Renal allograft eosinophilia: An unusual presentation of sudden graft dysfunction

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ABSTRACT

We present a case of sudden allograft dysfunction 11 months after renal transplantation which presented as severe peripheral and allograft eosinophilia and was managed as a case of an acute cellular rejection with significant interstitial graft eosinophilic infiltration. Patient had partial response to antirejection therapy and eventually ended up in a chronic allograft dysfunction.

Key words: Eosinophilic infiltration, graft loss, renal transplant, vascular rejection

Introduction

Eosinophils, besides being involved in inflammatory pathways, are also considered to have immunoregulatory function with roles in antigen presentation, T-cell regulation and polarization, B-cell priming, as well as regulation of dendritic cells, mast cells, basophils, and neutrophils.[1] They also play a crucial role in the mechanism of injury during acute renal allograft rejection.[2] We report a case of sudden, severe peripheral and renal allograft eosinophilia with subsequent graft loss.

Case Report

A 52-year-old multiparous homemaker, with unknown chronic kidney disease, was on maintenance hemodialysis for 4 years. Then, she had an uneventful deceased donor renal transplantation and a stable graft function with serum creatinine of 0.7 mg/dl and normal urine analysis for 11 months, presented with acute graft dysfunction. She was inducted with 75 mg of thymoglobulin and her maintenance immunosuppressive was prednisolone 2.5 mg OD, tacrolimus 1 mg BD, and mycophenolate mofetil 750 mg BD. She weighed 73.8 kg and had new onset diabetes after transplant. Serology for hepatitis B surface antigen, anti-hepatitis C virus antibody, and HIV was negative with cytomegalovirus (CMV) IgG positive. She was receiving diltiazem, clonidine, and atenolol. At the time of presentation, she had no fever, cough, dysuria, oliguria, hematuria, or pain in the graft. On examination, she was afebrile, her blood pressure was 160/90 mmHg, and heart rate was 80 beats/min. Her systemic examination was essentially normal. Her investigations revealed blood urea nitrogen 28.01 mg/dl and creatinine 1.3 mg/dl, hemoglobin 11.6 g/dl, white blood cells 2700/µl, polymorphs 44%, lymphocytes 8%, eosinophils 48%, platelet 260 × 10^3/µl, urine showing nil albumin with no active sediments, and urine eosinophils negative. Stool analysis showed no ova or cyst. BK and JC virus polymerase chain reaction (PCR) for blood and urine, CMV PP65 and PCR were negative.

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As the investigations were not conclusive, an allograft biopsy was done and three renal cores obtained which had five glomeruli. Light microscopy revealed normal glomerular structure, patchy tubular necrosis, and tubular atrophy [Figure 1]. There was no tubulitis, but the remarkable finding was interstitial infiltration by numerous eosinophils along with one patchy aggregate of lymphoid cells (<10% of the cortex). Interstitial fibrosis and tubular atrophy was about 5% of the cortex and blood vessels were mildly thickened. Immunofluorescence staining was negative for IgG, IgM, IgA, C3, C1q, kappa, and lambda. C4d was negative. Marked eosinophilia with renal involvement worldwide is most commonly caused by helminthic infections and drug-related allergic nephritis, which were excluded in our patient through stool examinations and a detailed drug history. Bone marrow aspiration and biopsy were performed to rule out eosinophilic leukemia which could be another etiological possibility in an immunocompromised patient with hypereosinophilia. Bone marrow aspiration and biopsy revealed marked increase in eosinophilic myeloid precursor with megaloblastoid red blood cells [Figure 1]. Bone marrow aspirate for karyotyping and next generation sequencing were normal and hence a leukemic process was excluded.

Hence, we came up with a most probable diagnosis of an acute cellular rejection with significant interstitial graft eosinophilic infiltration (SIGEI). Patient was treated with four doses of 500 mg of intravenous methylprednisolone following which the peripheral eosinophilia was completely suppressed and graft function improved. However, later, the patient continued to have allograft dysfunction which did not respond significantly with thymoglobulin and rituximab and our patient ended up in a chronic allograft dysfunction.

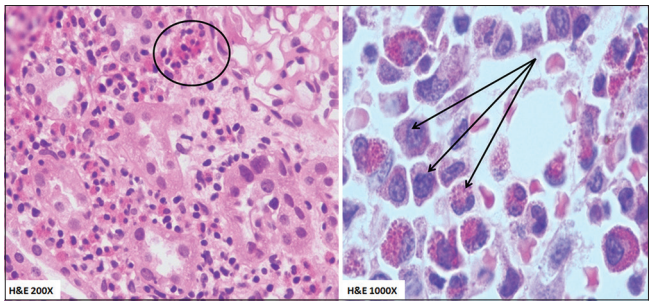

Figure 1: Renal graft biopsy (H and E, ×200) showing interstitial infiltration by numerous eosinophils (black circle) and bone marrow biopsy (H and E, ×1000) showing marked increase in eosinophilic myeloid precursors (black arrows)

Discussion

Eosinophils in the renal allograft have been previously implicated in allograft rejection, especially in vascular rejection and graft loss, the term commonly ascribed as acute cellular rejection with SIGEI. Meleg-Smith and Gauthier mentioned that SIGEI was significantly associated with vascular rejection (Banff Type II) but not with risk of allergic iatrogenic nephritis, suggesting that the presence of SIGEI may be a helpful criterion in the pathologic diagnosis of renal allografts.[3] Hongwei *et al*. mentioned that the sensitivity, specificity, and overall accuracy of predicting acute rejection with tissue eosinophil density ≥1 eosinophil per micron 2 × 10 (6) are 41%, 100%, and 52% and for peripheral blood eosinophilia ≥4% are 23%, 96%, and 40%, respectively.[4] The author also mentioned that the median peripheral blood eosinophilia (1.5–3.0%) in all grades of acute interstitial rejection and in acute vascular rejection was significantly higher than in controls. Management would include pulses of methyl prednisolone and thymoglobulin in cases of steroid resistance.[4] A study done by Jezior *et al*. concluded that eosinophilic infiltration of renal allograft is a negative predictor which can indicate more severe course of acute renal allograft rejection and increased resistance to an antirejection therapy.[4] It can determine an appearance of chronic allograft dysfunction hazard.[4] Similarly, our patient had partial response to augmented immunosuppressive therapy and her graft function continued to decline in spite of concurrent reduction in allograft and peripheral eosinophilia.

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Conflicts of interest
There are no conflicts of interest.

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