SWISS ONCOLOGY & HEMATOLOGY CONGRESS

Therapy refractory ICANS after CAR-T cell therapy with Brexucabtagene-Autoleucel (Tecartus) for Relapsed Mantle Cell Lymphoma: Successful Management with Intrathecal Triple Chemotherapy

Abstract category: Clinical hemato-oncology

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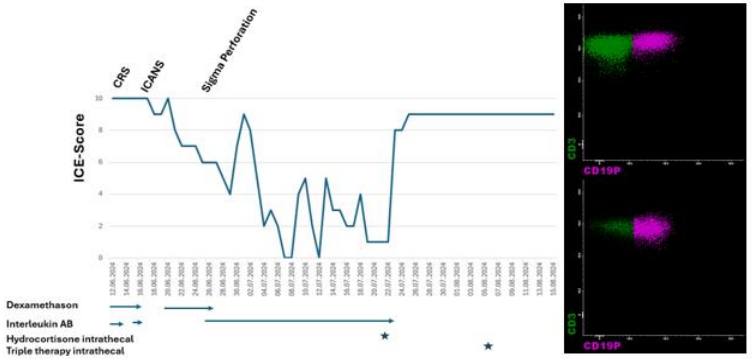
Background

Immune effector cell-associated neurotoxicity syndrome (ICANS) is a common complication of CAR T cell therapy, often linked to inflammatory cytokines disrupting the blood-brain barrier and causing neuroinflammation. The “on-target, off-tumor” effect is suggested by CD19 expression on brain mural cells and higher ICANS rates in CD19-directed CAR T therapies compared to BCMA or EGFRvIII targets. ICANS typically occurs 5 days to 3 weeks post-infusion, with symptoms ranging from mild confusion to coma, assessed by the ICE score. First-line treatment includes corticosteroids and interleukin receptor inhibitors like tocilizumab and anakinra.



Case report

A 67-year-old male with relapsed mantle cell lymphoma (MCL) was treated with CD19-directed CAR T cells. He developed Grade III cytokine release syndrome (CRS) on day 1, successfully managed with dexamethasone and tocilizumab. On day 5, he developed immune effector cell-associated hemophagocytic syndrome, followed by ICANS symptoms (somnolence, speech hesitancy, disorientation, ICE score 6). MRI was unremarkable, and lumbar puncture revealed no pathogens or infiltration of MCL but the presence of CAR T cells in the cerebrospinal fluid. Treatment included dexamethasone, tocilizumab and anakinra. Dexamethasone had to be discontinued after the patient suffered a sigmoid colon perforation and subsequent partial colon resection and stoma placement, likely due to significant reduction of intra-abdominal tumor mass.

Despite prolonged anakinra therapy, ICANS persisted for over a month. A second lumbar puncture confirmed CAR T cell presence, and to avoid systemic steroid therapy following abdominal surgery, intrathecal hydrocortisone was administered. The patient showed a rapid improvement of ICANS symptoms, which lasted for about 2 weeks, at which point he showed a discreet worsening of neurological symptoms that resolved completely after administration of intrathecal triple chemotherapy (methotrexate, cytarabine, dexamethasone).

Conclusion

This therapy-refractory ICANS case suggests intrathecal hydrocortisone and chemotherapy as promising second-line treatments. While small series show benefit, larger studies are needed. Identifying biomarkers and prophylactic strategies remain vital to improve outcomes.

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