
CASE SERIES**Parvovirus B 19 associated cytopenia in immunocompromised patients***Monica Puri¹, Gaurvi Piplani¹, Chhagan Bihari¹, Viniyendra Pamecha²**¹Department of Clinical Hematology, ²Liver Transplant Surgery, Institute of Liver and Biliary Sciences, New Delhi-110070 (Delhi) India*

Abstract

Parvovirus B19 (PVB19) infection is a significant yet overlooked cause of cytopenia in recipients of solid organ transplant. PVB19 can cause persistent infection due to poor viral clearance during immunosuppressive medication, with symptoms often presenting as refractory anemia or pure red cell aplasia. Diagnosis is frequently delayed because post-transplant anemia is common and standard screening for PVB19 is not done. The existing literature is primarily limited to a few case reports, with only a few series documenting the clinical spectrum among several solid organ transplants. This case series explores the presentation, diagnostic characteristics, and therapy of PVB19 infection in kidney and liver transplant recipients, emphasising the need for improved clinical vigilance in patients with unexplained cytopenias. Parvovirus B19 infection is a significant and frequently neglected cause of severe anaemia and pancytopenia in chronic liver illness and solid organ transplantation. Increased clinical awareness and timely pharmacological intervention, could considerably improve patient outcomes.

Keywords: Parvovirus B19, Solid organ transplant, Pure red cell aplasia, Immunosuppression, Intravenous immunoglobulin

Introduction

Parvovirus B19 (PVB19) is a non-enveloped, small deoxyribonucleic acid virus of the Parvo-viridae family (genus Erythroparvovirus) with a selective tropism for human erythroid progenitor cells, mediated by the blood group P-antigen. Transmission occurs via infected blood products, respiratory droplets and vertical routes. Seroprevalence studies show that 60-90% of persons have had previous exposure. Diagnosis relies on bone marrow examination, which characteristically demonstrates giant proerythroblasts with intranuclear inclusions, serology, and Polymerase Chain Reaction (PCR) [1-4]. In immunocompetent people, infection is typically self-limiting, manifesting as erythema infectiosum in children or arthropathy in adults. However, in immunocompromised hosts, particularly solid-organ transplant patients may develop chronic infection, resulting in serious clinical implications [1,5].

PVB19 is most typically seen in transplant recipients as chronic or refractory anemia, including pure red cell aplasia, because of poor virus clearance due to immunosuppressive medication. Additional manifestations include hepatitis, myocarditis, pneumonitis, vasculitis, and allograft failure. Despite these potential problems, PVB19 infection is often undiagnosed in the post-transplant context because anemia is common and routine viral surveillance is not undertaken. Molecular investigations have showed that the frequency of PVB19 infection in recipients of kidney transplant with anemia could be higher than previously thought [1,3,6]. The literature on PVB19 infection in transplant patients is mostly limited to single case reports, with just a few case series documenting the clinical spectrum across several solid-organ transplants. We present a case series of 12 patients with confirmed PVB19 infection, including kidney

and liver transplant recipients, to demonstrate their clinical features, laboratory findings, management strategies, and outcomes, as well as to highlight the importance of considering PVB19 when evaluating unexplained cytopenia in this population.

Case Series

Case 1

A 12-year-old male, known case of decompensated Chronic Liver Disease (CLD) due to progressive familial intrahepatic cholestasis 3, presented with high grade fever, abdominal pain, and distension for 2 days. On physical examination, developmental milestones were appropriate for the age [weight: 30.8 kg (5th percentile); height: 147 cm (50th percentile)]. Diagnostic and therapeutic ascitic tap was done. The laboratory parameters showed severe pancytopenia with hemoglobin of 9.1 g/dL, Total Leucocyte Count (TLC) $0.8 \times 10^3/\mu\text{L}$, and platelets $34 \times 10^3/\mu\text{L}$. Quantiferon-TB Gold (Gamma Interferon) turned out positive, and antitubercular treatment was initiated with intravenous amikacin, oral levofloxacin, and ethambutol. Bone marrow examination was done in view of severe pancytopenia, which revealed hypocellular marrow with erythroid suppression and was advised PVB19 serology. PVB19 IgM antibody was positive and confirmed active infection. The patient was managed with administration of intravenous fluids, supportive and nutritional care, with regular follow-up at the pediatric hepatology clinic. On follow-up, he had a liver transplant in December 2015 for CLD and was kept on immunosuppression with prednisolone and tacrolimus, with a positive clinical outcome.

