NSS

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30 Tweets • 2023-04-11 • See on Twitter

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1/ Hi #MedTwitter
Let's discuss about Post Transplant Lymphoproliferative Disorder (PTLD) in pediatric kidney transplants (PKT)
#Nephtwitter #tweetorial #ASPNFOAMgroup @ASPNeph #pedneph

2 Lets start with a poll!
Incidence of PTLD is lowest in which pediatric solid organ transplant recipients?

3 Ans: Kidney
PKT recipients have a relatively low incidence of PTLD of 1-3% as compared to intestinal (5%–20%), heart and lung (2%–10%) and liver (1%–5%) transplants.

4

Estimated incidence of PTLD ~1.2%

Median time of onset post-transplant (PT) - 190 days

Presentation- Early onset first 2 years after PKT, 80% of cases in 1st year

Late onset 5-10 years PT

PMID: 12482154

5. What are the risk factors for PTLD ?

6/ Ans: All of the above

2 major risk factors

EBV serostatus

Intensity of T cell immunosuppression

Table 2: Risk Factors for Development of PTLD

Category	Factors that Increase Risk
Age	Young age at time of transplant
EBV serologic states	EBV seriologically negative at time of transplant EBV-positive donor and EBV-negative recipient
Type of organ transplanted	Intestine (11%–20% incidence of PTLD) Lung, heart, and lung-heart (6%–20% incidence of PTLD) Liver (4%–15% incidence of PTLD) Kidney (1%–10% incidence of PTLD)
Other viral infections	Cytomegalovirus, hepatitis C virus, human herpesvirus 8
Intensity and duration of immunosuppression	T-cell mediated immune suppression regimens for a long time
Time from transplant	Less than 1 year

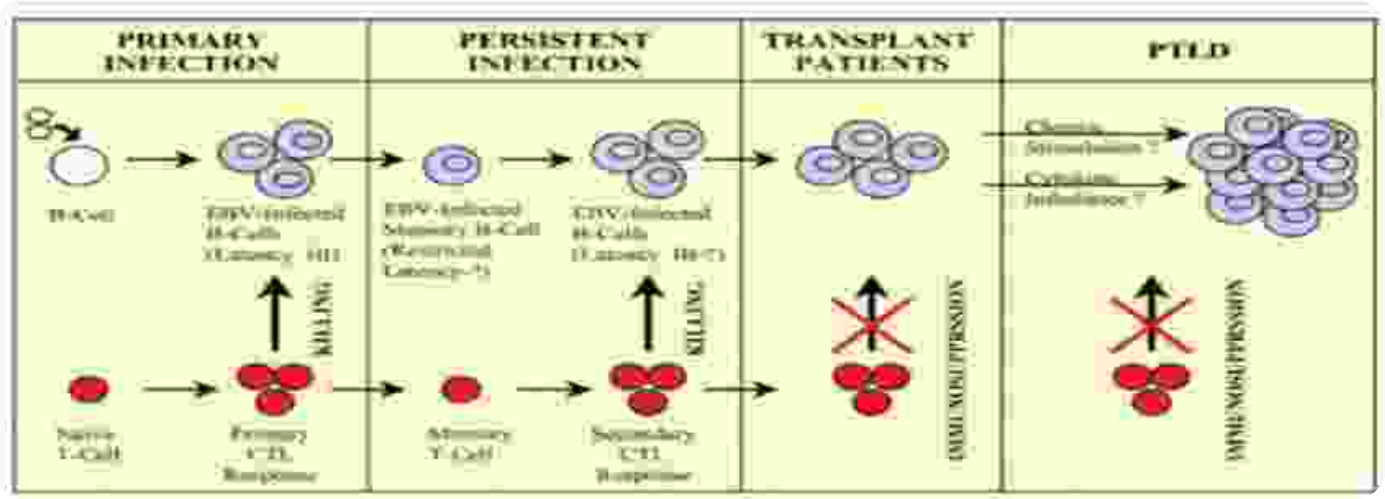
Sources.—References 14–22.

7/ What percentage of PTLD is EBV related?

