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Metachronous EBV-associated B-cell and T-cell Posttransplant Lymphoproliferative Disorders in a Heart Transplant Recipient

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Abstract

Posttransplant lymphoproliferative disorders (PTLDs) may occur as a complication of immunosuppression in patients who have received solid organ or bone marrow allografts. Most PTLDs are of B-cell lineage, whereas T-cell proliferations are rare. The majority of B-cell lesions are associated with Epstein-Barr virus infection. The occurrence of both B-cell and T-cell PTLDs in the same patient is extremely rare and only 6 cases have been previously published. We report a case of a 63-year-old man who developed 2 metachronous Epstein-Barr virus-related PTLDs beginning 10 years after heart transplantation. A polymorphic B-cell PTLD developed first that completely regressed after immunosuppressive therapy was partially with-drawn. Then, a monomorphic T-cell PTLD developed 31 months later. The patient died 17 months later owing to disease progression. We highlight the diagnostic challenge of this case that required numerous ancillary studies for lineage assessment and classification. Such studies are often needed in patients with a history of immunosuppression.

Keywords

posttransplant lymphoproliferative disorders; bilineal; Epstein-Barr virus; case report

Posttransplant lymphoproliferative disorders (PTLDs) comprise a heterogeneous group of lymphoid lesions. They develop as a consequence of immunosuppression in either solid organ or bone marrow allograft recipients. The risk of PTLD increases with the degree of immunosuppression. Patients who received human leukocyte antigen-mismatched or T-cell depleted marrow and patients who are treated with immunosuppressive therapy for graft-versus-host disease may have up to a 20% increased risk. In general, PTLD occurs in approximately 1% renal, 1% to 2% hepatic and cardiac, 5% heart-lung and liver-bowel, and 1% of bone marrow allograft recipients.^{10,22} The majority of cases (80% to 90%) are associated with Epstein-Barr virus (EBV) infection.¹⁰

On the basis of the 2001 World Health Organization (WHO) classification system of hematolymphoid malignancies, there are 4 morphologic categories for PTLD: early lesions,

polymorphic PTLTD, monomorphic PTLTD, and Hodgkin lymphoma and Hodgkin lymphomalike PTLTD.¹⁰ Early lesions are typically EBV-associated polyclonal expansions and include plasmacytic hyperplasia and infectious mononucleosislike PTLTD. Histologic architecture is usually preserved. Polymorphic PTLTDs are destructive B-cell lesions that show a full range of B-cell maturation, from immunoblasts to plasma cells. Although polymorphic in appearance, molecular genetic studies commonly show clonal immunoglobulin gene rearrangements or clonal EBV genomes. Monomorphic PTLTDs are morphologically B-cell or T-cell lymphomas and are classified according to the WHO classification system for lymphomas. PTLTDs may affect either nodal or extranodal sites.

Most of the monomorphic PTLTDs are of B-cell origin (85%) and can be classified as diffuse large B-cell lymphoma, Burkitt lymphoma, plasma cell myeloma, and plasmacytomalike PTLTD. Most of these cases are EBV+.^{10,25} T-cell neoplasms are rare and represent 10% to 15% of all PTLTDs. Reported cases include peripheral T-cell lymphoma unspecified, lymphoblastic lymphoma, large granular lymphocytic leukemia, cutaneous T-cell lymphoma, anaplastic large cell lymphoma, and hepatosplenic T-cell lymphoma. Seventy-five percent of T-cell PTLTDs lack EBV and have a more aggressive clinical course than the B-cell lesions.^{3,10,21,25} Classic Hodgkin lymphoma and Hodgkinlike PTLTD have also been reported in allograft recipients. These cases are virtually always EBV+.¹⁰ PTLTDs involving both B-cell and T-cell lineages in the same patient are extremely rare, and to our knowledge, only 6 cases have been reported.^{2,6,7,9,16,25} In this report, we review the literature and describe a case of a 63-year-old man who developed metachronous EBV-associated B-cell and then T-cell PTLTDs beginning 10 years after heart transplantation. This case highlights the need to perform ancillary studies for proper classification.

