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Cell based-therapies in patient with relapsing diffuse large B-cell lymphoma

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Relapse of diffuse large B-cell lymphoma (DLBCL) after autologous hematopoietic cell transplantation (auto-HCT) confers a poor prognosis. Many different regimens with a high-dose methotrexate (HD-MTX) backbone have demonstrated efficacy in relapsed or refractory cases, but the choice regarding subsequent lines remains a challenge [1–3]. It has been shown that chemotherapy alone is not sufficient for a cure. A cell-based consolidation with innovative chimeric antigen receptor (CAR) T-cells, or more standard allogenic hematopoetic cells, should be used to achieve long-term remission [4, 5].

Here, we present cell-based treatments in a patient with extranodal relapsing lymphoma after auto-HCT.

A 48-year-old male was diagnosed with a DLBCL (with unknown cell of origin subtype) in December 2009 with clinical stage (CS) IV. He was refractory to two cycles of CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) and received auto-HCT as a consolidation, partially responding to second-line R-ESHAP (rituximab, etoposide, methylprednisolone, high-dose cytarabine, cisplatin).

Eight years later, he relapsed with extranodal disease infiltrating the chest (with histopathological confirmation of primary diagnosis, non germinal center B-cell (GCB) subtype, no molecular test was done, immunohistochemistry: BCL2–/+; BCL6+/–, c-myc–). He received six more cycles of R-CHOP (rituximab, cyclophosphamide, adriamycin, vincristine, prednisone), achieving complete metabolic remission that was consolidated with a second auto-HCT in January 2019. In March 2020, he relapsed with extensive central nervous system (CNS) involvement. He recieved treatment specific for CNS lymphomas: high doses of R-MIV (methotrexate, rituximab, ifosfamide, and vincristine) [6]. After the third cycle, he achieved complete metabolic remission. He received three more R-MIV cycles with allogeneic cell consolidation from a matched unrelated donor after reduced-intensity conditioning comprising T-FluBu2 (thiotepa, fludarabine and busulfan) combined with anti-thymocyte globulin (ATG; 5 mg/kg) and standard cyclosporine and methotrexate immunosuppression. The post-transplant course was complicated only by neutropenic fever and urinary tract infection. He was engrafted in November 2020. He developed acute, and later chronic, graft-versus-host disease limited to the skin and was treated only with topical steroids.

In June 2022, the patient reported difficulties in concentrating and memory loss. Positron emission tomography–computed tomography (PET-CT) and brain magnetic resonance did not show any abnormality; the donor chimerism was 100%-donor. In August 2022, the patient's mental status began to worsen. In both magnetic resonance imaging (MRI) and PET-CT, infiltration of the ocular muscle was described with SUV_{max} 20.1 (Figure 1). In addition, infiltration of the sacral bone was also noticed (SUV_{max} 10.2) (Figure 2). Only those two regions were affected by lymphoma in PET-CT. Biopsy of the involved muscle suggested DLBCL relapse, but no CNS involvement by flow-cytometry was detected. The patient was qualified for CAR T-cell therapy (tisagenlecleucel) with polatuzumab vedotin (PV) bridging. Lymphocyte apheresis was done in September 2022, and two subsequent cycles of PV were given over the following two months. A clinical response was observed, but no control imaging was done. Infusion of CAR T-cells was carried out in November 2022 after limphodepletion therapy with fludarabine and cyclophosphamide with no severe early toxicity. An initial disease assessment was carried out in January 2023 with PET-CT, with no lymphoma presence (LPS 2).

