A Complex Case of Severe Myelitis Following CAR-T Cell Therapy for CNS Relapse of Diffuse Large B-Cell Lymphoma

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- **Chimeric Antigen Receptor T-cell (CAR-T) therapy is a breakthrough treatment for refractory/relapsed B-cell lymphomas [1]. While effective, it is associated with significant toxicities, primarily Cytokine Release Syndrome (CRS) and Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) [2,3]. We present a rare and severe case of longitudinal myelitis leading to irreversible paraplegia following CAR-T infusion, a toxicity pattern not fully captured by ICANS criteria [4].**

Case Presentation

A 60-year-old male presented with stage IV diffuse large B-cell lymphoma (DLBCL) involving testicle, kidneys, adrenal glands, heart, and lymph nodes.

· Initial Treatment: Achieved complete metabolic response (CMR) with R-CHOP.

· CNS Relapse: Despite CNS prophylaxis, he relapsed with clonal B-cells in the cerebrospinal fluid (CSF) and PET evidence of nerve root infiltration.

· Therapeutic Decision: Due to progressive and refractory disease, treatment with CAR-T cell therapy (axicabtagene ciloleucel - YESCARTA®) was initiated after bridging chemotherapy (R-ICE) [1].

Clinical Course & Neurological Toxicity

Post CAR-T cell infusion, the patient experienced a rapid and severe neurological decline consistent with high-grade ICANS but with unique features [2,3]:

· Symptoms: Acute onset of sciatic pain, rapidly progressing to flaccid paraplegia, urinary incontinence, a tonic-clonic seizure, and coma.

· Diagnostic Workup: MRI of the neuroaxis revealed extensive longitudinal myelitis with T2 hyperintensity spanning the cervical and thoracic spinal cord, suggesting direct inflammatory cord injury [4,5].

· Management & Outcome: The patient was managed in the ICU with high-dose corticosteroids (first-line for ICANS [3]). His consciousness improved, but he remained paraplegic. Follow-up imaging confirmed a complete metabolic response of the lymphoma [1], highlighting the dissociation between oncological efficacy and severe neurological toxicity.

Discussion &Conclusion

· This case illustrates a devastating neurological complication of CAR-T therapy, distinct in its presentation as a florid myelitis that may be under-recognized [4,5].

· It underscores that patients with active central nervous system (CNS) involvement may be at higher risk for severe and atypical neurotoxicity, necessitating extreme vigilance [4].

· While CRS and ICANS are well-described [2,3], this case of direct spinal cord inflammation (myelitis) is rare and carries a grave prognosis, suggesting a spectrum of neurotoxicity that extends beyond typical presentations [4,5].

· This outcome emphasizes the critical need for enhanced monitoring protocols, early intervention strategies, and further research into the pathophysiology and management of catastrophic neurological toxicities in CAR-T patients [4].

References

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