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Plasmacytic post-transplant lymphoproliferative disorder with hyperviscosity syndrome in a child after liver transplant

Christine H. Yang¹, Saurabh Gombar², Clare J. Twist³, Dita Gratzinger², Carlos O. Esquivel⁴, and Audrey H. Lau^{1,4}

¹Division of Pediatric Gastroenterology, Hepatology, and Nutrition, Department of Pediatrics, Lucile Packard Children's Hospital, Palo Alto, CA, USA.

²Division of Pathology, Stanford University School of Medicine, Stanford, CA, USA.

³Division of Pediatric Hematology and Oncology, Stanford University School of Medicine, Stanford, CA, USA.

⁴Division of Abdominal Transplantation, Department of Surgery, Stanford University School of Medicine, Stanford, CA, USA.

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Introduction

Post-transplant lymphoproliferative disorder (PTLD) encompasses a spectrum of lymphoproliferations that can occur after organ transplantation (1). PTLD rarely occurs as a monoclonal plasma cell proliferation, and even more rarely with hyperviscosity syndrome (HS). This is the first reported case of a pediatric liver transplant recipient presenting with HS from PTLD with extreme plasmacytic differentiation.

Case Description

A 4 year old female status post deceased donor reduced size liver transplant for maple syrup urine disease 18 months prior presented with newly elevated plasma Epstein-Barr Virus (EBV) viral load (224,318 IU/mL), cough, and myalgias. She was known to have serologic evidence of remote EBV infection prior to transplant. Viral loads up until presentation had been <100 IU/mL, and she was on valganciclovir prophylaxis for extensive immunosuppression secondary to multiple rejection episodes. Physical exam was significant for intermittent non-productive cough; no lymphadenopathy or hepatosplenomegaly. Her

Correspondence should be addressed to: Dr. Audrey H. Lau, Lucile Packard Children's Hospital/Stanford University, 750 Welch Road, Suite 116, Stanford, CA 94304, 650-723-5070, 650-498-5608 (FAX), audreylau@stanford.edu.
christine.yang@stanford.edu
sgombar@stanford.edu
clare.twist@stanford.edu
ditag@stanford.edu
esquivel@stanford.edu

blood was highly viscous, and serum IgM was elevated [806 mg/dL (41-186 mg/dL)]. She developed gastrointestinal and pulmonary hemorrhages, concerning for HS. Bone marrow biopsy revealed 10-15% IgM+ lambda light chain-restricted plasma cells, with flow cytometry immunophenotyping confirming lambda light chain-restricted monotypic plasma cells expressing CD38, CD45, CD19, and CD138, negative for CD56 and CD20, and positive for EBV via in situ hybridization (Figure 1A-F). Serum and urine protein electrophoresis identified an abnormal monoclonal IgM lambda light chain. Serum free light chains were elevated [41.5 mg/dL, (0.6-2.6 mg/dL)]; kappa chain levels were normal. PET/CT revealed FDG-avid cervical and mediastinal lymphadenopathy.

Her immunosuppression regimen, which included tacrolimus with fluconazole, sirolimus, and prednisone, was discontinued at the time of PTLT diagnosis. She underwent plasmapheresis, followed by PTLT-directed therapy with dexamethasone and bortezomib. After three courses, bone marrow biopsy and flow cytometry showed resolution of the abnormal plasma cell population and PET/CT normalized. She has now completed all six planned courses of chemotherapy and her PTLT is in remission. EBV viral load has remained <100 IU/mL. Two months after completion of chemotherapy, she presented with acute cellular rejection, and is back on tacrolimus and sirolimus.

Discussion

This case highlights a unique presentation of PTLT in a child. HS is described as a complication of lymphoplasmacytic lymphoma (LPL)/Waldenstrom macroglobulinemia (WM), an entity that has not been reported in children. Furthermore, HS has not been described with IgM <4000 mg/dL (2), although IgM concentrations and serum viscosity measurements have been reported to be unreliable predictors of clinical HS.

This patient does not fit classic adult criteria required for the diagnosis of WM, thus demonstrating the difficulty in classifying this subtype of PTLT. This case was characterized by phenotypically normal plasma cells, abnormal only due to EBV-positivity and cytoplasmic lambda light chain-restriction, and no light chain-restricted B-lymphocytes. The differential diagnosis included a B cell lymphoma like LPL with extreme plasmacytic differentiation, versus plasma cell myeloma (multiple myeloma, MM). In MM, the malignant plasma cells are usually phenotypically distinct from normal plasma cells, often CD45⁻, CD19⁻ and/or CD56⁺. Furthermore our patient did not meet clinical criteria for MM, including lack of bony lytic lesions, and had IgM paraprotein rather than the more usual IgG or IgA (3). Molecular studies did not reveal the *MYD88*^{L265P} mutation characteristic of LPL and cytogenetic analysis was normal.

Plasmacytic PTLT is a rare and unusual form of monomorphic PTLT which has been reported to present as plasma cell myeloma or as extramedullary plasmacytoma in pediatric and adult solid transplant recipients (3-5). We report for the first time a pediatric patient who developed HS as a consequence of plasmacytic PTLT with a WM-like presentation.

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List of abbreviations

PTLD	post-transplant lymphoproliferative disease
EBV	Epstein-Barr virus
HS	hyperviscosity syndrome
LPL	lymphoplasmacytic lymphoma
WM	Waldenstrom macroglobulinemia
MM	Multiple myeloma

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Figure 1. Histology and immunohistochemistry of plasmacytic PTLD

The patient's bone marrow biopsy demonstrates (A) clusters of atypical plasma cells located in both a paratrabecular and interstitial pattern. (B) Immunohistochemistry for CD138 highlights the clusters of plasma cells which are (C) positive for EBV via in situ hybridization for EBER. (D) The atypical paratrabecular and interstitial plasma cell aggregates express lambda light chain as assessed by in situ hybridization whereas (E) kappa light chain in situ hybridization highlights only rare scattered background plasma cells. (F) IgM immunohistochemistry brightly highlights both plasma cells and serum.