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ORIGINAL ARTICLE

# Plasmacytic post-transplant lymphoproliferative disorder: a case series of nine patients

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## Summary

Post-transplant lymphoproliferative disorder (PTLD) is a serious complication of organ transplantation. Although PTLD typically has a B-cell histology, an uncommon variant, plasmacytic PTLD can present as a monoclonal plasma cell proliferation similar to plasmacytomas seen in multiple myeloma. A retrospective analysis was performed on nine patients at our center with plasmacytic PTLD as characterized by plasmacytic histology with the presence of CD138 and lack of CD20. Of the 210 adult solid organ transplant PTLD patients diagnosed between 1988 and 2012, 9 (4%) had a histological appearance consistent with plasmacytic PTLD. The median time from transplant to diagnosis was 3.7 years (range 8 months–24 years). All patients presented with extranodal and often subcutaneous solid tumors. Laboratory features included elevated LDH and beta-2 microglobulin levels, monoclonal gammopathy, and EBV positivity of the tumor. Unlike conventional multiple myeloma, patients had normal calcium levels and only mild anemia. Six patients who have completed treatment achieved complete responses with radiation therapy and/or reduction in immunosuppression with two patients now greater than 5 years in continuous complete response. Plasmacytic PTLD, despite its plasmacytic histology, is responsive to conventional therapies used for B-cell PTLD including reduction in immunosuppression and radiation therapy.

## Introduction

Post-transplant lymphoproliferative disorder is a potentially life-threatening complication of organ transplantation, affecting 3–20% of solid organ transplant recipients [1–3]. It arises in the setting of pharmacologic immunosuppression leading to impaired T-cell function and loss of control over Epstein-Barr Virus (EBV)-infected cells. The majority of PTLD cases are associated with EBV infection, manifested by the presence of EBV early RNA, latent membrane protein, and/or DNA in the neoplastic tissue [4]. However, other oncogenic mechanisms are also likely involved as many cases of PTLD are EBV negative [5].

The term PTLD encompasses a heterogeneous group of lymphoproliferations involving B cells, T cells, and plasma cells [6,7]. The most commonly seen forms of PTLD are early lesions, polymorphic B-cell PTLD, and monomorphic B-cell PTLD. Early lesions are known to manifest as polyclonal proliferation of cells with normal cytogenetics. The presentation is often that of a mononucleosis-like syndrome, with the disease often responsive to reduction in immunosuppression alone. Polymorphic PTLD is histologically a heterogeneous lesion, typically EBV positive, often involving the allograft and occurring soon after transplantation. In contrast, monomorphic PTLD, histologically appears as sheets of malignant cells resembling traditional

non-Hodgkin lymphoma, is often EBV negative, occurs later after transplantation, and may carry a worse prognosis [4,8]. Although polymorphic and monomorphic B-cell PTLD make up the majority of cases, rarer forms of PTLD can occur.

Plasmacytic PTLD is an unusual form of monomorphic PTLD [9–14]. Unlike typical monomorphic PTLD, which is classically composed of B cells similar to that seen in diffuse large cell lymphomas, plasmacytic PTLD is composed of monoclonal monomorphic plasma cells similar to that in traditional plasma cell myeloma. The characteristic immunophenotype includes CD138 expression and lack of CD20 expression. Little has been reported on the clinical presentation and outcome of solid organ recipients with plasmacytic PTLD. Frequently lacking CD20, plasmacytic PTLD is not usually amenable to treatment with rituximab, limiting the treatment options usually used in B-cell PTLD [12]. We present our experience with nine adult solid organ transplant recipients with plasmacytic PTLD.

