Case Report: Hemolytic Anemia Following Deceased Donor Renal Transplantation Associated With Tranexamic Acid Administration for Disseminated Intravascular Coagulation

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ABSTRACT

Background. Long-term outcomes of kidney transplantation with organs from donors with disseminated intravascular coagulation (DIC) are comparable with those from other deceased donors. The use of tranexamic acid to impair fibrinolysis in the treatment of DIC is becoming increasingly frequent, particularly in the trauma setting. However, the effects of tranexamic acid on a transplanted kidney allograft are unknown.

Results. We report 2 cases of kidney transplantation following administration of tranexamic acid to the donor prior to organ donation. Microthrombi were present in the renal allografts. Both recipients experienced clinically significant hemolytic anemia, which typically occurs at a very low frequency.

Conclusions. These cases illustrate a potential concern for the use of tranexamic acid in deceased kidney donors with DIC.

KIDNEYS from donors with central nervous system trauma and/or multiple traumas often have disseminated intravascular coagulation (DIC), which is not uncommonly associated with glomerular microthrombi. Moreover, kidneys from these donors are often transplanted without substantial clinical sequelae. In addition, recent data suggest that donor DIC does not increase the risk of delayed or slow graft function (DGF/SGF). However, when donor DIC is associated with thrombocytopenia, the risk of DGF/SGF is significantly increased [1].

Tranexamic acid is a lysine analogue that suppresses fibrinolysis by inhibiting the proteolytic activity of plasmin (Fig 1) [2]. Tranexamic acid use is becoming increasingly frequent in trauma patients, having being shown to reduce mortality by up to 10% [3]. Further, multiple case reports in the literature demonstrate good outcomes with its use in patients with DIC and severe bleeding resulting from increased fibrinolysis.

Transplantation of kidneys from donors with tranexamic acid–treated DIC has not been reported in the literature. We report experience with 2 deceased donor kidney transplants from a donor with DIC who was treated with tranexamic acid prior to donation. Both donor kidneys demonstrated significant glomerular thrombi and experienced immediate graft function. However, both recipients developed marked thrombocytopenia and hemolytic anemia, and 1 recipient required alterations in immunosuppressive therapy. Experience in this case suggests that tranexamic acid may potentially exacerbate the risk of glomerular microangiopathy-like lesions and hemolytic anemia following kidney transplantation.

CASE REPORT

A 22-year-old, 70-kg Hispanic male multiorgan donor experienced brain death due to a self-inflicted gunshot wound to the head. He had no significant recorded past medical history, and renal function was normal on admission (serum creatinine [SCr], 1.16 mg/dL). Peak SCr level was 1.94 mg/dL (last value recorded prior to organ procurement) and was thought to be due to dehydration, as the final hourly urine output was >200 mL/h (3 mL/kg/h). The donor received epinephrine and norepinephrine infusions to maintain blood pressure, and methylprednisolone, levothyroxine, vasopressin, and desmopressin were administered as routine donor management.

The donor's platelet count decreased from 174×10^9/L at the time of admission to $<30 \times 10^9$/L within 24 hours. Prothrombin time and international normalized ration (INR) (33.9 seconds and 3.5,

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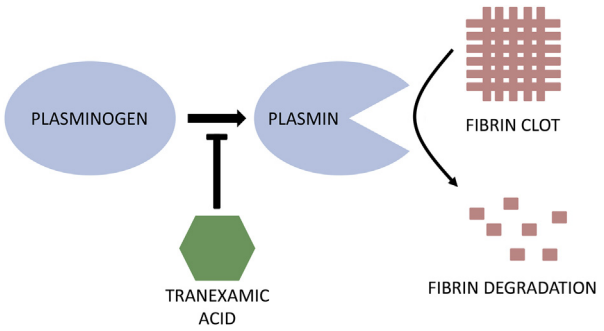

Fig 1. Mechanism of action of tranexamic acid. Tranexamic acid inhibits the activation of plasminogen to plasmin, thereby preventing the degradation of the fibrin clot.

respectively) peaked at 7 hours after admission. Hemoglobin and hematocrit levels decreased to 5.8 g/dL and 17.9%, respectively, and tranexamic acid was given to reduce fibrinolysis and minimize blood loss. Diffuse glomerular fibrin thrombi were observed on both kidney biopsies (performed after donation), involving 50% of glomeruli in the left kidney and 70% of glomeruli in the right kidney with 10%–20% of glomerular capillaries containing fibrin thrombi. Scattered granular casts were seen in the tubes (Fig 2A and B).

The kidneys were flushed in situ with Wisconsin solution and placed on a perfusion pump to evaluate perfusion and assess the effect of the glomerular fibrin thrombi. No evidence of poorly perfused areas were noted visually. Initial parameters on both kidneys revealed low flow rates with elevated resistices: left kidney initial flow rate of 60 mg/min with a resistance of 0.4, and after 1 hour the flow increased to 100 mg/min with a resistance index of 0.24. The right kidney initially had a flow rate of 40 mg/min with a resistance of 0.5, and after 2 hours the flow rate increased to 97 mg/min with a resistance index of 0.3. Donor kidneys were removed from cold perfusion after 4 hours for implantation.

