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LETTER TO THE EDITOR

Donor-derived extramedullary acute promyelocytic leukemia post kidney transplant

Ahmad Alhuraiji · Wahiba Chebbo · Ghada El-Gohary · Naeem Chaudhri · Fahad Almohareb · Khaled Ibrahim · Nasir Bakshi · Shamayel Mohammed · Hala Abalkhail · Syed Ahmed Osman

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Dear Editor,

Here, we describe what to our knowledge is the only case in the literature of donor kidney-derived extramedullary acute promyelocytic (EM-APL).

A 54-year-old physician with diabetes mellitus, hypertension, and ischemic heart disease, who had received a renal transplant of indeterminate origin for end stage kidney disease in China 2 years before presentation, was referred to our hospital with gross hematuria, deteriorating renal function, jaundice, and multiple subcutaneous nodules.

PET CT scan of the body revealed multiple FDG avid masses as shown in Fig. 1a. Biopsy of the transplanted kidney and subcutaneous nodule (FNA) was consistent with granulocytic sarcoma based on flow performed on the submitted specimen (axillary mass) showing a population of cells in the blast gate that co-express MPO, CD11b, CD13, CD33, CD34, CD38, and CD117 and HLA-DR (dim). Bone marrow was uninvolved and a FISH panel including *t*(15;17) was negative. Attempted cytogenetic analysis from FNA of the nodules failed.

A resection of the kidney was offered but the patient declined, and immunosuppression was continued with low-dose FK506 and prednisone; MMF was stopped. The final diagnosis at that stage was granulocytic sarcoma. Given the comorbidities, he was given upfront idarubicin and cytarabine "2+5" with a suboptimal response based on PET scan; then, he received salvage fludarabine/Ara-c (FA) protocol resulted in complete metabolic response. As per standard operating procedure at our hospital, PML-RARa is not sent from a diagnostic tissue sample other than bone marrow. In order to characterize the disease further, a FISH panel on the axillary biopsy was done and revealed positivity for *t*(15;17).

The patient was then given ATRA/idarubicin (AIDA) induction followed by 25 doses of arsenic trioxide (ATO) consolidation and then maintenance ATRA; mercaptopurine and methotrexate were not given due to cytopenias.

As the initial lesion seemed to be in the transplanted kidney, we sought to determine whether the leukemia may have been of donor origin. In order to address this hypothesis, DNA was extracted from the previously excised axillary block. This was compared with DNA from the patient's blood. To our surprise, DNA by short tandem repeat analysis revealed that axillary mass was not of recipient origin as shown (Fig. 1b).

Eighteen months on since first presentation, he has no demonstrable disease based on PET scan with good quality of life and stable renal function.

A case reported in *Blood* by Girsberger et al. described a case of donor kidney derived AML [1]. Kidney transplant recipients are at increased risk for development of malignancy compared with the general population [2]. There are case reports of AML post solid organ transplantation [3, 4]. Donor-derived APL has been reported [5]; however, the aleukemic extramedullary presentation in our case is unique. Treatment of acute leukemia in solid organ transplant remains one of the main challenges facing the hematologist with sparse literature focusing on this issue.

A. Alhuraiji (✉) · W. Chebbo · G. El-Gohary · N. Chaudhri · F. Almohareb · K. Ibrahim · S. A. Osman
Hematology Section, Oncology Centre, KFSHRC, Riyadh 11211, Saudi Arabia
e-mail: aalhuraiji@gmail.com