## Materials and methods

A retrospective analysis was performed on all patients diagnosed with plasmacytic PTLD after adult solid organ transplantation between 1988 and 2012 at the Hospital of the University of Pennsylvania. All patients had tumors that met criteria for plasmacytoma with populations of malignant cells with plasmacytic morphologic features and expression of the plasma cell marker CD138. Patients were excluded if their PTLD lesion did not express CD138 or was described as having a polymorphous population with a mixture of plasma cells and other forms (for example, numerous CD20+ B cells). Epstein-Barr virus involvement was determined by *in situ* hybridization for EBV-encoded RNA (EBER) transcripts and/or immunohistochemical staining for latent membrane protein (LMP). Data on the patient's medical histories, PTLD presentation, treatment, and outcome were collected and analyzed. Tumor staging was performed using the Ann Arbor staging system [15].

## Results

### Patient demographics

From January 1, 1988 to June 30, 2012, 7,428 adult patients underwent solid organ transplantation at the Hospital of the University of Pennsylvania of which 210 patients (3%) were diagnosed with PTLD. Nine (4%) patients of 210 were identified as having plasmacytic PTLD (Table 1). One of the nine patients in our series was not transplanted at our institution. All patients had previously undergone solid organ transplantation with a median age at diagnosis of 61 years (range 53–71). All patients received immunosuppressive medications at the time of their PTLD diagnosis (Table 2). The median time from transplant to diagnosis of PTLD was 3.7 years (range 8 months–24 years.). PTLD in three patients occurred early within the first 2 years after transplantation. Three patents were diagnosed long after transplant at years 13, 14, and 24.

### Clinical presentation

The clinical presentations were varied and related to the initial site of tumor involvement (Table 2). Patient 2 presented with diplopia as the initial manifestation of a CNS lesion. Patients 3, 6, 8, and 9 presented with subcutaneous skin lesions. Patients 1 and 5, who were liver transplant patients, had allograft lesions and presented with B symptoms (fatigue, weight loss, anorexia, and fever) in one case and were found incidentally in the other. Patient 4, a kidney transplant recipient, presented with acute gastrointestinal bleeding, secondary to a gastric lesion. Classic B symptoms (fever, weight loss, and night sweats), typical for lymphoma patients, were only seen in one patient. Patient 7 presented with headaches from his cavernous sinus mass.

Five patients had stage I disease consisting of solitary tumors only, and four had stage IV disease with multiple lesions. All patients were noted to have extra-nodal involvement with mass lesions, including 2 with liver allograft involvement. Unlike conventional lymphoma and B-cell

**Table 1.** Patient demographics.

| Patient number | Sex | Age at PTLD diagnosis | Organ transplant type | Reasons for organ transplantation | Organ transplant number | Prior rejection episodes |
|---|---|---|---|---|---|---|
| 1 | M | 69 | Liver | Hepatocellular carcinoma | 1 | 2 |
| 2 | M | 61 | Kidney | Focal segmental glomerulosclerosis | 1 | 1 |
| 3 | M | 65 | Lung | Chronic obstructive pulmonary disease | 1 | 1 |
| 4 | F | 56 | Kidney | Diabetic nephropathy | 1 | 1 |
| 5 | M | 62 | Liver | Cryptogenic cirrhosis | 2 | 0 |
| 6 | F | 59 | Lung | Chronic obstructive pulmonary disease | 1 | 2 |
| 7 | M | 71 | Heart | Idiopathic cardiomyopathy | 1 | 0 |
| 8 | M | 54 | Kidney | Alport syndrome | 1 | 0 |
| 9 | F | 53 | Islet cell & kidney | Diabetic mellitus | 2 | 0 |

PTLD, post-transplant lymphoproliferative disorder.

