POST TRANSPLANT LYMPHOPROLIFERATIVE DISORDER [PTLD]

DR VILESH VALSALAN

CONSULTANT NEPHROLOGIST AND TRANSPLANT PHYSICIAN

ACADEMIC CORDINATOR - ECNG

INTRODUCTION

- PTLD - A spectrum of lymphoid proliferations ranging from polyclonal B-cell hyperplasia to malignant monoclonal lymphoma that occurs after solid organ transplantation secondary to EBV infection and chronic immunosuppression.
- Incidence is 2-20%.
- Bimodal peak – less than 1 year [mainly EBV directed] and more than 10 years [chronic immunosuppression] , though can happen anytime post transplant.
- Biopsy is needed for diagnosis and classify the type which determines treatment.
- Reduction in Immunosuppression , Rituximab and chemotherapy are main stay of treatment.
- Clinical symptoms include constitutional B symptoms – fever , night sweats , loss of weight and organ specific [GIT- ulcerations, bleeding ; CNS – confusions, focal neurological deficit , seizures ; LUNGS – breathlesness , cough ; BONE MARROW – bone pain , cytopenias.]

PATHOPHYSIOLOGY /RISK FACTORS

- In EBV-positive PTLD, EBV infects circulating B cells, resulting in the coordinated expression of EBV proteins, including primary latent membrane proteins (LMP1, 2A-B) and EBV nuclear antigens

- In EBV-negative PTLD, several hypotheses have been proposed as potential pathogenic mechanisms, including:
    - "hit-and-run" EBV infection
    - other infectious agents
    - chronic immune activation triggered by the allograft.

- Genomic analysis suggests that EBV-negative PTLD is very similar to sporadic lymphoma in immunocompetent individuals and often contains mutations in the protein TP53.

Risk factors
EBV seronegativity at the time of transplantation
Active primary EBV infection at the time of transplantation
Variants of *LMP1* gene sequence
T-cell depletion
Immunosuppressive drug regimen and intensity
Type of transplanted organ
Age (children and older patients)
CMV coinfection
Acute or chronic graft versus host disease
Second transplant
Prior splenectomy
HLA type
Extent of HLA mismatch

CLASSIFICATION OF PTLD

1. Early lesions
   a. Reactive plasmacytic hyperplasia
   b. Infectious mononucleosis-like lesions
2. Polymorphic PTLD
   a. Polyclonal
   b. Monoclonal
3. Monomorphic PTLD
   a. B-cell neoplasms
      Diffuse large B-cell lymphoma
      Burkitt's lymphoma
      Plasma cell myeloma
      Plasmacytoma-like lesions
      Others
   b. T-cell neoplasms
      Peripheral T-cell lymphoma not otherwise specified
      Hepatosplenic T-cell lymphoma
      Others
4. Classical Hodgkin's lymphoma-type and Hodgkin's lymphoma-like PTLD

INVESTIGATIONS

- Detailed history and physical examination.

- Complete blood cell count (CBC) to evaluate unexplained anemia, thrombocytopenia or leukopenia.
- Comprehensive chemistry panel.
- Lactate dehydrogenase (LDH) to evaluate for tumor lysis syndrome.

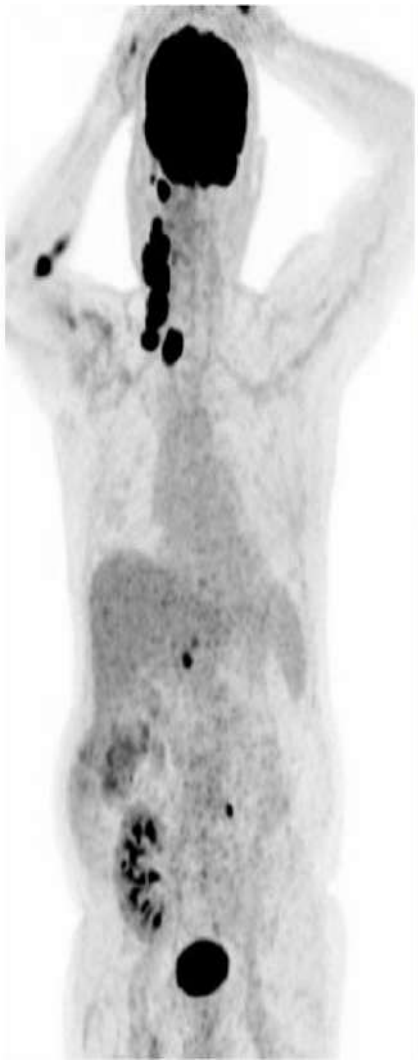
- Urine analysis for Monoclonal protein.

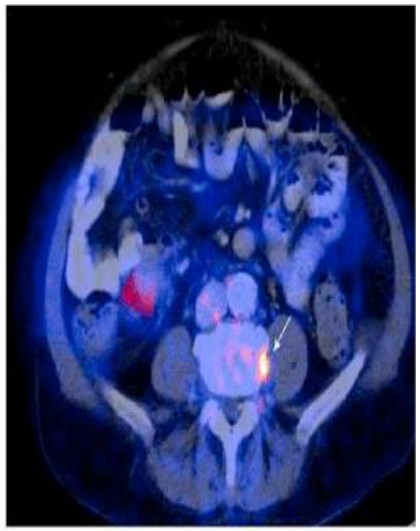
- EBV viral load (PCR) - serial EBV quantitative PCR measurement (that is rising) is more important and valuable than single positive EBV quantitative PCR. Negative EBV PCR does not exclude the possibility of PTLD.

