Very-late onset Primary CNS Post-transplant Lymphoproliferative Disease (PTLD): report of three cases and literature review

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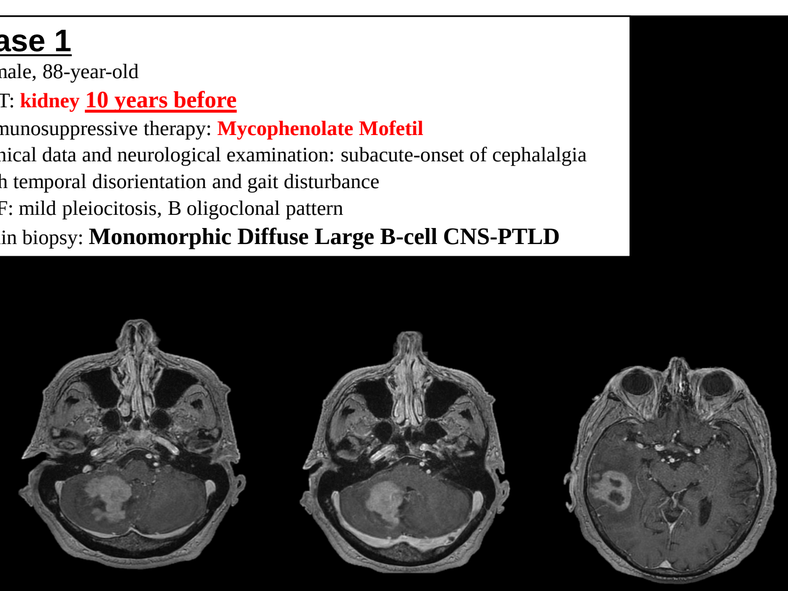
PTLD is an heterogeneous disease, affecting patients following solid organ transplant (SOT). Although considered historically a rare disease (<2% in transplantated population), its importance is increasing over the last 2 decades, because of the spreading of SOT and immunosuppression-associated complications.

Isolated CNS involvement occur in 7-15%.
The distinctive characteristics compared to systemic PTLD are the **stronger association with renal SOT**, **later onset** and **monomorphic histology**.

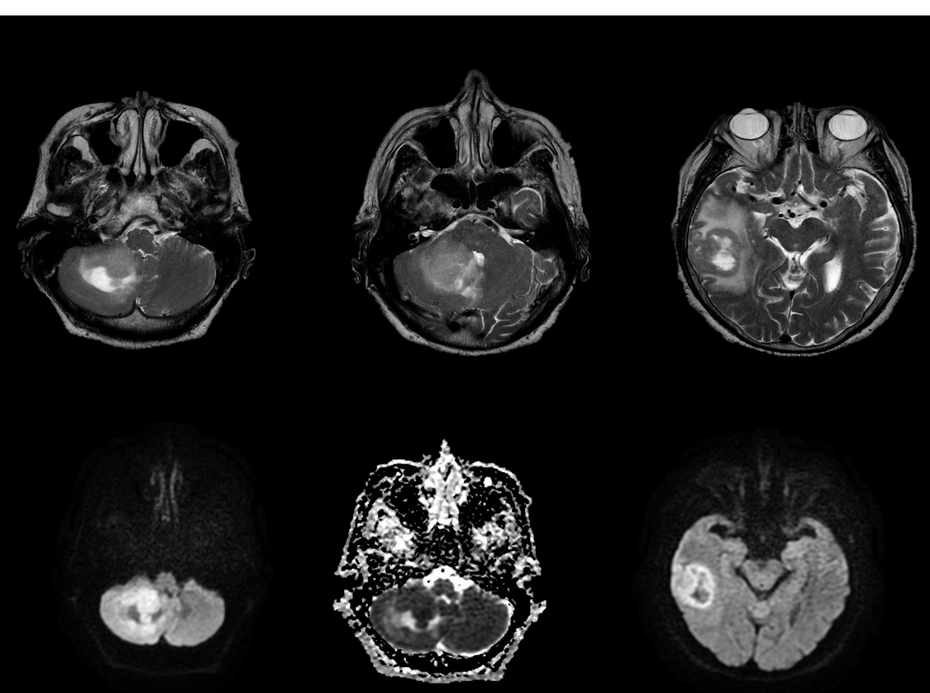
Up to date, the biggest retrospective and multicenter report included 84 patients (median latency 4.5 years)