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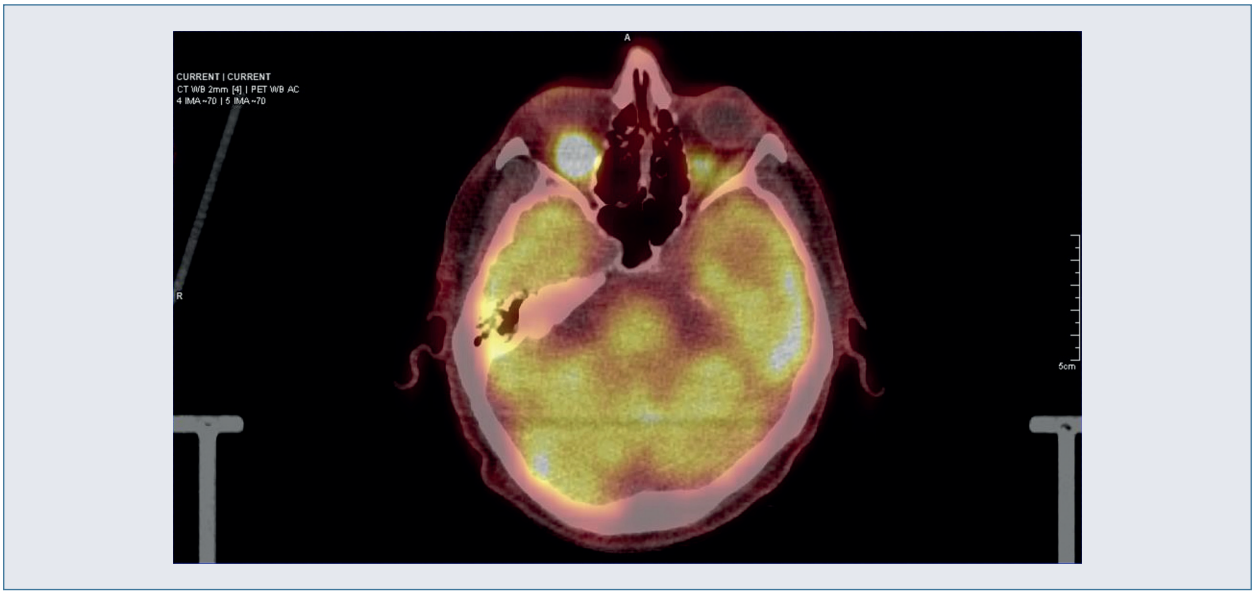

Figure 1. Positron emission tomography–computed tomography scan of head

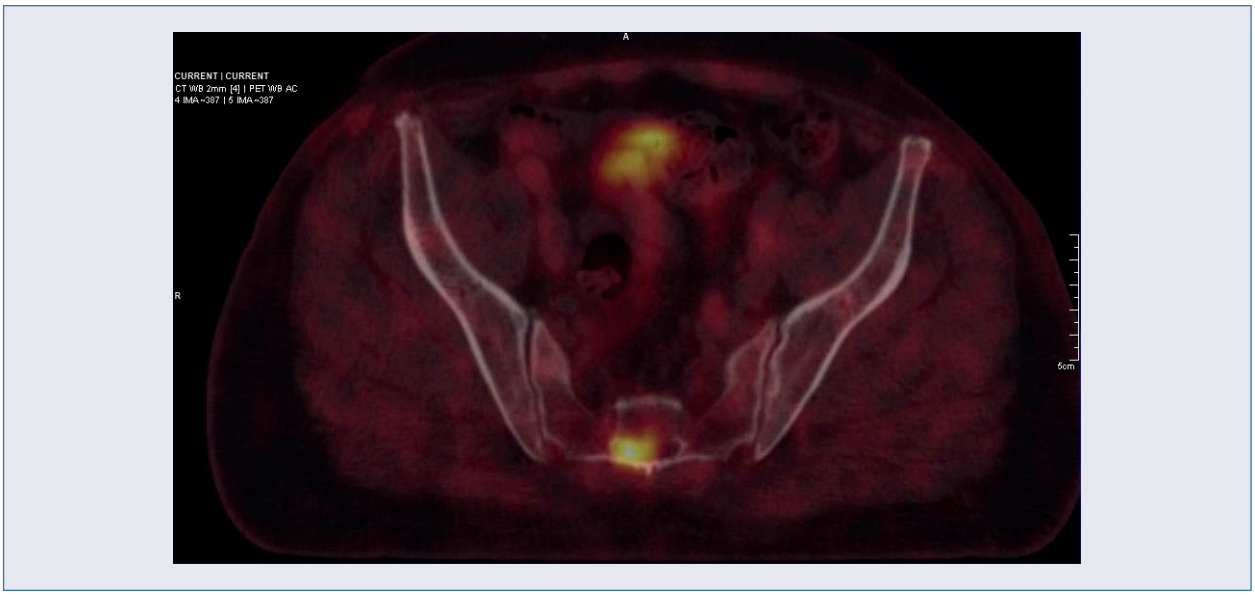

Figure 2. Positron emission tomography–computed tomography scan of pelvis

We conclude that cell-based therapies offer a unique opportunity to achieve remission in chemotherapy-resistant DLBCL. The optimal usage of CAR-T and allogeneic cells should be individualized.

Authors' contributions

AS wrote the manuscript with support from JMZ. MD and MT planned the treatment. All authors provided critical feedback and helped shape the manuscript.

Conflict of interest

The authors declare no conflict of interest.

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Ethics

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; EU Directive 2010/63/EU for animal experiments; Uniform requirements for manuscripts submitted to biomedical journals.

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