Aplastic anemia secondary to parvovirus B19 infection in a heart transplant recipient: Acase report.

Alberto Navarro Navajas[1]*, Helman Giral[2], Nicolas Ariza Ordoñez[2], John Alexander Ramirez[3]

[1]Department of Cardiology, Universidad El Bosque, FundaciónCardioinfantil-Instituto de Cardiología, Colombia
[2]Department of Internal medicine, Universidad del Rosario, FundaciónCardioinfantil-Instituto de Cardiología, Colombia
[3]Department of Cardiology, FundaciónCardioinfantil-Instituto de Cardiología, Colombia

Abstract

Parvovirus B19 infections represent a wide variety of severity and clinic spectrums, determined by the host's immune competence state; the most representative syndromes associated are erythema infectiosum, arthropathy and Transient aplastic crisis. We present a case of a masculine patient with an antecedent of heart transplant, who consults for constitutional symptoms, with posterior documentation of aplastic anaemia and parvovirus B19 infections, with requirement of human immunoglobulin treatment and resolution of symptoms.

Keywords: Parvovirus B19, Heart transplant, Case report, Aplastic anemia.

Accepted December 08, 2020

Case Report

We present the case of a 56-year-old male, with a history of gouty arthropathy and hypothyroidism, who had undergone cardiac transplant 3 months prior to consultation because of dilated cardiomyopathy with severely depressed left ventricular ejection fraction (10%), who presented at the emergency department referred from the outpatient hematology service complaining of asthenia, 3-day adynamia, associated with self-limited fever quantified peak of 39.5°C and findings of anemia in outpatient control hemogram (5.4 gr/dl; reference range:13.5-18.0). He reported no episodes of bleeding or other associated symptoms.

His immunosuppressive regimen and infectious prophylaxis included tacrolimus 8 mg/12 hours, mycophenolate 250 mg/12 hours, prednisolone 10 mg/day, valganciclovir 450 mg/12 hours and trimethoprim-sulfamethoxazole (TMP-SMX) 160/800 every 12 hours three times a week.

He was previously followed-up by hematology and heart transplant services for leukopenia and chronic multifactorial anemia, which required multiple blood transfusions (8 units of RBC in the last 3 months) and parenteral iron support with carboxymaltose in one occasion. The previous studies for this condition included bone marrow studies with evidence of hypocellularity for age, normal karyotype and studies for digestive bleeding without identification of bleeding sites (esophagogastroduodenoscopy and colonoscopy).

At admission, the following vital signs were obtained: blood pressure 127/87 mm Hg, heart rate 110 beats per minute, respiratory rate 17 breaths per minute, temperature 36.0°C, SaO_2 96% at environment. Generalized mucocutaneous pallor and tachycardic cardiac sounds were found, without other relevant alterations. Routine investigations showed a reduction of the cell count of the three cell lines and iron deficiency profile described in Table 1.

A Transthoracic echocardiogram was performed showing left ventricular ejection fraction of 51%, systolic dysfunction and akinesia in the apical segment of the right ventricle free wall, moderate tricuspid insufficiency, pulmonary artery systolic pressure (PSAP) of 42 mmHg and severe left atrial enlargement.

Initially, it was considered that the immunosuppressive medication and the persistent inflammatory state were the major causes of the documented pancytopenia. Valganciclovir and TMP-SMX were discontinued with subsequent improvement of the leukocyte count; however, there was persistence of moderate to severe anemia and thrombocytopenia. To study the infectious causes of pancytopenia, viral loads for Hepatitis B, Hepatitis C, Parvovirus B19, Cytomegalovirus and DNA for Histoplasmacapsulatum were requested, which reported negative results; however, Parvovirus B19 viral load greater than 106copies/ml was found. With these findings, infection with Parvovirus B19 was considered the cause of the patient´s clinical findings.