We report **three cases** whose key features are in line with published reports, but which can be considered
atypical due to the latency between SOT and CNS-PTLD

Case 1
Female, 88-year-old
SOT: **kidney** **10 years before**
Immunosuppressive therapy: **Mycophenolate Mofetil**
Clinical data and neurological examination: subacute-onset of cephalalgia with temporal disorientation and gait disturbance
CSF: mild pleiocitosis, B oligoclonal pattern
Brain biopsy: **Monomorphic Diffuse Large B-cell CNS-PTLD**



homogeneous contrast enhancement

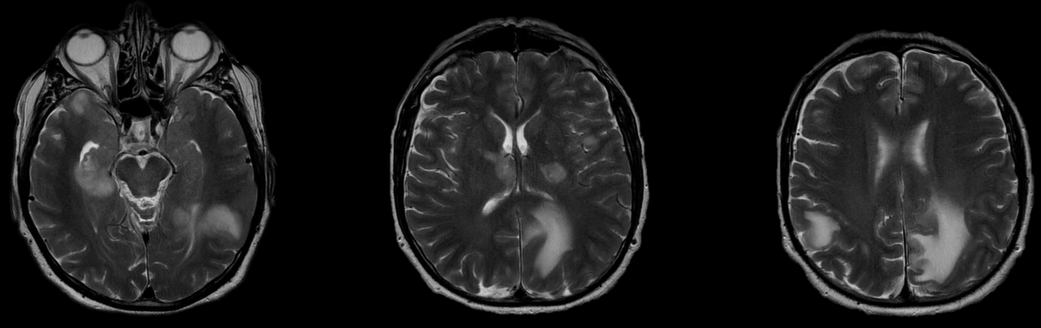


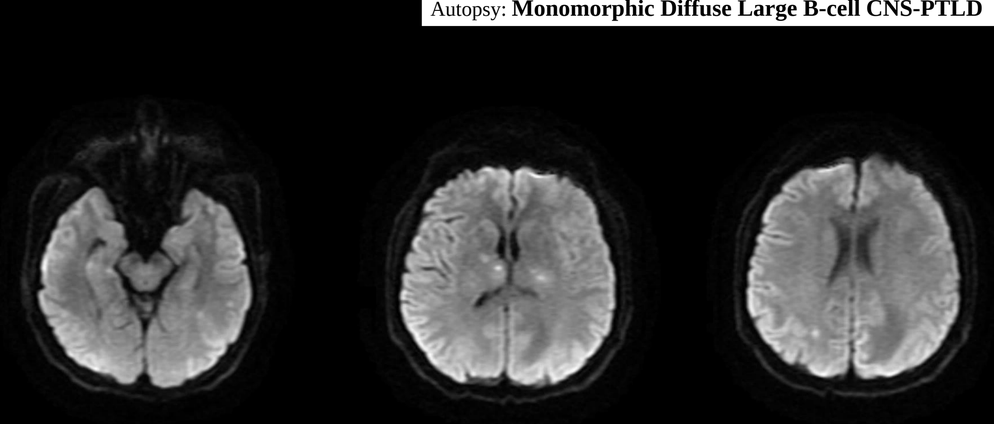
fronto-temporal and cerebellar T2 hyperintense lesion
necrosis, edema and mass effect

very high cellular density lesions,
as demonstrated by low ADC values

Case 2
Male, 67-year-old
SOT: **kidney** **10 years before**
Immunosuppressive therapy: **Mycophenolate Mofetil** and **Tacrolimus**
Clinical data and neurological examination: sensitive partial seizure with secondary generalization
CSF: mild pleiocitosis, B oligoclonal pattern
Autopsy: **Monomorphic Diffuse Large B-cell CNS-PTLD**