CASE REPORT

The patient was a 63-year-old African American male who had received a heart transplant for idiopathic dilated cardiomyopathy in the year 1992. He was seronegative for EBV; the EBV status of the donor is not known. He was on maintenance immunosuppression of cyclosporine (125 mg 2 times a day), mycophenolate mophetil (750 mg 3 times a day), and prednisone (5 mg every other day). In September 2002, he presented with recurrent fevers and progressive lymphadenopathy in axillary, pretracheal, subcarinal, iliac, and inguinal regions. EBV seroconversion was demonstrated and biopsy of an inguinal lymph node showed polymorphic EBV-associated B-cell PTLTD. Valganciclovir was added to his regimen to treat the EBV infection and cyclosporine and mycophenolate mophetil were decreased to 50 mg b.i.d. and 250 mg t.i.d., respectively. Follow-up computed tomography (CT) scan in August 2003 showed complete regression of lymphadenopathy in all affected regions.

In August 2004, he was diagnosed with adenocarcinoma of the prostate, Gleason score 3+3 = 6, and he received external beam radiation therapy (7600 cGy). In April 2005, he developed orbital fullness and compression of the right eye. CT scan showed a 2-cm enhancing right orbital mass that was not biopsied. It was assumed to be a recurrence of the B-cell PTLTD and he was treated initially with rituximab. However, the mass progressed causing severe pain, diplopia, and proptosis of his right eye. He received local radiation

therapy to the orbit consisting of 2400 cGy in 12 fractions. He responded well with significant improvement in eye function. Follow-up CT and positron emission tomography scans showed some residual infiltration of the orbital fat and an additional 1620 cGy were administered.

In December 2005, the patient developed a progressively enlarging mass in the right nasolabial area. The biopsy showed EBV-associated T-cell PTLD without evidence of residual B-cell PTLD. Radiation therapy was started, but was abandoned after 2000 cGy owing to extension of the tumor into maxillary sinus and inferior aspect of the orbit. CT scan in January 2006 showed progression of disease with involvement of pleura, liver, and retroperitoneal lymph nodes. He subsequently received 8 cycles of chemotherapy: cyclophosphamide, mitoxantrone, vincristine, and prednisone (CNOP) and cyclophosphamide, bleomycin, and cisplatin (CBP) protocols; however, the disease progressed and in August 2006 he was found to have multiple bone lesions involving the cervical spine, humerus, and ribs and also a brain mass in the temporal lobe. He was placed on ifosfamide, carboplatin, and etoposide (ICE) chemotherapy, but his clinical condition deteriorated with renal insufficiency, anemia, and progressive debilitation. After the first cycle, he had a seizure. Radiation therapy of the brain mass was initiated; however, he continued to have recurrent seizures and died in September 2006.

MATERIALS AND METHODS

Histologic Examination

Hematoxylin and eosin-stained sections from in-guinal lymph node (September 2002) and facial mass (December 2005) were reviewed.

Immunophenotypic Analysis

Immunohistochemical stains were performed on formalin-fixed, paraffin-embedded tissue sections, using heat-induced epitope retrieval, an avidin-biotin-peroxi-dase complex method, and an automated immunostainer (Ventana Benchmark, Tucson, AZ).⁴ Positive and negative control samples were run for each antibody. Antibodies to the following markers were used: CD3, CD4, CD5, CD7, CD20, CD45, CD56, CD79a, bcl-6, and prostate specific antigen (Ventana, Tucson, AZ); CD8 (Novocastra, Newcastle upon Tyne, England); CD30 (DAKO, Carpinteria, CA); CD15 (Becton Dickinson, San Jose, CA); granzyme B (Vector, Burlingame, CA); TIA-1 (Immunotech, Maravilla, France); cytokeratin (Enzo Biochem, New York, NY); and PAX-5 (Becton Dickinson, San Jose, CA). In addition, flow cytometric immunophenotypic analysis was performed on the inguinal lymph node tissue using a Beckman Coulter EPIC-C flow cytometry instrument (Coulter Electronics, Hialeah, FL) as described previously.⁸ The panel included antibodies to CD3, CD4, CD5, CD8, CD10, CD19, CD20, CD71, FMC-7, human leukocyte antigen-DR, and κ and λ light chains.

In Situ Hybridization

EBV was analyzed on formalin-fixed, paraffin-embedded tissue sections by in situ hybridization for EBV-encoded RNAs using the Epstein-Barr Early RNA Probe Reagent-

EBER 1–2 (Ventana INFORM EBER, Tucson, AZ) according to the manufacturer's recommendations. Appropriate positive and negative controls were run.