**Table 2.** Staging, treatment approach, and outcomes.

| Patient number | Organ involvement at diagnosis | Stage at diagnosis | Time from transplant to diagnosis | Immunosuppression at time of diagnosis | Treatments | Response | Outcomes |
|---|---|---|---|---|---|---|---|
| 1 | Liver allograft | I | 8 months | Pred 5 mg QD<br>MMF 500 mg Q12<br>Tac 3 mg Q12 | *Initial*: RI alone (Tac and MMF discontinued; Sirolimus 2 mg qd added; Pred increased to 20 mg qd) | *Initial*: SD | Died with SD 5 months post diagnosis (progressive liver failure secondary to recurrent Hepatitis C) |
| 2 | CNS & oral pharynx | IV | 9 months | Pred 5 mg QD<br>MMF 500 mg BID<br>Tac 2 mg QAM,<br>1 mg QPM | *Initial*: RI alone (MMF discontinued; Tac decreased to 1 mg q12) | *Initial*: CR | Alive in CR, 5 years and 8 months post diagnosis |
| 3 | Skin (subcutaneous) | I | 13 years 11 months | Pred 10 mg QD<br>MMF 500 mg BID<br>CSA 100 mg BID | *Initial*: RI alone (MMF discontinued; CSA decreased to 75 mg BID)<br>*Subsequent*: Complete excision + XRT | *Initial*: SD<br>*Subsequent*: CR | Died in CR, 1 month post resection (Bacterial Pneumonia) |
| 4 | GI tract (intestine & adenopathy) | IV | 14 years 4 months | Pred 7.5 mg QD<br>CSA 25 mg BID<br>Aza 100 mg QD | *Initial*: RI + complete surgical resection (Aza discontinued)<br>*Subsequent*: Further RI (CSA discontinued and Pred increased to 20 mg qd) | *Initial*: PD<br>*Subsequent*: CR | Alive in CR, 7 years 5 months post diagnosis, 6 years 7 months post relapse |
| 5 | Liver allograft | IV | 1 year 4 months | Tac 1 mg Q12 | *Initial*: RI (Tac discontinued) + cyclophosphamide + prednisone<br>*Subsequent:* CHOP chemotherapy Bortezomib. XRT | *Initial*: PD<br>*Subsequent*: PD | Died from Progressive PTLD 1 year post diagnosis |
| 6 | Skin (subcutaneous) | I | 2 years 10 months | Pred 5 mg QD<br>MMF 500 mg BID<br>Tac 2.5 mg BID | *Initial*: RI + complete surgical resection (Tac reduced)<br>*Subsequent*: Further RI and XRT (MMF discontinued) | *Initial* RI + surgery: PD<br>*Subsequent*: CR (with adjunctive radiation) | Died in CR, 14 months post initial diagnosis (respiratory failure from bronchiolitis obliterans) |
| 7 | Cavernous Sinus | I | 5 years 10 months | Pred 5 mg QD<br>Tac 1 mg QAM,<br>0.5 mg QPM<br>Aza 150 mg QD | *Initial:* XRT, RI (delete Aza)<br>*Subsequent:* etoposide + cyclophosphamide, further RI (reduce Tac to 0.5 mg BID) | *Initial:* PD<br>*Subsequent*: PD | Alive with active PTLD on treatment 1 year post diagnosis |
| 8 | Skin (subcutaneous) | IV | 24 years | Pred 5 mg QD<br>CSA 200 mg<br>QAM & 100 mg QPM | *Initial:* RI (Tac reduced to 100 mg BID) | *Initial:* CR | Alive in CR, 9 months post diagnosis |
| 9 | Lacrimal gland (subcutaneous) | I | 3 years, 8 months | Tac 1.5 mg BID<br>MMF 500 mg BID<br>Pred 5 mg QD | *Initial*: Surgical excision | *Initial:* CR | Alive in CR, 3 months post diagnosis |

MMF, mycophenolate mofetil; CSA, Cyclosporine; Aza, Azathioprine; Tac,Tacrolimus; Pred, Prednisone; CR, complete remission; SD, stable disease; PD, progressive disease; PTLD, post-transplant lymphoproliferative disorder; RI, reduction in immunosuppression. Tumor staging was done using the Ann Arbor Classification.

