CASE REPORTS

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HAPLOIDENTICAL HEMATOPOIETIC STEM-CELL TRANSPLANT FOR HIGH-RISK ACUTE MYELOID LEUKEMIA IN A KIDNEY TRANSPLANT RECIPIENT: CASE REPORT

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ABSTRACT

Solid organ transplantation is associated with a higher incidence of malignancies. Among them, acute myeloid leukemia has high morbidity and mortality, and its cure is only possible through allogeneic hematopoietic stem cell transplantation for high-risk disease. Case report: A 32-year-old female who underwent a kidney transplant eight years before was diagnosed with high-risk acute myeloid leukemia. She underwent induction therapy with "7+3", achieving complete remission with measurable residual disease detectable by flow cytometry. She then underwent a myeloablative haploidentical allogeneic transplant, achieving complete remission, free of graft-versus-host disease, with a functioning renal graft.

Keywords: Bone Marrow Transplantation; Kidney Transplantation; Leukemia, Myeloid, Acute.

INTRODUCTION

Solid organ transplants (SOT) and the resulting immunosuppression are known risk factors for the development of malignancies[1]. However, the rarity of acute leukemia cases and subsequent hematopoietic stem cell transplants in these patients makes the literature on this topic scarce. The recent expansion of haploidentical donor use and the incorporation of post-transplant cyclophosphamide in this context have not yet been reflected in publications that guide their safety and efficacy in post-SOT patients.

CASE PRESENTATION

A 32-year-old woman developed cytopenias eight years after receiving a kidney transplant from a deceased donor. At the time, she was on immunosuppression with mycophenolate sodium and tacrolimus. Following the development of cytopenias, mycophenolate was discontinued, and she continued with low-dose tacrolimus and prednisone.

Due to persistent and progressive cytopenias, bone marrow aspiration and immunophenotyping were performed. The results showed 51% myeloid blasts, which was consistent with high-risk acute myeloid leukemia (AML) due to a complex karyotype. The molecular assessment showed a wild-type FLT3 and non-mutated NPM1. Genomic evaluation was unavailable at the time of diagnosis.

The patient underwent induction chemotherapy with cytarabine (100mg/m^2) and daunorubicin (60 mg/m^2, protocol 3+7). She achieved complete morphological remission after one cycle of induction and received two subsequent cycles of consolidation with cytarabine (1.5 g/m^2 every 12 hours on days 1, 3, and 5). No renal graft dysfunction was noted after chemotherapy.

At the pre-transplant evaluation, a measurable residual disease (MRD) was identified by multiparameter flow cytometry (0.62% of abnormal myeloid precursors). A 23-year-old male brother was the only available donor. She then underwent haploidentical myeloablative peripheral blood hematopoietic cell transplantation with busulfan-fludarabine conditioning and post-transplant cyclophosphamide (PTCY), mycophenolate mofetil (MMF), and cyclosporine (CSA) for graft-versus-host disease (GvHD) prophylaxis[2]. All immunosuppressive drugs were paused from day -1 to day +5, and low-dose prednisone was restarted to prevent adrenal insufficiency and renal graft rejection at day +6.

At day +30, a bone marrow aspirate showed 14% myeloid blasts and 1.7% precursors with an abnormal immunophenotype and full donor chimerism. MMF was discontinued, and azacitidine (75 mg/m^2 for 5 days) was administered, followed by donor lymphocyte infusion (DLI) at 1 x 10^5 CD3+/kg. Subsequent evaluation revealed 5% myeloid blasts, 0.17% MRD by multiparameter flow cytometry (MFC), and mixed donor chimerism (90%). Cyclosporine was maintained with a new serum target of 50-100 ng/mL and continued on 28-day cycles of azacitidine (75 mg/m^2) for 5 days. By day +100, MRD was negative by MFC, and an incomplete hematologic recovery persisted.

On day +41, CMV reactivation was identified during routine post-HCT viral surveillance. The patient was treated with ganciclovir for 21 days without further reactivation. Letermovir was unavailable in the Brazilian public healthcare system at the time of transplantation.

After six months post-transplant and one year after the leukemia diagnosis, the patient remained in complete remission with negative MRD, experiencing mild anemia and moderate thrombocytopenia without requiring transfusions. She showed no signs of GvHD or renal graft rejection.

DISCUSSION

Patients undergoing kidney transplantation have a higher risk of developing acute myeloid leukemia, with an incidence ratio of approximately 1.9 times that of the general population[3]. AML after kidney transplantation, in particular, appears to occur later than liver transplantation and continues to contribute to new cases over time[4]. The prognosis remains poor, even in cases achieving complete remission, with a median survival of approximately six months[5].

Few publications have addressed hematopoietic stem cell transplantation, specifically in this scenario. A Japanese case series reported 17 cases of allogeneic transplantation post-SOT, including nine kidney transplant recipients and 4 with haploidentical donors using calcineurin inhibitor-based GVHD prophylaxis. Among these, eight developed renal graft dysfunction requiring dialysis[6].

The experience reported in Minnesota described nine allogeneic transplants after SOT, none involving haploidentical donors or post-transplant cyclophosphamide (PTCY)[7]. A series of European cases reported twenty-eight patients of allogeneic transplantation following solid organ transplantation, including twelve patients with prior kidney transplantation and four cases with haploidentical donors. No transplant utilized PTCY as GVHD-prophylaxis. This study demonstrated graft failure of the kidney transplant in 38% of patients post-HCT. The overall survival of the cohort was 60.2% at 12 months[8].

A recent case series described three patients undergoing allogeneic transplantation with GVHD prophylaxis based on post-transplant cyclophosphamide. Two of them received haploidentical donor grafts with peripheral blood stem cell sources[9].

Several uncertainties arise in the management of these cases: 1) Patients with prolonged immunosuppression due to prior solid organ transplantation have an increased risk of severe infections and multiple malignancies. 2) The use of immunosuppressive therapy during acute leukemia treatment and conditioning may interfere with its efficacy, increasing the risk of early relapse. 3) Donor-derived T lymphocytes may exhibit unpredictable alloreactivity against the kidney graft. 4) As of the submission date of this manuscript, there is no published data regarding the safety of early donor lymphocyte infusion in this setting that may trigger acute GVHD and rejection of the graft. 5) The risk of acute myeloid leukemia relapse with prolonged calcineurin inhibitor maintenance and the impact of PTCY on renal graft immunotolerance remain unknown.

Although this case's isolated experience provides limited insight into these questions, multicenter collaborative efforts and additional reports of transplantation in this setting may offer guidance for the treatment of high-risk acute leukemias following solid organ transplantation.

CONSENT FOR PUBLICATION

Written informed consent was obtained from the patient. This report was approved by the Institutional Review Board (CEP-HUWC N° 7.504.028).

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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