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Paraneoplastic Pyoderma Gangrenosum with Post Transplant Lymphoproliferative Disorder

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Dear Editor,

Pyoderma gangrenosum (PG) is an uncommon and serious ulcerating disease seen most often in females aged 20-50 years.[1] It is associated with malignancy in approximately 7% of cases. These are most commonly hematologic malignancies of which acute myelogenous leukemia is the most common.[2] To the best of our knowledge, there have been no prior reported cases of PG occurring during solid organ transplant (SOT)-related post-transplant lymphoproliferative disorder (PTLD).

A 62 year-old female with history of a liver transplant for severe non-alcoholic steatohepatitis presented 3 months following SOT with repetitive neutropenic fever and pancytopenia. The absolute neutrophil count was 900 cells/mm³, hemoglobin 9.8 gram/dL, and platelets of 92,000 cells/mm³. Early in clinical course, the patient developed significant, non-healing ulcers in the left inguinal region (**Figure 1A**).

Biopsy of the inguinal cutaneous lesion showed ulceration with extensive tissue necrosis without lymphocytic infiltrate; special stains and tissue cultures were negative. The findings were most consistent with PG. An ¹⁸F-fluorodeoxyglucose positron emission tomography (FDG-PET) showed a 3.1 cm hypermetabolic lymph node in the porta hepatis. Needle biopsy showed large lymphoid B-cells staining positive by immunohistochemistry for CD10 and CD20; Ki67 was 60%; Epstein Barr Virus (EBV) by EBV-encoded RNA in situ hybridization was negative. Clonal rearrangements of immunoglobulin heavy chain gene and kappa light chain gene were detected. Altogether, the diagnosis was consistent with B-cell PTLD, monomorphic subtype, EBV-negative.

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Consent

Informed consent was obtained from the patient for publication of this letter and any accompanying images.

Competing interests

AME is involved with Genentech Advisory Board and Speaker's Bureau.

The patient's immunosuppression was decreased by approximately 75%. In addition, she received weekly single-agent rituximab. After four doses/weeks, restaging FDG-PET documented that the patient was in complete remission and her pancytopenia resolved. Furthermore, the patient's PG began to improve (**Figure 1B**). She was treated with a total of 8 induction doses/weeks of rituximab and subsequently received maintenance rituximab every 3 months for 1 year. During this time, her PG progressively improved and ultimately resolved (**Figures 1C-D**). She has remained in complete remission 2 years following diagnosis.

There is no standardized approach to the treatment of PTLT. This in part relates to significant patient and disease heterogeneity as well as an absence of randomized studies. Reduction/cessation of immunosuppression still remains a mainstay of treatment and rituximab has been shown to have a significant impact on the disease.[3, 4] Further, single-agent rituximab (in combination with reduced immunosuppression) may result in in long-term disease-free survival, including for polymorphic and monomorphic B-cell PTLT.

Treatment of PG is challenging in part as there are no available randomized prospective trials. Therapy may include systemic steroids, cytotoxic drugs, and immunosuppressants.[2] The etiology of PG has not been fully elucidated, but it is linked in part to aberrant neutrophil activity.[2] There is a paucity of data regarding use of rituximab for treatment of PG. Two case reports of patients with granulomatosis with polyangiitis both associated with PG were successfully treated with infliximab followed by rituximab maintenance therapy[5] and rituximab alone, respectively, have been reported.[6]

In summary, PG may occur as a paraneoplastic manifestation of PTLT. Furthermore, therapy with single-agent rituximab and reduced immunosuppression may be an effective therapeutic strategy.

List of abbreviations

PG	Pyoderma gangrenosum
PTLT	Post transplant lymphoproliferative disorder

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Figure 1.

PTLD-related pyoderma gangrenosum. Multiple large, deep necrotic ulcers were noted in the patient's left inguinal region prior to treatment in panel A). Panel B) shows the same lesions 8 weeks thereafter (4 weeks following 4 doses of weekly rituximab. Panels C) and D) show the lesions 3 months and 1 year following diagnosis, respectively.