Refractory cardiogenic shock following idiopathic giant cell myocarditis in a 19-year-old woman

CLINICAL CASE

A 19-year-old woman with no medical history except for facial acne treated with tetracyclines during the previous year presented to the emergency room referring 1-week history of worsening muscle weakness, palpitations and exertional dyspnoea. Physical examination revealed a tachycardic (130 bpm), tachypnoeic and hypotensive (blood pressure 90/50 mm Hg) thin woman with fever of 38.5°C, rash and jugular vein distention.

An ECG showed sinus tachycardia with 0.5 mm elevation of the ST segment in the anterior and inferior leads. In laboratory studies, she had leukocytosis with neutrophilia and eosinophilia and mild rise of troponin I (4.8 μg/l), creatine kinase (524 U/l) and transaminases (aspartate aminotransferase of 765 U/l and alanine aminotransferase of 658 U/l). An echocardiogram revealed severe biventricular dysfunction with global hypokinesia and circumferential mild pericardial effusion. Signs of heart failure were found on her chest x-ray. In this clinical situation, we treated her with dobutamine, but she started to develop sustained ventricular tachycardia and refractory hypotension during the following hours. Coronary angiography showed no coronary lesions and an intra-aortic balloon pump was inserted for counterpulsation. The next morning, a new transthoracic echocardiogram revealed a left ventricular ejection fraction of 10% with a dilated left ventricle. She underwent a right heart catheterisation with endomyocardial biopsy and was diagnosed with giant cell myocarditis (GCM) (figure 1). We started treatment with intravenous, prednisolone (50 mg/day), intravenous immunoglobulin (30 g/day), ciclosporin and plasmaferesis with neither clinical nor haemodynamic improvement. Because of the patient's impaired clinical course, a biventricular assistance device (Abiomed BVS 5000) was inserted 5 days after her admission. As the prognosis of GCM is usually fatal, with no response to medical treatment, she was added to the emergency cardiac transplant waiting list, as her status was critical.

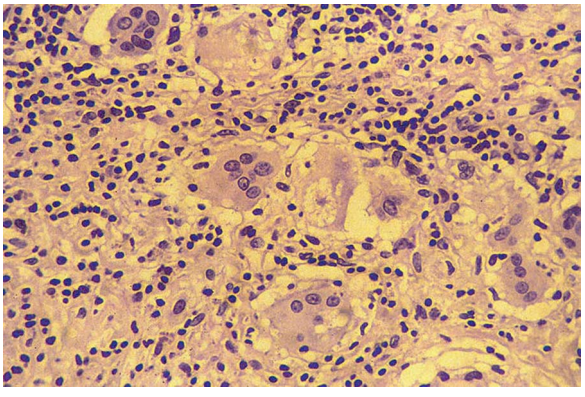

Figure 1 Histological study (H&E) showing numerous multinucleated giant cells and infiltration of lymphocytes and histiocytes.

She underwent transplantation but she developed acute transplant rejection and she received another assistance device (the same type). Two days after the implantation of the second device, she was haemodynamically stable but she had no neurological response. With the suspicion of anoxic injury, we performed an EEG that showed encephalic death.

DISCUSSION

GCM is a rare and frequently fatal type of myocarditis. Patients usually die of heart failure and ventricular arrhythmia unless cardiac transplantation is performed.[1 2] In addition to the idiopathic or primary form, GCM has been associated with other conditions including drug hypersensitivity,[3] granulomatosis, neoplastic conditions, autoimmune and inflammatory diseases.[4] However, the aetiology and pathogenesis of GCM is not well known.

The differential diagnosis for patients with cardiogenic shock in previously healthy hearts includes mostly acute myocardial infarction and myocarditis. In this case, the absence of cardiovascular risk factors, the clinical presentation (no chest pain), the non-specific ECG abnormalities and the global hypokinesia in the echocardiogram, without alterations in segmental contractility made it easy to exclude an acute coronary syndrome. The presence of fever in a healthy woman suggested myocarditis. An endomyocardial biopsy was performed to confirm this diagnosis and to exclude a GCM, because of the dramatic course of the patient. The sensitivity of transvenous endomyocardial biopsy for this devastating disease is 82–85% in some series.[5] Kandolin *et al* report that the sensitivity of this technique increased from 68% to 93% after up to two repeat procedures.[6]