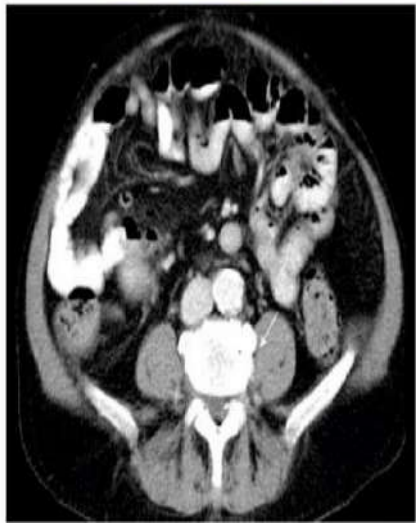
- Radiological studies : CT , MRI [CNS PTLD], and PET scanning to evaluate spread.

- Lumbar puncture with cerebral spinal fluid (CSF) analysis (EBV PCR in CSF fluid) in patients with PTLD with CNS involvement.

ROLE OF PET CT IN PTLD







ROLE :

Initial Diagnosis & Staging:

Highly effective for detecting PTLD.

It can identify the extent of disease - nodal and extranodal

Treatment Response Assessment:

Used to monitor the effectiveness of therapy and detect early relapse.

Biopsy Guidance:

PET/CT helps identify the most metabolically active tumor sites to target for biopsy.

Sensitivity:

The high sensitivity and negative predictive value (NPV) make it valuable for ruling out lymphoma in high-risk post-transplant patients.

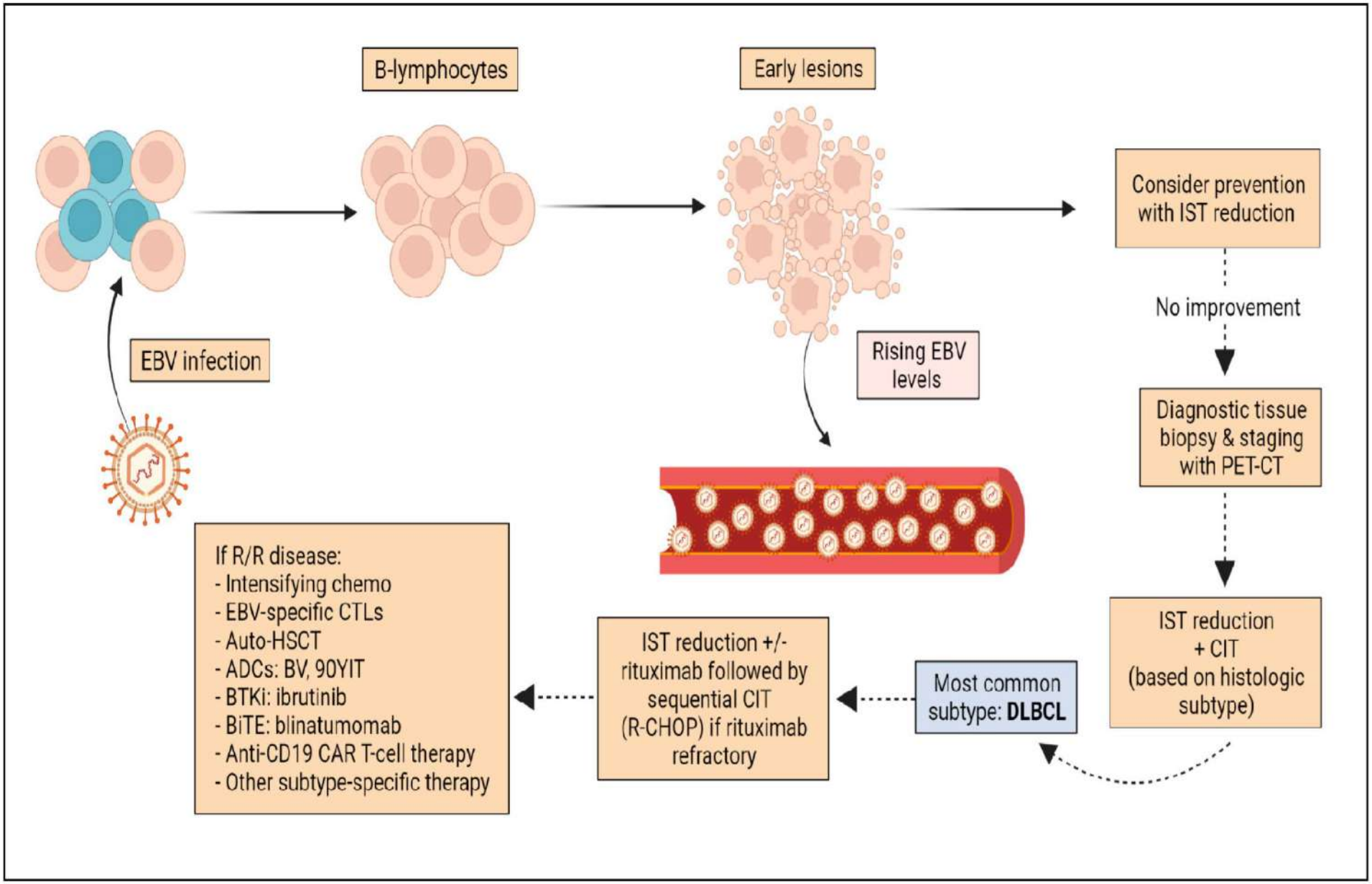
LIMITATIONS :

False Positives:

Also uptake in infectious or inflammatory conditions, so tissue biopsy is required for confirmation.

CNS PTLD – MRI is imaging of choice.

APPROACH TO PTLD



TREATMENT OF PTLD