Title

Atraumatic splenic rupture following IVlg for parvovirus B19 pure red cell aplasia post renal transplant

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Running title

Splenic rupture post parvovirus B19

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Introduction

Parvovirus B19 (PB19) infection is an uncommon but well reported cause of anemia in solid organ transplant recipients. Persistent cases may be treated with intravenous immunoglobulin (IVIg). We report a case of PB19 associated anemia in a renal transplant recipient who subsequently developed an atraumatic splenic rupture after administration of IVIg. Histological examination of the spleen after splenectomy showed evidence of previous extramedullary erythropoiesis (EMH) with the unusual finding of parvovirus infected cells.

Case

A 58-year-old male presented with progressive anemia 6 months after receiving his second allogenic renal transplant. He had achieved excellent graft function on standard doses of immunosuppression. He had received his first transplant 21 years prior, which had been viable for 18 years. His original renal pathology was an unspecified chronic glomerulonephritis.

He then developed progressive anemia (hemoglobin nadir 57 g/L) requiring significant transfusion support. He was iron replete with no abnormalities on hematinic screen. The anemia did not respond to reduction in myelosuppressive medications nor a trial of supplementary erythropoiesis stimulating agents.

Further hematological investigation demonstrated a suppressed reticulocytosis (nadir $1.9 \times 10^9/L$) with preserved platelet, myeloid and lymphoid lines, consistent with pure red cell aplasia (PRCA). Plasma cytomegalovirus PCR was negative but PB19 IgM was equivocal with negative IgG serology. Subsequent qualitative serum parvovirus B19 (PB19) PCR was positive. Bone marrow aspirate (Image 1A) and trephine (Image 1B) showed virtually absent

mature erythroblasts with the presence of abnormal giant proerythroblasts (arrows) consistent with a diagnosis of PB19 associated PRCA. Immunoperoxidase staining and in situ hybridization for PB19 were not used as they were not readily available and the clinical picture and morphological findings on histopathology were felt to be conclusive for PB19 associated PRCA.

The patient remained anemic despite reductions in immunosuppression and required substantive erythrocyte transfusions. He subsequently received pooled IVIg infusion (2g/kg in two divided doses, 3 days apart). Following treatment there was rapid recovery of his reticulocyte counts with spontaneous increment in hemoglobin levels. Repeat serum PB19 PCR was negative.

The patient re-presented 1-week after initial IVIg infusion with sudden onset abdominal pain and was found to have a spontaneous splenic hemorrhage on CT (Image 2). The hemorrhage was initially treated conservatively and he was discharged after a period of observation.

Over the following months the patient developed two relapses of PRCA. Both relapses coincided with a recurrence of positivity of PB19 serum PCR on serial testing. Each relapse of anemia responded to repeated treatment with IVIg, and PCR correspondingly returned to negative. The patient was eventually established on maintenance infusions at regular intervals.

Four months after initially presenting with splenic hemorrhage, an interval splenectomy was performed due to concerns of a potential underlying anatomical splenic abnormality and perceived risk of recurrent spontaneous rupture. The surgical specimen demonstrated splenic hematoma with surrounding normal splenic architecture. Within the hematoma there was hemosiderin (in keeping with past hemorrhage) and EMH in which there were giant proerythroblasts. These cells were identical to the PB19 affected cells originally seen in the bone marrow (arrows; Image 1C). The patient made an uneventful recovery from splenectomy and continues to receive regular IVIg maintenance treatment.

Comments

The initial components of this case are not common but are well described in solid organ transplant recipients. PRCA is a rare cause of profound anemia, characterized by severe reduction in the number of reticulocytes and erythroid precursors, but preservation of other cell lineages. The mechanism through which PB19 infection may cause PRCA is unclear, but spontaneous resolution is generally expected. Protracted anemia, caused by chronic infection, may occur in immunosuppressed hosts and may be treated with IVIg.¹

The subsequent atraumatic splenic rupture is a more remarkable aspect of this case, and the underlying etiology is less clear. This presentation involved a constellation of highly atypical features, making it difficult to discern the underlying process involved. There was an apparent temporal relationship between the splenic rupture and between the initial parvovirus infection, its treatment with IVIg and the subsequent restoration of normal erythropoiesis. However, we have been unable definitely to establish a causal relationship between any of these processes, particularly given the absence of any previously described comparable cases.

IVIg administration itself may trigger splenic sequestration of red-cells, but has only previously been associated with splenic rupture in association with primary cytomegalovirus infection.² Parvovirus infection has rarely been associated with splenic erythrocyte sequestration, but usually only in children with underlying sickle cell disease and this presentation is not associated with splenic rupture.³ In our patient, EMH was also seen within the spleen. While EMH may cause splenic enlargement, even in cases of massive splenomegaly, this does not usually lead to splenic rupture in isolation.⁴

The discovery of PB19 affected proerythroblasts within an area of splenic hemorrhage and extramedullary erythropoiesis is perhaps the most fascinating aspect of this case. Giant proerythroblasts are usually only reported when examining the bone marrow of patients with PB19 associated PRCA, although the spleen is not routinely examined in such cases. While giant proerythroblasts have previously been described in EMH in neonates, to the best of our knowledge, this has never been documented in an adult patient.^{5,6}

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Author Contribution Statement

All authors were involved in the care of this patient and contributed to the drafting and final approval of this work.

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