PROVEN INVASIVE PULMONARY ASPERGILLOSIS MIMICKING EARLY RELAPSE AFTER CD19 CAR-T THERAPY IN PRIMARY MEDIASTINAL B-CELL LYMPHOMA

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Background. Although invasive fungal infections occur in fewer than 5–10% of CAR-T recipients, they remain among the most life-threatening infectious complications, particularly in patients with prolonged neutropenia, corticosteroid exposure, and cumulative immunosuppression. Early evaluation of pulmonary lesions remains challenging, as infectious and neoplastic processes frequently present overlapping clinical and radiological features. Although the CAR-HEMATOTOX score predicts hematological toxicity and infectious risk, severe opportunistic infections may still occur in patients classified as low risk.

Case presentation. A 47-year-old woman with PMBCL, initially involving mediastinum and lungs, was refractory to first-line R-CHOP and achieved a partial response to brentuximab vedotin plus nivolumab. She subsequently received axicabtagene ciloleucel after IVAC bridging chemotherapy. Before lymphodepletion, her CAR-HEMATOTOX score was 0. Early toxicities included grade 2 CRS and grade 1 ICANS, both successfully managed with tocilizumab and corticosteroids. Thirty days after CAR-T infusion, during the high-risk susceptibility period to infectious complications, she presented with chest pain, dyspnea, profound pancytopenia, and new mediastinal lesions with pulmonary consolidations at sites of previous lymphoma, strongly suggesting early relapse. Histological evaluation was performed before salvage treatment. Bronchoscopic biopsy excluded lymphoma infiltration and demonstrated fungal hyphae, while bronchoalveolar lavage galactomannan supported the diagnosis of proven invasive pulmonary aspergillosis. Treatment with liposomal amphotericin B followed by isavuconazole resulted in clinical and radiological improvement.

Results. Antifungal therapy alone achieved progressive clinical, radiological, and metabolic improvement. Six-month PET/CT documented complete metabolic remission, while residual pulmonary uptake reflected resolving fungal infection. Nine months after CAR-T therapy, pulmonary lesions had further regressed, allowing discontinuation of antifungal therapy.

Conclusions. This case highlights that predictive tools such as the CAR-HEMATOTOX score should complement clinical judgment. Assessment of new pulmonary lesions after CAR-T therapy should consider the cumulative net state of immunosuppression, and histological confirmation should be pursued whenever feasible to distinguish opportunistic infection from lymphoma relapse.