

Could It Be Post Transplantation Lymphoproliferative Disorder at this period in a Live Donor Kidney Transplant Recipient

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ABSTRACT

Objectives: Post-Transplantation Lymphoproliferative Disorder (PTLD) is a well-recognized complication of renal transplantation. The typical histopathological changes of PTLD could be a large increase in the number of B cell lymphocytes in lymphoid tissues, accompanied by multiple focal areas of necrosis. Plasma cell-rich acute rejection (PCAR) is a relatively new clinical entity and is characterized by the presence of mature plasma cells that comprise more than 10% of the inflammatory cells infiltrating a renal graft. PCAR shows findings similar to those of post-transplantation lymphoproliferative disorder (PTLD). So we should differentiate between PTLD and PCAR for appropriate treatment.

Case Report: We report a 32-year-old male underwent living donor kidney transplantation from his 40-year sister at March, 2014. Unfortunately, at 8th day post transplantation his serum creatinine increased suddenly to 1.8 mg/dl with good urine output and unremarkable physical examination. Graft Ultrasound and Doppler showed no back pressure, perfect perfusion, so graft biopsy was carried out with starting empirical pulse steroid and plasma exchange. Graft biopsy revealed picture of Lymphoproliferative disorder which is uncommon picture at this early post-transplantation.

Conclusion: PCAR shows findings similar to those of PTLD and has a poor response to standard antirejection therapy and worse graft outcome. Hence, early diagnosis and management of this morphology in a renal allograft biopsy is essential for appropriate patient and graft survival.

INTRODUCTION

Post-Transplantation Lymphoproliferative Disorder (PTLD) is a well-recognized complication in renal transplant recipients. PTLD is usually caused by EBV infection due to therapeutic immunosuppression after renal transplantation [1]. The typical histopathological changes of PTLD could be a large increase in the number of B cell lymphocytes in lymphoid tissues, accompanied by multiple focal areas of necrosis [2]. Plasma cell-rich acute rejection (PCAR) is a relatively new clinical entity and is characterized by the presence of mature plasma cells that comprise more than 10% of the inflammatory cells infiltrating a renal graft [3]. PCAR shows findings similar to those of PTLD or BK virus nephropathy [4]. The findings of plasmacytic or plasma cell-rich tubulointerstitial inflammation portend a poor outcome of kidney transplantation [5]. So we should differentiate between PTLD and PCAR for appropriate treatment. We report a case of early post-transplantation lymphoproliferative disorder like picture in a live donor kidney transplant recipient.

CASE REPORT

A 32-year-old male diagnosed with end stage renal disease for bilateral vesico-ureteric reflux and maintained on regular hemodialysis for one year underwent living donor kidney transplantation from his 40-year sister at March, 2014. Pre-transplantation workup was negative for HIV (human immunodeficiency virus), hepatitis B virus, hepatitis C virus, and Epstein-Barr virus (EBV) with negative cross match, one HLA class II (DR) matching and zero percent for both class one and two panel reactive antibodies (PRA). The donor's cytomegalovirus and Epstein-Barr virus status was negative. Induction therapy with basiliximab was followed by tacrolimus, mycophenolate mofetil, and prednisolone immunosuppression. Nadir serum creatinine level was 1.4 mg/dL (corresponding to an estimated glomerular filtration rate of 78 mL/min/1.73 m² as calculated by the 4-variable MDRD [Modification of Diet in Renal Disease] Study equation). Unfortunately, at 8th day post transplantation his serum creatinine increased suddenly to 1.8 mg/dl with good urine output and unremarkable physical examination. Laboratory data showed a white blood cell count of 12,400/mL (neutrophils, 80%; lymphocytes, 10%; monocytes, 6%; and eosinophils, 1%), platelet count of 175,000/mL, Serum Albumin; 4.4g/dl, Cholesterol; 260 mg/dl, tacrolimus trough level; 9.8 ng /dl and normal urine analysis. Graft Ultrasound and Doppler showed no back pressure, perfect perfusion with resistive index (RI) 0.65, so graft biopsy was carried out with starting empirical pulse steroid(500 mg Methylprednisolone /day) and plasma exchange.