Besides, our patient was taking tetracyclines, which is one of the drugs that has been associated with hypersensitivity and myocarditis. Drug-associated myocarditis was first described in 1942 by French and Weller after sulfonamide administration.[7] The importance of the potential association of medications with GCM lies in the implications for prognosis and treatment. Hypersensitivity myocarditis (HSM) as described in the literature is an often fatal disease.[3] This may reflect delay in diagnosis or that it is not considered at all. Due to the lack of widespread necrosis and fibrosis in HSM, early withdrawal of the offending drug can lead to improved outcomes without long-term sequel. When diagnosed early in the course, discontinuation of the offending medication, often accompanied by the addition of corticosteroids, has resulted in successful recovery of some patients. There are no studies that directly compare the prognosis and treatment of GCM with HSM. But, in contrast to HSM, the corticosteroid administration is insufficient treatment for GCM. There are data suggesting that immunosuppressive therapy with regimens including ciclosporin, azathioprine, or both,[8] but not corticosteroids alone, may prolong the time to transplantation or death in patients with the idiopathic form of GCM. Our patient had been taking a drug from a class known to be associated with hypersensitivity and she presented with fever, rash and eosinophilia, some features of hypersensitivity reactions that support the presence of a hypersensitivity reaction.

One should consider the diagnosis of GCM in patients with left ventricular failure of new onset who decline clinically despite usual care, particularly if refractory ventricular tachycardia develops. In these patients, a biopsy-based diagnosis of GCM will yield prognostic information and allow them to be considered early for transplantation. A ventricular assist device is strongly recommended[8] as some studies show that patients with

end-stage GCM can be successfully bridged with ventricular assist devices to transplantation with very good post-transplantation survival.[9]

Particularly careful attention is warranted to rule out recurrent GCM in post-transplantation biopsies. Asymptomatic patients in whom routine biopsy reveals a prominent giant-cell infiltrate seem to do well with short-term heightened immunosuppression. Patients in whom left ventricular dysfunction is accompanied by giant-cell myocarditis may die despite aggressive immunosuppression.

GCM is a rare and frequently fatal disorder with no proven treatment. It is a disease of young, predominantly healthy adults. Without transplantation, patients usually die of heart failure and ventricular arrhythmias. Due to the poor prognosis of the condition, prompt recognition and diagnosis are of crucial importance.

Ana Viana-Tejedor,[1] Iago Sousa,[2] Héctor Bueno,[2] Francisco Fernández Avilés[2]

[1]Department of Cardiology, Hospital Clínico San Carlos, Madrid, Spain
[2]Department of Cardiology, Hospital General Universitario Gregorio Marañón, Madrid, Spain

Correspondence to Dr Ana Viana Tejedor, Department of Cardiology, Hospital Clínico San Carlos, C/Profesor Martín Lagos, s/n., Madrid 28040, Spain; ana_viana_tejedor@hotmail.com

Contributors All authors took an active part in the decisions made and in the care of the patient.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; internally peer reviewed.

To cite Viana-Tejedor A, Sousa I, Bueno H, *et al*. *Heart Asia* Published Online First: [*please include* Day Month Year] doi:10.1136/heartasia-2013-010279

Heart Asia 2013;**00**:34–35. doi:10.1136/heartasia-2013-010279

REFERENCES

1 Cooper LT, Berry GJ, Shabetai R. Idiopathic giant-cell myocarditis—natural history and treatment. Multicenter Giant Cell Myocarditis Study Group Investigators. *N Engl J Med* 1997;336:1860–6.
2 Cooper LT. Giant cell myocarditis: diagnosis and treatment. *Herz* 2000;25:291–8.
3 Daniels PR, Berry GJ, Tazelaar HD, *et al*. Giant cell myocarditis as a manifestation of drug hypersensitivity. *Cardiovasc Pathol* 2000;9:287–91.
4 Dennert R, Schalla S, Suylen RJ, *et al*. Giant cell myocarditis triggered by a parvovirus B19 infection. *Int J Cardiol* 2009;134:115–16.
5 Kandolin R, Lehtonen J, Salmenkivi K, *et al*. Treatment, and outcome of giant cell myocarditis in the era of combined immunosuppression. *Circ Heart Fail* 2012;6:15–22.
6 Magnani JW, Dec GW. Myocarditis: current trends in diagnosis and treatment. *Circulation* 2006;113:876–90.
7 French A, Weller C. Interstitial myocarditis following the clinical and experimental use of sulfonamide drugs. *Pathol* 1942;18:109–22.
8 Ziemba EA, John R. Mechanical circulatory support for bridge to decision: which device and when to decide. *J Card Surg* 2010;25:425–33.
9 Murray LK, González-Costello J, Jonas SN. Ventricular assist device support as a bridge to heart transplantation in patients with giant cell myocarditis. *Eur J Heart Fail* 2012;14:312–18.