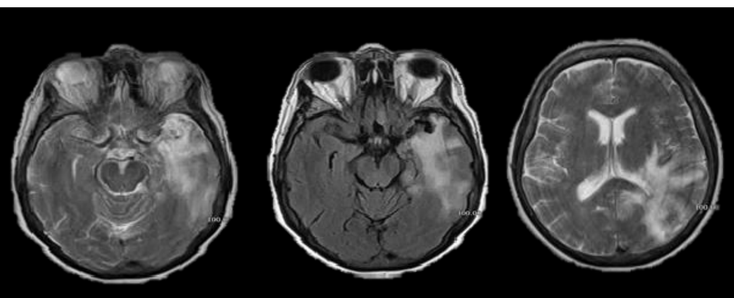
multiple T2 hyperintense supratentorial lesions
necrosis, edema and mass effect



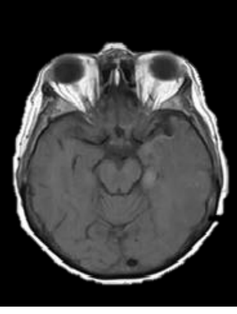


very high cellular density lesions, restricted on DWI sequences

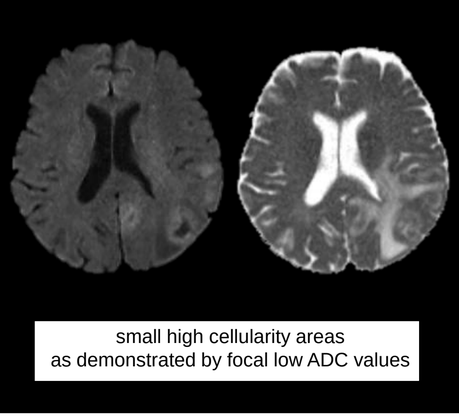
Case 3
Female, 71-year-old
SOT: **kidney** **20 years before**
Immunosuppressive therapy: **Mycophenolate Mofetil** and **Ciclosporin**
Clinical data and neurological examination: sudden onset of speech disturbances, progressively followed by poor orientation in time
CSF: single prevalent clone in oligoclonal B cells pattern, T policlonal pattern
Brain biopsy: **Monomorphic Diffuse Large B-cell CNS-PTLD**



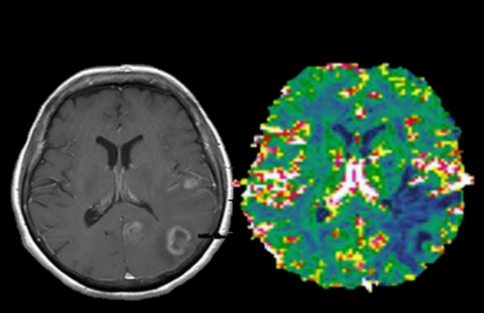
temporo-insular and temporo-parietal T2/FLAIR hyperintense lesions
necrosis, edema and mass effect



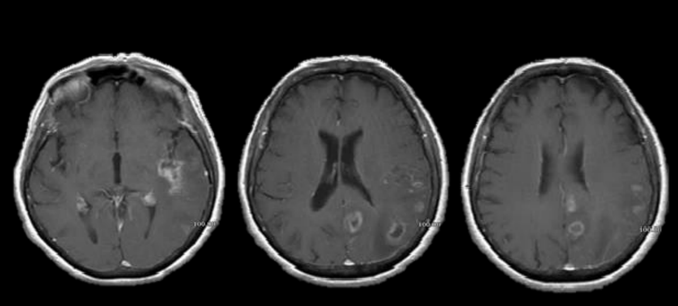
on T1w sequences,
hyperintense area referable to hemorrhagic spots



small high cellularity areas
as demonstrated by focal low ADC values



low rCBV values referable to poor perfusion



multiple, disomogeneous, ring-enhancing lesions

In our cases, the **latency** between SOT and onset of neurological symptoms is **significantly higher** (median time **13.5 years**) than that described in literature (median time 4.5 years)

THE DIAGNOSIS OF THE VERY-LATE ONSET CNS-PTLD IS A REAL CHALLENGE

The less deducible relation with past transplantation and the age-related comorbidities can lead to a misdiagnosis and to a subsequent inappropriate therapeutic approach.

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Epstein-Barr virus encephalitis in a renal transplant recipient manifesting as hemorrhagic, ring-enhancing mass lesions, Babik et al., Transpl Infect Dis, 2015