Assessment of Clonality

DNA was extracted from formalin-fixed, paraffin-embedded tissue slides of the inguinal lymph node and facial mass and analyzed for immunoglobulin (Ig) heavy chain (IgH) and T-cell receptor λ chain (TCR- λ) gene rearrangements by polymerase chain reaction (PCR). For IgH, PCR was performed using consensus primers to framework regions II and III and the IgH gene joining region (FRII-IgH and FRIII-IgH).¹⁹ For TCR- λ , 2 or 3 separate reactions were performed, with primers Vg101, Vg11, and Jg12 (set 1); primers Vg101, Vg11, and Jp12 (set 2); or primers Vg9 and Jg 12 (set 3).¹⁵ The products were analyzed by acrylamide gel electrophoresis. Assays were performed in duplicate to confirm the presence of a clonal population. CEM and MOLT-4 cell lines were used as positive controls.

RESULTS

The inguinal lymph node biopsied in the year 2002 showed diffuse effacement of the lymph node architecture by a polymorphous infiltrate of variably sized lymphocytes. The large cells displayed pleomorphic nuclei with prominent basophilic nucleoli and abundant amphophilic cytoplasm. Some cells had an immunoblastic appearance. Mitoses and apoptotic debris were numerous. Intermediate and smaller-sized lymphocytes displayed vesicular chromatin, conspicuous nucleoli, and irregular nuclear outlines. Numerous plasma cells were also present (Fig. 1A). Immunohistochemical studies showed the large atypical cells to be positive for CD20 (Fig. 1B) that also stained numerous immunoblasts and plasmacytoid lymphocytes. CD79a stained the plasma cells. Lesser numbers of CD3/CD5⁺ T cells consisting of an appropriate ratio of CD4 and CD8 subsets were present in the background. In situ hybridization for EBV was positive in the large atypical cells (Fig. 1C). The analysis of IgH and TCR- λ gene rearrangements showed polyclonal rearrangement patterns. Flow cytometric evaluation showed an absence of surface light chain expression on the B cells. The overall findings were consistent with EBV-associated PTLT with features of polymorphic B-cell lymphoma.

The right nasolabial mass biopsied in the year 2005 showed an atypical lymphoid infiltrate invading skeletal muscle and adipose tissue. It was composed of pleomorphic lymphoid cells with scattered large atypical cells, some of which had Hodgkinlike features (Fig. 2A). Immunohistochemically, the infiltrate was composed of numerous atypical T cells positive for CD3, CD5, and CD7. No B cells were identified with CD20, PAX-5, and CD79a. The Hodgkinlike cells were weakly positive for CD30 and negative for CD15, PAX-5, and CD79a. Some of the pleomorphic cells contained cytoplasmic positivity for CD3 (Fig. 2B). In situ hybridization for EBV was positive in numerous cells (Fig. 2C). PCR for TCR- λ gene rearrangement generated a band of appropriate size in both replicates using primer set 1, consistent with a clonal rearrangement (Fig. 3). PCR for IgH gene rearrangement was suboptimal, with no reaction products generated, consistent with no B cells identified immunohistochemically. These results were consistent with EBV-associated monomorphic PTLT with features of peripheral T lymphoma, unspecified.

DISCUSSION

This report describes a case of a heart transplant recipient who developed metachronous EBV-associated B cell and then T-cell PTLDs. Only 6 other bilineal PTLD cases have been published.^{2,6,7,9,16,25} Their clinical, morphologic, immunophenotypic, and molecular characteristics are summarized in Table 1.