Graft biopsy showed: tubules with focal areas of moderate lymphocytic infiltration 2-7 lymphocytes / tubular section with disturbed basement membrane and focal areas of dilated peritubular capillaries with more than 20 lymphocytes, neutrophils and eosinophils. The interstitium show marked diffuse inflammatory infiltrates: plasma cells, activated lymphocytes, eosinophil and neutrophils admixed with normal blood vessels. There are focal areas of serpinginous necrosis. Immunofluorescent staining was negative for C4D and positive for CD20. Picture in favour of post-transplant Lymphoproliferative disorder was made as a diagnosis but a diffuse lymphocytic infiltrate of such severity that it is difficult to visualize tubular architecture, which can occasionally be observed in patients with severe cellular rejection (**fig 1**).

Since the treatment options for rejection and PTLD are markedly different, so studies to exclude PTLD were done like EBV work up , careful examination for missed

lymphadenopathy ,revision the previous radiological work up to exclude hidden lymphadenopathy before transplantation and we also reexamined the donor with revision of her pre-transplantation abdominal CT with contrast for lymphadenopathy with no positive findings ,so we considered the acute rejection and anti-rejection therapy (pulse steroid & plasma exchange) was given –being that It may be difficult to distinguish between acute antibody-mediated rejection and severe acute cellular rejection, and the two processes may also coexist - with good response and the serum creatinine returned to its basal value.

DISCUSSION

We report a case of early post-transplantation lymphoproliferative disorder like picture in a live donor kidney transplant recipient. It was difficult to clearly differentiate PCAR from plasma cell-rich PTLD because of the monoclonality of plasma cell infiltration. Acute cellular rejection(ACR) of the renal allograft usually shows interstitial infiltrate of activated cellular rejection of T-cell origin along with scattered plasma cells, eosinophils, and neutrophils. PCAR is a relatively newly described entity characterized by the presence of plasma cells constituting more than 10% of the infiltrating cell population [3]. There are very few reports/studies of PCAR in the available literature [5-12].

Many possibilities were considered in the pathogenesis of PCAR [5]. Desvaux et al. suggested that acute antibody mediated rejection (AMR) may be involved in most PCAR cases [3]. Furuya et al. reported the possibility that de novo HLA-DQ donor specific antibodies (DSA) induced AMR and may contribute to the occurrence of PCAR [13]. On the contrary, Chikamoto et al. reported a pediatric PCAR case that showed a T cell-mediated rejection (TMR) pattern [14]. However, Suzuki et al. suspected that PCAR may be an atypical form of PTLD [9]. Plasmacytic infiltrates in the renal graft may also be seen in PTLD, viral infections, and exposure to toxins or drugs [11].

PTLD is a well-recognized complication of both solid organ transplantation (SOT) and allogeneic hematopoietic stem cell transplantation (HSCT) [15].In renal transplant recipients, PTLD is usually caused by EBV infection due to therapeutic immunosuppression after renal transplantation [1]. In normal condition, EBV infection activates innate immunity (both humoral and cellular immunity) to control EBV replication and proliferation of EBV-infected B-cells. However, when immunosuppressants such as Calcineurin inhibitors are used to prevent graft rejection after renal transplantation, these

drugs will impair CD4 and CD8 T-cell immunity by inhibiting T cell function, thus leading to uncontrolled proliferation of EBV- infected B-cells to form lymphoid hyperplasia or B cell lymphoma [16]. The typical histopathological changes of PTLD could be a large increase in the number of B cell lymphocytes in lymphoid tissues, accompanied by multiple focal areas of necrosis [2]. The lesion may include plasmacytic hyperplasia, B-cell hyperplasia, B-cell lymphoma, or immune blastic lymphoma. Histopathological evidence for the presence of EBV DNA, RNA, or protein is very important to make an accurate diagnosis of PTLD, and can be obtained by using immunohistologic staining of paraffin-embedded tissue, *In situ* hybridization with the EBV-encode dRNA probe, and qualitative and quantitative EBV polymerase chain reaction (PCR) [17]. However, approximately 10%–20% of PTLD were EBV negative [18].