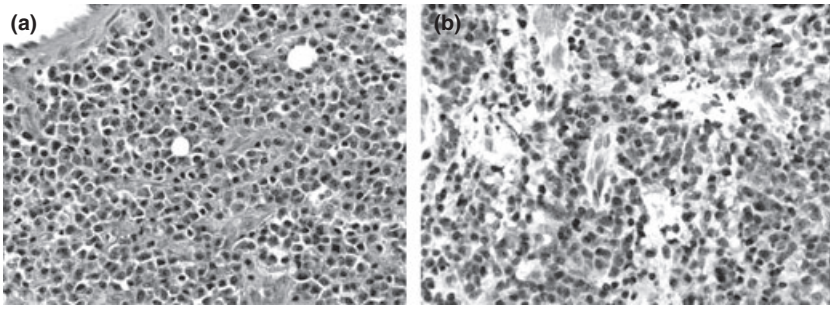


**Figure 1** PTLD, plasmacytoma (40×) (a) H and E stain, plasma cells in the lesion are noted to have a variable morphology. They are best characterized by eccentric nucleus, ample cytoplasm, and peri-nuclear clear zone that correlate with the golgi apparatus. The nuclear chromatin is condensed, distributed on the outer rim of the nuclear membrane, rendering what is known as a clock face appearance of the plasma cells. (b) EBER stain, plasmacytic cells stain positive for EBV-encoded RNA (EBER) in a typical nuclear pattern.

PTLD where adenopathy is frequently seen, only one patient had detectable adenopathy.

Tumor biopsies were performed in all patients. All tumors contained sheets of plasma cells that expressed CD138 and lacked expression of CD20 (Fig. 1a), consistent with the diagnosis of monomorphic plasmacytic PTLD (Table 3). Seven of nine patients had detectable intracellular EBV through the use of in situ hybridization for EBER and/or LMP stains (Fig. 1b). A bone marrow biopsy was done only on one patient and was negative for malignancy.

Laboratory data at the time of diagnosis (Table 3) revealed elevations in serum LDH levels in 7 of 9 patients and beta 2 microglobulin levels in 7 of 7 patients tested. Eight patients were noted to have some degree of renal insufficiency though similar to their baseline (median creatinine 1.5 mg/dL range 0.9–2.9 mg/dL). All patients were noted to have normal calcium levels. Cytopenias were generally mild consisting of anemia only (median hemoglobin 11 g/dL range 7.7–14). Quantitative plasma EBV levels were measured in seven patients at diagnosis and found to be elevated in five by PCR. Serum protein electrophoresis (SPEP) was performed in all patients, four of whom showed a monoclonal gammopathy measuring less than 2 g/dL. One patient was also noted to have minor bands consistent with free lambda light chain. Three patients had a negative SPEP despite having light chain-restricted immunoglobulin present on their tumor cells.

### Treatment and outcome

Eight patients have completed treatment and are fully assessable for response. Patient #7 is still undergoing treatment. Initial treatment approach for all but one patient (#9) involved reduction in immunosuppression (RI) (Table 2). Four patients (#1, #2, #3, and #8) were treated with initial RI only. Patient #1 had stable disease, but died a few months later from liver allograft failure as a result of progressive hepatitis C. Patients #2 and #8 despite having stage IV disease, including CNS involvement in patient #2, achieved complete responses with RI alone. Patient #3 had stable disease after RI and subsequently achieved a CR after complete surgical excision of a subcutaneous skin nodule and subsequent radiation therapy.

Two patients (#4 and #6) were initially treated with surgery and RI and noted to have a complete response following complete surgical resection. Both subsequently relapsed while on RI. Patient #4, presenting with a gastric mass, was noted to have a relapse of his disease after 1 month, and achieved complete remission 3 months after further reduction in immunosuppression (discontinuation of tacrolimus). Patient #6 relapsed 4 months after being treated with RI and complete surgical excision. She ultimately achieved a second complete remission after further RI (discontinuation of mycophenolate mofetil) and concurrent radiation therapy. Patient #9 is still in remission after surgical resection though follow-up is short at only 9 months.