Frankel et al⁷ reported a case of a 56-year-old male renal transplant recipient who, after 2.5 years, developed an EBV+ B-cell PTLT of the scalp and had a concurrent peripheral blood clonal T-cell population. Euvrard et al⁶ described a case of a 38-year-old man who received a renal allograft for nephrotic syndrome and subsequently developed squamous cell carcinoma and cutaneous T-cell lymphoma, followed by a nodal lymphoma that contained both T-cell and B-cell clonal populations by immunohistochemical and molecular studies. Hollingsworth et al⁹ reported a 12-year-old girl who developed a B-cell lymphoproliferative disorder in the renal allograft by histologic and immunophenotypic features and had molecular evidence of clonal IgH and clonal TCR gene rearrangements, presumably in the same cell. Nelson et al¹⁶ reported a 45-year-old male liver transplant recipient who developed concurrent T-cell and B-cell PTLTs at multiple sites. In the case reported by Chuhjo et al,² a 31-year-old man underwent allogeneic bone marrow transplant for aplastic anemia. Within 42 days after transplantation, he developed simultaneous B-cell and T-cell PTLTs, both of which were EBV+. Yin et al²⁵ described a 4-year-old EBV-seronegative girl who received 2 allogeneic kidney transplants, both of which were from seronegative donors, owing to end-stage renal disease secondary to postinfectious glomerulonephritis. She developed an EBV+ B-cell PTLT 2.5 years after the second transplant and then an EBV+ T-cell PTLT 12 months later.

As detailed in Table 1, the histologic appearance of these cases comprised a wide spectrum with both polymorphic and monomorphic B-cell lesions. Among T-cell neoplasms, cutaneous T-cell lymphoma, PTLT with Hodgkinlike features, and PTLT resembling hepatosplenic T-cell lymphoma were reported. EBV positivity was found in all 6 patients. Gene rearrangement studies for immunoglobulin and/or T-cell receptor were carried out in all the cases, but not in all specimens. All tested lesions contained evidence of a clonal population.

The risk of developing PTLT is related to multiple factors including the degree and type of immunosuppression, the type of allograft, and the EBV status of the recipient before transplantation.^{1,10,12} EBV IgG-negative allograft recipients have a 70-fold increased risk of developing PTLT after transplantation from an EBV+ donor compared with EBV seropositive recipients. Seroconversion after transplantation has been reported in multiple studies as one of the most important risk factors for the development of PTLT.^{1,12,14} The patient reported here was EBV naive before transplant and thus, was at a very high risk for the development of PTLT. EBV infection was detected at the time of initial PTLT diagnosis. The case described by Yin et al²⁵ is similar. A 10-year-old girl developed primary EBV infection after allogeneic kidney transplantation and subsequently was diagnosed with a nodal B-cell PTLT. Approximately 12 months after successful treatment, recurrent lymphadenopathy contained a B-cell PTLT. In addition, liver and bone marrow specimens

at this time showed an EBV- associated T-cell PTLT. Our case, however, showed no evidence of the residual B-cell clone, which may, in part, be owing to the recent treatment with rituximab. As the orbital mass was not biopsied, one can only speculate on the possibility of a biphenotypic (1 clone containing dual lineage markers) or bilineal (2 distinct clones) PTLT.

The initial PTLT in the present case was diagnosed as a polymorphic EBV+ B-cell PTLT by morphologic and immunophenotypic findings. However, IgH gene rearrangement studies showed a polyclonal pattern. Indeed, an overall false negative rate of up to 20% can be observed by PCR IgH studies.¹⁹ Interestingly, flow cytometric studies showed most of the B cells lacked surface light chains. This is an abnormal finding and often associated with diffuse large B-cell lymphoma.^{11,13} Two and a half years later when the patient developed an orbital mass, it was apparently assumed to be a recurrence of the B-cell PTLT and was not biopsied. He was empirically treated with rituximab. The mass did not respond, but subsequent local radiation therapy was successful. However, a few months later, a right facial mass developed, which was biopsied. Perhaps in part owing to the patient's recent treatment with rituximab, determining the cell lineage of the facial mass required numerous immunohistochemical and molecular studies to rule out a possible B-cell origin. Rituximab causes down-regulation of surface CD20 and cell death by apoptosis.²⁰ Even months after treatment, CD20 may not be present on repopulating B cells. However, in the facial mass lesion, the pan-B-cell marker CD79a and the B-cell transcription factor, PAX-5, were negative. Furthermore, molecular studies for IgH failed to show the presence of cells undergoing rearrangement of the B-cell receptor gene. Some of the atypical cells showed cytoplasmic positivity for CD3. Although this has been described in some EBV+ B-cell lymphomas,¹⁷ as EBV infection may result in down-regulation of the B-cell program, with subsequent loss of B-cell markers¹⁸; a T-cell PTLT is favored on the basis of the immunohistochemical findings and the presence of a clonal rearrangement of the TCR- λ gene.