A diagnosis of red cell aplasia caused by parvovirus B19 infection in immunocompromised host was made, and treatment with human Intravenous Immunoglobulin (IVIG) (500 mg/Kg/day) was initiated for 5 days, with poor initial response (decrease of 2 g/dl of hemoglobin and persistence of thrombocytopenia 50,000/ul after 5 days of IVIG course). A new therapeutic cycle of immunoglobulin (400 mg/Kg/day) was prescribed for 10 days, receiving a 15 days total course of treatment. Subsequent resolution of the pancytopenia was documented, with normal blood count results after IVIG course conclusion (Hb 11.4 g/dl, hematocrit 34%, leukocytes 5740 cells/mm^3 and platelets 396,000/ul).

Noteworthy, complications associated to health care were presented after IVIG treatment, consisting in hospital-acquired pneumonia, without microbiological isolation, that required a course of empirical antibiotic management with meropenem, linezolid and amphotericin B, with subsequent improvement of respiratory symptoms. Afterall, patient was discharged with prescription for cyclosporine and prednisolone immunosuppressive therapy, and prophylaxis with IVOIG 250

Table 1. *Laboratory test results at hospital admission.*

Laboratory tests results	
Whole blood count: 3400 cells/µg (5000-10000)	Total iron 236 ug/dL (59-158)
Neutrophil count 1260 cells/µg (2000-7000)	Total iron binding capacity: 240 µg/dL(228-428)
Lymphocytes count 1000 cells/µg (1500-4000)	Unsaturated iron binding capacity: 4 µg/dL (110-370)
Hemoglobin concentration 5.26 grams/dL (13.5-18.0)	Transferrin 1.88 g/L (2-3.6)
Hematocrit 15% (40-54)	Ferritin 3235 ng/mL (21.8-274.7)
Mean corpuscular volume: 85 fL (86-96)	Vitamin B12 186 pg/mL (187-883)
Platelet count 123000/µg (150.000-450.000)	Folic acid 33.6 ng/mL (3.1-20.5)
	Haptoglobin 215 mg/dL (15-200)
Reference ranges in parentheses	

mg/kg/day for 3 days, 4 weeks after the last dose. Outpatient control 5 months after mentioned consultation, showed normal complete blood count (leukocytes: 6620/mm^3, hemoglobin: 13.3 g/dl, platelets: 222,000/ul) and viral load of Parvovirus B19 of 402 copies/ml.

Discussion

Parvovirus B19 (PVB19) is a single-stranded, non-enveloped DNA virus, with an extreme tropism for erythroid CD36+ progenitor cells [1] due to its binding to blood group P-antigen (a globoside abundant in erythroid cells and also found to a lesser extent in endothelial cells, myocytes, and megakaryocytes). It was discovered in 1975 during screening for hepatitis B virus in asymptomatic donors and It was associated with disease in 1981 [2].

Erythema infectiosum is the classic presentation of parvovirus B19 infection, generally affecting children. In adults, arthropathy and severe anemia can occur especially in individuals with hemolytic disorders, and hydropsfetalis if the infection is acquired during gestation [3,4]. Among solid organ transplant and allogeneic/autologous hematopoietic stem cell transplant recipients, persistent anemia has been described as the main manifestation. However, hepatitis, pneumonitis, myocarditis and graft rejection have also been documented have also been documented [5].

The incidence of PVB19 infection in transplant patients is unknown. A systematic literature review reported 98 cases of transplant patients with PVB19 among which 54% had undergone kidney transplantation, 24% allogenic or autologous hematopoietic stem cell transplantation, 9% liver transplantation, and 12% cardiac and lung transplantation [5]

With regard to cardiac manifestations, the infection can cause severe lesions in patients undergoing heart transplantation. The mechanisms by which they produce such lesions include acute cell rejection, antibody-mediated rejection, microvascular pathology [6]; which in turn negatively affects the prognosis of these patients.

The spectrum of possibilities of cardiac manifestations by PVB19 ranges from myocarditis to dilated cardiomyopathy. The clinical course of PVB19 myocarditis is usually severe [7]. Parvovirus B19-induced myocarditis has a variable prevalence (2.5%) and accounts for 60% of positive cases of endomyocardial biopsies due to viral infections [8,9].

Serological tests with IgM detection and a 4-fold increase or IgGseroconversion in paired serum samples are useful markers for acute PV B19 infection. IgG persists for life; therefore, it is a marker of past infection [7].

