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Case Report

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Donor Cell-Derived Myelodysplastic Syndrome Following Allogenic Peripheral Blood Stem Cell Transplant

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ABSTRACT

Donor cell-derived leukemia is a rare but well-described complication of allogeneic hematopoietic stem cell transplant (HSCT). This clinical case report aims to highlight the importance of recognizing this unusual disorder and thus, ensuring its appropriate management. We herein describe a case of a 9-year-old male diagnosed with acute lymphoblastic leukemia (ALL) and relapsed after initial chemotherapy. Subsequently, the patient had an allogenic peripheral blood stem cell transplant (PBSCT) from an HLA-matched, unrelated donor. Unfortunately, the patient then developed progressive thrombocytopenia, and following investigation, including bone marrow examination and cytogenetic analysis, he was diagnosed with donor cell-derived myelodysplastic syndrome. The literature review emphasizes the importance of considering it as a differential diagnosis of disease relapse following allogeneic HSCT.

Keywords: Lymphoid leukaemia; Bone marrow transplantation; Myelodysplastic syndromes

Case presentation

A 9-year-old male was diagnosed with low count (white cell count of 15.8 x 10^9/L) acute lymphoblastic leukaemia (ALL) in July 2013. He had no central nervous system (CNS) disease (CNS1) at the time of diagnosis. The patient was enrolled in UKALL 2011 trial and started on treatment on Regimen A. Cytogenetic and molecular analysis showed the presence of the Philadelphia chromosome with t (9;22) and BCR-ABL transcripts, respectively. His treatment was subsequently changed, and he entered the CA 180372 trial with Dasatinib. He tolerated his chemotherapy reasonably well and finished treatment in June 2015. Unfortunately, the patient then had an isolated bone marrow relapse, 16 months after completing therapy.

He was started on ALL R3 induction therapy with Imatinib (after approval of individual funding application) in November 2016. At initial presentation, the patient's younger sister was tissue typed, but sadly was not a match. The patient had an allogenic peripheral blood stem cell transplant (PBSCT) from a 10/10 HLA-matched unrelated donor in April 2017 with cyclophosphamide and total body irradiation as conditioning regimen. The donor was 30 years old and was genetically female with no significant past medical history. In addition, her investigations (including full blood count, biochemistry, and clotting profile), prior to donation, were all normal.

Following the PBSCT, the patient had poor graft function secondary to viral reactivation and mild skin allogenic graft -versus-host disease, which were later resolved.

In May 2019, the patient developed progressive thrombocytopenia, which required transfusion support. Bone marrow examination showed morphological and molecular remission with no evidence of BCR-ABL transcripts and 100% donor chimerism. Cytogenetic analysis revealed donor karyotype (46XX) with only additional finding of Trisomy 8 in donor cells. Repeat bone marrow examination showed dysplasia in erythroid and megakaryocyte precursors with no excess of blasts. He was subsequently diagnosed with donor-cell derived myelodysplastic syndrome in July 2019. Following confirmation of trisomy 8, the donor registry was informed and to the best of our knowledge, the donor is in good health. The treatment was discussed at the national bone marrow transplant multi-disciplinary team (MDT), and it was agreed to proceed with a second allogeneic haematopoietic stem cell transplant (HSCT) from an unrelated donor. The patient consequently had a successful second transplant and is currently under follow-up.

DISCUSSION

Haematological disorders, including malignancies, can be treated with allogenic HSCT. Donor cell-derived leukaemia (DCL) is a rare but well-described complication of allogenic HSCT. This is the development of de novo haematological malignancy originating in donor cells. However, the most common cause of failed allogenic HSCT is relapse of the host's underlying disease[1].

DCL has garnered significant interest as it can provide valuable insights into the mechanisms involved in leukemogenesis. More than 130 cases of DCL have been described in the literature since 1971[2], with a reported incidence of 124 cases per 100, 000 transplants[3]. In most of these patients, DCL was observed in patients whose stem cells were acquired from bone marrow, whereas DCL was reported in only 26 patients after allogenic PBSCT[2].

The first case of DCL was reported in 1971 by Fialkow et al[4]. The authors described a 16-year-old girl with ALL who received a HSCT from an HLA- matched brother and had a relapse of her leukaemia 62 days after the bone marrow transplant. Cytogenetic studies confirmed that the recurrence was in XY donor cells. Thus, it was concluded that the leukaemia was donor derived.

Several cases of DCL have been described following this initial report, albeit, sporadically. However, much more recently, there has been a surge in the number of cases, as the majority (83%) of the cases have been published in the last 20 years[2]. Due to the intermittent frequency of reporting, it has been challenging to estimate the incidence of DCL. In 1982, Boyd et al.[5] approximated that DCL accounts for 5% of recurrent leukaemia after bone marrow transplant. A survey conducted by the European Group for Blood and Marrow Transplantation3 in 2005, reported an incidence of 0.12%. A similar figure of 0.13% was reported by the Japan Society for Hematopoietic Cell Transplantation[6] in 2016. Furthermore, there may be an underestimation in the incidence of DCL due to mortality following allogenic HSCT.

A review by Suárez-González et al.[2] found that paediatric patients (≤16 years) account for 23% of all DCL cases, with a median age of 6 years at the time of diagnosis of primary disease. The authors also report that ALL was the most common primary disease (occurring in 43% of children), and the source of stem cells was peripheral blood for only 2% of children, while the most common source was bone marrow (73%).

CONCLUSION

DCL is an intriguing entity. This case highlights the importance of considering it as a differential diagnosis of disease relapse following allogenic HSCT. In conclusion, there is a need to conduct further research to determine the pathogenesis of DCL and thus recognize measures to prevent its occurrence.

CONFLICTS OF INTEREST

The authors report no conflict of interest.

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