It is speculated that EBV infects a subset of T cells that express the viral receptor CD21.²¹ It has been suggested that infection of T cells occurs in cases of high level of uncontrolled viral replication.²⁵ In the 6 reported cases, all tested T-cell lesions, except 1, were EBV+, which suggests profound immunosuppression with high viral replication and can offer a possible explanation for the occurrence of 2 PTLTs in the same patient.

In 4 of the 6 cases, B-cell and T-cell lesions occurred in distinct anatomic sites. However, in 2 patients, clonal rearrangements of both IgH and TCR- λ genes were identified within the same lesion.^{6,9} Several mechanisms have been proposed for the occurrence of such biphenotypic lymphoid malignancies. More often, these occur in precursor lymphoid malignancies. One of the proposed theories is persistence of the recombinase enzyme. Recombinases are responsible for IgH and TCR gene rearrangements, and they may remain active until some functional stop signal is given.²⁴ If the stop signal is not generated appropriately, biphenotypic clones can be created.^{5,23}

Five of these 6 cases contained simultaneous B-cell and T-cell PTLTs^{2,6,7,9,16}; the other case, like ours, developed a B-cell PTLT followed by T-cell PTLT with no evidence of the

original clone.²⁵ By definition, the usual unilineage PTLDs comprise a heterogeneous category, so the discovery of an additional lineage, albeit an extremely rare occurrence, further underscores the importance of ancillary testing for classification. Although no clear relationships can be gleaned from these few cases regarding clinical outcome, the emergence of a subsequent lesion of a different (or additional) lineage may impact management decisions. Morphology, comprehensive immunophenotyping, and in situ hybridization for EBV are the mainstay of diagnosis in PTLT lesions. IgH and TCR- λ gene rearrangement studies are also very useful to confirm clonality. Such ancillary studies are critical for the correct classification of these complex lesions, especially with the advent of monoclonal antibody therapy that may cause diagnostic challenges in subsequent biopsies. Unanswered questions include— Should patients who were EBV naive before transplant be more closely monitored and then treated more aggressively at the first sign of an EBV-associated PTLT? Do these patients portend a worse prognosis than their latently EBV-infected counterparts who also develop PTLT? Are these patients at higher risk for PTLTs of more than 1 lineage? If clinically possible, biopsy of a new mass should be considered in patients with a history of PTLT to investigate the possibility of a distinct clonal process.

REFERENCES

1. Aucejo F, Rofaiel G, Miller C. Who is at risk for post-transplant lymphoproliferative disorders (PTLT) after liver transplantation? *J Hepatol* 2006;44:19–23. [PubMed: 16298453]
2. Chuhjo T, Yachie A, Kanegane H, et al. Epstein-Barr virus (EBV)- associated post-transplantation lymphoproliferative disorder simultaneously affecting both B and T cells after allogeneic bone marrow transplantation. *Am J Hematol* 2003;72:255–258. [PubMed: 12666136]
3. Costes-Martineau V, Delfour C, Obled S, et al. Anaplastic lymphoma kinase (ALK) protein expressing lymphoma after liver transplantation: case report and literature review. *J Clin Pathol* 2002;55:868–871. [PubMed: 12401829]
4. Davey FR, Elghetany MT, Kurec AS. Immunophenotyping of hematologic neoplasms in paraffin-embedded tissue sections. *Am J Clin Pathol* 1990;93:S17–S26. [PubMed: 2180277]
5. Davey MP, Bongiovanni KF, Kaulfersch W, et al. Immunoglobulin and T-cell receptor gene rearrangement and expression in human lymphoid leukemia cells at different stages of maturation. *Proc Natl Acad Sci USA* 1986;83:8759–8763. [PubMed: 3464980]
6. Euvrard S, Noble CP, Kanitakis J, et al. Brief report: successive occurrence of T-cell and B-cell lymphomas after renal transplantation in a patient with multiple cutaneous squamous-cell carcinomas. *N Engl J Med* 1992;327:1924–1926. [PubMed: 1454087]
7. Frankel AH, Thompson M, Vulliamy T, et al. A T cell clone in association with an Epstein-Barr virus-related B cell lymphoma. *Transplantation* 1991;52:1108–1109. [PubMed: 1661038]
8. Gervasi F, Lo Verso R, Giambanco C, et al. Flow cytometric immunophenotyping analysis of patterns of antigen expression in non-Hodgkin's B cell lymphoma in samples obtained from different anatomic sites. *Signal Transduct Commun Cancer Cells* 2004; 1028:457–462.
9. Hollingsworth HC, Stetler-Stevenson M, Gagneten D, et al. Immunodeficiency-associated malignant lymphoma. Three cases showing genotypic evidence of both T- and B-cell lineages. *Am J Surg Pathol* 1994;18:1092–1101. [PubMed: 7943530]
10. Jaffe E, Harris NL, Stein H, et al. WHO Classification, Pathology and Genetics Tumors of Haematopoietic and Lymphoid Tissues Lyon, France: IARC Press; 2001:264–269.
11. Kaleem Z, Zehnbaue BA, White G, et al. Lack of expression of surface immunoglobulin light chains in B-cell non-Hodgkin lymphomas. *Am J Clin Pathol* 2000;113:399–405. [PubMed: 10705821]
12. Katz BZ, Pahl E, Crawford SE, et al. Case-control study of risk factors for the development of post-transplant lymphoproliferative disease in a pediatric heart transplant cohort. *Pediatr Transplant* 2007;11:58–65. [PubMed: 17239124]

