

Photo Vignette

A Violaceous Nodule in a Lung-transplant Patient

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Dermatology Online Journal 22 (6): 16

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Abstract

Posttransplantation lymphoproliferative disorder (PTLD) is a rare complication of solid organ or allogenic bone marrow transplantation. Cases localized to the skin are even rarer, with only around 100 cases recorded in the literature [2]. We present a case of 60 year-old-woman, a lung transplant recipient, who presented with an asymptomatic violaceous nodule on her left medial calf. Histopathology was consistent with PTLD of the B-cell subtype, EBV negative. This case is unique in that it was of the B cell subtype of cutaneous PTLD, which has been less commonly observed than the T cell subtype. In addition, the case was EBV negative, which is rare in B cell cutaneous PTLD. The patient was treated with rituximab 600 mg IV weekly for four weeks and cytomegalovirus immune globulin (Cytogam) 100 mg/kg once, with resolution of the nodule.

Key words: cutaneous posttransplantation lymphoproliferative disorder; posttransplantation lymphoproliferative disorder of B-cell origin; skin cancer in immunosuppressed; skin cancer in transplant recipients

Introduction

Posttransplantation lymphoproliferative disorder is a rare yet potentially serious complication of solid organ or allogenic bone marrow transplantation that should be considered in the differential diagnosis of one or multiple violaceous nodules in an immunosuppressed patient.

Case synopsis

A 60-year-old woman with end stage COPD received an orthotopic right lung transplant in October 2011. She experienced no episodes of rejection. Posttransplantation immunosuppressive therapy consisted of prednisone, tacrolimus, and azathioprine. In March 2015, three and a half years posttransplantation, she began experiencing congestion, cough, and dyspnea on exertion. Pulmonary function testing revealed a decrease in FEV1. Transbronchial biopsy showed no evidence of acute cellular rejection and a viral screen was negative. Treatment with IV corticosteroids resulted in some improvement of symptoms. However, two months later the patient again experienced dyspnea on exertion, increased oxygen requirements, a drop in FEV1, and difficulty sleeping on her right side owing to soreness over her right chest. A right pleural effusion was noted on chest x-ray. Transbronchial biopsy was repeated showing evidence of focal organizing pneumonia with no evidence of acute cellular rejection. Cultures and viral screen were again negative. In early June 2015, the patient developed an asymptomatic lesion on her left medial calf. Physical examination revealed a 3 x 3 cm violaceous nodule with an erythematous border (Figure 1).

