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A Challenging Case of Refractory PMBCL with CNS Involvement Successfully Treated with CAR-T Cells

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Introduction :

Primary mediastinal B-cell lymphoma (PMBCL) is an aggressive lymphoma affecting young patients, while it generally has a favorable prognosis with first-line treatment, refractory forms or cases of early relapse remain associated with poor survival. In these patients, failure of standard treatments—including immunochemotherapy, salvage therapy, and sometimes autologous stem cell transplantation—leads to a genuine therapeutic impasse.
In this context, anti-CD19 CAR-T cells are now playing an increasingly important role in the management of relapsed or refractory aggressive B-cell lymphomas, with encouraging results in multirefractory PMBCL. Their use is all the more relevant in settings such as Morocco, where treatment options after failure of conventional regimens remain limited.

Case presentation :

A 27-year-old man was diagnosed with primary mediastinal large B-cell lymphoma (PMBCL), staged IVA according to the Ann Arbor classification, with an IPI score of 3, an age-adjusted IPI of 2, and an NCCN-IPI of 3.

The patient initially received six cycles of rituximab plus dose-adjusted EPOCH (R-DA-EPOCH). End-of-treatment assessment by 18F-FDG PET/CT showed only a partial metabolic response, with persistent residual mediastinal disease.

Given the inadequate response, a second-line salvage chemotherapy regimen consisting of dexamethasone, cytarabine, and cisplatin (DHAP-like regimen) was initiated. However, the response remained unsatisfactory, with persistent refractory disease.

During the course of the disease, the patient developed seizures, prompting further neurological evaluation. Brain magnetic resonance imaging (MRI) revealed a fronto-parieto-temporal lesion, highly suggestive of secondary central nervous system (CNS) involvement by lymphoma.

In this context, the patient received symptomatic anticonvulsant management and was subsequently treated with multiple CNS-directed and systemic salvage approaches. An initial regimen combining gemcitabine, vincristine, and dexamethasone, associated with anti–PD-1 immunotherapy (sintilimab), temozolomide, and targeted agents including venetoclax and zanubrutinib, was introduced. However, this treatment was poorly tolerated and could not be continued.

A subsequent salvage strategy was then administered, consisting of rituximab, polatuzumab, gemcitabine, vinorelbine, and dexamethasone, in association with additional CNS-active agents including pemetrexed, temozolomide, orelabrutinib, and lenalidomide.

Reassessment after this treatment showed a partial radiological response at the CNS level, with reduction of the intracranial lesion on brain MRI, while PET/CT demonstrated persistent residual mediastinal disease, although with decreased metabolic activity.

Given the persistence of localized thoracic disease, the patient subsequently underwent consolidative mediastinal radiotherapy, delivered to the residual mediastinal mass at a dose of 4 fractions of 8 Gy.

Given the multiply relapsed and refractory disease course, the presence of secondary CNS involvement, and the failure of several prior treatment lines, the patient was considered a candidate for academic anti-CD19 CAR-T cell therapy, representing a potentially curative option in a setting of otherwise very limited therapeutic alternatives.

He first received an infusion of murine CD19-directed academic CAR-T cells (mCD19 CAR-T) at a dose of 2.6×10^6/kg. The infusion was well tolerated, with no major acute adverse events. Importantly, the patient did not develop cytokine release syndrome (CRS) or immune effector cell-associated neurotoxicity syndrome (ICANS), despite his prior history of CNS involvement, making the treatment particularly notable from a safety perspective.

Because of this suboptimal expansion profile, a second CAR-T infusion was administered. This was followed by a more favorable expansion pattern, reaching a peak of approximately 10^7, before gradually declining thereafter.

As part of the post–CAR-T therapeutic strategy, pomalidomide and sintilimab were maintained transiently, but were subsequently discontinued because of hematologic toxicity.

Post-treatment evaluation showed a marked response. Contrast-enhanced brain MRI demonstrated a major reduction of the fronto-parieto-temporal lesion, with a clear decrease in the associated perilesional edema. In parallel, 18F-FDG PET/CT revealed a significant decrease in the anterior mediastinal mass, with complete metabolic response, corresponding to a Deauville score of 1.

The patient was therefore considered to be in complete metabolic remission.

Discussion and conclusion :

This case highlights an aggressive and refractory form of Primary Mediastinal Large B-Cell Lymphoma, complicated by secondary central nervous system involvement and resistance to standard therapies. Despite the sequential use of multiple targeted and immunomodulatory treatments, disease control remained limited, reflecting high-risk biology.
The key finding is the achievement of complete remission after CAR-T cell therapy, delivered in two infusions due to insufficient initial expansion, with an excellent safety profile and no occurrence of CRS or ICANS, despite prior CNS involvement.
This case underscores the central role of CAR-T therapy as a potentially curative salvage option in highly refractory PMBCL, including cases with CNS involvement, and highlights the value of academic CAR-T platforms and adaptive strategies such as repeat infusion and optimization of cell expansion.

Références :

- Safety and efficacy of CAR T-cell therapy in central nervous system lymphoma: a systematic review and meta-analysis : 2026 Mar 23:16:1790444
- CAR-T therapy for large B-cell lymphoma with CNS involvement (CLML 2024 meta-analysis) : *Clinical Lymphoma, Myeloma & Leukemia (2024)*
- CAR-T therapy in relapsed/refractory B-cell lymphoma (Systematic review) : 2024 Dec 17;16(12):e75854.