13. Li S, Eshleman JR, Borowitz MJ. Lack of surface immunoglobulin light chain expression by flow cytometric immunophenotyping can help diagnose peripheral B-cell lymphoma. *Am J Clin Pathol* 2002; 118:229–234. [PubMed: 12162683]
14. Lim WH, Russ GR, Coates PT. Review of Epstein-Barr virus and post-transplant lymphoproliferative disorder post-solid organ trans- plantation (review article). *Nephrology (Carlton)* 2006;11:355–366. [PubMed: 16889577]
15. McCarthy KP, Sloane JP, Kabarowski JH, et al. A simplified method of detection of clonal rearrangements of the T-cell receptor- gamma chain gene. *Diagn Mol Pathol* 1992;1:173–179. [PubMed: 1342963]
16. Nelson BP, Locker J, Nalesnik MA, et al. Clonal and morphological variation in a posttransplant lymphoproliferative disorder: evolution from clonal T-cell to clonal B-cell predominance. *Hum Pathol* 1998;29:416–421. [PubMed: 9563796]
17. Petitjean B, Jardin F, Joly B, et al. Pyothorax-associated lymphoma: a peculiar clinicopathologic entity derived from B cells at late stage of differentiation and with occasional aberrant dual B- and T-cell phenotype. *Am J Surg Pathol* 2002;26:724–732. [PubMed: 12023576]
18. Portis T, Longnecker R. Epstein-Barr virus LMP2A interferes with global transcription factor regulation when expressed during B-lymphocyte development. *J Virol* 2003;77:105–114. [PubMed: 12477815]
19. Ramasamy I, Brisco M, Morley A. Improved PCR method for detecting monoclonal immunoglobulin heavy chain rearrangement in B cell neoplasms. *J Clin Pathol* 1992;45:770–775. [PubMed: 1401205]
20. Seliem RM, Freeman JK, Steingart RH, et al. Immunophenotypic changes and clinical outcome in B-cell lymphomas treated with rituximab. *Appl Immunohistochem Mol Morphol* 2006;14:18–23. [PubMed: 16540725]
21. Sivaraman P, Lye WC. Epstein-Barr virus-associated T-cell lymphoma in solid organ transplant recipients. *Biomed Pharmacother* 2001;55:366–368. [PubMed: 11669498]
22. Snow AL, Martinez OM. Epstein-Barr virus: evasive maneuvers in the development of PTL. *Am J Transplant* 2007;7:271–277. [PubMed: 17229074]
23. Waldmann TA. The arrangement of immunoglobulin and T cell receptor genes in human lymphoproliferative disorders. *Adv Immunol* 1987;40:247–321. [PubMed: 3109221]
24. Yancopoulos GD, Blackwell TK, Suh H, et al. Introduced T cell receptor variable region gene segments recombine in pre-B cells: evidence that B and T cells use a common recombinase. *Cell* 1986; 44:251–259. [PubMed: 3484682]
25. Yin CC, Medeiros LJ, Abruzzo LV, et al. EBV-associated B- and T-cell posttransplant lymphoproliferative disorders following primary EBV infection in a kidney transplant recipient. *Am J Clin Pathol* 2005;123:222–228. [PubMed: 15842046]

FIGURE 1.