Patient #5 presented with advanced stage IV disease, which included the presence of lytic bone lesions. He underwent initial therapy that not only included reduction in the tacrolimus dose but also cyclophosphamide and prednisone for three cycles, with subsequent stabilization of disease. He was then switched to bortezomib, to which his disease was noted to have no response. Next, the patient received image-guided radiotherapy to the liver allograft, his main site of involvement, with marked decrease in the size of the lesion. Five months later, he developed progressive disease with diffuse intra-abdominal lymphadenopathy and additional bony lesions, and was initiated on combination chemoimmunotherapy using the CHOP regimen (cyclophosphamide, doxorubicin, vincristine, and prednisone). Unfortunately, no improvement was noted after the completion of six cycles, and the patient ultimately opted for palliative radiotherapy prior to his demise.

Patient #7 underwent radiation therapy and RI for a cavernous sinus mass with only minimal response. At progression, he was treated with cyclophosphamide and etoposide

**Table 3.** Laboratory finding and pathology.

| Patient number | Tumor CD138 | Tumor CD20 | Tumor EBER | Tumor LMP | Plasma EBV PCR (copies/ml) | SPEP | Elevated LDH | Elevated Beta 2 Microglobulin (mg/l) | Hypercalcemia (mg/dl) | Elevated Creatinine (mg/dl) | Anemia (Hgb g/dl) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Y | N | Y | N | At Diagnosis: 55800<br>s/p Treatment: <818 | IgG Lambda1.9 g/dl | Y | H (7.8) | N (8.5) | Y (1.5) | Y (7.7) |
| 2 | Y | N | Y | N | At Diagnosis: 600<br>s/p Treatment: 0 | IgG Kappa<br>0.9 g/dl | Y | N/A | N (9.8) | N (1.0) | Y (10.5) |
| 3 | Y | N | Y | N | N/A | N/A | Y | H (5.6) | N (9.2) | Y (1.7) | Y (12.4) |
| 4 | Y | N | Y | Y | At Diagnosis: N/A<br>s/p Treatment: <100 | IgA Kappa<br>0.4 g/dl | Y | H (3.4) | N (8.6) | Y (1.4) | Y (10.5) |
| 5 | Y | N | Y | N/A | N/A | Negative | Y | H (15.1) | N (9.1) | Y (1.8) | N (12.4) |
| 6 | Y | N | Y | N | At diagnosis: 959<br>s/p Treatment: 959 | IgG Kappa + Lambda<br>Too low to quantify | Y | N/A | N (9.0) | Y (2.9) | Y (11) |
| 7 | Y | N | N | N | At Diagnosis: 2910 | Negative | N | H (2.69) | N (9.5) | N (1.2) | Y (11.1) |
| 8 | Y | N | Y | Y | At diagnosis: 611 | Negative | Y | H (3.6) | N (8.8) | Y (1.9) | N (14.0) |
| 9 | Y | N | N | N | At diagnosis<br>Not detected | Negative | N | H (3.07) | N (9.2) | N (0.88) | N (12.6) |

chemotherapy with an initial response, but then progression. He is currently undergoing further treatment.

Of the patients included in the case series, four are still alive and in complete remission. Patient #2 is alive for more than 5 years from diagnosis, whereas Patient #4 is alive for more than 7 years from her original diagnosis and more than 6 years from relapse. Both patients achieved complete response with RI alone. Two patients (#8 and #9) are alive in CR, but with short follow-up of less than a year. Two patients (#3 and #6) achieved complete responses, but died from unrelated causes while still in remission. Patient #1 died with stable disease, 4 months following his diagnosis of PTLD because of progressive liver failure secondary to hepatitis C recurrence in the allograft. Only one patient (Patient #5) died from progressive PTLD 1 year following diagnosis with stage IV disease, after failure of RI in addition to several chemotherapy regiments (Table 2). Patient #7 is still undergoing treatment.

## Discussion

PTLD encompasses a broad histologic spectrum ranging from polyclonal expansions mediated by EBV to monomorphic lymphomas indistinguishable from aggressive lymphomas in nontransplant patients. Of the 210 cases of PTLD seen in our institution in the past 20 years, nine (4%) have met the diagnostic criteria of plasmacytic PTLD.

