction. During the course, he was hospitalized and consulted to dermatology department, as for the skin lesions on his forearm. Physical examination revealed hemorrhagic bullae on the left forearm (Fig. 2). Laboratory examination showed increased levels of CRP (14.7 mg/dl). A biopsy specimen revealed prominent red blood cells, diffuse neutrophil infiltration in the entire dermis (Fig. 3). There were

no atypical cells. He was initially treated with antibiotics without effects, but successfully treated with oral prednisolone (30 mg/day).



Figure 1. Hemorrhagic shallow bullae on the shin of Case 1.



Figure 2. Bullous hemorrhagic lesions on the forearm of Case 2.

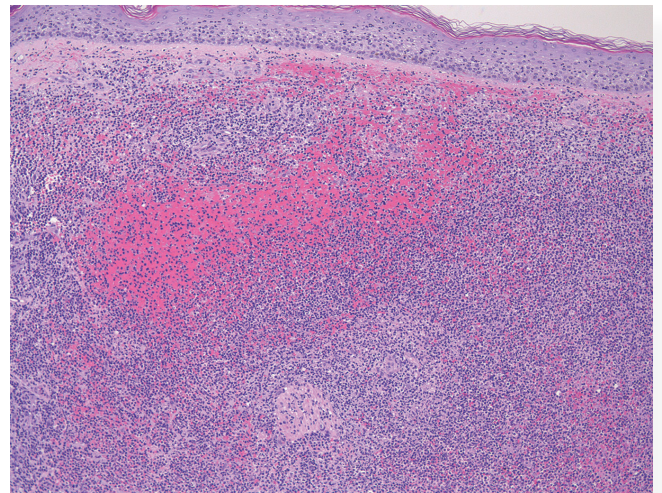


Figure 3. Skin biopsy specimen showing numerous neutrophils infiltration with a number of erythrocytes in the dermis.

PG is clinically classified into 4 types, i.e. ulcerative, bullous, pustular and vegetative type. Bullous PG is relatively rare, and to date, more than 30 cases of bullous PG have been reported [1,2]. This type is characterized by rapid development of vesicles and enlarging bullae with central necrosis and shallow erosions. Previous reports indicate that extremities are the most frequently involved, and hematological malignancies, i.e. preleukemic conditions and leukemia, are mostly associated [2]. We describe herein 2 cases of bullous PG occurred on the upper and lower extremities. Case 1 had UC, and Case 2 had multiple myeloma. In both cases, development of bullous PG was related with the activity of gastrointestinal and hematological conditions, respectively. Case 1 presented with typical clinical features of bullous PG. In Case 2, we at first suspected myeloma cells infiltration in the skin, because previous reports showed that leukemia cells recruited to the sites of leakage of a drip infusion on the forearm [3]. However, histological features denied atypical cells and demonstrated PG.

In the lesional skin of PG, not only neutrophils but also a number of CD3-positive T cells are infiltrated [4], which is implicated to play an important role in the induction of PG, via T cell-derived cytokines and chemokines. IL-8 has been implicated to play an important role in neutrophil recruitment in the lesional skin. Tumor necrosis factor- α (TNF- α) induces IL-8 production by peripheral mononuclear cells [5]. Also, therapies targeting TNF- α result in beneficial effects on refractory PG [6,7], suggesting a crucial role of TNF- α in the pathogenesis of PG. TNF- α enhances vascular permeability in endothelial cells [8] as well as endothelial barrier dysfunction, which may be relevant to bullous formation of PG. TNF- α plays an important role in inflammatory bowel disease, whereas role of TNF- α in

hematological malignancy is unclear. The etiology of bullous PG in hematological conditions needs further studies.

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