

**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** – breathlessness , 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

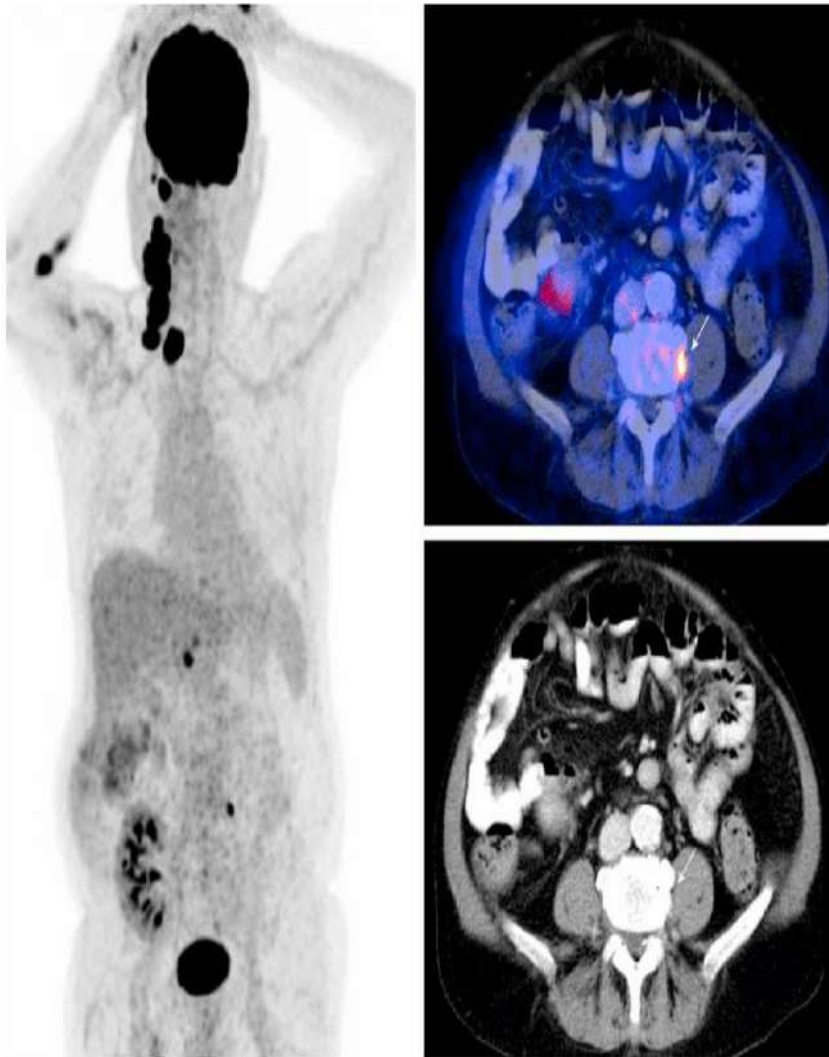
CLASSIFICATION OF PTLD

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.

