Parovirus B19-induced red cell aplasia in solid-organ transplant recipients. Two case reports and review of the literature

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Abstract

Two solid-organ transplant recipients (one heart and one lung) developed severe anemia with reticulocytopenia. Both were heavily immunosuppressed. Bone marrow aspiration revealed almost complete absence of erythroid precursors. A few giant megaloblastic proerythroblasts with cytoplasmic vacuolisation and intranuclear inclusions were seen. Human parvovirus B19 (B19V)-DNA genome was found by nested-PCR assays in blood and bone marrow samples in both cases. Twelve similar cases are described in the literature. When looked for, B19V DNA was positive either in serum or bone marrow or both. Twelve of the fourteen patients were successfully treated by high dose i.v. immunoglobulin (IVIG). One patient recovered spontaneously and another after treatment with recombinant human erythropoietin (rHu-EPO) only. Transplant patients should be considered at risk for severe erythroblastopenic anemia due to B19V infection. Diagnosis is based on bone marrow examination and detection of B19V DNA by PCR in serum and/or marrow. IVIG is an effective and safe treatment. The role of erythropoietin in this indication needs further study.

Human parvovirus B19 (B19V) is a small, single-stranded DNA virus discovered in 1975. It was subsequently shown to be responsible for transient aplastic crisis in sickle cell anemia [20], erythema infectiosum (fifth disease) [1] and has been directly or indirectly implicated in a number of clinical syndromes reviewed in Heegaard [11].

The pathogenesis of B19V infection can be accounted for by its tropism and direct cytotoxicity for erythroid progenitor cells where B19V bind to blood-group P antigen [3, 23]. Thus, in patients with underlying hemolytic anemias, the infection can produce an aplastic crisis usually resulting in the appearance of specific antibodies. In immunocompetent patients, B19V causes a self-limited illness: in general, this suppression of erythrocyte production does not last more than one to two weeks and is not clinically manifest. Unlike immunocompetent patients, immuno-compromised individuals are unable to produce an effective antibody response to the virus and anemia may be persistent.

Few previous cases of parvovirus B19 producing anemia in solid-organ transplant recipients have been reported in the literature [2, 6, 7, 18, 19, 21, 24, 26]. In the present study, we report the occurrence, in a heart and in a lung transplant recipient, of severe erythroblastopenic anemia associated with active parvovirus B19 infection, treated successfully with i.v. immunoglobulin (IVIG) infusion. To our knowledge, this is the first reported case of parvovirus B19-induced pure red cell aplasia (PRCA) in a lung transplant patient.
Patients, material and methods

A nested-PCR assay for B19V-DNA was performed on blood and bone marrow samples obtained from two patients. The presence of anti-B19 specific antibody was tested in patient's sera using commercial enzyme immunoassays (EIA). A computerized search of the Medline database was performed seeking all the reported cases concerning parvovirus B19-induced pure red cell aplasia in solid-organ transplant recipients from 1984 up to December 1996.

Case no. 1

A 45 year-old woman underwent bipulmonary transplant in January 1994 for cystic fibrosis and progressive respiratory failure. She received ciclosporin A (CSA) (150 mg bid), azathioprine (Az) (2 mg/kg/d) and prednisone (Pred) (25 mg/d) for immunosuppression in association with prophylactic trimethoprim-sulfamethoxazole. At the time of transplantation, the recipient's serologic titers were negative for hepatitis B surface antigen, anti-hepatitis B antibody, anticytomegalovirus IgM and anti-HIV antibody, while titers were positive for anticytomegalovirus IgG. Donor's serologic titers were negative for anti-cytomegalovirus, hepatitis and HIV antibodies. Parvovirus titers were not determined on donor or recipient sera, as they are not included in routine pretransplant serologic screening. By month 12 she developed a stage Ib chronic graft rejection with obliterative bronchiolitis, and immunosuppression was adapted accordingly: Az and CSA were discontinued and replaced by FK 506 (tacrolimus) (2 x 4 mg/d), mycophenolat mofetilum (2 x 500 mg/d) and prednisone (15 mg/d).

By month 22, she complained of a flu-like syndrome with myalgia and asthenia. Complete blood count revealed anemia (10.9 g/dl) which became rapidly severe: her hemoglobin level dropped to 6.9 g/dl ten days later. Total WBC count was 11 x 10^9/l, with severe lymphopenia related to the immunosuppressive treatment, platelet count 464 x 10^9/l and reticulocyte count 3.7 x 10^9/l, with normal red cell indices. Serum iron and total iron binding capacity were high. Folic acid and B12 were normal. No hemolysis or blood loss was observed. Examination of peripheral blood smear revealed a discrete anisopoikilocytosis. Examination of bone marrow aspirates revealed discrete hypocellularity. Giant megaloblastic proerythroblasts showing vacuolization of the cytoplasm and intranuclear inclusion were observed (Fig. 1). No others forms of erythroid precursors were found. Normal megakaryocytes and myeloid precursors were present. Repeat cytomegalovirus cultures and early antigen detection were negative in blood, bone marrow, urine and saliva, but positive in bronchoalveolar lavage, with detection of anticytomegalovirus IgM antibodies. Intravenous therapy with ganciclovir was initiated. Parvovirus B19 DNA was detected in the patient's serum and bone marrow by polymerase chain reaction (PCR). No anti B19V IgM or IgG was detected. The diagnosis of B19V-induced PRCA was made. The patient received rHu- EPO (erythropoietin alpha) at a dose of 10'000 U s.c. 3 times a week associated with IVIG 0.4 g/kg/d for five days. She was also transfused with 2 units of packed erythrocytes. Evolution was favorable and the patient was discharged at day nine in good condition. At day 10, hemoglobin rose to 10.5 g/dl with an absolute reticulocyte count of 280 x 10^9/l.

Fig. 1
Bone marrow morphology. Giant proerythroblast with vacuolisation of the cytoplasm