Our group of nine adult patients included adult lung, heart, liver, and kidney recipients. The small number of patients studied makes the determination of incidence in different organ transplant subtypes difficult. However, our overall incidence of 4% is identical to a previously reported series suggesting that plasmacytic PTLD represent a uncommon variant of PTLD [12]. Given the use of multiple concurrent immunosuppressive agents, one cannot identify a specific causative drug. As in other cases of PTLD, it is likely that immunosuppression, in general, rather than a specific drug led to the development of plasmacytic PTLD.

Similar to other types of PTLD, although many of our patients were diagnosed within 2 years of transplantation, it appears that plasmacytic PTLD can also occur many years after transplantation. Certain features seen in our patients appear to characterize plasmacytic PTLD and set it apart from classical plasma cell myeloma and other subtypes of PTLD. Unlike traditional multiple myeloma, which commonly involves the bone marrow only and can present with lytic boney lesions, plasmacytic PTLD uniformly presented with plasmacytomas [12]. Extra-nodal mass lesions, frequently subcutaneous, were universal in our series. Adenopathy, as seen in classic PTLD, was only seen in one patient. Unfortunately, bone marrow biopsies are not routinely performed in PTLD cases at our institution, so we


 

were unable to determine the extent of bone marrow involvement in our series. However, in a previous report, in eight patients with plasmacytic PTLD, none had bone marrow involvement [12]. Classic myeloma lab findings, such as LDH and beta-2-microglobulin levels were elevated in almost all of our patients. For both myeloma and PTLD in general, elevated LDH and beta-2 microglobulin are associated with poorer outcomes [16–18]. Furthermore, with PTLD, high LDH has even been seen to be a poor prognostic factor for response to therapies such as reduction in immunosuppression and rituximab, although not for combined chemoimmunotherapy [4,19,20]. Given the near universally elevated LDH and beta-2 microglobulin levels in our series, we were unable to determine their effect on outcome, although a number of our patients did well despite these poor prognostic signs. Although the majority of our patients had a monoclonal gammopathy, this was not universal. Unlike traditional multiple myeloma, lytic bone lesions, hypercalcemia, and severe anemia were not features in our series. While similarities exist, plasmacytic PTLD appears to be distinct from traditional multiple myeloma, presenting as solid plasmacytomas with a different laboratory profile.

Besides a unique clinical and laboratory presentation compared with conventional myeloma, the presence of EBV within the tumor cells in this case series distinguishes plasmacytic PTLD from classical plasma cell myeloma seen in nontransplant patients where EBV is rarely present. It is critical to distinguish traditional multiple myeloma from plasmacytic PTLD. Short of an allogeneic stem cell transplant, conventional myeloma is not felt to be curable and requires long-term treatment to control. In contrast, our series shows that plasmacytic PTLD may respond to reduction in immunosuppression alone with long-term disease-free survival and possibly cure. In transplant patients with plasmacytomas, knowing if it is PTLD may allow patients to be treated and cured without traditional chemotherapy for multiple myeloma, which otherwise might induce unneeded complications in immunosuppressed transplant patients. The presence of EBV also provides a potential method for monitoring patients as they proceed through treatment by following their EBV load through the use of peripheral blood quantitative EBV PCR [21,22].

Interestingly, although both plasmacytic PTLD and plasma cell myeloma are characterized by a clonal proliferation of plasma cells, plasmacytic PTLD tends to present and behave in a manner more similar to a lymphoma with mass lesions rather than with bone marrow involvement and lytic bone lesions seen in conventional myeloma. In many patients with traditional B-cell PTLD, there is some degree of plasmacytic differentiation. Plasmacytic PTLD, given its clinical presentation and behavior, is more similar to a lymphoma than conventional myeloma and may represent an extreme case of differentiation of a B-cell PTLD. This case series underscores the importance of tissue biopsies and appropriate pathological work-up for a transplant patient presenting with a mass lesion. It cannot be inferred that a mass lesion in a transplant patient is a CD20-positive B-cell PTLD and treatable with rituximab (anti-CD20 monoclonal antibody), as plasmacytic PTLD and other rare subtypes such as T-cell PTLD and Hodgkin-like PTLD are often CD20-negative. In classic myeloma, while the vast majority of cases do not express CD20, some do. It remains unclear how often plasmacytic PTLD expresses CD20, although our series and the literature would suggest that it would be the minority of patients [12].