Case 2

A 43-year-old male with ethanol-induced CLD underwent liver transplantation in August 2025. His

post-transplant treatment was complicated by biopsy-proven acute cellular rejection, biliary anastomotic stricture requiring balloon dilatation and bilateral percutaneous transhepatic biliary drainage (PTBD), and a relaparotomy for purulent peritonitis.

He presented with upper Gastrointestinal (GI) bleed, sepsis-like symptoms, jaundice, and abdominal distension. On examination, he had tachycardia, hypotension, and ascites. The laboratory results indicated hemoglobin of 9.3 g/dL, TLC $11.9 \times 10^3/\mu\text{L}$, platelets $102 \times 10^3/\mu\text{L}$, total bilirubin 32.3 mg/dL, aspartate aminotransferase/ alanine aminotransferase (AST/ALT) 132/110 IU/L, and serum creatinine 1.34 mg/dL. He underwent upper GI endoscopy and hemo-clip application was done. *Klebsiella pneumoniae* was detected in both blood PTBD cultures, and cytomegalovirus IgM was reactive. Bone marrow examination revealed maturation arrest at pronormoblastic stage with intranuclear viral inclusion, suggestive of parvo-virus infection and the same was confirmed by PVB19 IgM. Despite receiving Intravenous Immunoglobulin (IVIG), broad-spectrum antibiotics, antivirals, transfusions, and supportive care, the patient died due to multiorgan failure and refractory septic shock.

Case 3

A 48-year-old male with a 20-year history of chronic ethanol use was diagnosed with CLD in 2012 after presenting with ascites. He experienced recurrent decompensation, followed by acute kidney injury, requiring diuretic modifications. The patient presented with severe anemia (hemoglobin 4.1 g/dL) and thrombocytopenia (platelets $79 \times 10^3/\mu\text{L}$) with reticulocyte count of 11.02%. The peripheral blood smear revealed target cells,

schistocytes, and significant anisopoikilocytosis. Direct antiglobulin test was strongly positive (4+), which is consistent with warm autoimmune hemolytic anemia. Bone marrow aspirate and biopsy revealed few giant pronormoblasts with focal cytoplasmic blebs and intranuclear inclusions—likely parvo-virus infection and the same was confirmed by PCR for PVB19. He was treated with IVIG (400 mg/kg/day for 5 days), rituximab, and oral prednisolone (40 mg/day), and his hemoglobin level stabilized at 7-8 g/dL and discharged.

Case 4

A 32-year-old male, post-kidney transplant, presented with a three-day history of fever and maculo-papular cutaneous lesions over trunk. Laboratory assessment revealed severe anemia, with a hemoglobin level of 5.2 g/dL, TLC ($9.7 \times 10^3/\mu\text{L}$) and platelet count ($286 \times 10^3/\mu\text{L}$). Iron profile, peripheral blood smear and reticulocyte count was suggestive of hypoproliferative anemia. Bone marrow examination showed significant erythroid suppression, and advised PVB19 serology. PVB19 PCR was positive. The skin biopsy findings were consistent with dermatomycosis. Immunosuppression was modified, Mycophenolate Mofetil (MMF) was stopped, and supportive management included a low-sodium diet, avoidance of nephrotoxic drugs, and tailored fluid intake. The patient was treated with oral terbinafine, erythropoietin (5,000 IU subcutaneously twice weekly), and supportive medications, and was discharged.

