Recalcitrant cutaneous pyoderma gangrenosum with pulmonary involvement resolved with treatment of underlying plasma cell dyscrasia

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INTRODUCTION

Pyoderma gangrenosum (PG) is a rare inflammatory ulcerative disease with unknown pathophysiology and etiology. It is associated with many systemic inflammatory, autoimmune, and neoplastic diseases.1,2 The clinical presentation varies widely but commonly manifests as painful, progressive, and well-demarcated ulcers with blue/gray serpiginous borders.2 The histopathology of PG is non-specific but typically includes dense neutrophilic infiltration with necrosis and hemorrhage.3 These variations and inherent uncertainties of PG can make definitive diagnosis challenging, and more common processes such as infections, vasculitides, and malignancies must first be excluded. Suggested criteria for PG are: progression of the ulcer(s), ruling out more common ulcerative diseases and atypical infections, confirmation of associated systemic diseases, and response to treatments.4 Therapy typically includes immunosuppression and wound care, but treatment of underlying systemic diseases, seen in this case report, has been shown to be successful.3

CASE REPORT

A 51-year-old female presented with a history of three episodes of suspected PG over two years. She was initially evaluated at an emergency department in 2017 and was found to have rust-colored sputum and a presumed pneumonia. After she did not respond to antibiotics and her chest computed tomography images worsened, a transthoracic lung biopsy was performed revealing bronchocentric granulomatous inflammation and fibrosis. Bacterial, fungal, and acid-fast bacilli cultures were negative. She was noted to have a nasal septum perforation, which raised concern for granulomatosis with polyangiitis, but no vasculitis was seen on biopsy, and the antineutrophil cytoplasmic antibodies were negative. The cutaneous site of her lung biopsy developed an ulcer that quickly expanded and was clinically diagnosed as PG (Fig 1). This required skin-grafting and pulse-dosed methylprednisolone before resolving. The pneumonitis also resolved with methylprednisolone. Months later, she again developed a progressive ulceration of her trunk (Fig 2). This ulcer again responded to pulse steroids and skin-grafting.

At presentation in our clinic, on her left anterior hip, she had a 1-cm erosion with yellowish exudate and granulation tissue with surrounding redness but no drainage or fluctuance (Fig 3). Intralesional triamcinolone 10 mg/cc was injected in the office along with a superficial bacterial culture which was negative for Staphylococcus aureus. Over several weeks, her ulcer grew, despite increasing doses of oral prednisone of up to 60 mg/day and cyclosporine 100 mg twice a day (Fig 4). Pulse IV methylprednisolone therapy was again required for control.

Laboratory work-up was notable for antinuclear antibody positivity (titer, 1:360), slightly elevated...
rheumatoid factor (16.7 IU/ml), erythrocyte sedimentation rate (63 mm/hr), and CRP (4.0 mg/L). Rheumatology performed serum protein electrophoresis, showing a faint IgA lambda monoclonal spike of 0.1 g/dL. Bone marrow aspiration revealed a clonal population of neoplastic plasma cells on flow cytometry, fluorescence in-situ hybridization analysis, and histopathology. After the healing of the ulcer, immunosuppression was discontinued and the oncology team initiated six cycles of cyclophosphamide, bortezomib, and dexamethasone. The patient's IgA monoclonal gammopathy became undetectable, and the patient has been in remission of PG for over one year.

DISCUSSION
PG represents one of the neutrophilic dermatoses. These are clinically dissimilar diseases united by morphological overlap, polymorphonuclear infiltrates on histopathology, extracutaneous neutrophilic infiltrates, and frequent associations with systemic disease. Manifesting this clinical heterogeneity, this patient's pulmonary involvement by PG was difficult to diagnose due to this uncommon location and mimicry of pneumonia. Additionally, it is exceedingly rare for the lungs to be the initial and sole site of PG involvement. However, pulmonary involvement is the most common extracutaneous site of PG, and such cases are more often associated with hematologic disease than classic PG. As we observed, PG with pulmonary involvement is often presumed to be a pneumonia until it becomes clear that antibiotics are ineffective. A lung biopsy was performed, resulting in an ulcer at the surgical incision. In light of this pathergy, cutaneous PG with pulmonary involvement was more strongly considered. This demonstrates the difficulty of diagnosing PG, particularly when it does not manifest in a typical location. In fact, her diagnosis was still in question, when we considered granulomatosis with polyangiitis, given her lung lesions and perforated nasal septum, though the absence of primary vasculitis on biopsies and a negative test for antineutrophil cytoplasmic antibodies made PG more likely.

Once a working diagnosis of PG is established, immunosuppression with systemic corticosteroids, steroid-sparing agents, and tumor necrosis factor inhibitors are often required. This patient had recurrent PG despite aggressive parental steroid use in combination with a steroid-sparing agent. In recalcitrant clinical cases, an underlying systemic disease may be present. Our evaluation for typical
associated conditions such as inflammatory bowel disease, inflammatory arthritis, solid organ malignancies, myelodysplastic syndrome, and hematologic malignancy was negative. Urine and serum electrophoresis demonstrated a subtle IgA lambda gammopathy, which was confirmed on subsequent bone marrow biopsy to represent a plasma cell dyscrasia. Although unusual, PG of the lungs with histology showing pulmonary granulomatous inflammation was reported in one of two cases by Gade et al, and their literature review indicated that granulomatous histology was seen in 2% of cases of PG with pulmonary involvement. The letter by Bostan et al reporting PG with pulmonary involvement, large truncal cutaneous ulcers, and an IgA gammopathy responsive to bortezomib was strikingly similar to our case. While the specific underlying mechanism of this association has not been fully elucidated, dysregulation of the immune system through defective cell-mediated responses or deposition of immunoglobulins in vessels has been postulated. Treatment of the present patient’s underlying hematologic disorder will hopefully prevent future episodes of PG. The purpose of this case report is to highlight an unusual case of recalcitrant cutaneous PG with pulmonary involvement associated with an underlying plasma cell dyscrasia and IgA gammopathy. In future cases of atypical PG, consideration of a similar underlying process may result in a timely diagnosis and successful treatment plan, preventing additional morbidity and even mortality.

Conflicts of interest
None disclosed.

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