Case Presentation

# Primary cutaneous B-cell post-transplant lymphoproliferative disorders mimicking pyoderma gangrenosum in a renal transplant recipient

Yasutoshi Hida, MD, PhD[1a], Emi Kunikata, MD[1], Tomoko Hara, MD[2], Takahiko Kasai, MD, PhD[3], Yoko Hamada, MD[4]

[1] Division of Dermatology, Tokushima Red Cross Hospital, Komatsushima, Tokushima, Japan, [2] Division of Hematology, Tokushima Red Cross Hospital, Komatsushima, Tokushima, Japan, [3] Division of Diagnostic Pathology, Tokushima Red Cross Hospital, Komatsushima, Tokushima, Japan, [4] Division of Surgery, Tokushima Red Cross Hospital, Komatsushima, Tokushima, Japan

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## Abstract

Post-transplant lymphoproliferative disorder is an uncommon complication of immunosuppression following solid organ or hematopoietic stem cell transplants. Primary cutaneous post-transplant lymphoproliferative disorder with isolated skin involvement but without systemic involvement is rare. We report a 50-year-old woman, a renal transplant recipient on long-term immunosuppression, who presented with a rapidly expanding ulcer on her right posterior thigh after a skin incision. Although the clinical presentation was similar to that of pyoderma gangrenosum, pathological investigation confirmed Epstein-Barr virus-associated primary cutaneous B-cell post-transplant lymphoproliferative disorder. Initially, we reduced her immunosuppression. As the ulcer rapidly expanded, we initiated R-CHOP chemotherapy, consisting of rituximab, cyclophosphamide, doxorubicin, and prednisolone. Owing to the complications from cytomegalovirus retinitis, we were only able to administer two courses of chemotherapy. However, after continuous administration of ganciclovir, the skin ulcer regressed and completely healed, leaving a scar five months after her first visit. Since pyoderma gangrenosum is a diagnosis of exclusion, ulcerative skin lesions, similar to the clinical presentation of pyoderma gangrenosum, should be subjected to pathological investigation for accurate diagnosis.

## Introduction

Post-transplant lymphoproliferative disorder (PTLD) is an uncommon complication of immunosuppression following solid organ or hematopoietic stem cell transplants.[1] Extranodal lesions in PTLD can involve several organs, including the central nervous systems, lungs, gastrointestinal tract, and skin.[2-4] Isolated skin involvement without systemic involvement is rare in PTLD.[5] Herein, we report a renal transplant patient with primary cutaneous B-cell PTLD who presented with a rapidly progressing skin ulcer on the right posterior thigh with a clinical presentation that mimicked that of pyoderma gangrenosum (PG).

## Case Synopsis

A 50-year-old woman with a history of a renal transplant from her mother for focal segmental glomerulosclerosis in 2007 underwent dialysis for a failed renal transplant in February 2024. Simultaneously, she noticed a single erythematous lesion on her right posterior thigh (Figure 1). A local physician considered the erythema to be a subcutaneous abscess and incised it, which evolved into a necrotic ulcer and progressively expanded. The patient was referred to our hospital with a suspicion of PG. Physical examination revealed a 10×7cm ulcer marginated with a slightly raised violaceous undermined border and an exudative base on the right posterior thigh (Figure 2). She started immunosuppressive therapy that consisted of prednisolone 10mg/day, mycophenolate mofetil 500mg/day, and tacrolimus 4.5mg/day in 2007. Maintenance immunosuppressive therapy at the time of skin ulcer development consisted of prednisolone 3.75mg/day, mycophenolate mofetil 750mg/day, and tacrolimus 1.5mg/day.

a Corresponding Author: Yasutoshi Hida MD PhD, Division of Dermatology, Tokushima Red Cross Hospital, 773-8502, Tokushima Komatsushima Komatsushima-cho Irinoguchi 103, Japan, Tel: +81 885-32-2555, Email: yasutoshi@ae.auone-net.jp

