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Case report

Pericardial effusion and cardiac tamponade: clinical manifestation of chronic graft-versus-host disease after allogeneic hematopoietic stem cell transplantation

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ABSTRACT

The authors report a case with pericardial effusion and cardiac tamponade as a rare clinical manifestation of chronic graft-versus-host disease in a young man with acute myelogenous leukemia submitted to an allogeneic hematopoietic stem cell transplantation from a related donor.

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Graft-versus-host disease (GVHD) is a syndrome with variable clinical manifestations associated with the time of clinical evolution, affected organ and severity of lesions. It arises as a result of immunocompetent cells attacking different tissues of the recipient.¹ Acute GVHD begins at approximately the 19th day after transplantation, chronic GVHD usually develops after Day (D)+100; however, the same clinical criteria are employed for diagnosis, as chronic GVHD can occur even before D+100. The acute form of GVHD affects three organs: skin, liver and intestine; while the chronic form of GVHD is clinically characterized by cutaneous, mucosae, hepatic, gastrointestinal, serous tissue, pulmonary and ocular lesions. The most common factors that increase the risk of GVHD are donor/recipient human leukocyte

antigen (HLA) mismatch, patient and donor age, donor/recipient opposite gender and number of T lymphocytes in the inoculum.² Despite scientific advances in the area of hematopoietic stem cell transplantation (HSCT), including prophylaxis against infection, immunosuppressive medications and better intensive clinical support techniques for DNA typing, this complication still remains the most common cause of morbidity and mortality in patients undergoing allogeneic HSCT.³ GVHD with pericardial effusion and cardiac tamponade is a rare complication after HSCT and its impact is not well defined yet.⁴ The authors report on a case of this complication in a young man with acute myelogenous leukemia (AML) submitted to allogeneic HSCT from a female donor.

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Case report

A 39-year-old man was admitted to Hospital Santa Marcelina (HSM) on July 28, 2007 and was diagnosed with AML [French-American-British (FAB M2)], confirmed by myelogram (20% of myeloid blasts) and immunophenotyping (34% positive for CD45 low; CD4, CD13, CD33, CD11 and CD117 positive; immature: CD34, CD38, and aberrant expression of CD7). Induction therapy was initiated with the D3A7 regimen: Daunorubicin (60 mg/m²/day for three days) and Cytarabine (200 mg/m² for seven days). The patient achieved complete remission, and consolidation therapy was subsequently prescribed. After chemotherapy, the patient was submitted to allogeneic HSCT on December 26, 2007 from a female HLA-identical related donor, but with major ABO blood group incompatibility (patient A Rh⁺ and donor B Rh⁺). Stem cells were collected by apheresis and the total CD34 count was 5.35 × 10⁶/kg. The patient received prophylactic treatment against GVHD with cyclosporin and methotrexate. Grafting was observed on D+17 after stem cell infusion. The patient evolved during transplantation without any complications except for febrile neutropenia which was treated with cefepime. He was discharged to an outpatient follow-up and received methotrexate, arabinoside-C and dexamethasone (MADIT) every two weeks for six cycles and cyclosporine (10 mg/kg/day). On March 26, 2008, a bone marrow biopsy showed 30% cellularity with the three series well represented and absence of malignant cells. Yet, bone marrow karyotyping (20 metaphases) showed cells being 46 XX. The patient was progressively weaned off cyclosporine (10/10 days) however on D+142 after HSCT he developed chronic GVHD with skin lesions similar to scleroderma, mucositis and hepatitis. At that time the medical team decided to increase the dose of cyclosporine and start prednisone therapy (1 mg/kg/day). By D+173, the lesions of the skin and mucous membranes had improved; at which time prednisone weaning was begun. On April 3, 2009, he was readmitted to the hospital with dyspnea, orthopnea, paroxysmal nocturnal dyspnea and generalized edema (cardiac tamponade) and was submitted to an urgent pericardiocentesis to drain about 1600 mL of sero-bloody fluid. An analysis of the liquid showed the following characteristics: hemorrhagic aspect, ph = 7.8; glucose = 135 mg/dL; protein = 4.6 g/dL albumin = 3.4 g/dL; amylase = 20 U/dL; lactate dehydrogenase (dehydrogenase accumulation threshold) = 335 U/dL; adenosine deaminase (ADA) = 17.3 U/dL; acid-fast bacilli (AFB) and fungal cultures were negative. At that time, it was decided to treat the patient with empirical treatment for tuberculosis and restart prednisone (1 mg/kg/day). The patient evolved clinically well and after two weeks of treatment was discharged from the hospital in good condition. In June, 2009, he was again admitted with signs and symptoms of cardiac tamponade. Because of his history, an echocardiography was immediately performed which showed pericardial effusion with signs of cardiac tamponade. Because of the recurrence without a well-defined diagnosis his case was discussed with the heart surgeon, who decided to proceed with a pericardiostomy and biopsy; a drain was placed in