Recipient 1 was a 52-year-old white male with end-stage renal disease (ESRD) due to hypertension (weight, 90.7 kg), who had been on peritoneal dialysis for 51 months. Immunosuppression included alemtuzumab (Campath) 30 mg × 1 dose and a 5-day steroid taper for induction with belatacept (Nulojix) and mycophenolate mofetil (CellCept) 1000 mg orally twice daily for maintenance. Standard thromboprophylaxis with subcutaneous heparin was administered postoperatively.

Recipient 1 received the left kidney and experienced good initial graft function with a decrease in SCr from 15.07 mg/dL to 3.55 mg/dL on postoperative day (POD) 4 when he was discharged from the hospital (Table 1). Post-transplantation the platelet count decreased from 262 × 10^9/L to 93 × 10^9/L on POD 4, but rebounded to 204 × 10^9/L by POD 6. Consistent with thrombocytopenia, the patient's hemoglobin also decreased from 13.3 g/dL at admission to 9.8 g/dL in the first 4 days post-transplantation, which was associated with an undetectable haptoglobin level, and a peripheral smear that demonstrated schistocytes. The hemolytic anemia and thrombocytopenia were, therefore, thought to result from thrombotic microangiopathy secondary to the donor glomerular fibrin thrombi. His course was otherwise uncomplicated, except for deep vein thrombosis of the left popliteal vein diagnosed on POD 40. Three months post-transplantation the patient continues to do well, with stable SCr level of 0.9 mg/dL and platelets of 271 × 10^9/L.

Recipient 2 was a 68-year-old African American female (weight, 63.2 kg) with ESRD due to glomerulonephritis and type 2 diabetes mellitus. The patient underwent transplantation pre-emptively with the right donor kidney and experienced immediate graft function with improvement in SCr level from 3.63 mg/dL pretransplantation to 1.61 mg/dL on POD 1 (Table 2). The immunosuppressive regimen included rabbit anti-thymocyte globulin (rATG; 1.5 mg/kg) × 4 doses and a 5-day steroid taper for induction with belatacept and mycophenolate mofetil 1500 mg orally twice daily for maintenance. The platelet count decreased from 120 × 10^9/L pretransplantation to 50 × 10^9/L on POD 1 with a nadir at 32 × 10^9/L on POD 3. rATG doses were delayed due to thrombocytopenia, however, other immunosuppression was not affected. Platelet count recovered to 86 × 10^9/L by POD 6, when rATG induction was reinitiated. Hemoglobin decreased following transplantation from 8.6 g/dL to 6.1 g/dL on POD 3, and serum haptoglobin levels were undetectable on POD 3 when the peripheral smear also demonstrated schistocytes (Fig 3). The hemolytic anemia and thrombocytopenia were, therefore, thought to be due to a thrombotic microangiopathy secondary to the donor glomerular fibrin thrombi. The patient was discharged home on POD 10, and 3 months post-transplantation renal function was excellent with a SCr level of 0.7 mg/dL and platelets of 262 × 10^9/L.

DISCUSSION

This report describes successful transplantation of kidneys from a donor who was administered tranexamic acid to treat a clinically significant DIC with a hemolytic diathesis. Significant

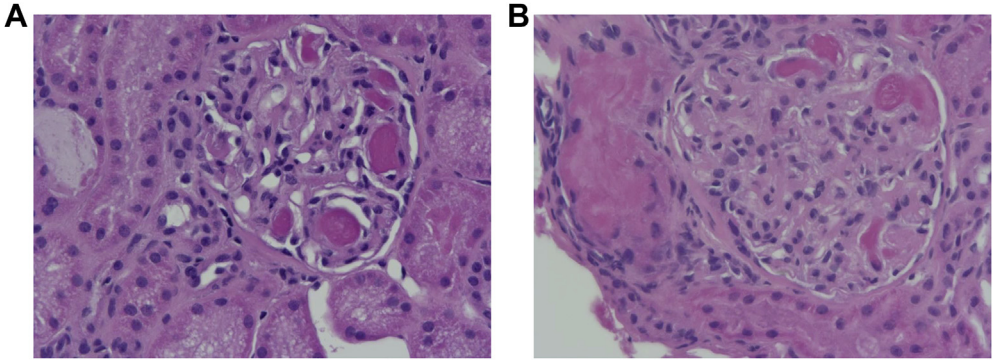

Fig 2. Donor kidney biopsy specimens. (**A**) Left and (**B**) right kidneys demonstrated substantial glomerular thrombi, involving 50% and 70%, respectively, of glomeruli pretransplantation.