A Case of Very Late-Onset, EBV-Negative, Post-Transplant Lymphoproliferative Disease in a Liver Transplant Recipient with Chronic EBV Viremia

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Background

- **Post-Transplant Lymphoproliferative Disease (PTLD)** is a pathologic proliferation of lymphoid and/or plasmocytes in immunosuppressed patients who received solid organ or hematopoietic cell transplantation.
- PTLD occurs in approximately 2.7% of liver transplant recipients with a reported mortality range of 25-35%.[1,2]
- We present a patient with congenital autoimmune hepatitis (AIH) who received a living donor liver transplant (LDLT) at 1 year of age and presented 20 years later in acute liver failure secondary to late-onset PTLD.

Presentation

- A 21-year-old woman with history of autism spectrum disorder and congenital AIH (LDLT at 1 year of age) presented to the hospital for evaluation of confusion and several days of progressive abdominal pain, distension, nausea, and vomiting.
- Her most recent maintenance therapy includes azathioprine (AZA) 150mg daily, tacrolimus (tac) 0.5 mg twice daily, prednisone 5mg daily
- Notable labs:

WBC 9.2 x 10^9/L	total bilirubin 1.2 mg/dL
PLT 259 x 10^9/L	AST 160 U/L
INR 3.4	ALT 55 U/L
Cr 8.1 mg/dL	ALP 281 U/L
lactate 5.5	NH3 >100 mmol/L

- Non-contrasted abdominal CT scan revealed notable findings in **Figure 1A-1C**.

Hospital Course

- Right inguinal node biopsy revealed monomorphic PTLD of a large B-cell lymphoma that was EBV negative, seen in **Figure 1D**.
- Her AZA and tac were discontinued, and she was started on weekly rituximab and high dose steroids with initial positive response.
- Chemotherapy was initiated with cyclophosphamide, doxorubicin, vincristine sulfate, and prednisone.
- Clinical course was complicated by severe neutropenia with sepsis and shock from an upper GI bleed, leading to multisystem organ failure and death.

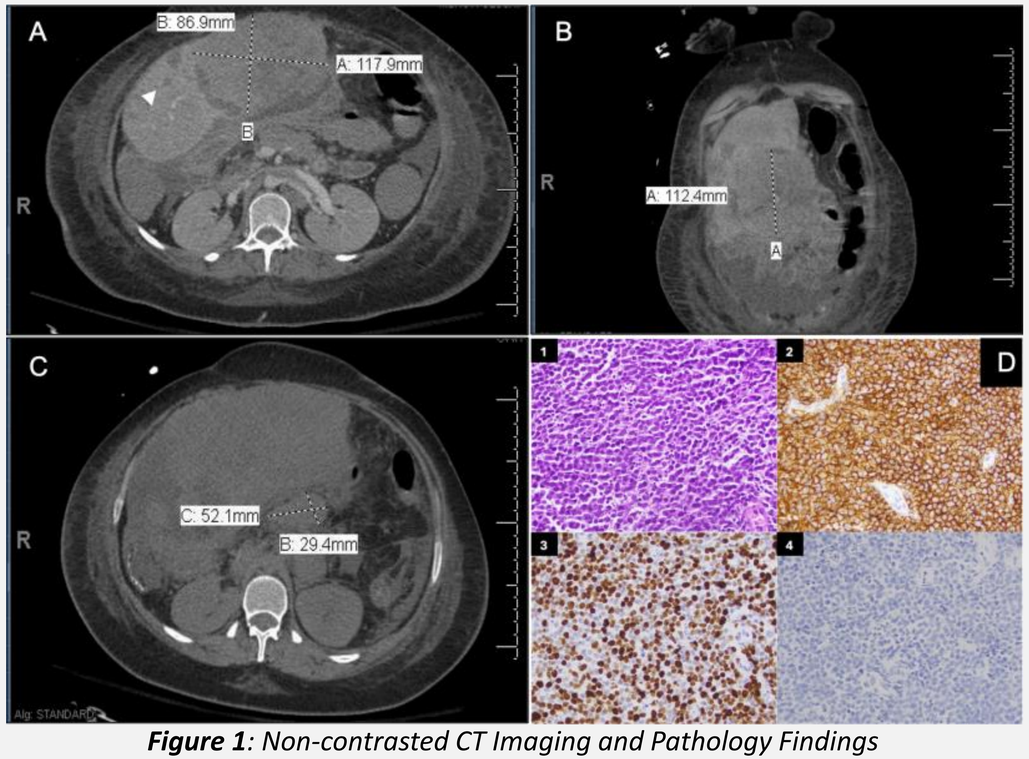

***Figure 1**: Non-contrasted CT Imaging and Pathology Findings*

A. Heterogenous lesions within the allograft liver, largest measuring 11.8 x 8.7 cm
B. Cross-section demonstrating the largest infiltrative tumor, measuring 11.2 cm
C. Bulky lymphadenopathy involving peripancreatic nodes, measuring 5.2 x 2.9 cm
D. Pathology evaluation (all 50x objective)
  1) H&E shows monotonous population with extensive apoptotic debris
  2) CD20 highlights the large cells
  3) Ki-67 proliferation index is high (~70%)
  4) EBV RNA in situ hybridization (EBER) is negative in the tumor cells

Discussion

- **Post-Transplant Lymphoproliferative Disease (PTLD)** is a relatively common malignancy complication of liver transplantation with a high mortality rate.
- Main risk factors for PTLD include chronic immunosuppression, EBV serostatus, and very young recipient age.[3]
- There is a paucity of information about EBV-negative, very late-onset PTLD in liver transplant recipients.
- Recent literature details the most delayed PTLD presentation among all solid organ transplants was 18.4 years.[4]
- Our case demonstrates a very late-onset EBV-negative PTLD in a patient with multiple risk factors.

Learning Points

1. This case highlights a rare instance of acute liver failure from PTLD in a patient **over 20 years out from transplantation**.
2. Treatment of PTLD is challenging, necessitating a careful balance amongst eradication of PTLD, preservation of graft function, and complications of immunosuppression.

References

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