Treatment with Allogeneic JCV-Specific T Cells in a Lung Transplant Recipient with PML: A Case Report

Alessandro Petullà[1], Francesca Rinaldi[1], Luca Bello[1, 2], Elena Sogus[1], Nathalie Scarpulla[3], Federica Meloni[4], Patrizia Comoli[5], Paolo Gallo[1, 5], Paola Perini[1], Maurizio Corbetta[1, 5]

[1] Department of Neuroscience, University of Padova, Padova, Italy; [2] Padova Neuroscience Center, University of Padova, Padova, Italy; [3] Department of Advanced Medical and Surgical Sciences, University of Campania "L. Vanvitelli", Napoli, Italy; [4] Department of Cardiac, Thoracic, Vascular Sciences and Public Health, University of Padova, Padova, Italy; [5] Cell Factory & Pediatric Hematology/Oncology, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy

Background

Progressive multifocal leukoencephalopathy (PML) is a rare and often fatal infectious disease of the central nervous system caused by reactivation of the John Cunningham virus (JCV) in immunocompromised patients. Current therapeutic strategies primarily focus on restoring immune competence, a challenging task in solid organ transplant recipients. Recently, treatment with allogeneic JCV-specific T cells has emerged as a promising therapeutic approach.

Case report

We report the case of a 66-year-old woman who underwent bilateral lung transplantation for severe chronic obstructive pulmonary disease and was on immunosuppressive therapy with tacrolimus, mycophenolate mofetil, and corticosteroids. Approximately one year post-transplant, she developed *expressive language disturbance*. *Brain CT scan and MRI* revealed subcortical demyelinating lesions in the left temporo-parietal-occipital region (Figure 1 and 2), and *cerebrospinal fluid* PCR testing was positive for JCV-DNA, confirming the diagnosis of **PML**.

Intervention

Given the lack of effective antiviral therapies and the necessity to maintain some level of immunosuppression, treatment with **allogeneic JCV-specific T cells** was proposed. After careful reduction of immunosuppressive therapy, the patient received two infusions of allogeneic JCV-specific T cells two weeks apart. The therapy was well tolerated, with no significant adverse effects.

Outcomes

Clinically, a progressive *improvement in language abilities* was observed, corroborated by repeated speech therapy assessments. Follow-up magnetic resonance imaging showed *gradual resolution of demyelinating lesions with malacic evolution*. Cerebrospinal fluid analysis performed two months after therapy demonstrated ***negativization of JCV-DNA***. Six-month clinical and neuroradiological follow-up (Figure 3) confirmed disease stabilization.

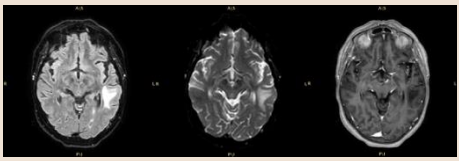

Figure 1A. Brain FLAIR (left), DWI (middle) and contrast-enhanced (right) MRI sequences showing PML left temporal lesion at the diagnosis.

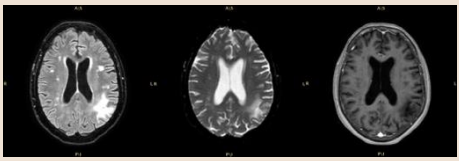

Figure 1B. Brain FLAIR (left), DWI (middle) and contrast-enhanced (right) MRI sequences showing PML left parietal-occipital lesion at the diagnosis.

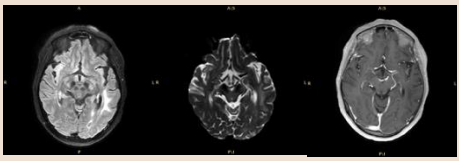

Figure 2A. Brain FLAIR (left), DWI (middle) and contrast-enhanced (right) MRI sequences showing PML left temporal lesion pre-treatment.

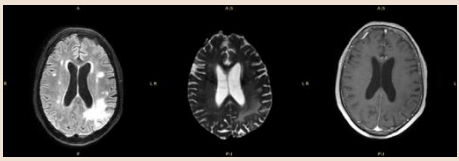

Figure 2B. Brain FLAIR (left), DWI (middle) and contrast-enhanced (right) MRI sequences showing PML left parietal-occipital lesion pre-treatment.

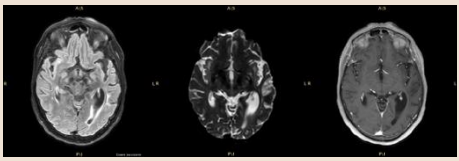

Figure 3A. Brain FLAIR (left), DWI (middle) and contrast-enhanced (right) MRI sequences showing PML left temporal lesion post-treatment.

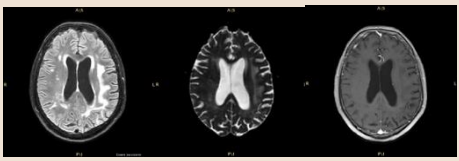

Figure 3B. Brain FLAIR (left), DWI (middle) and contrast-enhanced (right) MRI sequences showing PML left parietal-occipital lesion post-treatment.

Discussion and conclusions

Allogeneic JCV-specific T cell therapy proved to be **effective** and **safe in the treatment of PML** in a lung transplant recipient.
This case supports the potential role of this novel therapeutic strategy in managing severe acquired immunodeficiency-associated PML.

Presenter and contacts: Dr. Alessandro Petullà, E-mail: alessandro.petulla@studenti.unipd.it

References

1. Berzero G, Basso S, Stoppini L, Palermo A, Pichiecchio A, Paoletti M, Lucev F, Gerevini S, Rossi A, Vegezzi E, Diamanti L, Bini P, Gastaldi M, Delbue S, Perotti C, Seminari E, Faraci M, Luppi M, Baldanti F, Zecca M, Marchioni E, Comoli P - Adoptive Transfer of JC Virus - Specific T Lymphocytes for the Treatment of Progressive Multifocal Leukoencephalopathy - Annals of neurology - 2021 - 89(4)
2. Bernard - Valnet R, Koralnik IJ, Du Pasquier R - Advances in Treatment of Progressive Multifocal Leukoencephalopathy - Annals of neurology - 2021 - 90(6)
3. Schweitzer F, Laurent S, Cortese I, Fink GR, Silling S, Skripuletz T, Metz I, Wattjes MP, Warnke C - Progressive Multifocal Leukoencephalopathy: Pathogenesis, Diagnostic Tools, and Potential Biomarkers of Response to Therapy - Neurology - 2023 - 101(16) – 700-713