ELSEVIER

Acute Renal Failure Caused by Hyperuremic Acidemia in ABO-Incompatible Kidney Transplant Maintained With Cyclosporine and High-Dose Mizoribine: A Case Report

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ABSTRACT

Introduction. The shortage of cadaver organs has led to expansion of living donor kidney transplantations with, 30% increase among ABO-incompatible cases in Japan and the use of marginal extended donors. Herein we have reported the outcome after an ABO-incompatible kidney transplantation from an aged living-related donor who suffered from mild diabetes mellitus and hypertension.

Case Report. A 48-year-old man underwent ABO-incompatible kidney transplantation from his 76-year-old father, using anti-CD20 antibody induction, followed by cyclosporine (CsA), mycophenolate mofetil (MMF), and prednisolone. After the operation, MMF was switched to high-dose mizoribine (MZ). He was discharged from the hospital on postoperative day (POD) 28 with a serum creatinine (sCr) of 1.47 mg/dL. On POD 34 when the sCr was 8.14 mg/dL, his urine examination showed uric acid crystals with serum uric acid of 24.6 mg/dL. Biopsy findings showed no evidence of acute rejection but mild tubulointerstitial injury. Hemodialysis performed twice to reduce uric acid was accompanied by hydration. CsA/MZ was switched to tacrolims/MMF; benzbromarone, to febuxostat to treat hyperuric acidemia. On POD 58, sCr reduced to 1.75 mg/dL he was discharged. On POD 416, graft function was stable with sCr of 1.70 mg/dL.

Conclusion. Common side effect of MZ is hyperuricemia which presumably caused acute renal failure of this aged marginal donor kidney.

EVEN AFTER amendment of the brain death law in Japan, there was only a modest increase in the number of cadaveric donors. Thus, more than 85% of cases for use kidneys from living donors. To expand the living donor pool, the number of ABO-incompatible transplantations has increased by 30% in Japan. As the ages of recipients has become older and older, that of donors has also become older and older. However, older donors often have their own complications, such as obesity, hypertension, and diabetes. It is difficult to find an appropriate donor for an older recipient. Therefore, marginally appropriate individuals are considered, to extend donor criteria. Herein we have reported an ABO-incompatible kidney transplantation from an aged living-related donor with mild diabetes, hypertension, and obesity.

CASE REPORT

The patient was an 48-year-old man who had suffered end-stage renal failure of unknown cause and began hemodialysis 4 months prior. He desired an ABO-incompatible renal transplantation from his 76-year-old father, who had mild diabetes, hypertension, and obesity. This donor candidate was prescribed medications for hypertension and diabetes. At the first visit hemoglobin A1c (HbA1c) was 6.4% of 6.7%, and body mass index (BMI), 34.1 kg/m^2. However, his renal function was normal: sCr, 0.84 mg/dL, 24-hour Cr clearance, 103.1 mL/min, and daily total urine protein, 30 mg/day. Before the operation, he was able to decrease the HbA1c and BMI to 6.0% and 31.9.

Immunosuppression was induced with anti-CD20 antibody (Ab), cyclosporine (CsA), MMF and prednisolone (PSL). Anti-B blood

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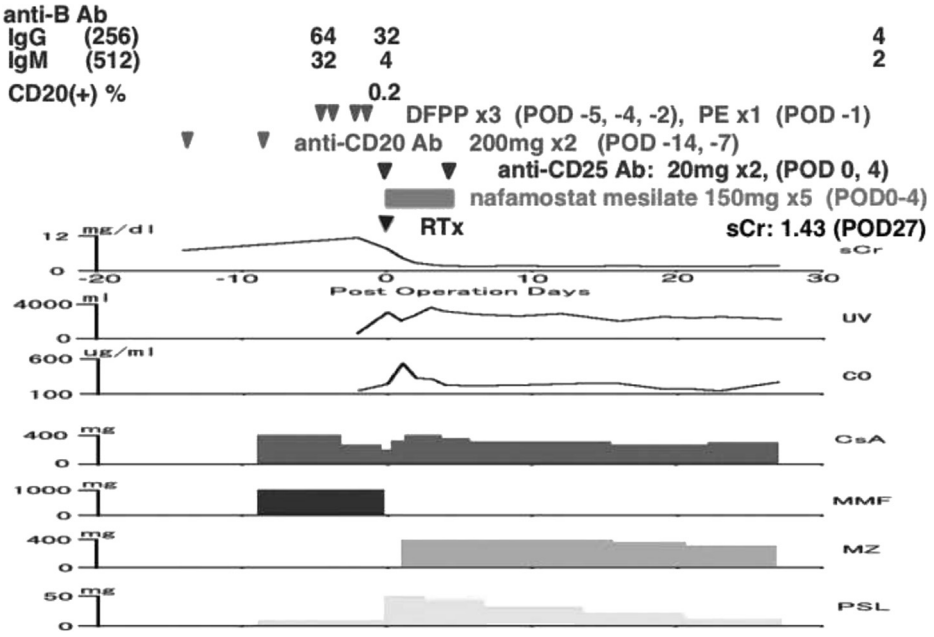

Fig 1. Postoperative course. Induction and maintenance of immunosuppressants are shown in the time course after the kidney transplantation. He discharged from our hospital on postoperative day (POD) 27 and serum creatine (sCr) was 1.47 mg/dL.