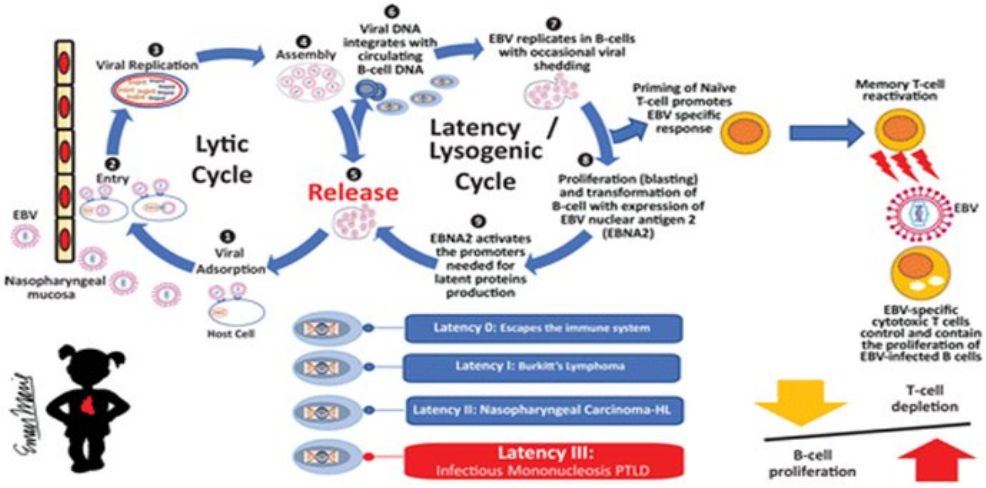
8. Ans- > 80%

Pathogenesis of PTLD

Chronic immunosuppression of EBV-specific cytotoxic T cells → unchecked proliferation of EBV infected B-cell → malignant transformation.



9. Pathophysiology of EBV related # PTLD- figure shows the pathogenesis and interplay between virology and tumor biology in PTLD



10. EBV negative PTLD- 20-30 % of cases
Pathogenesis is unclear- likely due to chronic antigenic stimulation, infection with other viruses HHV6/CMV.
Usually late presentation 7-10 years post-transplant.

11: Morphological classification of # PTLD @ WHO 20167 Criteria

Table 1: PTLD Pathologic Classification according to WHO 2016 Guidelines

PTLD Types and Subtypes	EBV Serologic Status	Histopathologic Results	
		Tissue Architecture	Main Features
Nondestructive lesions			
Plasmacytic hyperplasia	Positive	Maintained	Many plasma cells, small lymphocytes, and rare normal-appearing immunoblasts
Florid follicular hyperplasia	Positive (usually)	Maintained	Marked follicular hyperplasia, without interfollicular changes that are characteristic of other early lesions
Infectious mononucleosis-like	Positive	Maintained	Paracortical and/or interfollicular expansion, often many immunoblasts, transformed cells in a background of T cells and plasma cells
Polymorphic PTLD	>90% are positive	Effaced	Destructive proliferation of polymorphic cell infiltrates* Scattered large atypical immunoblasts that resemble Reed-Sternberg cells, geographic necrosis, or many mitoses can be present Does not fulfill the criteria for a typical lymphoma
Monomorphic PTLD			
B-cell neoplasms†			
Diffuse large B-cell lymphoma	Variable	Effaced	Predominance of large transformed cells that can be very pleomorphic
Burkitt lymphoma	Variable	Effaced	Sheets of medium-sized lymphoid cells with multiple nucleoli, basophilic cytoplasm, and many mitoses Variable scattered tingible body macrophages can be seen
Plasma cell myeloma	Variable	Effaced	Should fulfill all criteria for plasma cell myeloma in a normal host
T-cell or natural killer–cell neoplasms	>30% positive	Effaced	Most fulfill the criteria for peripheral T- cell lymphoma, not otherwise specified Others are a variety of specific types of mature T-cell lymphomas
Classic Hodgkin lymphoma	>90% positive	Effaced	Fulfill morphologic and immunophenotypic criteria for classic Hodgkin disease, usually mixed-cellularity type Reed-Sternberg or Hodgkin cells in a background of polymorphic cell infiltrates‡

12. Risk factors for poor prognosis in PTLD include?

13- Ans: All of the above
Scoring system from the French registry found that older age (>55 years), serum creatinine >1.5 mg/dL, high LDH, disease location- CNS or serous membrane invasion, & monomorphic, T cell histology had worse outcome.