The detection of nucleic acids in blood, serum or plasma is important both for the diagnosis of PV B19, and for the screening of blood products. PCR may be useful for diagnosis at a very early stage of infection, before the appearance of the antibody and also in the late stage of convalescence, being the only diagnostic method in patients with immunodeficiency [7], taking into account that transplant patients are unable to mount sufficient Ig anti PV B19 [8].

Assays with PV B19 antigen are relatively insensitive and unreliable for the detection of acute infection, except perhaps for patients with aplastic crisis or for detecting blood donors [7]. In patients with blood-negative PCR, but with suspected disease, the diagnosis can be confirmed by bone marrow examination [9].

On treatment, IVIG is associated with favorable outcomes in patients with Parvovirus B19 induced anemia; however, there is not a specific regime of treatment. Modification of the patient's immunosuppressive drugs regime should be considered to ameliorate immune response to control viral replication. At following after treatment, Parvovirus B19 viral load should be monitored as relapses can occur several months after [10].

Conclusion

Anemia after solid organ transplantation is a common condition, reporting prevalences up to 91.6% in heart transplant recipients. Among the diverses etiologies of this disorder are side effects of immunosuppressive and antibiotic prophylaxis drugs, the appearance of chronic kidney disease, the persistence of a chronic inflammatory state and, as in our case, the occurrence of infections secondary to microorganisms with red blood cells tropism (including parvovirus B19, Plasmodium spp, Dengue virus, Babesiaspp, etc). The recognition of this multiples etiologies in the approach to this patients can make a difference in the decision making process and the achievement of successful treatments.

Conflict of Interest

None

References

1. Human Parvovirus B19. American Journal of Transplantation. 2004;4:92-94.
2. Rouger P, Gane P, Salmon CH. Tissue distribution of H, Lewis and

P antigens as shown by a panel of 18 monoclonal antibodies. C Rev FrTransfus Immunohematol. 1987;30(5):699-708.

3. Brown T, Anand A, Ritchie LD, et al. Intrauterine parvovirus infection associated with hydropsfetalis. Lancet. 1984;2(8410):1033-4.
4. Serjeant GR, Topley JM, Mason K, et al. Outbreak of aplastic crises in sickle cell anaemia associated with parvovirus-like agent. Lancet. 1981;2(8247):595-7.
5. Eid AJ, Brown RA, Patel R, et al. Parvovirus B19 Infection after Transplantation: A Review of 98 Cases. Clin Infect Dis. 2006;43(1):40-8.
6. Invernizzi R, Bastia R, Quaglia F. Pure red cell aplasia caused by parvovirus B19 in a heart transplant recipient. Clin Case Rep. 2016;4(9):870–71.
7. Qiu J, Söderlund-Venermo M, Young NS. Human Parvoviruses. ClinMicrobiol Rev. 2017;30(1):43–113.
8. Bhattacharya S, Paneesha S, Chaganti S, et al. "Viral" myocarditis in a patient following allogenic stem cell transplant: Diagnostic dilemma and management considerations. J Clin Virol. 2009;45(3):262-4.
9. Verdonschot J, Hazebroek M, Merken J, et al. Relevance of cardiac parvovirus B19 in myocarditis and dilated cardiomyopathy: review of the literature. Eur J Heart Fail. 2016;18(12):1430–41.
10. Crabol Y, Terrier B, Rozenberg F, et al. Intravenous Immunoglobulin Therapy for Pure Red Cell Aplasia Related to Human Parvovirus B19 Infection: A Retrospective Study of 10 Patients and Review of the Literature. Clin Infect Dis. 2013;56(7):968–77.
11. Cursack GC, Crespo-Leiro MG, Paniagua-Martín MJ, et al. Chronic anemia in heart transplant patients: prevalence, predisposing factors and prognostic significance. Rev EspCardiol. 2007;60(11):1144-50.

***Correspondence to:**

Alberto Navarro Navajas
Cardiology fellow, Universidad El Bosque
FundaciónCardioinfantil-Instituto de Cardiología
Colombia
E-mail: nicolasariza19972011@hotmail.com