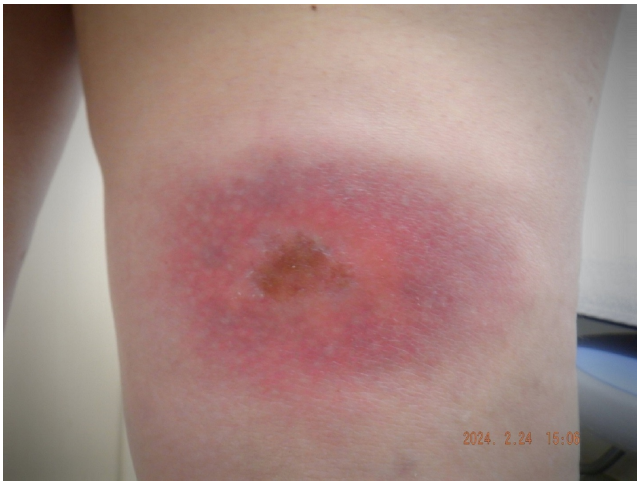

**Figure 1.** *Infiltrated erythema over the right posterior thigh.*

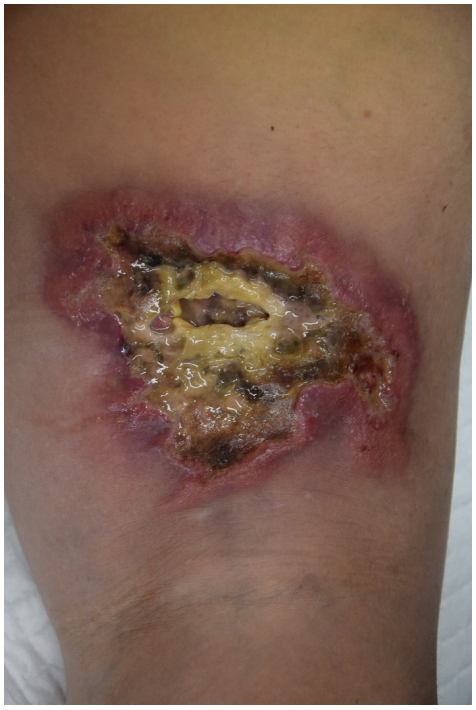

**Figure 2.** *Rapid expansion of a necrotic exudative ulcer shortly after a skin incision.*

Skin biopsy was performed on the infiltrated ulcer margins. Histopathological examination of the biopsy specimen revealed a dense monomorphous atypical lymphocytic infiltrate (Figure 3) that extended throughout the dermis into the subcutaneous tissue. The infiltrates spared the epidermal surface. The proliferative activity was brisk (MIB-1 labeling index, 60%). The lymphoid cells were positive for *CD20* (Figure 4), bcl-2, MUM-1, and *CD79*. They were negative for bcl-6, *CD3*, *CD5*, *CD10*, *CD23*, *CD30*, and *CD56*. Epstein-Barr virus (EBV)-encoded ribonucleic acid in situ hybridization was positive (Figure 5). Positron emission tomography-computed tomography images revealed increased tracer uptake limited to

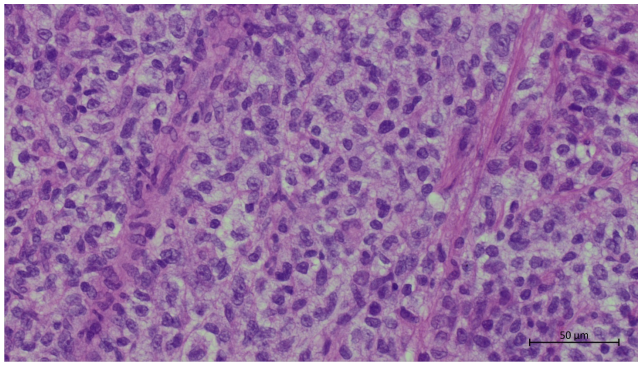

**Figure 3.** *Hematoxylin and eosin histopathological findings showing medium to large-sized atypical lymphoid cells (Bar, 50$\mu$m).*