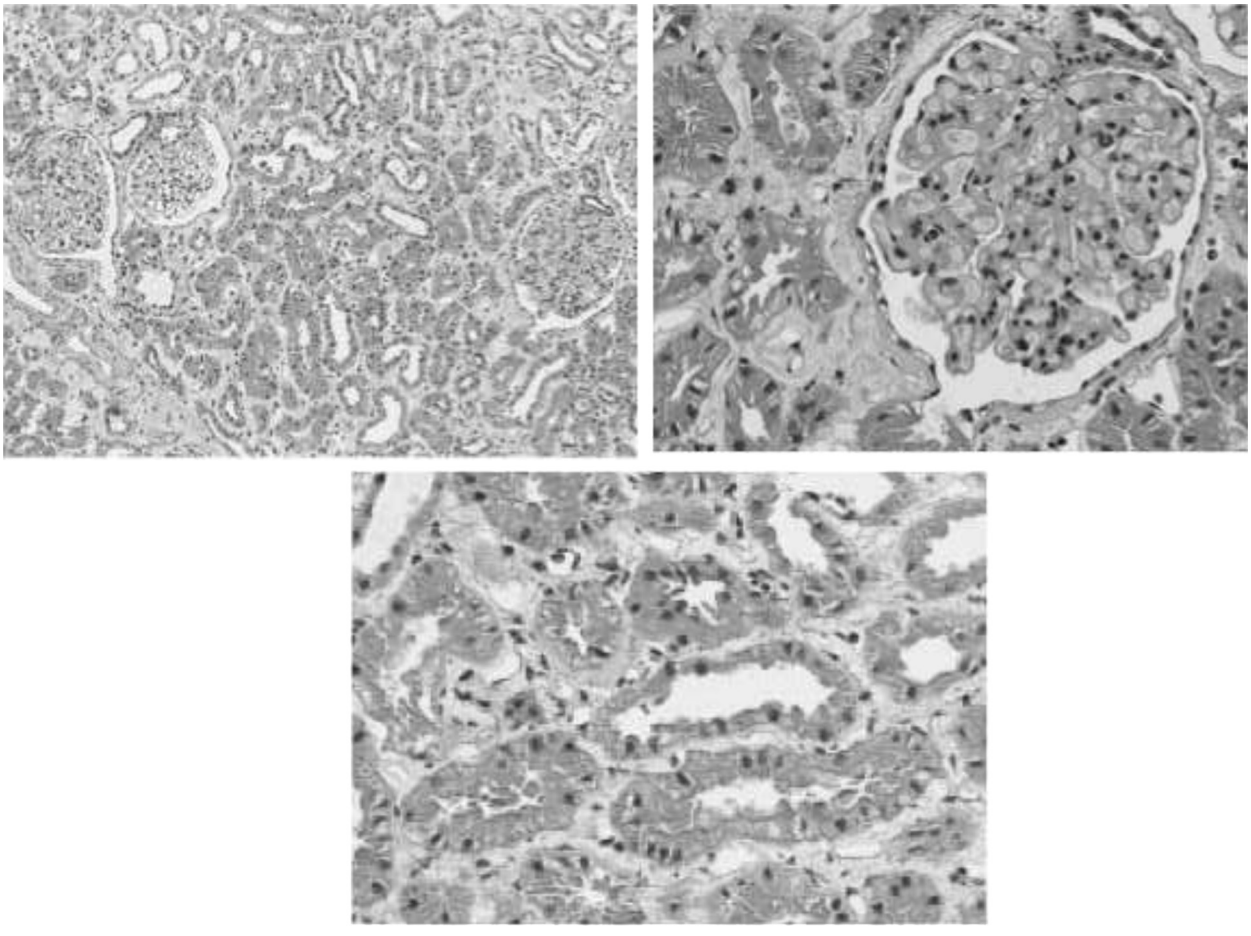

Fig 2. Microscopic section of needle biopsy specimen on postoperative day (POD) 34. Pathologic findings showed no evidence of acute rejection but mild tubulointerstitial injury. (Stain: Hematoxylin and eosin; original magnification, ×40–×200).