The patients with plasmacytic PTLD included in this series had a relatively good disease outcome, with only one patient expiring as a result of progressive disease. Overall, 6 of 9 assessable patients ultimately achieved a complete response. As in the case of conventional B-cell PTLD, reduction in immunosuppression appears to be an effective and potentially curative therapy [23]. Unlike conventional B-cell PTLD, all of the patients in our series were CD20-negative and were unlikely to benefit from rituximab therapy. Despite being a rare variant of PTLD with different histology, the disease process of plasmacytic PTLD noted in our patients appeared to behave much like B-cell PTLD, and was treated and cured by similar means. It has been recently reported that in monomorphic CD20-positive PTLD, the sequential use of rituximab followed by CHOP chemotherapy results in a 68% overall response rate and median overall survival of 6.6 years [4]. These results suggest a possible standard of care of monomorphic CD20-positive PTLD. However, in our series, none of the patient's tumors expressed CD20 and the one patient that did receive CHOP chemotherapy did not respond. It remains unclear what the optimal therapy is for plasmacytic PTLD, although radiation, resection, and reduction in immunosuppression appeared effective in our patients. Bortezomib, a proteasome inhibitor that is highly efficacious in classical plasma cell myeloma, failed to work in our one patient.

Our series, while suggesting interesting features of plasmacytic PTLD, does have some weaknesses, which must be noted. This is a small retrospective series of patients treated at one center opening up the possibility of bias in their individual care. In addition, bone marrow biopsies were not routinely done, which leaves an open question of whether these patients had bone marrow involvement concurrently with their extranodal plasmacytomas and whether that involvement had any prognostic effect on their outcome. Unfortunately, in practice, bone marrow biopsies are not routinely done on PTLD patients at our center leading to the lack of data in this series. As in any small series of a rare variant of a rare disease such as plasmacytic PTLD, large-scale prospective clinical trials are difficult to per-

form. Small series such as this may still provide helpful insight into the presentation and treatment.

Plasmacytic PTLD is a rare subtype of PTLD that, despite its different histology, presents, behaves, and can be treated successfully using similar approaches to traditional B-cell PTLD. Patients can be cured of their disease without resorting to conventional chemotherapy for multiple myeloma. As in all cases of PTLD, treatment should be individualized and managed in collaboration between an oncologist and a transplant physician.

## Authorship

MK, NS, RR, DT: design of study, data analysis, wrote manuscript. DF: pathology review and analysis. OF, RR, VNA, MB, TF, SG, SJS, EAS: conduct of study, data collection.