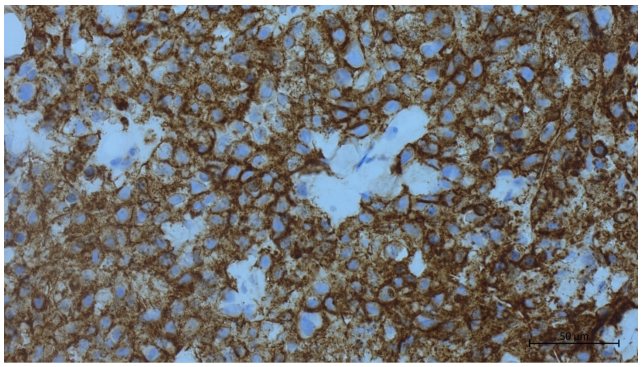

**Figure 4.** *Immunohistochemistry with an anti-*CD20 *antibody showing positivity (Bar, 50$\mu$m).*

the site of the cutaneous ulcer. Based on these findings, we diagnosed the patient with primary cutaneous B-cell PTLD related to EBV, which was categorized as monomorphic PTLD. To reduce immunosuppression, mycophenolate mofetil was discontinued and prednisolone and tacrolimus were reduced to 2.5mg/day, and 1mg/day, respectively. In addition, owing to the rapid expansion of the ulcer, we initiated R-CHOP chemotherapy, consisting of rituximab, cyclophosphamide, doxorubicin, and prednisolone. The patient developed cytomegalovirus retinitis three weeks after the second course of chemotherapy.

Chemotherapy was discontinued and the patient received ganciclovir intravenously three times a week. Following continuous administration of ganciclovir, the skin ulcer rapidly regressed and completely healed, leaving a scar (Figure 6) five months after her first visit. Tacrolimus was discontinued in October 2024. Ganciclovir is scheduled to be discontinued in January 2025, as the cytomegalovirus retinitis has improved.

## Discussion

The incidence of PTLD varies with type of transplant. Small intestine transplant recipients are at the highest risk for development of PTLD (up to 32%), whereas renal

