Case Report

Renal transplant in a patient of severe hemophilia

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ABSTRACT

Hemophilia is a rare disorder that is difficult to diagnose and manage. The prevalence of end-stage renal disease is increasing in hemophilic patients because of improved life expectancy. Renal transplant surgery in such patients is often complicated by adverse hematological events such as bleeding and intravesical thrombosis, both with a risk of renal allograft rejection. We report a case of a 46-year-old hemophilia A patient on hemodialysis who underwent renal transplant and show that although challenging, renal transplant in hemophilic patients is possible.

INTRODUCTION

Hemophilia A and B are genetic X-linked recessive bleeding disorders caused by mutations in genes encoding factor VIII and IX, respectively.[1] According to NHR statistics, people with hemophilia numbered 21,824, of which 17,606 had hemophilia A.[2] Severity level of hemophilia A was categorized according to residual clotting factor levels: severe with activity <1% and FVIII <0.01 IU/mL, moderate with 1%–5% and FVIII 0.01–0.05 IU/mL, and mild with >5% and FVIII: 0.06–0.40 IU/ml.[3] The prevalence of end-stage renal disease (ESRD) is increasing in hemophilic patients because of improved life expectancy. The associated bleeding risks make renal replacement therapy in hemophilic patients challenging. However, the replacement therapy with factor concentrate using novel dosing methods has made surgical procedures, including renal transplantation, possible.

CASE REPORT

A 46-year-old Indian male weighing 58 kg was diagnosed with severe hemophilia A in 2007 when he was operated for intestinal perforation and developed excessive bleeding. He underwent right nephrectomy in 2013 for pyonephrosis and started taking analgesics. He developed end-stage renal failure in 2019 due to analgesic-induced nephropathy. He presented to us in 2019 for maintenance hemodialysis (HD). On presentation, his factor VIII level was <1% (0.75 IU/ml).

The patient was planned for renal transplant with his wife being the donor. One day before transplant, his activated partial thromboplastin time (APTT) was 99s and prothrombin time/international normalized ratio was normal. On two-dimensional echo, ejection fraction was 40% with moderate mitral regurgitation and left ventricular dysfunction of Grade II. The patient was kept on factor replacement as per the hemophilia protocol.[3,4] Two days before transplant, immunosuppressive induction was done with mycophenolate mofetil (MMF) (720 mg BD) and tacrolimus (2 mg BD). Anti-thymocyte globulin (ATG) and Methylprednisolonewere given for induction on the day of transplant. On the day of transplant, his APTT was 33s and factor VIII level was 93%.

A right lower abdominal Gibson's incision was given, and donor renal vessels were anastomosed to external iliac vessels in an end-to-side manner. The ureter was anastomosed to the bladder over 5-Fr double J (DJ) by

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Lich-Gregor technique. After proper hemostasis, a single abdominal drain was placed. The procedure was uneventful with blood loss of approximately 100 ml.

Recombinant factor VIII was administrated according to the hemophilia protocolfor renal transplant[4], and the patient did not have any bleeding complications. The baseline factor level of the patient was 0.75. Factor VIII replacement was started the day before transplant with 6000 IU in divided dose morning and evening with required factor level 100% in the sample taken 10 min after morning infusion. On the day of surgery, 3000 IU just before surgery and 3000 IU in the evening with required factor level 100% in the sample were taken 10 min after morning infusion. On day 1 again, 6000 IU in divided dose was administered required factor level 100%. On days 2 and 3, a divided dose of 4000 IU with trough factor level 66% in the sample was taken immediately prior to morning dose and day 4–7 a divided dose of 2000 IU with trough factor level 33%. On day 8, dose of 1500 IU and, day 9–12, dose of 1000 IU were administered all in divided dose morning and evening and required trough factor level 15%.

Postoperatively, urine output was 11–12 l in 24 h and was clear. The patient was on double dose Nitroglycerin at 10 ml/h with blood pressure of 170/80 mmHg. Drain output was 50 ml and was serous. Postoperative ATG was given on day 1 and day 3. MMF, Tacrolimus , and Prednisolone were given as oral immunosuppressant in postoperative period. Abdominal drain was removed on the 3rd postoperative day, Foley catheter on the 4th postoperative day, and DJ stent on 9th postoperative day.

The patient was discharged under stable condition with no hematuria or proteinuria and normal serum creatinine. At present, the patient is on regular follow-up with 5 months posttransplant. The graft is functioning well, measured with respect to serial serum creatinine level and urine output. No bleeding episode encountered during this follow-up period.

DISCUSSION

Hemophilia is a rare disorder that is difficult to diagnose and manage. Renal transplant surgery in such patients is often complicated by adverse hematological events such as bleeding and intravesical thrombosis, both with a risk of renal allograft rejection.

Due to improved life expectancy of hemophilic patients, aging-related diseases such as diabetes, hypertension, cancer, and chronic infections are emerging as new challenges.[5] Among chronic diseases, renal diseases are a major issue of concern and slowly progress to ESRD requiring RRT initiation. Because of high bleeding tendency, the choice of renal replacement modality and placement of intravascular accesses are particularly important. Both peritoneal dialysis (PD) and extracorporeal hemodialysis (HD) have been reported in hemophilic patients.[6]

In our patient, different conditions, i.e., nephrectomy, use of nephrotoxic drugs (analgesics), and sepsis-induced AKI, coexisted, ultimately leading to the development of chronic kidney disease.

PD is considered the treatment of choice in patients affected by coagulopathy due to reduced risk of bleeding and nonrequirement of coagulation factor infusions after treatment.[7] In our patient, considering the previous history of major abdominal surgery (which is one of the most important contraindications to PD) and infections, we opted for HD.

After the treatment has been chosen, placement of dialysis access is mandatory. While venous catheter is considered only a temporary access, arteriovenous fistula is thought to be the optimal permanent access.[8]

Limited data exist with renal transplant done in these rare bleeding disorders.

Gompers *et al*.[9] performed a cadaver transplant in a 15-year age hemophilic patient. Postoperatively, massive intravesical hemorrhage complicated the case and graft rejection occurred 3 months postoperatively. They did the second cadaveric transplant in the same patient at 23 years of age, again complicated by massive intravesical hemorrhage, but the graft survived 27 months of follow-up.

Koene *et al*.[10] also performed renal transplant in a patient with severe hemophilia A after 1 year of uneventful dialysis. There was no rejection and no postoperative bleeding. The patient postoperative factor requirement was unchanged; hence, they concluded that the kidney does not contribute to clotting factors.

El Bakkouri *et al*.[11] in a case report of renal transplant in a hemophilic patient, concluded that surgical intervention is possible with good factor replacement with no bleeding and rejection.

Our experience, together with those previously reported, demonstrates that, although challenging, renal transplant in hemophilic patients is possible.

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