Correspondence
Constrictive pericarditis due to Candida albicans: An unexpected cause of pericardial effusion after heart transplantation

Pericarditis constrictiva por Candida albicans: una causa inesperada de derrame pericárdico tras el trasplante cardíaco

To the Editor:

Constrictive pericarditis may follow any cardiac surgical procedure, with an incidence varying between 0.1% and 0.3%. However, this complication has been rarely described after orthotopic heart transplantation (OHT). Since diagnosis requires a high index of suspicion in those recipients presenting with symptoms of right heart failure and preserved left systolic function, diagnosis may be delayed for several months. Candida pericarditis constitutes a rare condition associated to immunosuppression, broad-spectrum antibiotic therapy, or previous pericardiectomy.

A 54-year-old male, diagnosed 4 years before of non-ischemic dilated cardiomyopathy, was admitted to our institution in September 2008 because of rapidly progressive congestive heart failure. Despite intensive treatment persistent hemodynamic instability prompted us to use an intra-aortic balloon pump as a bridge to urgent OHT. Perioperative cultures routinely obtained from the donor and preservation fluid were negative. Both the transplant procedure and the early postoperative period were uneventful. Basiliximab was administered as induction therapy, whereas the maintenance immunosuppression included cyclosporine A, mycophenolate mofetil, and prednisone. An echocardiography (EC) performed two weeks later revealed a moderate-to-severe pericardial effusion with some fibrin strands, with no signs of hemodynamic compromise. In view of the absence of symptoms of cardiac tamponade or heart failure the patient was discharged home. Over the next month he developed slight ankle edema. EC disclosed the persistence of severe pericardial effusion with multiple, highly mobile, filamentous strands arising from a thickened pericardium. He remained afebrile throughout the entire episode. Physical examination showed tachycardia, jugular vein distention, and paradoxical pulse. Laboratory data included a white cell count of $9.1 \times 10^9$ L$^{-1}$ (81.9% neutrophils), platelets $228 \times 10^9$ L$^{-1}$, serum creatinine 1.56 mg dL$^{-1}$, and through levels of cyclosporine A and mycophenolate mofetil within therapeutic range. Echocardiographic-guided pericardiocentesis yielded 1500 cm$^3$ of sero-hematic fluid. Analysis of the effusion showed a leukocyte count of $8 \times 10^9$ L$^{-1}$ (80% neutrophils), glucose concentration of 20.0 mg dL$^{-1}$, and lactic dehydrogenase level of 6690 IU L$^{-1}$. On the fifth day pericardial fluid cultures yielded Candida albicans (C. albicans). The patient underwent a pericardial window via left anterior minithoracotomy with evacuation of 450 cm$^3$. Significant pericardial thickening was confirmed, and C. albicans was isolated from the pericardial tissue culture. Blood and urine cultures were negative; there were no fundoscopic signs of chorioretinitis. Liposomal amphotericin B (L-AmB) (3 mg/kg daily) was prescribed for 2 weeks. A new EC revealed progressive, irregular thickening of both pericardial layers and respiratory variations of mitral and tricuspid inflows velocities. A median sternotomy and a bilateral antephrenic pericardiectomy with epicardial decortication were completed. Pericardium was markedly thickened with organized pleuropericardial adhesions. C. albicans was cultured from surgical specimens. L-AmB was switched to oral fluconazole (200 mg twice a day) after 6 weeks. EC showed normal graft function and filling pressures, and the patient was discharged. Fluconazole was continued for 12 months on an ambulatory basis. Three years later the patient remains asymptomatic.

Primary pericarditis caused by Candida spp. is a rare condition. Rabinovici et al. identified a number of predisposing factors: malignancy (27%), previous antibiotic (62%) or corticosteroid therapy (15%), diabetes mellitus (15%), and pericardiotomy (38%). Cardiac tamponade was present in 8 of 12 patients for whom data were available. Pericardiocentesis alone constituted the definitive treatment in only one of 10 patients, and surgical drainage of the pericardial sac was required in the remaining cases, with an overall survival of 56%. The diagnosis relies on the culture of pericardial fluid or pericardium specimens, accompanied or not by the histological documentation of tissue invasion by the fungus. Molecular methods based on polymerase chain reaction may also provide a reliable and earlier diagnostic approach.

In our knowledge, we herein describe the third case of Candida pericarditis in an OHT recipient (PubMed search using terms "heart transplant", "Candida" and "pericarditis"). Canver et al. reported a 52-year-old
patient who presented 14 months after the procedure with symptoms of heart failure; postoperative period had been unremarkable and immunosuppression regimen was not specified; due to rapid hemodynamic deterioration the patient underwent surgical drainage and total pericardectomy, associated with an 8-week course of L-AmB followed by oral fluconazole indefinitely. Puius and Scully described a 37-year-old female who received rabbit antithymocyte globulin and daclizumab as induction therapy; early postoperative period was complicated with acute renal failure requiring continuous veno-venous hemofiltration; clinical condition did not resolve until retained epicardial pacing wires were removed and a pericardial window was done. In contrast to these cases, our patient only had mild symptoms of heart failure, and no evidence of systemic infection. *Candida* constrictive pericarditis appeared prematurely in the post-transplant period, without any significant postoperative events or additional risk factors for invasive fungal infection. We hypothesize the possibility of a donor-derived infection through the cardiac allograft, since the cause of the donor's death was a road traffic trauma with severe hemothorax which required the insertion of chest tubes at the site of the accident under non-aseptic conditions.

Pericardial effusion occurs frequently in the setting of OHT and has been observed in up to 35% of patients in the immediate postoperative period. Although this complication appears to be benign, close echocardiographic monitoring is required to rule out the progression to cardiac tamponade. In our patient, pericardial effusion did not spontaneously resolve during the first weeks and pericardiocentesis became mandatory in order to obtain an etiologic diagnosis. The present case exemplifies that both pericardial fluid and pericardectomy specimens should be sent routinely for microbiological investigation even in the absence of apparent infection.

Current guidelines state that treatment of *Candida* pericarditis should include amphotericin B, an echinocandin, or fluconazole, in combination with either a pericardial window or pericardectomy. Although Puius and Scully reported a favorable outcome using combination therapy with caspofungin and fluconazole, we chose L-AmB followed by step-down to oral fluconazole as the regimen most often employed in the previous, albeit limited, literature. Paucity of data precludes firm recommendations about the length of treatment, which should continue for several months until complete resolution of pericardial inflammation.

Source of funding

M. Fernandez Ruiz enjoys a ''Contract Research Training’’ Rio Hortega (CM11/00187) of the Health Institute ’’Carlos III’’.

References


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http://dx.doi.org/10.1016/j.rce.2012.05.017