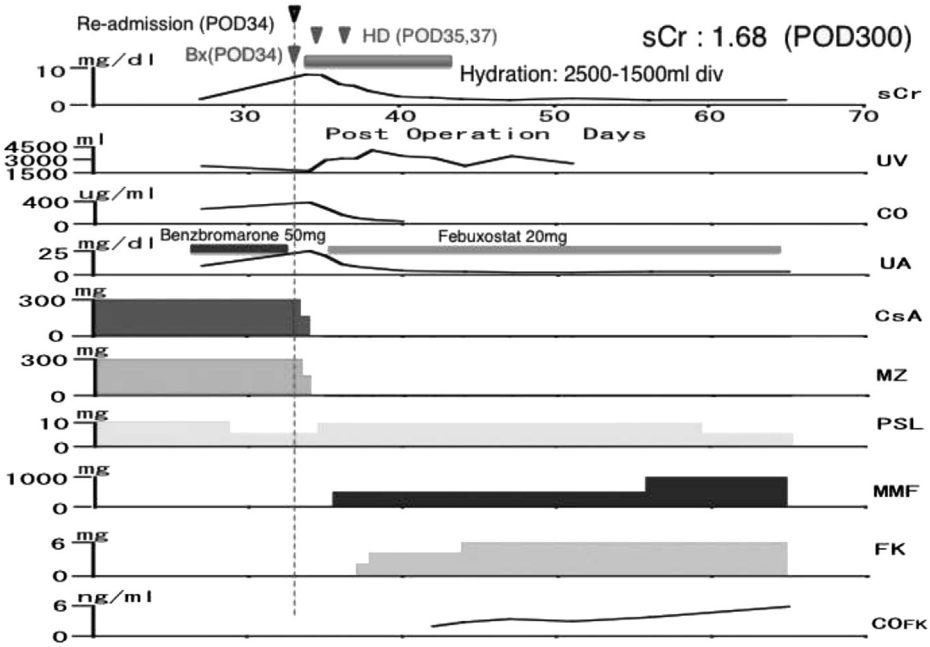

Fig 3. Postoperative course after rehospitalization. He had acute renal dysfunction, serum creatine (sCr) was 8.14 mg/dL, and uric acid was 24.3 mg/dL. He discharged from our hospital on postoperative day 52 and sCr was improved to 1.75 mg/dL.

group Ab reduced IgG to: 32 and, IgM: 4 by double filtration and plasmapheresis (DFPP) and plasma exchange (PE) before the transplantation. After the operation, MMF was switched to high-dose mizoribine (MZ). The postoperative course was uneventful; free of acute rejection episodes or drug toxicity upon a graft biopsy. He was discharged from the hospital on POD 27, with a sCr of 1.47 mg/dL (Fig 1). On POD 34, he visited the outpatient clinic because he noticed tongue numbness. Laboratory examinations showed sCr of 8.14 mg/dL; he was re-hospitalized for a graft biopsy. Ultrasonography of the grafted kidney showed no evidence of hydronephrosis. There was normal blood flow to the graft. Urine examination showed uric acid crystals; the serum uric acid was 24.6 mg/dL. Tubulointerstitial renal injury caused hyperuricemia was highly suspected. CsA trough was 382.4 g/mL. It was high enough to not be a cause of rejection. Pathological findings showed no evidence of acute rejection. Only mild tubulointerstitial injury was found (Fig 2). Tubulointerstitial renal injury causing hyperuricemia was suspected; however, the CsA through concentration was high 382.4 ug/mL.

Hemodialysis was performed twice to reduce the uric acid concentration, diuresis was accompanied by good hydration. CsA/MZ were switched to tacrolimas MMF and Benzbromarone and, to Febuxostat to treat the hyperuric acidemia. On POD 58, the sCr was reduced to 1.75 mg/dL and he was discharged from the hospital (Fig 3). At 14 months after the operation, graft function was stable. The sCr was 1.70 mg/dL. The donor was healthy with a sCr of 1.34 mg/dL.

DISCUSSIONS

High-dose MZ has been reported to be effective for maintenance of immunosuppression in cases of ABO-compatible kidney transplantations.[1] Recently, an high-dose MZ regimen has also been reported to be effective for ABO-incompatible kidney transplantations.[2] We employed an high-dose MZ regimen for ABO-incompatible kidney transplantation in several cases. In the present case, the donor not only had a marginally appropriate age but also mild diabetes and hypertension. Graft function was expected to be relatively poor.[3] Renal hypofunction itself can worsen hyperuricemia which is a common side effect of MZ. Acute renal failure observed after kidney transplantation seemed to be caused by severe hyperuricemia, which created a vicious spiral with the impaired renal function. Previous publications have reported uric acid to contribute to deterioration of glomerular filtration rate in renal transplant cases.[4,5]

Benzbromarone has been utilized to treat and prevent hyperuricemia, but it is not effective to reduce uremic acid. Benzbromarone accelerates excretion of uric acid in patients with appropriate but possibly not those with impaired renal function. In contrast, febuxostat inhibits production of uric acid, so it is effective to reduce uric acid for recipients with relative renal hypo function. Therefore, we switched benzbromarone to febuxostat.

Since we suspected the acute renal failure to be induced by MZ, we believed that there immunosuppressive regimen must be carefully considered in cases employing aged marginal donors. These transplantations require long-term careful observation of both the donor and recipient.

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