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ORIGINAL ARTICLE

Unrelated cord blood transplantation for adult-onset EBV-associated T-cell and NK-cell lymphoproliferative disorders

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Abstract

Adult-onset EBV-associated T-cell and NK-cell lymphoproliferative disorders (EBV-T/NK-LPDs) often progress rapidly, and require allogeneic stem cell transplantation early in the course of treatment. Unrelated cord blood transplantation (UCBT) is a readily available option for patients without HLA-matched donors. We retrospectively analyzed the outcomes of 12 UCBT in adult patients with chronic active EBV infection (CAEBV, $n=8$), EBV-positive hemophagocytic lymphohistiocytosis following primary EBV infection ($n=2$), hydroa vacciniforme-like lymphoproliferative disorder ($n=1$), and systemic EBV-positive T-cell lymphoma of childhood (STCLC, $n=1$). The median age at transplantation was 31.5 years (range 19–58). At the median follow-up time for survivors, which was 6.3 years (range 0.3–11.3), 3-year overall survival (OS) rates in all patients and 8 CAEBV patients were 68.2% (95% CI 28.6–88.9) and 83.3% (95% CI 27.3–97.5), respectively. Graft failure occurred in 4 of 8 CAEBV patients, requiring a second UCBT to achieve neutrophil engraftment. The cumulative incidence of grade II–IV acute GVHD was 33.3% (95% CI 9.1–60.4%). The EBV-DNA load became undetectable or very low after UCBT in all cases. UCBT may be a promising treatment option for adult-onset EBV-T/NK-LPDs.

Keywords EBV-associated T-cell and NK-cell lymphoproliferative disorders · Chronic active EBV infection · Hemophagocytic lymphohistiocytosis · Allogeneic stem cell transplantation · Cord blood transplantation

Introduction

EBV-associated T-cell and NK-cell lymphoproliferative disorders (EBV-T/NK-LPDs) encompass a broad spectrum from reactive conditions, such as hemophagocytic lymphohistiocytosis (HLH), to neoplastic diseases, including T/NK-cell lymphoma [1, 2]. In the 2017 revised World Health Organization (WHO) classification, EBV-positive T-cell and NK-cell proliferation is classified into 8 categories: EBV-positive HLH (EBV-HLH), chronic active EBV infection (CAEBV), hydroa vacciniforme-like lymphoproliferative disorders (HV-LPD), severe mosquito bite allergy (SMBA), systemic EBV-positive T-cell lymphoma of childhood (STCLC), aggressive NK-cell leukemia (ANKL), extranodal NK/T-cell lymphoma, nasal type (ENKL), and nodal peripheral T-cell lymphoma, EBV-positive [3]. EBV-T/NK-LPDs in the pediatric age group include two major types of CAEBV and STCLC. HV-LPD and SMBA are localized forms of cutaneous CAEBV. Each type of EBV-T/NK-LPD may overlap or progress to another aggressive form, and all types have a risk of systemic inflammation leading to multiple organ failure [4, 5]. Kawa et al. established the 3-step treatment strategy for CAEBV, which comprises cooling therapy, chemotherapy, and allogeneic stem cell transplantation (allo-SCT) [6]. Allo-SCT is currently regarded as the only curative therapy for EBV-T/NK-LPDs [2, 6–12].

EBV-T/NK-LPDs may also develop in adult age groups and an older age at onset is associated with a poor prognosis [2, 13, 14]. Adult-onset CAEBV progresses more rapidly and shows more severe manifestations than pediatric cases [15]. The duration of responses to steroids, immunosuppressive drugs, and chemotherapy is often short and allo-SCT may be required earlier following a confirmed diagnosis. If a patient does not have a HLA-matched donor, unrelated cord blood transplantation (UCBT), which may be promptly performed, is a therapeutic option. A retrospective study of UCBT in

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