PMID: 23423742

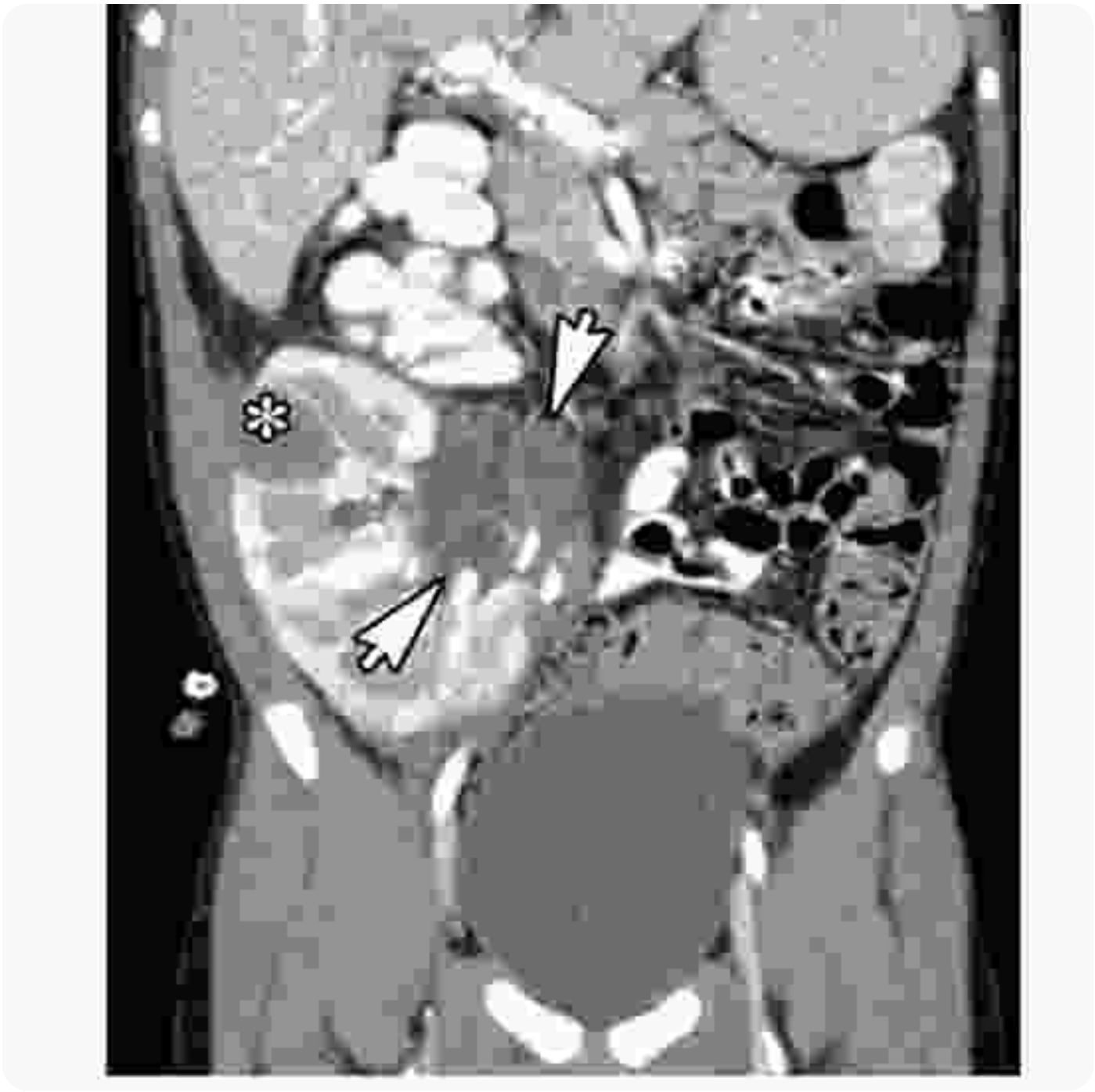
12.Symptoms of PTLD

Symptoms/complaints	Signs
Swollen lymph glands	Lymphadenopathy
Weight loss	Hepatosplenomegaly
Fever or night sweats	Subcutaneous nodules
Sore throat	Tonsillar enlargement
Malaise and lethargy	Tonsillar inflammation
Chronic sinus congestion and discomfort	Signs of bowel perforation
Anorexia, nausea and vomiting	Focal neurologic signs
Abdominal pain	Mass lesions
Gastrointestinal bleeding	
Symptoms of bowel perforation	