Polymorphic B-cell posttransplant lymphoproliferative disorder of groin lymph node. A, Diffuse proliferation of small to large atypical lymphoid cells. B, The atypical cells are CD20⁺. C, Numerous cells are Epstein-Barr virus+ by ISH (hematoxylin-eosin and CD20, original magnification $\times 400$; ISH, original magnification $\times 200$). ISH indicates in situ hybridization.

FIGURE 2.

Monomorphic T-cell posttransplant lymphoproliferative disorder of facial mass. A, Atypical lymphoid infiltrate invading skeletal muscle is composed of pleomorphic cells with scattered large cells some of which have Hodgkinlike features. B, The atypical cells are CD3⁺, some showing cytoplasmic staining. C, Numerous cells are Epstein-Barr virus⁺ by ISH (hematoxylin-eosin, original magnification $\times 400$; CD3 and ISH, original magnification $\times 200$). ISH indicates in situ hybridization.

FIGURE 3.

Acrylamide gel electrophoresis of polymerase chain reaction products showing clonal T-cell receptor λ gene rearrangement of facial mass. Arrow indicates patient (1 replicate shown); CEM, positive control lane; MW mix, molecular weight markers.

TABLE 1.

Summary of Reported PTLTD Cases Affecting B-cell and T-cell Lineages

Case Reports												
(Sex/age, y)	Trans-plant	Interval*	Site	Histology/IP	EBV	Molecular Studies	Treatment	Follow-up [†]	Outcome	Reference		
M/56	Kidney	28 mo	Scalp	B-cell lymphoma (large cells)	+	ND	RAD	NA	B-PTLD regression	Frankel et al ⁷		
M/38	Kidney	132 mo	PB		ND	TCR-C			T-clone persistence			
			Skin	T-cell lymphoma	−	TCR-C	DID, CHEM	13 mo			DOD	Euvrard et al ⁶
			LN	Immunoblastic	+	TCR-C IgH-C						
F/12	Kidney	45 d	Kidney	T-cell and B-cell lymphoma					NA	Hollingsworth et al ⁹		
				Polymorphic B-PTLD with plasmacytoid differentiation	+	IgH-C TCR-C	NA	NA			NA	NA
M/45	Liver	52 mo	BM no. 1	T-PTLD with Hodgkin-like features	+	ND	DID, AVT, CHEM	34 mo	NED	Nelson et al ¹⁶		
				T-PTLD and B-PTLDs with Hodgkinlike features	+	TCR-C IgH-P						
				Plasma cell rich PTLD	+	TCR-ND IgH-P						
M/31	BM	45 d	Liver	T-PTLD and B-PTLDs with numerous plasma cells	+	TCR-C IgH-C			DOD	Chuhjo et al ²		
				CD3, CD8	+	TCR-C	DID, DBI	56 d				
				CD19, CD20, κ	+	IgH-C						
F/10	Kidney	30 mo	LN	Large atypical B-cells	ND	ND			DOD	Yin et al ²⁵		
				Rare T-cells (UCLH-1)								
				Polymorphic B-PTLD	+	IgH-C TCR-P	DID, AVT	30 mo				
M/63	Heart	120 mo	Liver	T-PTLD resembling hepatosplenic T-cell lymphoma	+	TCR-C IgH-P			DOD	Present case		
				Same as BM	+	TCR-C IgH-P						
				Polymorphic B-PTLD	+	IgH-P TCR-P	DID, AVT	48 mo				
			Orbital mass	Not biopsied			Rituximab, RAD					
			Facial mass	Monomorphic T-PTLD	+	IgH-NP TCR-C	RAD, CHEM					

* Interval between organ transplantation and development of PTLTD.

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[†]Interval between initial diagnosis of PTLD and outcome.

AVT indicates antiviral therapy; BM, bone marrow; C, clonal; CHEM, chemotherapy; DBI, donor blood infusion; DID, decrease of immunosuppressive drugs; DOD, died of disease; F, female; IgH, immunoglobulin heavy chain gene; IP, immunophenotype; LN, lymph node; M, male; NA, not available; ND, not done; NED, no evidence of disease; NP, no polymerase chain reaction products; P, polyclonal; PB, peripheral blood; PTLD, posttransplant lymphoproliferative disorder; RAD, radiation; TCR, T-cell receptor gene.