the pericardium and 1500 mL of serohematic fluid was removed. The biopsy of the pericardium concluded: presence of fibrinous exudate with chronic pericarditis and diffuse inflammatory lymphoplasmacytic infiltration, more intense around the vaso-histological structure compatible with GVHD. The immunohistochemical study of the pericardium indicated CD20⁺ (pan B), L26/CD45 Ro (pan T), (UCHL1)/CD138 plasma cells, CD4 negative, concluding that the pericardium was affected by an inflammatory process rich in B and T cells, as well as plasma cells. A computed tomography (CT) of the thorax on June 26, 2010 showed thickening of the pericardium with minimal pericardial effusion, and significant bilateral pleural effusion. The drain was kept in the pericardium until no more cardiac debit was observed and the patient remained on prednisone (1 mg/kg/day) to control the pericardial GVHD. The patient evolved with significant clinical improvement and was discharged to outpatient follow-up.

Discussion

HSCT is an effective therapy for AML. Although used in patients with on-going disease, the best results are documented in patients undergoing the procedure while in first remission.⁵ In the current case, HSCT was performed after chemotherapy and the patient achieved complete remission. Pathological and clinical features of chronic GVHD are similar to some collagen diseases, in which there is a deregulation of the immune system with eosinophilia, presence of autoantibodies, hypergammaglobulinemia and plasmacytosis. There is frequent involvement of the skin, liver, eyes, lungs and gastrointestinal tract. However involvement of other tissues, such as serosal tissues, has rarely been reported. Sullivan et al. reported serosal tissue involvement in 2% of patients with chronic GVHD after HSCT.⁶ It is known that GVHD presents similar clinical manifestations to autoimmune diseases, such as systemic sclerosis, systemic lupus erythematosus, lichen planus, Sjögren's syndrome, rheumatoid arthritis and primary biliary cirrhosis. It is surprising that the incidence of polyserositis is so low.⁶ The patient developed pericardial effusion and cardiac tamponade sixteen months after HSCT, in addition to bilateral pleural effusion. Pleural tuberculosis is a frequent cause of pleural effusion in Brazil. The risk of tuberculosis appears to be increased in patients with chronic rheumatic diseases such as systemic lupus erythematosus, and in patients on prolonged corticosteroid or immunosuppressant therapies.⁷ In view of epidemiological data showing that tuberculosis is a major cause of serositis in Brazil and since the patient's immune system was highly suppressed and the adenosine deaminase concentration in the pericardial fluid was very close to the normal upper limit (17.3 U/dL), we chose to start empirical treatment for tuberculosis until the results of the biopsy and immunohistochemistry confirmed pericardial GVHD. From then on, the patient remained on specific treatment for GVHD with cyclosporine and prednisone. There are few reports of pleural effusion and pericardial fluid in chronic

GVHD. Seber et al. described polyserositis in seven patients with recurrent serous effusions after HSCT.⁸ There are some important differences between these cases and the present one. In the previously referenced study, four of the HSCT used unrelated donors and in six cases serosal effusions occurred before D+100 after HSCT; considered as the period for acute GVHD. Only three of the seven patients had pericardial effusions. The authors of this article highlight the extension of pericardial effusion (April: 1600 mL and June: 1500 mL of serohematic fluid), the association with pleural effusion, the recurrence of serositis, the time of clinical manifestation (16 months after transplantation) and the severity of it leading to cardiac tamponade with imminent risk to life for the patient. The pericardium contains, on average, about 50 mL of fluid. When there is an accumulation of fluid in the pericardial space capable of producing pressure above intracardiac levels, cardiac tamponade occurs. This is characterized by increasing intracavity pressures with limitation of ventricular filling and consequent reduction of cardiac debit leading to hemodynamic instability.⁷ Although pericardial effusion is a rare clinical manifestation of GVHD with few cases described in the literature, it should not be underestimated by hematologists accompanying patients submitted to allogeneic HSCT.

Conflicts of interest

The authors declare no conflicts of interest.

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