Case 5

An 18-year-old male presented with pain in abdomen and progressive jaundice for 20 days. On examination, hepatosplenomegaly was present. Laboratory parameters showed anemia (hemoglobin 7.1 g/dL),

TLC ($9.0 \times 10^3/\mu\text{L}$), and platelet count of $187 \times 10^3/\mu\text{L}$. Peripheral blood smear revealed severe anisopoikilocytosis, schistocytes and nucleated RBCs, suggestive of hemolysis. Hemoglobin electrophoresis was sent and revealed thalassemia trait. Bone marrow examination showed erythroid hyperplasia with maturation arrest and intranuclear viral inclusion likely PVB19 and the same was confirmed by PVB19 IgM. The patient was managed conservatively with a high-protein, low-salt diet, folic acid supplements, hepatoprotective supplements, and multivitamins, with a planned follow-up after two weeks.

Case 6

A 2-year-10-month-old male child presented with progressive ecchymotic skin lesions over multiple sites from 2 weeks. Child also appeared pale to the parents. He had a history of resolved acute liver failure three months back. Child was born out of non-consanguineous marriage. Antenatal and birth history was uneventful and the child was immunised as per scheduled. Laboratory evaluation demonstrated pancytopenia with hemoglobin 5.6 g/dL, TLC $3.09 \times 10^3/\mu\text{L}$, and platelet count $40 \times 10^3/\mu\text{L}$. Liver function tests were near normal at the time of admission. Bone marrow aspiration was hemodiluted and biopsy demonstrated intranuclear viral inclusions in erythroid series, suggestive of PVB19 infection, subsequently confirmed by PCR. During hospitalization, the child developed generalized seizures followed by pulmonary hemorrhage and cardiac arrest. Despite resuscitative efforts and intensive care support, the child could not be revived and was declared deceased.

Case 7

A 55 years old male, two months post deceased donor liver transplant for decompensated cirrhosis,

presented with four days of high-grade fever, oliguria and a generalized macular rash over the face and extremities. He was on triple immunosuppression regimen consisting of tacrolimus, MMF, and steroids, alongside prophylactic valganciclovir. Physical examination revealed oral ulcers and a diffuse macular exanthema suggesting clinical suspicion for drug induced eruption or Graft-Versus-Host Disease (GVHD). Initial hematological evaluation revealed life-threatening pancytopenia, (hemoglobin 7.4 g/dL, TLC $90 \times 10^3/\mu\text{L}$, platelet $43 \times 10^3/\mu\text{L}$) and acute kidney injury (serum creatinine- 2.30 mg/dL). Peripheral blood smear showed normocytic normochromic erythrocytes with marked leukopenia and moderate thrombocytopenia. Bone marrow aspirate and trephine biopsy demonstrated marked hypocellularity (5%) replaced by fat cells, secondary hemophagocytosis, and pathognomonic giant proerythroblasts with intranuclear inclusions (Figure-1- D). While screens for sepsis and common viruses [Cytomegalovirus (CMV), Epstein Barr Virus (EBV), hepatitis B/C virus) were negative, PCR confirmed PVB19-induced marrow exhaustion. Severe renal impairment precluded IVIG therapy. Management included MMF withdrawal and supportive care (IV fluids, G-CSF); however, fever and pancytopenia persisted. Due to potential GVHD overlap and the need for specialized hematological salvage therapy, the patient was transferred to a tertiary center.