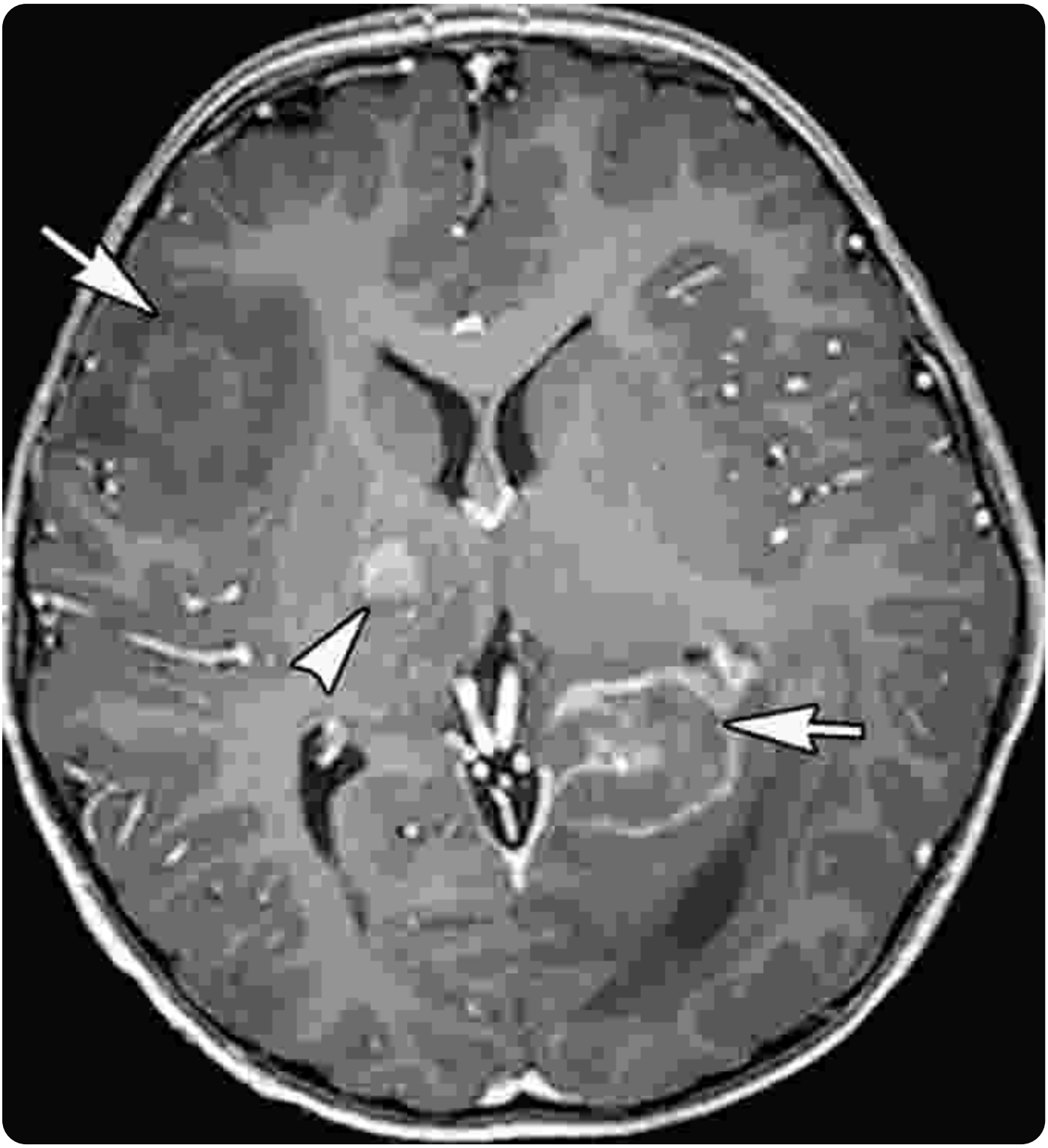
13. Diagnosis of PTLD includes:
High EBV viral load
CT/MRI/PET Scan
Biopsy

14. High EBV load
-No consensus about the EBV threshold at which intervention should be done due to wide interlab variability and differences in sensitivity and specificity between whole blood, serum and plasma.
-Trends of viral load more valid and useful than single values

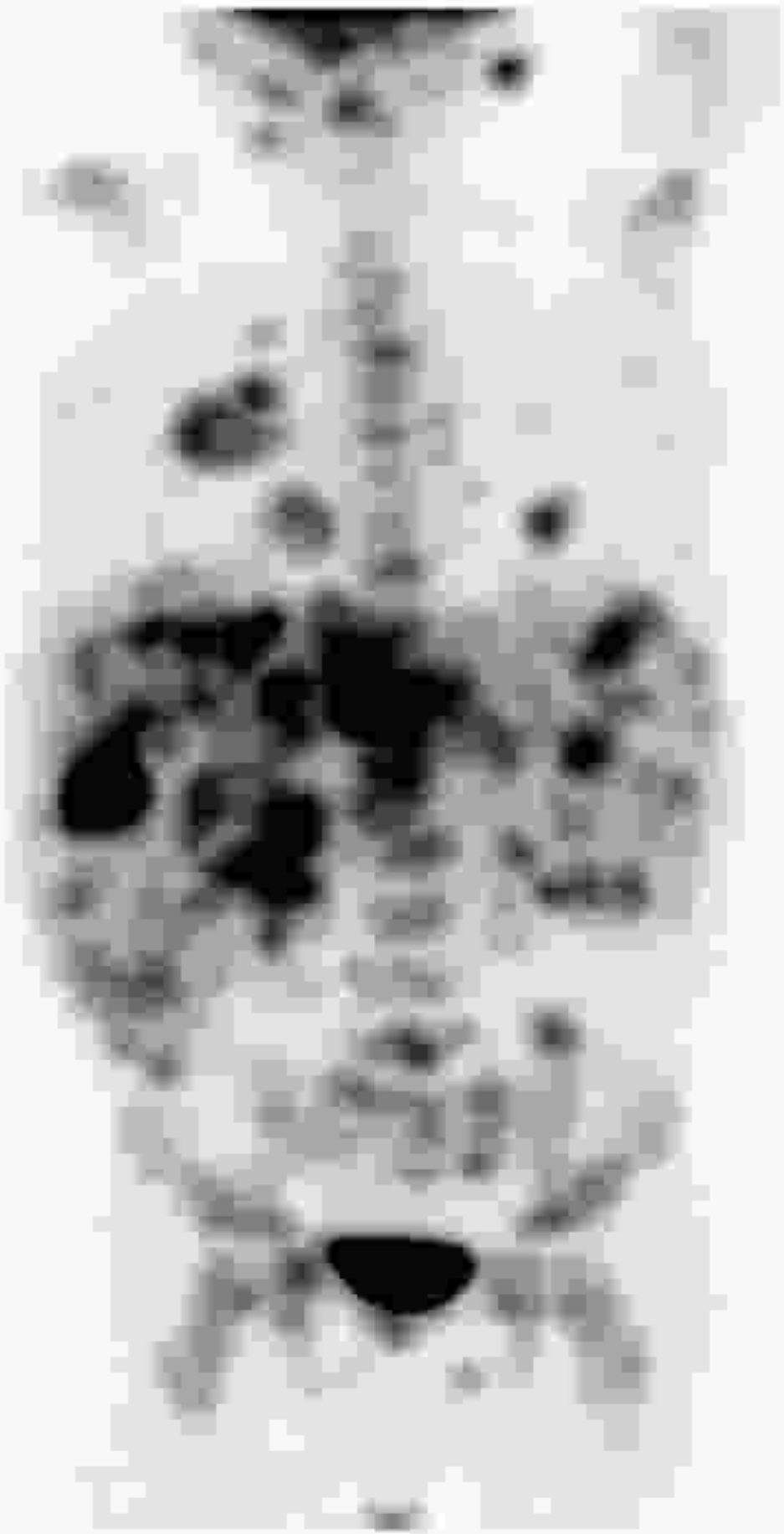
15: Imaging to assess for tumour
CT Scan



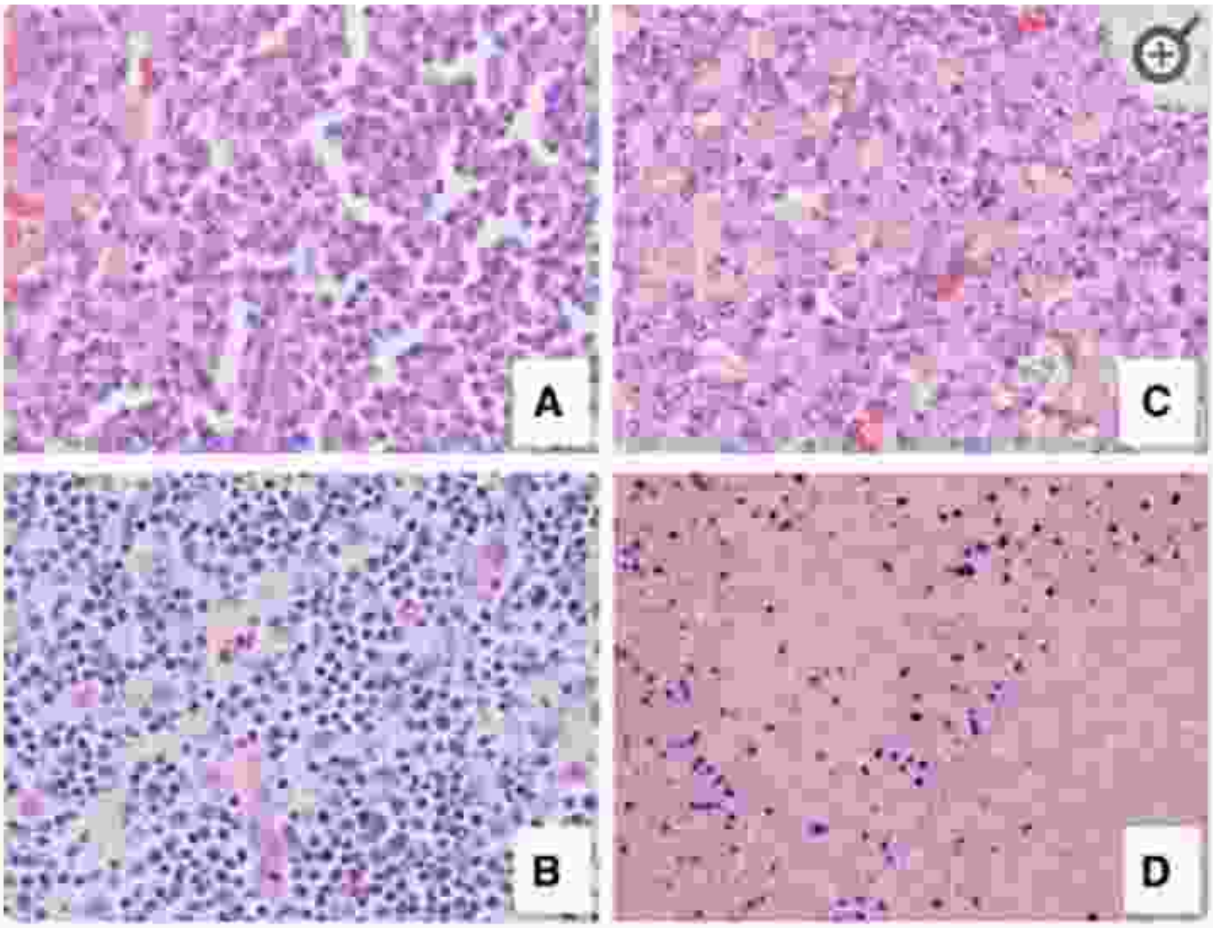
16.MRI Scan



17. PET Scan



18. Histopathological features of PTLD



19. Prevention of PTLD in high-risk patients (EBV -ve R/ EBV + D) PT
EBV viral load monitoring:
Weekly- biweekly- first 3 month
Q month for the first 3–6 month,
Q 3 months until 12 months PT
Other patients- less frequent monitoring, monthly
EBV PCR levels post-acute rejection t/t

20. Prophylaxis PT for EBV in high risk patients is controversial
1. Routine anti-viral prophylaxis for first 3 months (100 days) post-Tx
2. Serial monitoring of viral load and pre-emptive treatment of viral re-activation

https://onlinelibrary.wiley.com/doi/full/10.1111/ajt.14020

21. Immunoprophylaxis
Anti-CMV IVIG (Cytogam) reduced the incidence of non-Hodgkin lymphoma in kidney transplant recipients but only in the first posttransplant year
Cytogam may have some effect in reducing the short-term risk of PTLD, data is limited.