In our case differentiation of PCAR from PTLD is a sophisticated problem. Plasma cell infiltration is common in AMR; however, some AMR cases were C4d negative like this case [19]. We suspected PCAR because the infiltrating inflammatory cells were not only lymphoplasma cells but also neutrophils and monocytes. Lymphoproliferative disorder is uncommon picture at this early post-transplantation period as most cases of PTLD usually occur with 1–2 months of organ transplant. The incidence rate of PTLD varies between 1 and 5% in renal transplant recipients [20].

In conclusion: PCAR, a rare morphologic type of ACR of renal allograft, shows findings similar to those of PTLD and has a poor response to standard antirejection therapy and worse graft outcome when compared with cases with a comparable Banff grade of ACR. Hence, early diagnosis and management of this morphology in a renal allograft biopsy is essential for appropriate patient and graft survival

Conflict of interest statement

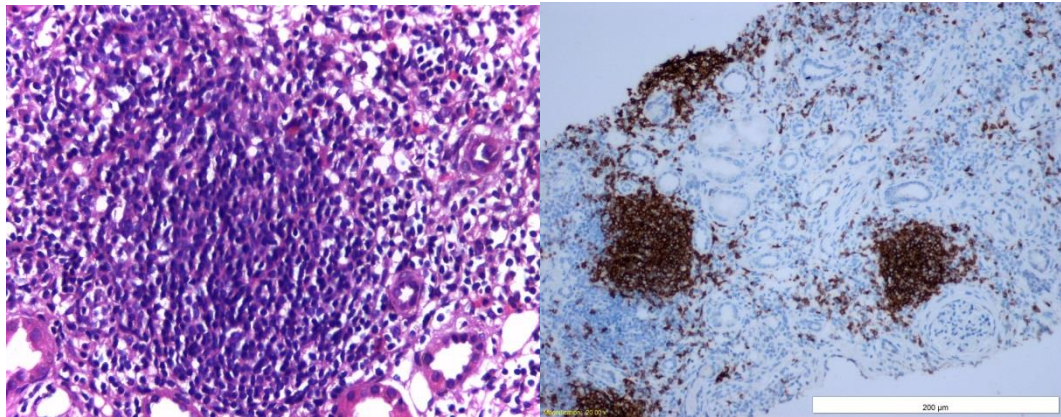
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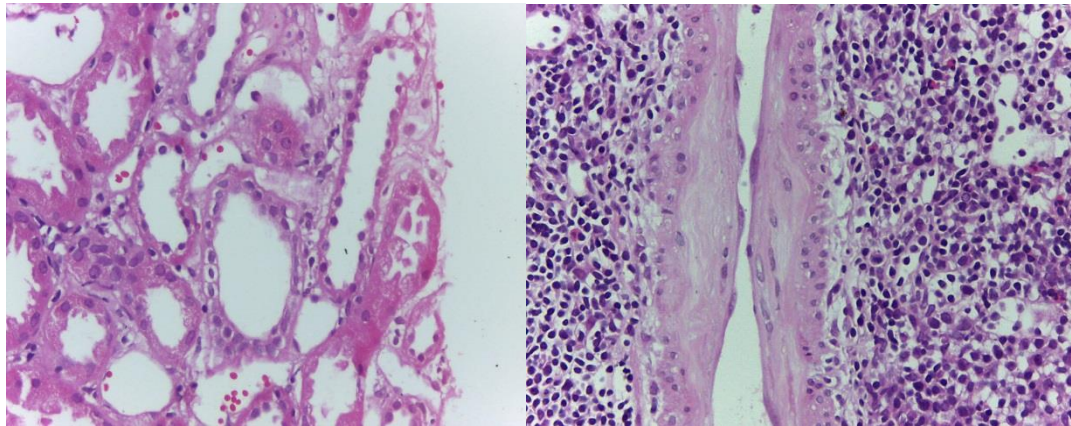
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Fig (I)



A. Dense inflammatory infiltrate up to formation of lymphoid follicles .

B. CD20 positive cells in the follicles .



C. Evidence of tubulitis without viral cytopathic effect and dense interstitial inflammation without evidence of Vasculitis .