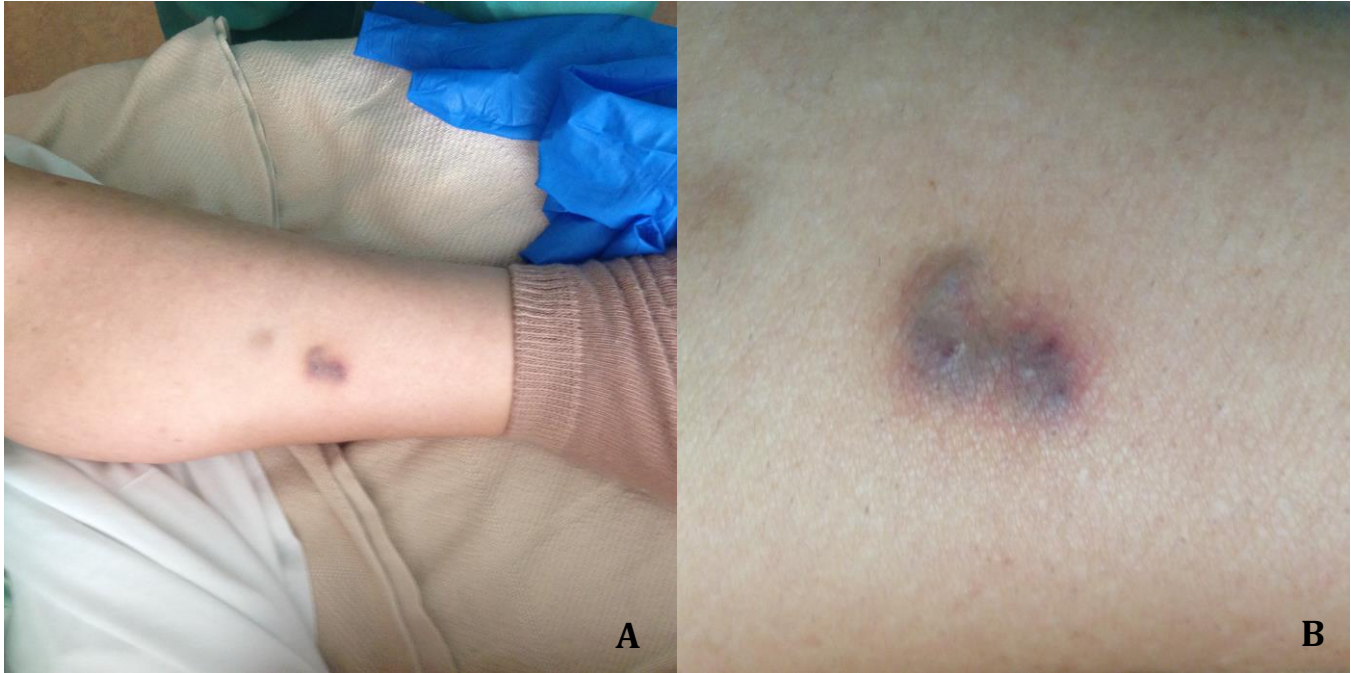


Figure 1. (A & B) 3 x 3 cm violaceous nodule with an erythematous border on the left medial calf.

A punch biopsy of the skin nodule was performed. Histopathology revealed an atypical lymphoid infiltrate distributed throughout the dermis (Figure 2).

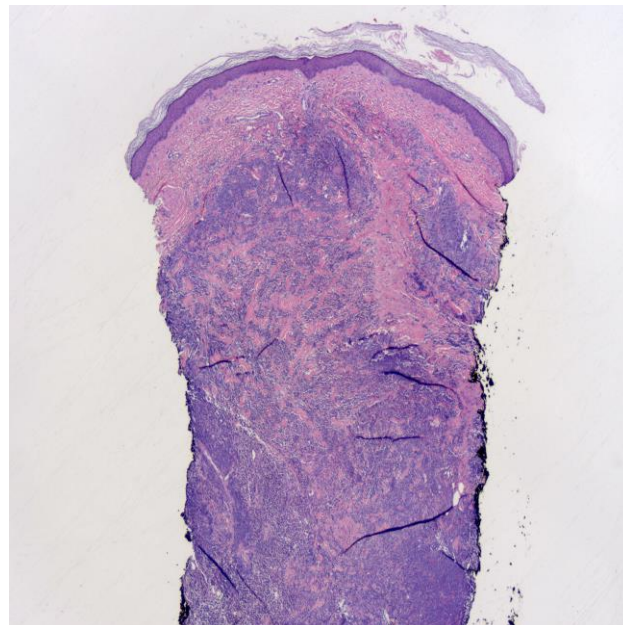


Figure 2. Atypical lymphoid infiltrate extending from the superficial to deep dermis, sparing the epidermis (Hematoxylin-eosin, original magnification x20)

High power examination showed enlarged tumor cells with pleomorphic nuclei and prominent nucleoli (Figure 3).