https://www.sciencedirect.com/science/article/pii/S1470204507700402

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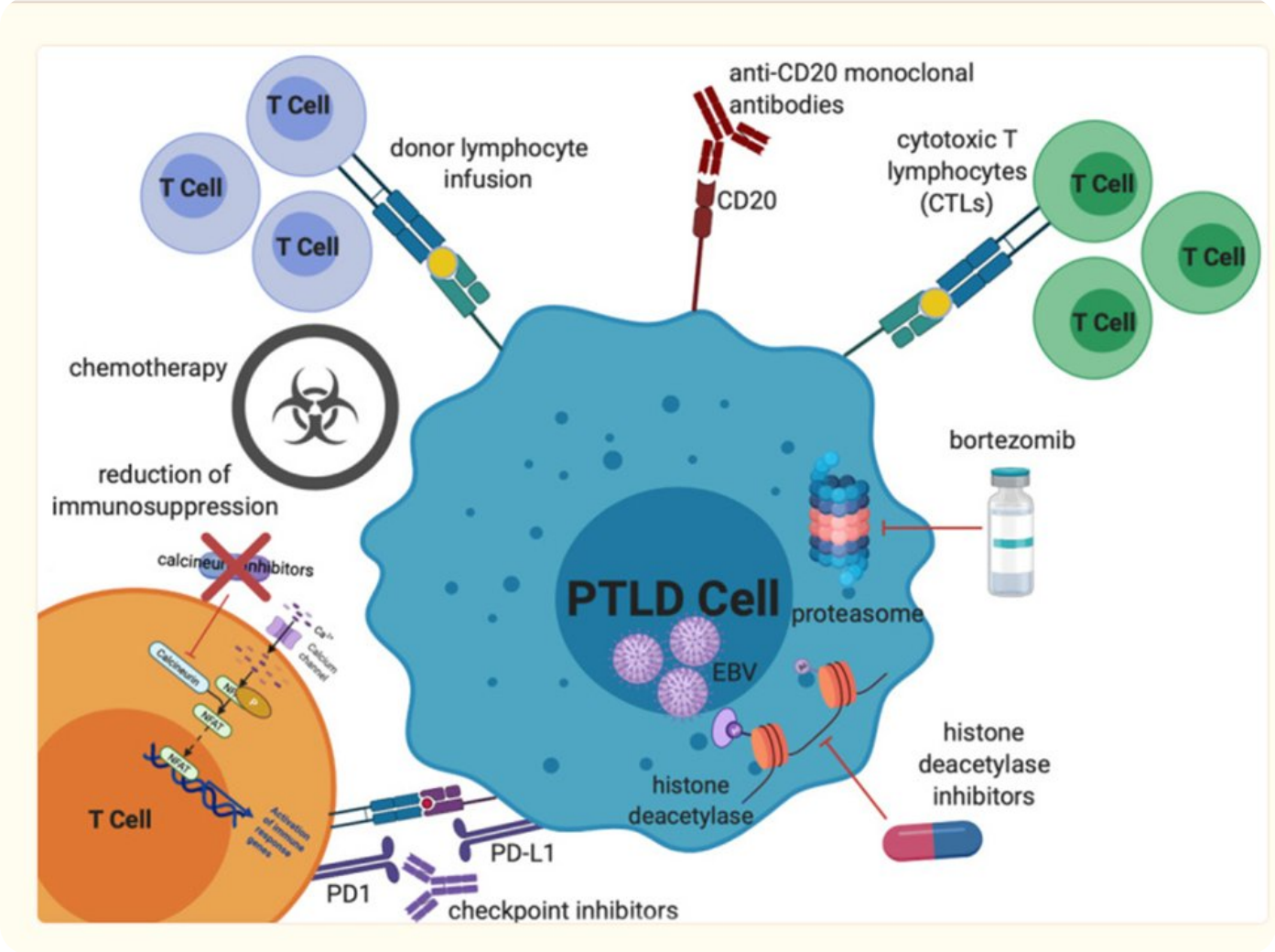
Therapy :
Referral to Oncology
Reduction of IS
Rituximab
Chemotherapy
Radiation Therapy



23: Reduction/Withdrawal of Immunosuppression (IS)

KDIGO recommends reduction of IS if increasing EBV viral load

Reducing CNI dose (targeting 50% reduction of trough levels),

Discontinuing antimetabolites such as MMF or Azathioprine

24:
Therapy: Rituximab
CD20- positive PTLD, in particular diffuse large B cell lymphoma
Dose- 375 mg/m2 weekly for 3–4 doses.
70-75% remission rate

doi: 10.1182/blood.V104.11.746.746

25: Therapy: Chemotherapy
Cyclophosphamide, doxorubicin, vincristine and prednisone (CHOP)
In conjunction with rituximab, complete remission rate 65-69%
2 year event free survival (alive with functioning allograft and no PTLD) of 83%

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https://doi.org/10.1111/j.1600-6143.2012.04206