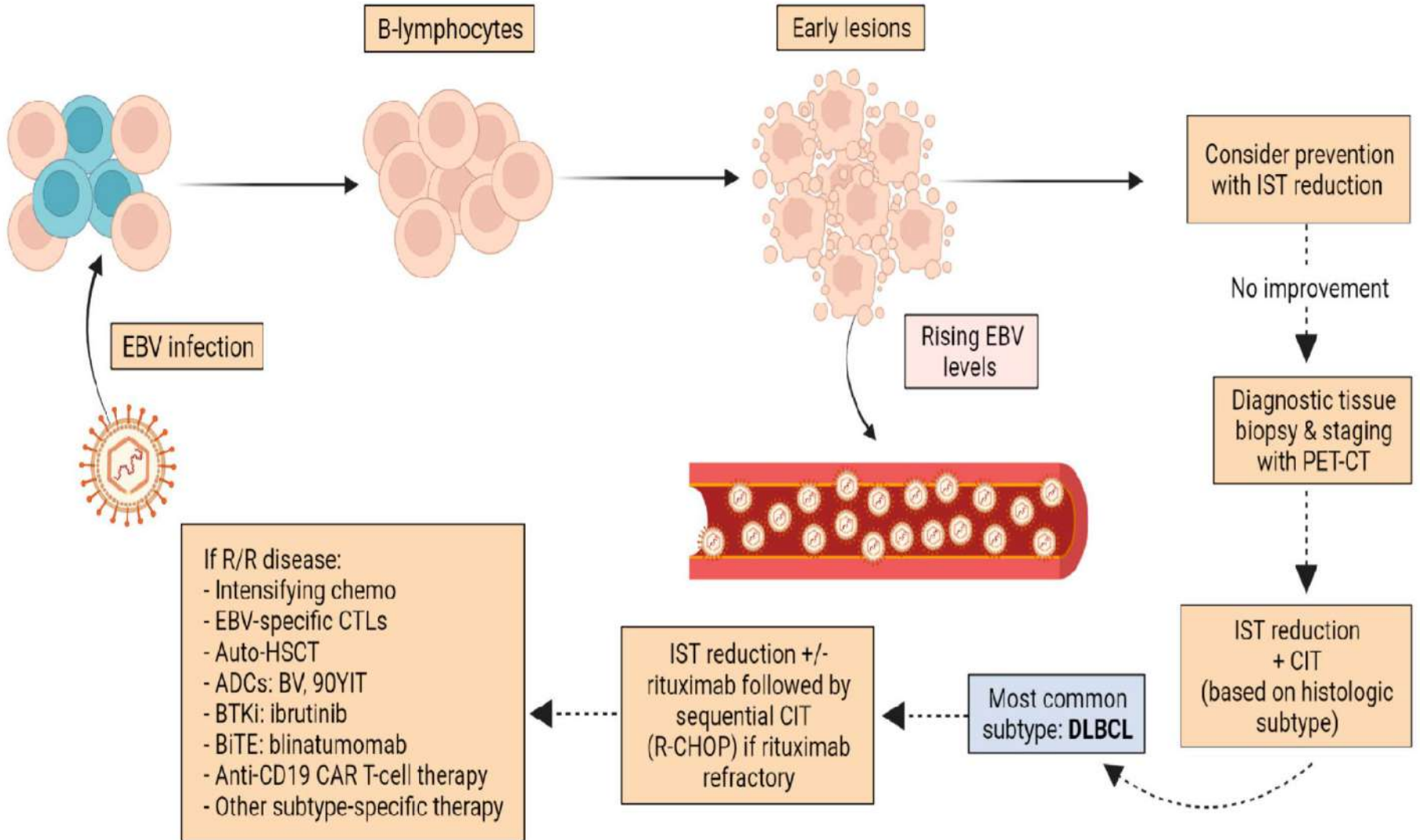
LIMITATIONS :

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

RIS (reduce/stop CNI, continue low-dose prednisone 5 mg/d; restart immunosuppression with mTOR after CTx) dependent on (1) risk of organ dysfunction/loss, (2) health risk upon organ loss, (3) availability of new organ

Supportive treatment analog current cancer treatment guidelines (high risk)

	Early lesion	Polymorphic		Monomorphic		
		CD20+ ▪ rituximab	Others	CD20+ ▪ rituximab	Others	
	Assess comorbidities and performance status					
				Hodgkin/ Hodgkin-like	T-cell lymphoma	CNS lymphoma
Fit	Consider concomitant CTx (CHOP) in high tumor burden	Consider CTx (CHOP)	Concomitant/ sequential CTx (CHOP)	ABVD	CHOP	HD MTX
Frail		No concomitant CTx		Palliative RTx	Monotherapy analog primary PTCL Palliative RTx	RTx decompressing surgery

Response assessment

If no CR after RIS	If no CR after RIS/first line	If no CR after RIS/first line
CD20+ rituximab CD20- consider CTx (CHOP) RTx of localized disease	CTx if prior treatment included rituximab mono 2nd line CTx if prior treatment included CTx RTx of localized disease	Second line chemotherapy according to histological type and performance status