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## References

1. Finn L, Reyes J, Bueno J, *et al.* Epstein-Barr virus infection in children after transplantation of the small intestine. *Am J Surg Pathol* 1998; **22**: 299.
2. Armitage JM, Kormos RL, Stuart RS, *et al.* Posttransplant lymphoproliferative disease in thoracic organ transplant patients: ten years of cyclosporine-based immunosuppression. *J Heart Lung Transplant* 1991; **10**: 877.
3. Opelz G, Henderson R. Lymphomas after solid organ transplantation: a collaborative transplant study report. *Am J Transplant* 2003; **4**: 222.
4. Trappe R, Oertel SH, Leblond V, *et al.* Sequential treatment with rituximab followed by CHOP chemotherapy in adult B-cell post-transplant lymphoproliferative disorder (PTLD): the prospective international multicentre phase 2 PTLD-1 trial. *Lancet Oncol* 2012; **13**: 196.
5. Nelson BP, Nalesnik MA, Bahler DW, *et al.* Epstein-Barr virus-negative post-transplant lymphoproliferative disroders: a distinct entity? *Am J Surg Pathol* 2000; **24**: 375.
6. Nalesnik MA. The diverse pathology of post-transplant lymphoproliferative disorders: the importance of a standardized approach. *Transpl Infect Dis* 2001; **3**: 88.
7. Harris NL, Ferry JA, Swerdlow SH. Posttransplant lymphoproliferative disorders: summary of Society for Hematopathology Workshop. *Semin Diagn Pathol* 1997; **14**: 8.
8. Vegso G, Hadju M, Sebestyen A. Lymphoproliferative disorders after solid organ transplantation- classification, incidence, risk factors, early detection and treatment options. *Pathol Oncol Res* 2011; **17**: 443.
9. Borenstein J, Pezzella F, Gatter KC. Plasmablastic lymphomas may occur as post-transplant lymphoproliferative disorders. *Histopathology* 2007; **51**: 774.
10. Vishnu P, Jiang L, Cortese C, *et al.* Plasmacytoma-like post-transplant lymphoproliferative disorder following orthotopic liver transplantation: a case report. *Transplant Proc* 2011; **43**: 2806.
11. Willoughby V, Werlang-Perurena A, Kelly A, *et al.* Primary cutaneous plasmacytoma in a heart transplant patient. *Am J Dermatopathol* 2006; **28**: 442.
12. Trappe R, Zimmermann H, Fink S, *et al.* Plasmacytoma-like post-transplant lymphoproliferative disorder, a rare subtype of monomorphic B-cell post-transplant lymphoproliferation, is associated with a favorable outcome in localized as well as in advanced disease: a prospective analysis of 8 cases. *Haematologica* 2011; **96**: 1067.
13. Reid-Nicholson M, Kavuri S, Ustun C, *et al.* Plasmablastic lymphoma: cytologic findings in 5 cases with unusual presentation. *Cancer* 2008; **114**: 333.
14. Richendollar BG, Hsi ED, Cook JR. Extramedullary plasmacytoma-like post-transplantation lymphoproliferative disorders: clinical and pathologic features. *Am J Clin Pathol* 2009; **132**: 581.
15. Carbone PP, Kaplan HS, Musshoff K, *et al.* Report of the committee on Hodgkin's disease staging classification. *Cancer Res* 1971; **31**: 1860.
16. Terpos E, Katodritou E, Pouli A, *et al.* High Serum lactate dehydrogenase adds prognostic value to the international myeloma staging system even in the era of novel agents. *Eur J Haematol* 2010; **85**: 114.
17. Tsai DE, Hardy CL, Tomaszewski JE, *et al.* Reduction in immunosuppression as initial therapy for posttransplant lymphoproliferative disorder: analysis of prognostic variables and long- term follow-up of 42 adult patients. *Transplantation* 2001; **71**: 1076.
18. Greipp PR, San Miguel J, Durie BG. International staging system for multiple myeloma. *J Clin Oncol* 2005; **23**: 1.
19. Choquet S, Oertel SH, Leblond V, *et al.* Rituximab in the management of post-transplantation lymphoproliferative disorder after solid organ transplantation: proceed with caution. *Ann Hematol* 2007; **86**: 599.
20. Reshef R, Vardhanabhuti S, Luskin MR, *et al.* Reduction in immunosuppression as initial therapy for posttransplant lymphoproliferative disorder. *Am J Transplant* 2011; **11**: 336.
21. Tsai DE, Nearey M, Hardy CL, *et al.* Use of EBV PCR for the diagnosis and monitoring of post-transplant lymphoproliferative disorder in adult solid organ transplant patients. *Am J Transplant* 2002; **2**: 946.
22. Gulley ML, Tang W. Using Epstein–Barr viral load assays to diagnose, monitor and prevent posttransplant lymphoproliferative disorder. *Clin Microbiol Rev* 2010; **23**: 350.
23. Starzl TE, Nalesnik MA, Porter KA, *et al.* Reversibility of lymphomas and lymphoproliferative lesions developing under cyclosporin-steroid therapy. *Lancet* 1984; **1**: 583.