Parvovirus-related anaemia and thrombotic microangiopathy in a renal transplant recipient

Prabhu Kanchi, Ankur Gupta, SE Dhanasegaran, Kaniyappan Nambiyar, Ashwani Kumar

A 35-year-old female renal allograft recipient presented with sudden onset of anaemia six months post-transplant. Her native renal disease was CKDu (chronic kidney disease of unknown etiology). Her native kidneys were never biopsied as she presented late with end-stage renal disease and shrunken kidneys. Prior to her transplant, she was on hemodialysis for three years and her dialysis period was uneventful with respect to haematology aspects. She was on intravenous darbepoetin on dialysis. Post-transplant, her graft function was good with serum creatinine of 97µmol/L and haemoglobin of 110g/L on prednisolone 5mg/day, tacrolimus 3mg/day and mycophenolate mofetil.

Figure 1: A: Bone marrow trephine biopsy reveals mildly hypocellular marrow for the age (haematoxylin and eosin, 50X), B: There is paucity of erythroid precursors with few giant proerythroblasts (arrow heads) in the bone marrow. No intranuclear viral inclusion is noted. Occasional focus of lymphoid aggregate is also seen (arrow) (haematoxylin and eosin, 400X), C: Thickened glomerular capillary wall and focal interstitial fibrosis are noted (haematoxylin and eosin, 200X), D: Glomerulus shows closed glomerular capillary lumen and appear ‘bloodless’. Intraluminal thrombi are also present in the glomerulus. An arteriole shows luminal narrow due to endothelial swelling (arrow) (haematoxylin and eosin, 400X).
mofetil (MMF) 1,500mg/day. The other medications were ranitidine and sulfamethoxazole-trimethoprim prophylaxis.

Six months post-transplant, she presented in outpatient clinic with weakness and lethargy for a week. She denied any history of fever, cough, sputum, bleeding, vomiting, diarrhoea, any sick contacts or over-the-counter medications. Examination showed marked pallor, temperature 36.8°C, respiratory rate 16/min, pulse 90/min and blood pressure 110/68mmHg. There was no edema or rash. Cardiac auscultation revealed a grade 3 systolic murmur most prominent over left upper sternal border. Chest, abdominal and neurological examinations were normal. Investigations done a week prior to clinic visit showed haemoglobin of 50g/L, leucocyte count 9.2 x10^9/L with normal differentials, platelet count of 230 x10^9/L, serum urea 8mmol/L, serum creatinine 124µmol/L, normal plasma glucose, electrolytes and liver function tests. Urine did not show protein or red cells. Peripheral blood film did not show any evidence of red blood cell fragmentation. Coagulation profile, serum lactate dehydrogenase, haptoglobin, CMV polymerase chain reaction (PCR) and antinuclear antibody were normal. Fecal occult blood was negative. She underwent a bone marrow examination and was transfused four units of leukodepleted packed red cells.

Her bone marrow biopsy showed marked erythroid hypoplasia and occasional giant proerythroblasts with relative myeloid predominance. (Figures 1A and B) Meanwhile, her qualitative blood PCR for parvovirus B19 came back as positive. Serum creatinine further worsened to 194µmol/L and a renal graft biopsy was done which revealed thrombotic microangiopathy (TMA). (Figures 1C and D) There were no features of acute rejection or any chronicity. The renal biopsy was positive for Parvovirus B19 DNA by nested PCR. She was treated with five-day course of intravenous immunoglobulin (IvIG) 400mg/kg/day with reduction of MMF to 500mg/day. Her haemoglobin improved to 100g/L and her serum creatinine decreased to 106µmol/L and remained stable at four months of follow-up.

**Figure 2:** Timeline depicting hemoglobin trend after intravenous immunoglobulin therapy (Hb: hemoglobin, PRBC: packed red blood cells, IvIG: intravenous immunoglobulin).
Discussion
Renal transplant patients can develop symptomatic Parvovirus B19 infections as a result of primary infection acquired via the usual respiratory route or via the transplanted organ, or because of reactivation of latent or persistent viral infection. The common manifestations include pure red cell aplasia and/or other cytopenias, though collapsing glomerulopathy and TMA have also been reported.1,2

TMA can occur as a recurrence of the disease involving the native kidney or as de novo disease.3 The common precipitating factors include immunosuppressives like calcineurin inhibitors or mTOR inhibitors, antibody mediated rejection, viruses like CMV, HCV, Parvovirus, etc and genetic abnormalities in the complement cascade. TMA manifestations are quite variable and can vary from a limited form confined to the kidney to a full-blown systemic variant. Our patient had a renal-limited form suggested by absence of hemolysis in the peripheral blood film and normal platelet counts.

The diagnosis of Parvovirus B19 requires confirmation by PCR. The diagnosis may be missed, especially in immunosuppressed patients, when only antibody levels are measured.4 Parvovirus B19 produces lysis of proerythroblast through the P antigen, a receptor present in erythroid cells and glomerular endothelial cells. This results in endothelial cell dysfunction/cell death, leading to capillary thrombosis and glomerular death. This is the plausible mechanism of TMA5,6 supporting the hypothesis of B19 as a uniform common diagnosis involving bone marrow and kidney in our case.

IvIG is an important source of anti-Parvovirus 19 antibodies providing passive immunity.7,8 Our patient responded well to this treatment along with reduction of MMF. The long-term effect of Parvovirus on renal functions are still unknown. Moreover, the relatively low incidence of this infection make donor/recipient screening for this virus not worthwhile.

Our case highlights the importance of high index of suspicion for diagnosing B19 infection. A timely diagnosis along with IvIG and reduction in immunosuppression helped in achieving base-line renal functions and resolution of anaemia in our case. The treating physician should be vigilant enough to keep this possibility in an immunocompromised patient presenting with anaemia and acute kidney injury.

Competing interests:
Nil.

Author information:
Prabhu Kanchi, Consultant Nephrology, GEM Hospital, Chennai, India; Ankur Gupta, Fellow Nephrology, The Ottawa Hospital, University of Ottawa, Ottawa, Canada; SE Dhanasegaran, Senior Consultant Nephrology, Bilroth Hospital, Chennai, India; Kaniyappan Nambiyar, Senior Resident Histopathology, PGIMER, Chandigarh, India; Ashwani Kumar, ICMR-Post-doctoral Research Associate, PGIMER, Chandigarh, India.

Corresponding author:
Dr Ankur Gupta, Division of Nephrology, The Ottawa Hospital, 1967 Riverside Drive, K1H 7W9, Ottawa, ON, Canada.
parthankur@yahoo.com

URL:
REFERENCES:


