CASE REPORT
Concurrent pyoderma gangrenosum and subcorneal pustular dermatosis in a patient with monoclonal IgA/\(\lambda\) gammopathy

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Abstract
Subcorneal pustular dermatosis (SPD) and pyoderma gangrenosum (PG) are two neutrophilic dermatoses. Coexistence of these diseases in the same patient is rare and may be a strong indicator of IgA dysglobulinemia. We describe a 69-year-old man who presented with waxing and waning flaccid pustules covering his trunk and four limbs. Poorly healing ulcerations, which usually progressed into larger nodules after debridement, were also noted. Repeated cultures were negative for bacteria, and the patient was diagnosed with SPD and PG. Serum protein electrophoresis and immunofixation revealed a monoclonal IgA lambda protein. A subsequent bone marrow biopsy revealed a normocellular marrow. While PG and SPD can occur individually in a variety of associated diseases, such as rheumatoid arthritis, systemic lupus erythematosus and inflammatory bowel disease or infection; however, their coexistence is strongly indicative of IgA dysglobulinemia.

Introduction
Pyoderma gangrenosum (PG) and subcorneal pustular dermatosis (SPD) belong to the neutrophilic dermatoses spectrum. SPD is an uncommon disease with only 200 reported cases and the majority of these cases are associated with monoclonal gammapathy, and a few cases subsequently progress to IgA myeloma. PG is a rare ulcerative cutaneous condition of uncertain origin. In at least 50% of patients, it is associated with systemic diseases such as inflammatory bowel disease, rheumatoid arthritis, paraproteinemia or hematological malignancy. We report a patient who presented with both of these neutrophilic dermatoses and developed monoclonal IgA/\(\lambda\) gammapathy the following day. Therefore, we suggest that routine urine analysis for Bence–Jones protein, serum protein electrophoresis and subsequent bone marrow biopsy should be performed in such patients.

Case presentation
A 69-year-old male presented to our clinic with dozens of pustules covering the trunk and limbs (Figure 1A) and a large ulceration on the right upper back (Figure 1B). He had had waxing and waning pustulosis for the past 10 years. These tiny yellowish pustules were flaccid, studded on an erythematous base and ruptured easily, resulting in superficial erosion, scaling, crusting and faint hyperpigmentation (Figures 1C and 1D). Mucous membranes were not involved. Two years before coming to our clinic, he developed an ulcerated wound with focal necrosis over the right upper back. Poor healing of this wound increased its size to 9 cm \times 8 cm with an undermined border; however, there was no discharge or foul smell. Repeated wound cultures were negative. He had undergone surgical debridement several times in the surgical department; however, the debridement typically led to a larger wound. The patient had a history of ischemic heart disease and post-bypass surgery, but there was no diabetes mellitus or other systemic disease. He had been treated irregularly with oral corticosteroids for the relapsing pustular eruptions. A skin biopsy from the pustule showed a subcorneal cleft containing numerous neutrophils (Figure 2). The dermis revealed perivascular infiltration of monoclonal cells and scattered neutrophils. Direct immunofluorescence studies were negative. According to the clinical features and the
pathological findings, we diagnosed the patient with concurrent SPD and PG. Laboratory investigation indicated an elevated level of lactic dehydrogenase (LDH) of 270 U/L (reference range 125–215 U/L). Serum protein electrophoresis revealed a monoclonal spike in the gamma region and immunofixation electrophoresis indicated the presence of a monoclonal IgA lambda protein. The amounts of immunoglobulins present were: IgA 589 mg/dL (reference range 70–400 mg/dL), IgG 928 mg/dL (reference range, 700–1600) and IgM 47.10 mg/dL (reference range 40–230). Further investigation of the patient was conducted to search for possible associated malignancy. A bone marrow biopsy revealed a normocellular marrow. Urinalysis for Bence–Jones protein was negative, and radiological and skeletal surveys were also normal. The final diagnosis was therefore PG with SPD in association with a monoclonal IgA/lambdopathy. Combined therapy with dapsone (50 mg/day) and a low-dose oral corticosteroid was started resulting in excellent control. The ulceration healed gradually over the next 4 weeks resulting in a scar, and prednisolone was then tapered to 5 mg/day. Follow-up examination found that localized small ulcers had developed but were controlled through intralesional injections of steroids. There is no evidence of progression into a malignant plasma-cell disorder to date.

Discussion

We report a rare case of concurrent PG and SPD. The patient also had underlying IgA monoclonal gammapathy. PG is an uncommon, inflammatory, non-infective, non-neoplastic and ulcerating process. PG is characterized by painful, large necrotic ulcers with blush undermined borders surrounded by an advancing zone of erythema. No confirmatory diagnostic test exists for PG. Specific criteria suggest that the diagnosis of PG must exclude other possible conditions, such as infection, vascular disease or malignancy. PG is associated with an underlying disease, including inflammatory bowel disease, rheumatoid arthritis, paraproteinemia or hematological malignancy in 50–70% of patients. A monoclonal gammapathy is present in approximately 10–20% of patients with PG. In the largest reported series of 86 patients, nine with PG had monoclonal gammapathy and of these, seven had IgA, one had IgG and one had IgM paraprotein.
SPD is an uncommon relapsing symmetric pustular eruption that usually involves the flexural and intertriginous areas, and is frequently associated with various forms of immune dysfunction, most commonly IgA monoclonal gammopathy. The exact pathophysiology is unknown, and its nosological classification is still controversial. Direct and indirect immunofluorescence is negative in classic SPD. In contrast, IgA pemphigus refers to cases that are clinically identical with SPD according to standard histopathologic pictures, but direct immunofluorescence reveals that IgA is localized to the intraepidermal spaces.

Both PG and SPD are neutrophilic dermatoses characterized by inflammatory infiltration consisting of mature polymorphonuclear leukocytes. The neutrophils are usually located within the dermis in PG and are found in the uppermost epidermis in SPD. However, whether the coexistence of these conditions reflects a common pathogenic mechanism is an interesting question. PG and SPD share the same inflammatory cells and similar associated systemic disease. We propose that IgA dysglobulinemia may have a causal relationship with the migration and activation of neutrophils; the responsible chemotactic factors are currently under investigation.

Conclusion

The concurrence or sequential development of PG and SPD in the same patient is rarely reported. To date, only 12 cases have been reported in the English literature. Importantly, the coexistence of PG and SPD is considered to be a strong indication of dysglobulinemia. Eight of the 12 reported cases had IgA monoclonal gammopathy; one had biclonal IgA and IgG gammopathy and one had underlying IgA myeloma. In a recent case reported by Ahmad and Ramsay, a 57-year-old woman had PG for 5 years before developing SPD and biclonal IgA and IgG gammopathy, and IgA myeloma 12 years later. This IgA association is remarkable, because IgA gammopathy comprises only 10% of all monoclonal gammopathies with a prevalence rate of 1%–3% in the general population. Therefore, annual gammopathy tests and close follow-up must be conducted in patients with these two neutrophilic dermatoses.

References