Case 8

A 45 years old male with ethanol-related CLD (MELD-Na 22) underwent an elective living donor liver transplant in December 2022. The intraoperative course was uneventful, with a graft-to-recipient weight ratio of 0.81. His recovery was complicated on post op day 11 by fever and refractory anemia requiring frequent transfusions, despite a stable

graft and no visible bleeding. Hematological evaluation for refractory anemia revealed bicytopenia (hemoglobin 8.2 g/dL, platelet count $79 \times 10^3/\mu\text{L}$) with microcytic hypochromic anemia, moderate anisocytosis, lymphopenia, thrombocytopenia, and a low reticulocyte count (0.54%), consistent with hypoproliferative anemia. Iron studies showed reduced total iron binding capacity with markedly elevated ferritin levels (920 $\mu\text{g/L}$). CMV testing was negative. Bone marrow aspiration and biopsy demonstrated marked erythroid suppression with numerous giant proerythroblasts exhibiting characteristic intranuclear inclusions, suggestive of PVB19 infection. Molecular testing revealed a high viral load of 10^6 copies/mL. Klebsiella-positive intra-abdominal collections were treated with percutaneous drainage and targeted antibiotics, Parvovirus B19-induced marrow suppression was managed conservatively.

Immunosuppression was carefully titrated using daily liver function. The patient's clinical status stabilized and was discharged afebrile, with a healthy surgical wound and resolving liver function.

Case 9

A 16-year-old male, status post living donor liver transplantation (September 2017) for acute liver failure, presented with a 15-day history of progressive fatigue, anorexia, and exertional dyspnea. His post-transplant course was complicated by three episodes of acute cellular rejection requiring triple immunosuppression with tacrolimus, MMF, and prednisolone. Clinical examination revealed marked pallor. Hemoglobin declined rapidly from 13.4 to 4.9 g/dL over three months with reticulocytopenia (1%) and elevated ferritin (536 ng/mL), despite normal iron and vitamin B12 levels. Stool for occult blood were negative. Rising creatinine suggested acute kidney injury.

Differentials included immunosuppressant-induced myelosuppression, renal anemia, and viral associated pure red cell aplasia. Viral evaluation showed negative EBV and CMV-deoxyribonucleic acid PCR. Bone marrow examination (January 17, 2020) revealed a hypocellular marrow with selective, marked erythroid suppression suggestive of PVB19 infestation and was confirmed by molecular testing (PCR). Immunosuppression was temporarily withheld, and the patient was managed with packed red blood cell transfusions and recombinant erythropoietin. This case underscores the diagnostic and therapeutic challenges of refractory anemia in heavily immunosuppressed pediatric transplant recipients, with PVB19 as a key precipitant of acute hematopoietic failure.

Case 10

A 52-year-old male with non-alcoholic steatohepatitis-related CLD, type 2 diabetes mellitus, diabetic neuropathy, and transfusion-dependent anemia presented with progressive abdominal distension, bilateral pedal edema, and significant fatigue. He had severe anemia (hemoglobin 3.9 g/dL), acute-on-chronic kidney injury (serum creatinine 5.29 mg/dL), and decompensated cirrhosis (hepatic venous pressure gradient 20 mmHg). Hematological evaluation showed a complex anemia, with iron studies indicating deficiency (transferrin saturation 10.9%) but anemia severity disproportionate, necessitating repeated transfusions. Despite erythropoietin and supportive therapy, hemoglobin continued to decline, raising suspicion for viral-induced marrow suppression.

Bone marrow examination showed hypocellularity with erythroid suppression with possibility of PVB19 infestation and PCR confirmed PVB19 as

the primary cause of marrow failure and hematologic instability. The clinical course was complicated by chronic kidney disease requiring multiple sessions of hemodialysis. Upper gastrointestinal endoscopy demonstrated severe portal hypertensive gastropathy and gastric antral vascular ectasia, managed with argon plasma coagulation. Despite advanced multisystem involvement and poor prognosis related to concurrent PVB19 infection and renal failure, the patient was stabilized through multidisciplinary nephrology and hepatology care and discharged hemodynamically stable at family request for home-based palliative support.

Case 11

A 13-year-old male child was diagnosed as CLD with pancytopenia with increased transaminases under evaluation, presented with fever, yellowish discoloration, pallor, and abdominal distension. Hemogram showed pancytopenia (hemoglobin-8.0 g/dl, TLC $1.0 \times 10^3/\mu\text{L}$ and platelet count- $44 \times 10^3/\mu\text{L}$).

