Positive impact of high-throughput drug sensitivity assay and salvage autologous CD19 CAR-T therapy on second marrow relapse of acute lymphoblastic leukemia with NT5C2 mutation

Xue Tang[1], Lijiao Qin[1], Lulu Wang[1], Cheng Jiao[2], Fen Chen[1], Yuchen Liu[2], Guichi Zhou[1], Sixi Liu[1], Ying Wang[1], Shilin Liu[1], Feiqiu Wen[1], Lung-Ji Chang[2], and Huirong Mai[1]

[1]Shenzhen Children's Hospital
[2]Shenzhen Geno-immune Medical Institute

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Abstract

Background: A 12-year-old girl diagnosed with intermediate risk B-ALL in 2017 received chemotherapy according to CCLG-2008 ALL protocol and achieved a complete remission (CR) after induction. However, four years later, she had a first bone marrow relapse and received treatment with HKPHOSG Relapsed ALL 2007 protocol. During maintenance chemotherapy, approximately one year after the first relapse, she developed a second bone marrow relapse with NT5C2 gene mutation detected. Tumor burden was not well controlled after DEAV chemotherapy, with the blasts in bone marrow increasing from 49.3% to 96%. The analysis of high-throughput drug sensitivity of tumor resistant genes was consistent with the poor response to chemotherapy. Procedure: CAR-T cell immunotherapy bridged to HSCT was introduced at this stage. Following peripheral lymphocyte apheresis, the patient received lymphodepleting conditioning with fludarabine and cyclophosphamide three days before CAR-T cell infusion. Dexamethasone and carfilzomib were then given according to the outcome of high-throughput drug sensitivity test. Result: Around 68.6% blasts were detected by flow cytometry at the day of CAR-T cell infusion. The patient experienced grade 1 CRS without ICANS. CR of morphology and molecule biology was achieved on day 28 after CAR-T cell infusion. Finally the child received haploid-HSCT and remained in remission. Conclusion: Overall, this report reveals that the combination of drug sensitivity test with lymphodepleting conditioning could significantly reduce the tumor burden before infusion of CART cells, and patients may achieve deeper remission and obtain opportunity for transplantation.

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