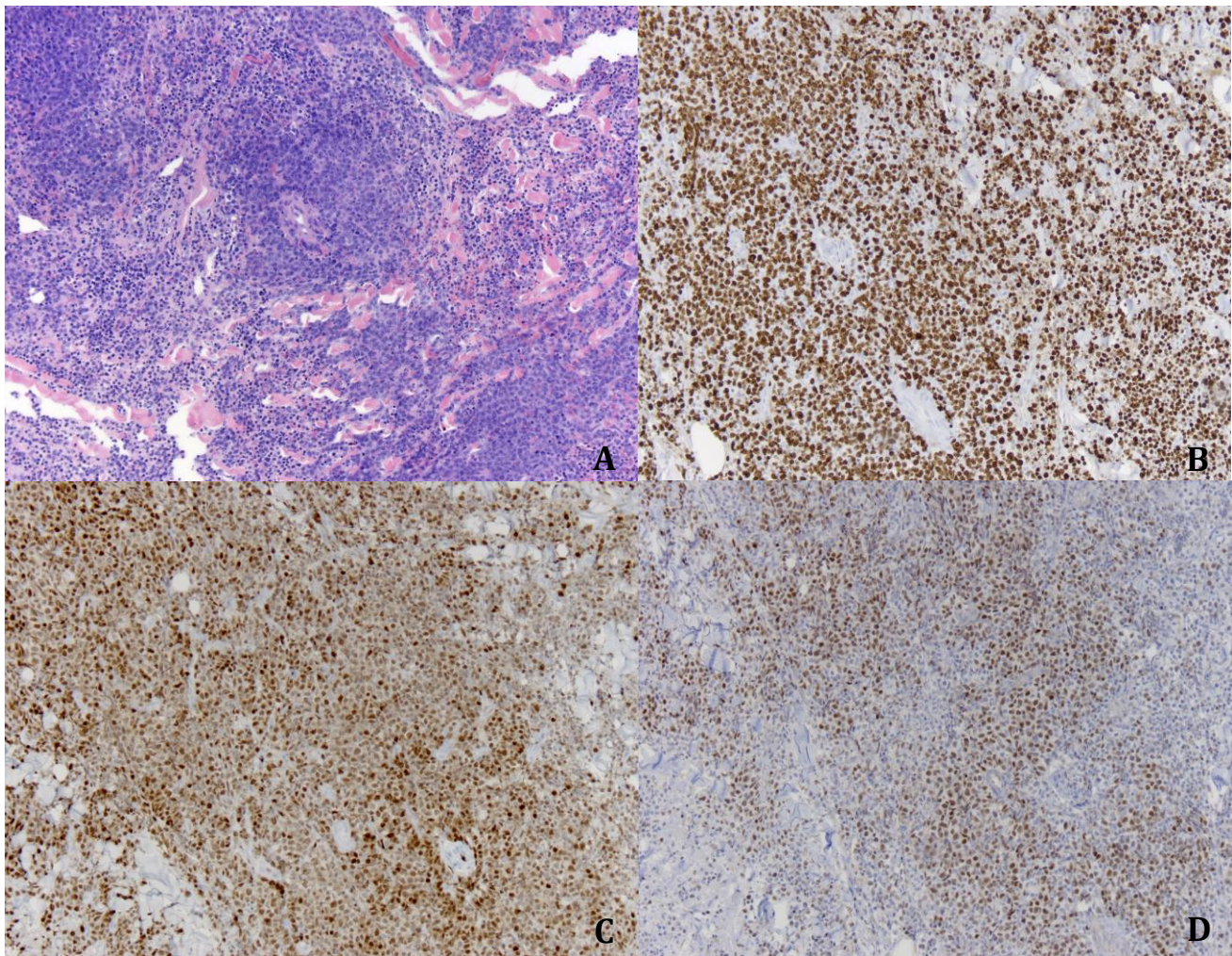


Figure 3. Large tumor cells with enlarged, pleomorphic nuclei and prominent nucleoli. A) Hematoxylin-eosin, original magnification x100, B) positivity for MIB-1, C) positivity for MUM1, D) positivity for PAX-5.

Immunohistochemistry was performed showing tumor cell positivity for CD20 and PAX-5, demonstrating B cell lineage, and MUM1, indicating an activated B cell subtype. MIB-1 was expressed in approximately 90% of tumor cells. Tumor cells were negative for CD3, CD10, and CD30. EBV in situ hybridization was negative. These findings were consistent with PTLN, diffuse large B-cell lymphoma (DLBCL) CD20+ subtype, EBV negative. The patient was treated with rituximab 600 mg IV weekly for four weeks and cytomegalovirus immune globulin (Cytogam) 100 mg/kg once. She remained on her immunosuppressive regimen. The nodule on her left medial calf resolved leaving behind a hyperpigmented patch. In November of 2015, the patient had two episodes of acute rejection, both treated with methylprednisolone. When she returned for follow-up in January 2016, three grouped violaceous nodules with an erythematous border were noted on the left lower calf, inferior to where the first lesion had resolved (Figure 4).