His peripheral smear revealed normocytic normochromic anemia, leukopenia, and moderate thrombocytopenia. His kidney function analysis showed serum bilirubin -28 mg/dl, serum creatinine-0.3 mg/dl, urea- 29 mg/dl. His coagulation profile was normal with INR- 1.08. His liver function tests revealed AST-1046 IU/L, ALT-1012 IU/L, and serum albumin levels-2.3 g/dl. Bone marrow examination showed hypocellular marrow replaced by fat cells, presence of few giant pronormoblasts along with presence of cytoplasmic blebs and intra-nuclear inclusions in few erythroblasts suggestive of PVB19. The diagnosis was of PVB19 was confirmed by qualitative PCR testing. The patient was managed with intravenous colloid therapy, supportive care, multivitamins, and

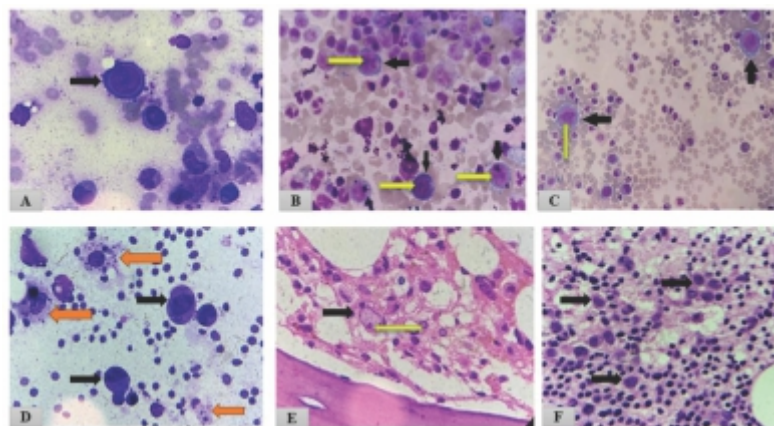
diuretics as required and was discharged with improving blood parameters.

Case 12

A 61-year-old male was a known case of type 2 diabetes mellitus, hypertension, chronic kidney disease with acute kidney injury requiring hemodialysis. He presented with abdominal distension, loose stools and losing weight. His radiological findings revealed moderate ascites with bilateral pleural effusion. Complete blood count showed bicytopenia (hemoglobin-8.2 g/dl, TLC $4.5 \times 10^3/\mu\text{L}$ and platelet count- $143 \times 10^3/\mu\text{L}$). His peripheral smear revealed normocytic normochromic RBC picture and mild thrombocytopenia. His kidney function analysis showed serum creatinine- 8.3 mg/dl, and urea- 121 mg/dl. His coagulation profile was normal with INR- 1.02. His liver function test revealed AST-26 IU/L, ALT-37 IU/L, and serum albumin level was 2.2 g/dl. Bone marrow aspirate and biopsy revealed megaloblastic erythroid hyperplasia with nuclear inclusions, suggestive of PVB19. The diagnosis of PVB19 was confirmed by qualitative PCR testing. The patient was managed with intravenous albumin, hemodialysis, supportive care, and was discharged with improving blood parameters.

Figure 1: Microscopic demonstration of Parvo virus B19 on bone marrow aspirate and biopsy.

