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LETTER TO THE EDITORS

Successful renal transplantation for end-stage renal insufficiency developed in a patient with Castleman's disease

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Sirs,

Multicentric Castleman's disease (CD) is an uncommon lymphoproliferative disease characterized by systemic inflammatory reactions including hypergammaglobulinemia because of dysregulated production of interleukin-6 (IL-6) and vascular endothelial growth factors [1]. Five-year overall survival is 65% and approximately 5% of multicentric CD patients had various renal complications [1–3], including the development of chronic renal failure in 45% [4]. To the best of our knowledge, there has been no report of renal transplantation for the treatment of end-stage renal disease (ESRD) secondary to CD.

A 47-year-old Japanese male, with a history of proteinuria and hypergammaglobulinemia presented to our hospital with palpitations, nasal bleeding, and general fatigue. His initial workup revealed a hemoglobin 4.8 g/dl, fibrinogen 620 mg/dl (normal: 166–375), serum creatinine 2.4 mg/dl, C-reactive protein (CRP) 7.0 mg/dl, γ-immunoglobulin (IgG) 6360 mg/dl (826–1840), and IL-6 24.7 pg/ml (<4). A chest-abdominal-pelvic computed tomography was obtained which revealed multiple systemic lymphadenopathies, prompting a submaxillary lymph node biopsy that revealed massive plasma cell infiltration among increased numbers of small lymphatic follicles, that was suggestive of multicentric plasma cell type CD.

Immunosupressive treatment with prednisolone and cyclophosphamide resulted in the improvement of lymphadenopathy, however, he developed ESRD in 3 years and underwent ABO-compatible renal transplantation from a living donor (wife). Methylpredonisolone was initiated 6 days prior to transplantation, which resulted in normalization of IL-6 (3.2 pg/dl), but not IgG (2980 mg/dl). Postoperative immunosuppressive therapy consisted in a triple drug regimen combining tacrolimus at a starting dose of 0.075 mg/kg/day, and adjusted according to the blood trough levels over 10 ng/ml, micophenol mofetil (MMF) 1500 mg/day and a 2-month tapered dose of predonisolone from 125 to 5 mg/day.

On postoperative day 4, the patient became oligouric and serum creatinine was elevated from 2.1 to 3.7 mg/dl. Doppler ultrasound showed decreased blood flow indicating acute rejection. Pulse steroid, plasmapheresis, and anticoagulant therapies were unsuccessful. Thus, the patient received anti-CD3 (muromonab CD3) at 5 mg/day and anti-CD20 (rituximab) at 5 mg/kg/day for a total of 10 days, which resulted in decreased serum IgG levels to 844.9 mg/dl, and eventual normalization of kidney function. Now, 8 years after renal transplantation, the patient continues to have excellent graft function (serum creatinine approximately 1.1 mg/dl), without clinical, pathological evidence of rejection. In addition, surveillance with radiologic and hematologic follow-up demonstrates no evidence of CD recurrence.

Despite normalization of serum IL-6 by pretransplant immunosuppression, the patient sustained high serum IgG and developed an acute rejection on postoperative day four. Treatment with anti-CD3 and anti-CD20 therapies normalized creatinine and IgG levels. Serum levels of IL-6 and IgG reflect disease severity in CD, as they both mediate various inflammatory symptoms. Accumulated evidence clearly shows that IL-6 reflects acute rejection of renal graft after kidney transplantation [5,6]. However, a causal relationship is unclear, particularly in the present case, as the patient developed acute rejection despite a normal IL-6. Hypergammaglobulinemia, generally does not affect graft function in renal transplantation [7], although there has been a report on accelerated graft failure in monoclonal gammopathy of undetermined significance [8].

An excellent long-term control of CD was achieved after renal transplantation. Most of CDs are idiopathic, although it is at least partly attributed to dysregulated acceleration of inflammatory process. Consistently, there have been a number of published case series on successful immunosuppressive treatments for multicentric CD [9,10]. Therefore, we expected that immunosuppression after renal transplantation was also effective for CD. However, previous reports

showed some renal allograft recipients who newly developed CD after transplantation [11–13]. Notably, these cases are related to viral infections such as human herpesvirus 8 or Epstein–Barr virus secondary to immunosuppression, which is distinct from primary CD developed in an otherwise healthy patient.

In conclusion, we report a case of ESRD because of multicentric CD in which both diseases were successfully treated by renal transplantation followed by immunosuppressive therapy. Renal transplantation should be considered for patients with CD.

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