Pure red cell aplasia in a simultaneous pancreas-kidney transplantation patient: inside the erythroblast

Francesca Labbadia, Eduardo Salido-Fierrez, Juliana Majado-Martinez, Valentín Cabañas-Perianes, José M. Moraleda Jiménez
Hospital Universitario Virgen de la Arrixaca, Murcia, Spain

Abstract

A case of pure red cell aplasia in a simultaneous kidney-pancreas transplant recipient on immunosuppressive therapy is reported here. The patient presented with anemia unresponsive to erythropoietin treatment. Bone marrow cytomorphology was highly suggestive of parvovirus pure red cell aplasia, which was confirmed with serology and polymerase chain reaction positive for parvovirus B19 DNA in peripheral blood. After the administration of intravenous immunoglobulin the anemia improved with a rising number of the reticulocytes.

Introduction

Parvovirus B19 (PVB19) is a non-enveloped, icosahedral small virus containing a single-strand of DNA. It is highly tropic to human bone marrow and replicates only in erythroid progenitor cells, due to the unique tissue distribution of the PVB19 cellular receptor, the blood group P antigen. Clinical manifestations of PVB19 infection vary according to the blood group P antigen. Beside the importance of the viral antigen cannot be infected in vitro by Parvovirus.1 The presence of the P antigen is essential for the infection, so that people who lack P antigen cannot be infected in vitro by Parvovirus.1 Beside the importance of the viral receptor as determinant of host susceptibility, there is also evidence of the existence of a co-receptor and an intracellular blockade in non permissive cells. The PVB19 replication specificity, there is also evidence of the existence of nonstructural proteins.3

Case Report

A 42-year old female patient with an end-stage renal disease due to diabetic nephropathy received a simultaneous renal and pancre-
Seroepidemiologic studies demonstrate that 60-90% of adults have antibodies against PVB19. It is responsible for a wide range of diseases (acute and chronic) depending on the host immune response.4

The first reported human disease associated to PVB19 infection was a transient aplastic anemia in a patient with sickle cell disease.5 In immunocompromised patients, persistent infection results from the inability to produce neutralizing antibodies. It can occur in congenital, iatrogenic and infective immunodeficiency. The dominant clinical manifestation is anemia secondary to pure red cell aplasia.6

The first report of PVB19 infection after transplantation was published in 1986.7 PVB19 induced PRCA associated with solid organ transplantation is a significant but rare infectious complication.

Although large, prospective surveillance studies are lacking, some studies reported an incidence of PVB19 disease of ~2% after transplantation.8 More recently, it has been suggested that up to 20% of organ transplant recipients develop PVB19 viremia after transplantation.9 In the largest series of transplanted patients reported in the literature,10 the patient population consisted of kidney transplant (54%), liver transplant (9%), heart or lung transplant (12%), and autologous (4%) or allogenic (24%) hematopoietic stem cell transplants. To our knowledge, no case of PVB19 infection has been described in simultaneous kidney-pancreas transplantation.

The median time to onset of PVB19 disease is 7 weeks after transplantation and most cases reported 1 year after transplantation are due to persistent infection.11

Our patient had an acute non-regenerative normocytic anemia unresponsive to EPO with a moderate neutropenia and a normal platelet count. The clinical onset of acute PVB19 infection was eight years after double transplantation, since we did not have evidence of a positive serology and PCR for PVB19 until now. As she had neutropenia and anemia, a marrow aspiration was performed to exclude drug toxicity. The bone marrow cytology disclosed the typical cytological findings of PVB19 infection and oriented the final diagnosis.

There are not established guidelines for the screening or for the treatment of PVB19 infection in organ transplant recipients. Nevertheless, there are sufficient data to give some recommendations in patients with erythropoietin-resistant anemia once all other causes of anemia have been excluded.12

In this regard, the diagnostic test with the highest specificity in the appropriate clinical setting is the PVB19 PCR in peripheral blood, a noninvasive test particularly useful in immunocompromised patients in whom the PVB19 serology can be negative at the onset of the disease.13 In patients with a suspected PVB19-induced red cell aplasia, a bone marrow examination provides fast and helpful diagnostic information.

The distinctive morphologic abnormalities include the presence of very large pronormoblasts with occasional intranuclear inclusions along with a relative paucity of more mature polychromatophilic erythroid precursors. Examination of formalin-fixed bone marrow aspirate smears seems to facilitate the identification of the typical intranuclear inclusions.14

Regarding the treatment, most patients benefit from IVIG therapy and/or reduction of immunosuppressive therapy. The standard doses of 0.4-1.0 g of IVIG/kg daily for 5 days appear to be clinically effective in most cases with no subsequent adverse effects. The goal of the treatment should be the eradication of viremia as evidenced by a negative PCR study, not only the clinical remission as judged by resolution of the anemia.15

Conclusions

We report the first case of PRCA due to PVB19 infection in a combined kidney-pancreas transplant recipient. Our case confirms that PVB19 infection is a rare but possible cause of anemia unresponsive to EPO in immunosuppressed transplanted patients. We underline the importance of a diagnostic screening using the PCR-PVB19 test and bone marrow cytology, and the rapid response to IVIG therapy.

References


Figure 1. Giant proerythroblasts with nuclear inclusions.

Figure 2. Blood count evolution after treatment with intravenous immunoglobulin.