A) Bone marrow aspirate- Giant pronormoblast showing cytoplasmic blebs and intranuclear viral inclusion ((black arrow) (Oil immersion view) (Giemsa stain). B) Giant pronormoblast showing cytoplasmic blebs (black arrow) and intranuclear viral inclusion (Yellow arrow) (Oil immersion view) (Giemsa stain). C) Giant pronormoblast showing cytoplasmic blebs (black arrow) and intranuclear viral inclusion (Yellow arrow) (Oil immersion view) (Giemsa stain). D) Bone marrow aspirate- Giant pronormoblast showing cytoplasmic blebs and intranuclear viral inclusion (black arrow), with Hemophagocytosis of erythroid, band forms (orange arrow) (Oil immersion view) (Giemsa stain). E) Bone marrow biopsy- Giant pronormoblast showing cytoplasmic blebs (black arrow) and intranuclear viral inclusion (Yellow arrow) (Oil immersion image) (Hematoxylin & Eosin stain). F) Bone marrow biopsy- Giant pronormoblast showing cytoplasmic blebs and intranuclear viral inclusion (black arrow) (Oil immersion image) (Hematoxylin & Eosin stain)



Discussion

PVB19 infection is an important but frequently undetected cause of cytopenia in patients with chronic liver illness and solid organ transplantation. The virus selectively targets erythroid progenitor cells via the P antigen receptor, resulting in acute or long-term inhibition of erythropoiesis [7]. In immunodeficient hosts, infection is generally self-limiting; but, in immunocompromised people, inadequate virus clearance can develop to chronic infection with severe and persistent hematological symptoms [2,7]. In the present case series, severe anaemia was the most common clinical characteristic, accompanied by reticulocytopenia and, in some cases, pancytopenia. These findings are consistent with previous studies that identified PVB19 as a major cause of pure red cell aplasia and transfusion-dependent anaemia in transplant recipients [3]. Molecular investigations show that persistent viremia in immunosuppressed patients leads to marrow suppression, which explains the chronicity and severity observed in this population [2].

Compared to large transplant cohorts, current case series has a broader haematological spectrum, including significant pancytopenia and marrow hypocellularity. According to Eid *et al.* (2006) anaemia is the most common indication of PVB19 infection after solid-organ donation, with other haematopoietic lineages being involved less frequently [3]. In contrast, majority of our patients, particularly those on intensive immunosuppression or with severe liver illness, suffered life-threatening multilineage cytopenias. Similar findings have been described in smaller cohorts of immunocompromised patients, implying that long-term viral persistence and immunological instability may extend marrow suppression beyond the erythroid lineage [8].

Bone marrow investigation was critical to the diagnosis. Giant proerythroblasts with intranuclear viral inclusions are a pathognomonic sign, especially in immunocompromised patients when serological responses may be compromised [9]. Molecular confirmation via PCR improved diagnosis accuracy and enabled for distinction from drug-induced myelosuppression, rejection-related cytopenias, and other viral infections typically seen in the post-transplant environment [1-3]. Patients with CLD formed a unique subgroup in our dataset. Cirrhosis-associated immune dysfunction, hypersplenism, and dietary deficits may exacerbate the hematological effects of PVB19 infection, culminating in severe cytopenias that outweigh the severity of the liver disease. While PVB19 is rarely documented in chronic liver illness with few emerging studies suggesting that the virus may contribute considerably to unexplained cytopenia in this population, which is consistent with our observations [10].

The management of PVB19 infection in immunocompromised individuals is not standardised and is mostly determined by illness severity and host immunological status. Supportive treatment and careful lowering of immunosuppressive therapy are the foundation of management and may aid immune-mediated virus clearance [3]. IVIG has been found to be useful in promoting haematological recovery in patients with chronic infections by delivering neutralising antibodies, especially in transplant recipients and other immunocompromised hosts [3,7-8].

Therapeutic response varied among our cases, most likely due to variances in immune reconstitution, viral burden, and associated organ failure. These findings emphasise the need of early detection and

individualised treatment techniques for better outcomes.

Conclusion

PVB19 infection is a significant and frequently neglected cause of severe anaemia and pancytopenia in patients with CLD and solid organ transplantation. It frequently presents as medication

toxicity, rejection, or sepsis-related marrow suppression. Bone marrow examinations and molecular tests are essential for early detection. Increased clinical awareness and timely intervention, such as immunosuppression modification and IVIG therapy, could considerably improve outcomes in this high-risk population.

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