Figure 4. Inferior: Recurrent violaceous nodules with an erythematous border on the left medial calf. Superior: hyperpigmented patch representing resolved previous lesion.

The biopsy revealed features consistent with recurrent PTLD of the DLBCL subtype. Azathioprine was discontinued and the patient was again treated with rituximab. Owing to evidence of rejection, the patient is currently undergoing workup for another lung transplant.

Discussion

Posttransplantation lymphoproliferative disorders are lymphoid proliferations that develop in solid organ or allogeneic bone marrow transplant recipients. Extranodal PTLD occurs in up to 2% of all allograft recipients [1, 3]. It is the most frequent malignant complication of transplantation in childhood and the second most frequent complication in adults after non-melanoma skin cancers [2]. In both pediatric and adult populations, PTLD is the leading cause of cancer-related mortality and graft loss [2]. PTLD includes a spectrum of lymphoproliferative diseases, ranging from an EBV-driven polyclonal hyperplasia in an infectious mononucleosis-like picture to malignant B- and T-cell lymphomas indistinguishable from their counterpart in immunocompetent individuals [1, 2]. The most commonly reported extranodal sites include the gastrointestinal tract, lungs, central nervous system, and the allografted organ [1]. Cutaneous PTLD is rare, with only around 100 cases reported in the literature [2]. In isolated skin involvement, T-cell variant of PTLD is more common than B-cell variant [2]. B-cell PTLD differs from cutaneous B-cell lymphoma in the general population with a predominance of EBV-associated forms [2].

Incidence varies with a number of factors. Renal allografts have the lowest risk (1.4%), whereas heart/lung allografts have the highest risk (5%) [1, 4, 3]. Risk is increased with HLA-mismatched or T-cell-depleted bone marrow allograft, primary EBV infection posttransplantation, cytomegalovirus disease, cyclosporine and tacrolimus induction therapy, and T-cell specific immunosuppressive therapy [1, 2, 4]. Younger age at transplantation increases risk, possibly because of increased risk of primary EBV infection [1]. Cumulative dose of immunosuppression correlated with increased risk of PTLD development [1].

Patients with cutaneous PTLD present at a median interval of 7 years posttransplantation and rarely exhibit systemic symptoms [1,2]. Primary cutaneous B-cell PTLD usually presents with one or multiple purple-red nodules, sometimes with ulceration [2]. Less commonly, erythematous indurated plaques, an erythematous maculopapular eruption, single or widespread ulceration, and erythroderma can develop [2]. The lesions are usually asymptomatic, but may be tender, painful, or hypoesthetic and are most commonly found on the extremities [2]. Histologically, primary cutaneous B-cell PTLD contains dense diffuse or nodular monomorphous aggregates of large cells [2]. In EBV positive tumors, plasmablastic cells predominate [2]. In most cases, the tumor cells express CD20 and/or CD79a as well as MUM-1 positivity [2].

The majority of B-cell PTLD is associated with an EBV infection [2]. Although the pathogenesis is not well understood, the decrease in EBV-specific T-cells from immunosuppression is thought to allow for growth of EBV-infected monoclonal proliferations of B-cells [1]. The depressed immune system, chronic antigenic stimulation by transplanted organ, and direct oncogenic potential of immunosuppressive agents allows for uncontrolled EBV proliferation and expansion of multiple EBV-infected and immortalized clones of B-cells [3, 5].

The mainstay of therapy is reduction in immunosuppression, with approximately 25% responding to that alone [1]. If reduction in immunosuppressive therapy cannot be done or fails, anti-CD20 antibody therapy (rituximab), chemotherapy, surgical resection, and radiation therapy have also been used [1]. Cutaneous PTLD has a more favorable response to therapy than other forms of PTLD, with overall survival rates for primary cutaneous B-cell and T-cell PTLD at 45.4% and 45.8%, respectively [1, 2].

Conclusion

With increasing rates of life-saving solid organ transplantation, dermatologists must be aware of PTLD as a rare, yet potentially serious complication of immunosuppression.

Acknowledgements

The authors would like to acknowledge Nicholas Nguyen, MD, University of Colorado School of Medicine Pediatric Dermatology Fellow, for his assistance in editing the manuscript.

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