26 Therapy: Radiation/Surgery

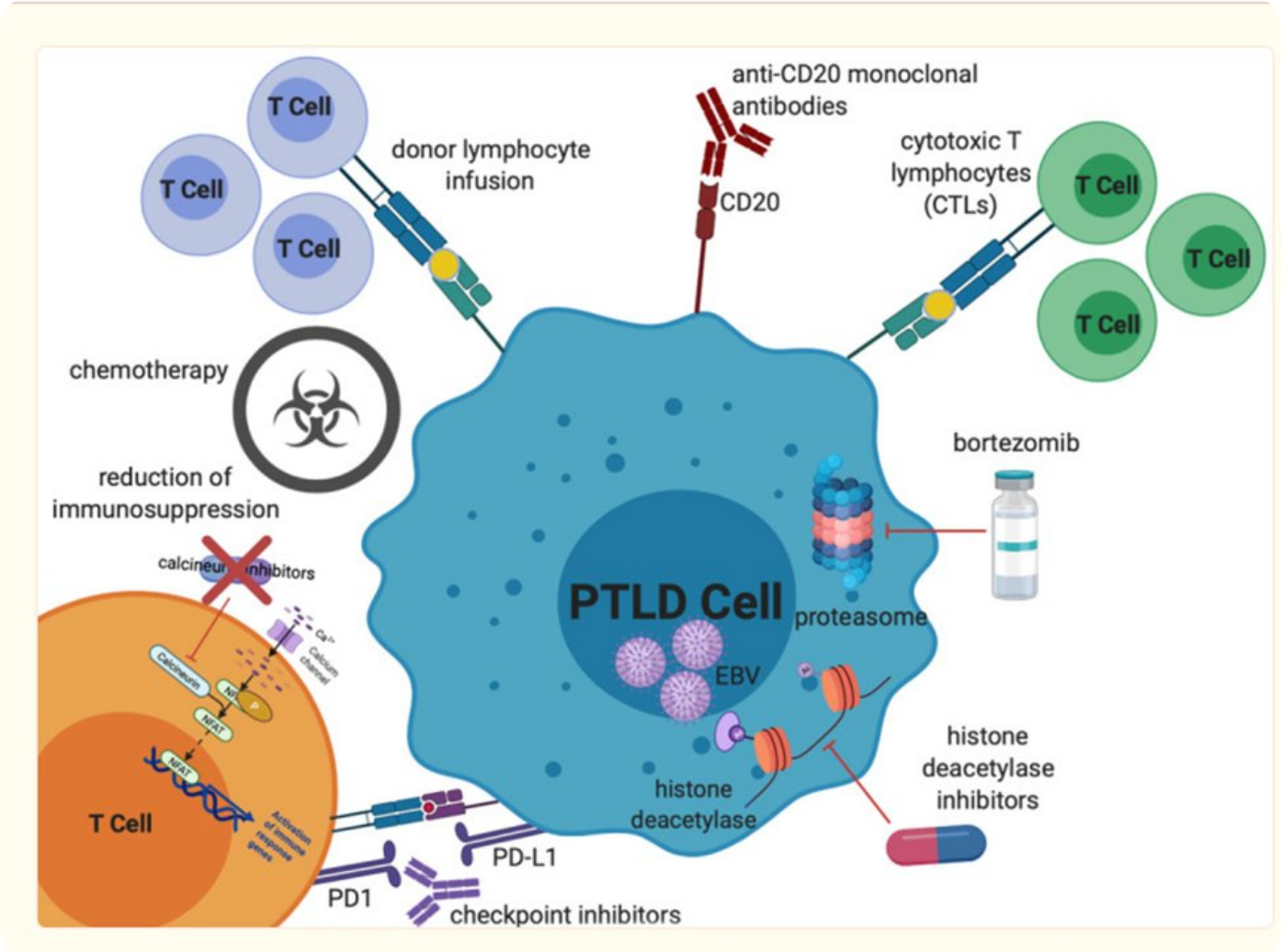
Rarely used- treatment of local disease, symptomatic control, or palliative care

26: Newer treatment options

Brentuximab vedotin -CD30 monoclonal antibody

Checkpoint Inhibition and Chimeric Antigen Receptor T Cells (CAR-T therapy)

EBV-Specific Cytotoxic T Cells



Thank you for scrolling till the end!
For a case-based clinical discussion with an expert - login to @ASPNeph website, Jan 2023 webinar #Membereducation

Special thanks to #ASPNFOAM group members @drM_sudha @RoshanPGeorgeMD @SwastiThinks @nefron1310
That’s all for today.