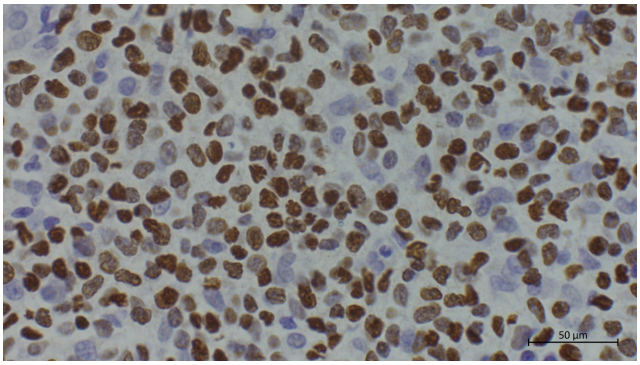


**Figure 5.** *In situ hybridization with an Epstein-Barr virus encoding region probe showing positivity. Bar, 50µm.*

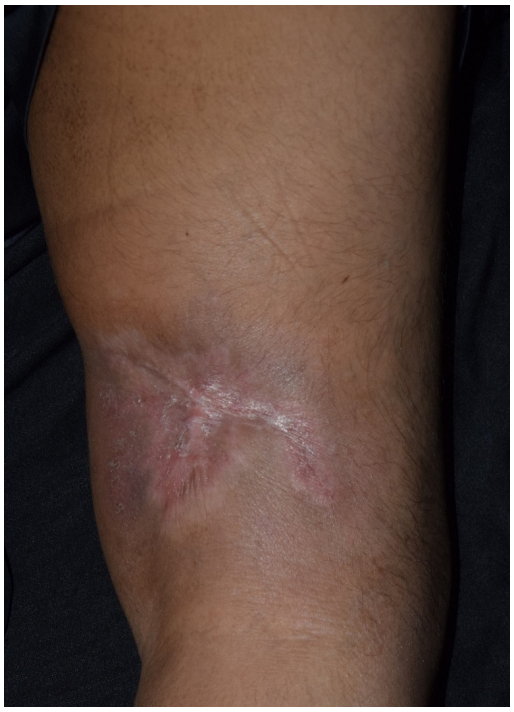

**Figure 6.** *Clinical image of scar following healing skin ulcer.*

transplant recipients are at relatively low risk (1%-2%), which may reflect immunosuppressive regimens.[3] Although the exact frequency of primary cutaneous PTLD is unknown, it was estimated to comprise 1% or less of the total cases of PTLD.[5] According to multicenter case series, approximately 30% of the cases of primary cutaneous PTLD were classified as primary cutaneous B-cell PTLD and 90% of the cases of primary cutaneous B-cell PTLD were EBV-associated lymphoproliferation.[6] One major etiology of primary cutaneous B-cell PTLD is persistent EBV infection owing to immunosuppressive agents of cytotoxic T cells, whose response is necessary to control EBV infection.[7] Uncontrolled EBV replication and expression of EBV-derived oncogenes leads to the transformation from polyclonal lymphoproliferation to monoclonal lymphoma.[7]

Wang et al analyzed 50 cases of primary cutaneous B-cell PTLD reported in the literature.[5] The median age at onset was 56 years, with a male-to-female ratio of 2:1. The median interval from transplantation to diagnosis was eight years with a range of 0.4 to 30 years. Although any body part can be involved, the most common site is the extremities, accounting for 64.6% of cases. Patients with primary cutaneous B-cell PTLD usually present with one or more purple-red nodules or tumors, which may ulcerate. These nodules are usually asymptomatic but can be tender or painful.

Pyoderma gangrenosum is a rare inflammatory skin disease that presents as sharply marginated exudative ulcers with violaceous, undermined borders.[8] New ulcers may develop because of minor skin trauma. This phenomenon, known as pathergy, can be observed during a surgical incision.[8] In this case, a surgical incision led to inflammatory erythema into rapid expansion of the skin ulcer, mimicking pathergy. Weening et al studied 240 patients with a presumed diagnosis of PG and identified 12 cases of cutaneous involvement of malignant lymphoma.[9] As PG is a diagnosis of exclusion, overriding the fear of exacerbating skin conditions and performing a biopsy are necessary. The clinical resemblance of primary cutaneous B-cell PTLD and PG may relate to the rapid growth and angiocentric distribution of $EBV^+$ B cells in primary cutaneous B-cell PTLD, leading to tissue ischemia and necrosis with minor trauma.[10]

However, the optimal management of EBV-induced PTLD remains controversial. Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice recommend the reduction of immunosuppression as the initial therapy in patients who do not have rapidly progressive disease.[3] They recommended rituximab monotherapy as the next-line treatment for $CD20^+$ PTLD in patients with progressive disease and cytotoxic chemotherapy for those with progressive disease after rituximab-induction therapy.[3] Other treatment modalities include the use of antiviral agents.

Ganciclovir has an active antiviral effect against EBV and has been used in the management of early EBV-induced PTLD.[3] In this case, we initiated reduction of immunosuppression followed by R-CHOP chemotherapy because of the rapid expansion of the skin ulcer. Owing to cytomegalovirus retinitis, only two courses of R-CHOP chemotherapy were possible, but the skin ulcer healed after continued intravenous ganciclovir. We believe that reduction of immunosuppression and continuous intravenous ganciclovir therapy are effective treatments for this disease. Because primary cutaneous B-cell PTLD generally has a relatively better prognosis than extracutaneous PTLD, patients with primary cutaneous B-cell PTLD should initially be treated less aggressively.[11]

## Conclusion

An aggressive primary cutaneous PTLD presents rapid skin ulcer expansion, similar to the clinical presentation of PG. Although a few reports of PG development in renal

post-transplant recipients exist, ulcerative skin lesions mimicking PG should undergo pathological investigation for an accurate diagnosis.[12]

## Potential conflicts of interest

The authors declare no conflicts of interest.

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