DOI: 10.1111/ajt.15117

Donor-derived Philadelphia chromosome-positive B cell lymphoblastic leukemia presenting with renal allograft involvement in the first year posttransplant

To the Editor:

Donor malignancy transmission is a rare but well-recognized solid organ transplantation complication that carries high mortality risk. Here, we report a case of donor-derived *BCR-ABL1*-positive B cell acute lymphoblastic leukemia (ALL) in which the diagnosis was made through renal allograft biopsy indicated for graft dysfunction. Subsequent investigations revealed secondary bone marrow involvement by blasts containing donor HLA consistent with donor origin disease.

The donor was a 57-year-old woman who had last seen her primary care practitioner a month prior to death and was deemed in good health. She presented to the hospital with flu-like symptoms and was found to have thrombocytopenia (11×10^9/L) and leukopenia (4.4×10^9/L), prompting assessment by hematology-oncology. She was eventually diagnosed with infectious mononucleosis complicated by idiopathic thrombocytopenic purpura. One day after admission, she developed a large cerebral hemorrhage and progressed to brain death. The family agreed to kidney donation.

The recipient had immediate graft function and relatively uneventful posttransplant course. At the 1-year posttransplant visit, she complained of worsening fatigue and was noted to have increased creatinine (1.9 mg/dL from baseline of 1.3). Donor-specific antibodies were detected and a kidney biopsy was indicated.

Biopsy, which showed diffuse renal infiltration by B cell lymphoblastic leukemia (Figure 1), prompted a bone marrow biopsy, which revealed partial bone marrow involvement (47% blasts), suggesting that the primary site could be the allograft. Cytogenetic studies showed a 46,XX,del(9)(p21),t(9;22)(q34.1;q11.2) karyotype, consistent with Philadelphia chromosome. HLA subtyping of bone marrow biopsy sample by sequence-specific oligonucleotides probes detected both recipient and donor HLA alleles with a similar magnitude.

After diagnosis, immunosuppression was reduced to steroids alone and the patient started a 6-cycle regimen of hyperfractionated cyclophosphamide (300 mg/m^2 every 12 hours on days 1-3), vincristine (2 mg/d on days 4 and 11), doxorubicin (50 mg/m^2 on day 4), and dexamethasone chemotherapy with rituximab (375 mg/m^2 on day 1) and dasatinib (100 mg on days 1-14 of each cycle) alternating with cycles of methotrexate (1 g/m^2 on day 1), cytarabine (3 g/m^2 every 12 hours on days 2-3), and methylprednisolone. She then received a peripheral blood stem cell transplant (SCT) from her sister. Creatinine has remained stable throughout treatment, ranging from 1.16 to 2.20 mg/dL.

The contralateral kidney recipient was contacted and has shown no evidence of hematologic malignancy up to this date, 22 months after transplant.

Allograft involvement by hematological disease is typically seen in early posttransplant lymphoproliferative disorder, often of donor origin,[1] which can be a cause of early graft disfunction.[2] Leukemia involving the allograft is a much rarer event, with only 1 case of

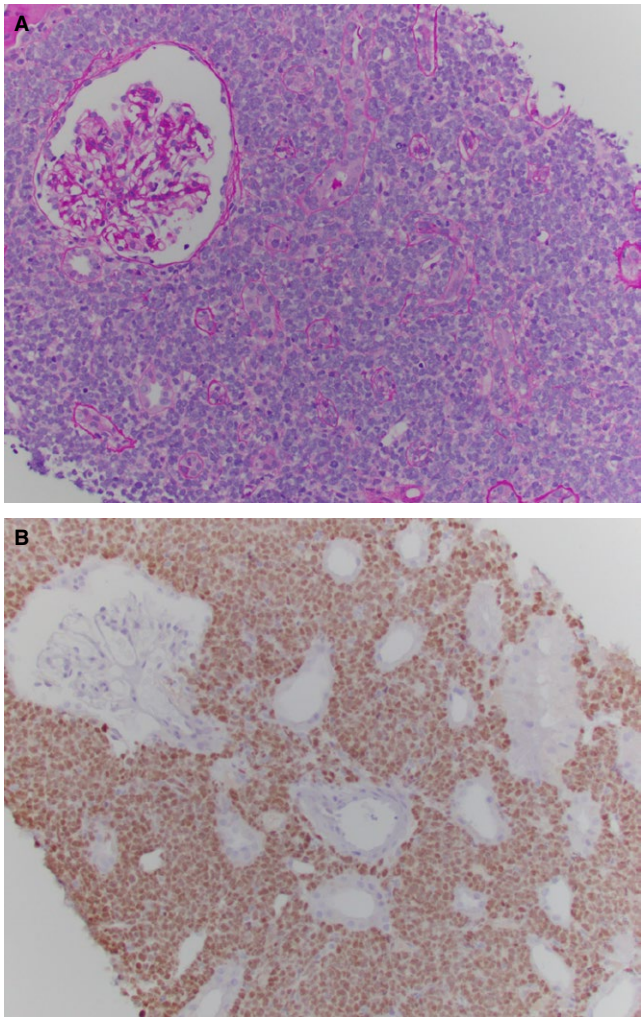

FIGURE 1 Diffuse renal parenchymal infiltration by B cell acute lymphoblastic leukemia blasts (A) that were diffusely positive for terminal deoxynucleotidyl transferase (TdT), (B). A—periodic acid–Schiff stain, B—TdT immunoperoxidase, both 200× magnification

donor-transmitted T cell ALL reported in an adult renal recipient.[3] To the best of our knowledge, this is the first reported case of transmission of a *BCR-ABL1*-positive B cell ALL to a renal transplant recipient.

Our case highlights the fact that donor tumor transmission, although rare, is likely unavoidable in spite of thorough donor assessment, as occurred in our case. It also highlights the potential of allograft sparing, at least in cases of hematolymphoid malignancies for which surgical removal is not the mainstay of regular treatment.

Whereas many have advocated donor organ removal and withdrawal of immunosuppression as the only way to achieve remission,[4,5] our patient was successfully treated while keeping her allograft and is currently in remission, 11 months after diagnosis and 5 months after SCT.

DISCLOSURE

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation*.

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Keywords

cancer/malignancy/neoplasia: hematogenous/leukemia/lymphoma, clinical research/practice, complication: malignant, kidney (allograft) function/dysfunction, kidney transplantation/nephrology

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