N. Bakshi · S. Mohammed · H. Abalkhail
Pathology and Laboratory Medicine, KFSHRC, Riyadh 11211, Saudi Arabia

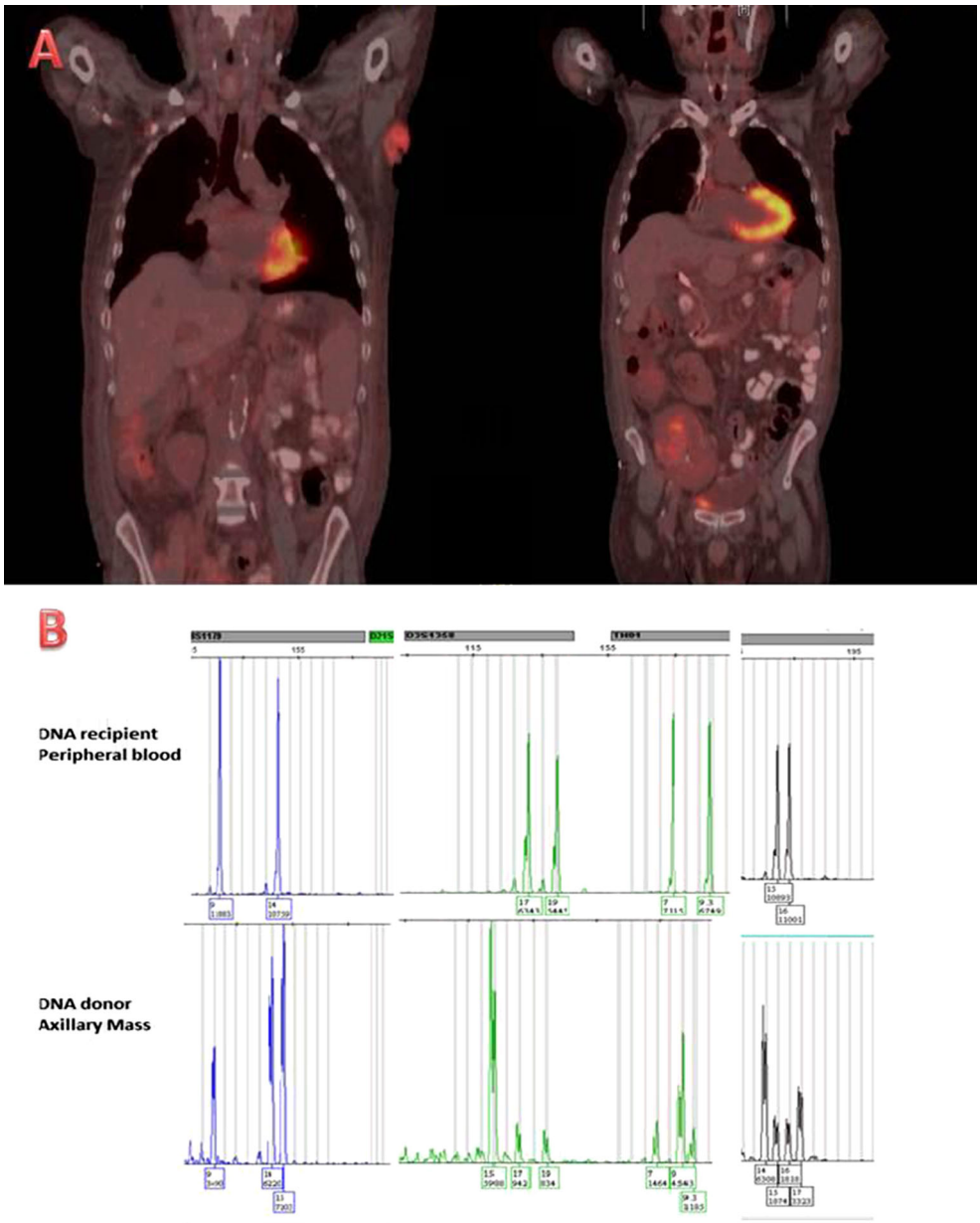

Fig. 1 **a** PET scan at presentation revealed hypermetabolic masses on the transplanted kidney causing obstruction (*arrow 1*), a lesion on the ampulla of Vater, a left axillary mass (*arrow 2*) multiple subcutaneous nodules, peritoneal deposits intraabdominal lymph nodes, and a left adrenal lesion. Post treatment PET scan showed no FDG uptake (not shown) **b** STR analysis of donor (axillary mass DNA) and recipient genomic DNA was performed. The genetic profile using exhibited additional allele peaks that is present only in the axillary mass DNA and absent in genomic DNA. The percentage of donor DNA in comparison to genomic DNA was calculated from informative alleles

This case highlights few unique issues: (1) donor kidney-derived disseminated extramedullary APL as sparing the bone marrow, and responding to combination chemotherapy, ATRA, and ATO; (2) the challenge of monitoring response in aleukemic presentations—in this case PET scan, urine cytology, and peripheral blood PCR for PML-RARa were used; and (3) though convention would dictate resection of the allograft and cessation of immunosuppression, in this case, and mainly due to patient's choice, the renal allograft was preserved. The case also highlights ethical issues relating to unregulated transplant practices. Donor-derived malignancy must be suspected in any malignancy arising in transplant recipients, and our case confirms the feasibility of STR analysis to determine this.

Conflict of interest The authors declare that they have no conflict of interest.

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