Ventricular assist surprise: Giant cell myocarditis or sarcoidosis?

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Idiopathic giant cell myocarditis (GCM) is a rapidly fatal disease with a worse natural history than lymphocytic myocarditis.¹ Transplantation is the best available therapy, despite the risk of disease recurrence in the allograft. However, patients with GCM often die before a donor heart becomes available.² Mechanical assist for acute myocarditis dramatically improves the natural history of the underlying disease. Particularly when the picture is of lymphocytic myocarditis, there is a good chance of successful bridge to recovery.³ There are no reported cases of bridge to recovery for GCM, and the world experience of bridge to transplant totals 9 cases. Furthermore, the outcome of these patients was poorer than that of other patients with GCM who underwent transplantation without prior requirement of a ventricular assist device (VAD).²

Secondary GCM is associated with other systemic illnesses (eg, sarcoidosis).⁴ From a clinical and pathologic standpoint, idiopathic GCM and cardiac sarcoidosis (CS) are considered different entities.⁵ We present a case that challenges this traditional view.

Clinical Summary

A 36-year-old previously healthy man presented to the local hospital with a 1-week history of breathlessness and malaise. An echocardiogram showing a globally dilated heart, with a left ventricular ejection fraction of 15%, confirmed the clinical diagnosis of acute failure. Serial chest radiographs and comprehensive viral screens remained unremarkable throughout his illness. His clinical condition deteriorated to cardiogenic shock, and he was referred to our unit where a Thermo Cardiosystems HeartMate left VAD (Woburn, Mass) was inserted on an emergency basis.

The left ventricular core biopsy was typical for GCM in its acute phase (Figure 1, A). Although the literature suggests a beneficial effect for immunosuppression,¹ this was kept in reserve postoperatively because of ongoing infection. A pulmonary transbronchial biopsy (obtained from the patient during bronchial toilet while he was still in intensive care) demonstrated an appearance indicative of sarcoidosis (Figure 1, B). The patient was bridged to transplantation, which took place uneventfully 87 days later. Analysis of the explanted heart showed features of GCM in its healing phase but also persistent giant cells with an appearance more typical of CS (Figure 1, C). Immunosuppression was routine with triple cyclosporine-based therapy. Fifteen months posttransplantation, the patient remains free of symptoms and of disease recurrence in the allograft.

Discussion

Differentiation of GCM from CS may be difficult, particularly when there is very limited extracardiac involvement by sarcoidosis. The typical case of GCM presents with cardiac failure. Histologically, there is myocyte necrosis without granuloma formation. Conversely, CS is an interstitial granulomatosis presenting with arrhythmias or sudden death.⁵ The first case of bridge to transplant for CS has only recently been described, showing that patients with established sarcoidosis are less likely to require mechanical assist.⁶ The existing classifications are based on small autopsy or in vivo studies. As opposed to Litovski and colleagues⁵ series of 15 autopsy cases, in which the 2 patterns of presentation were described, Davidoff and colleagues⁴ did not find differences in the demographic, clinical, or hemodynamic characteristics of patients in whom GCM or CS was diagnosed antemortem.

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Figure 1. A, Left ventricular biopsy showing replacement of cardiac myocytes by lymphocytes, macrophages, a few eosinophils, and macrophage giant cells. There are no granulomas. B, Transbronchial biopsy with a single giant cell granuloma. C, Explanted heart shows replacement granulation tissue, fibrosis, myocyte loss, lymphocytes, and eosinophils. However, there are persistent giant cells with Schaumann bodies, which are described in cardiac sarcoidosis but considered to be absent in the healing phase of giant cell myocarditis.

From the larger series of the Multicenter GCM Study,¹ it is apparent that some patients die or are lost from follow-up before serial histologic evaluation is possible. It is therefore not surprising that a complex inflammatory and healing process is difficult to characterize by a snapshot of tissue pathology. Clearly, some patients are in the middle.^{7,8} We found a report in which a case very similar to ours, with discrete sarcoidosis diagnosed on lung autopsy tissue, was classified as CS.⁷ Perhaps GCM and CS represent 2 ends of a disease spectrum. An analogy is possible with the lung, in which the aggressive form of necrotizing sarcoid granulomatosis is described.⁹

With the advent of ventricular assist, this speculation gains more substance. The effect of hemodynamic unloading extends to the level of cellular phenotype, with decreased susceptibility to myocardial apoptosis and a reduction in the level of circulating CD4 T cells.^{6,10} These changes are relevant for the cardiac recovery of patients supported for myocarditis. In this context, one can attempt to explain some of the distinguishing features of idiopathic GCM and CS. The presence of myocyte necrosis, characteristic of all forms of GCM, may indicate the early phase of a grave variant of disease. If time were allowed, dead myocytes could be cleared and granulomas could slowly organize. Fibrosis, a nonspecific

indicator of tissue damage and repair, could also become more widespread. VADs possibly allow the more severely ill patients to survive to a healing phase, when more typical pathology is discernible.

Until the pathology of this twilight zone is clarified, there are practical implications. Patients with myocarditis who do not require a VAD urgently benefit from endomyocardial biopsy, because the type of pathology influences the prognosis and the choice of device. In our patient, the diagnosis of pulmonary sarcoidosis was incidental. When GCM is diagnosed in surgical candidates, there is a case for actively excluding lung sarcoidosis by tissue histology. Finally, the combination of immunosuppression and mechanical support is better described for lymphocytic myocarditis.¹¹ Such novel combinations may also improve the poor outcome of bridge to transplant in GCM, regardless of the primary or secondary nature of the cause.

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Intraparenchymal replacement of the left pulmonary artery with implantation of segmental arteries in a 26-year-old patient

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Aneurysms of the pulmonary artery are associated with primary or secondary pulmonary hypertension,¹ chronic pulmonary embolism, or pulmonary valve stenosis.² Systemic disorders, such as Behçet disease,³ Osler disease, and other acquired cardiovascular or congenital diseases,⁴ are known to produce such aneurysms. Lethal complications include bronchial rupture,^{3,4} dissections, and intrapulmonary erosion. Compression of neighboring structures is also a source of morbidity. We report on a patient who was referred to our hospital after demonstration of bilateral, dilative changes of the segmental arteries of the apicoposterior segments of the upper lobes, as well as an aneurysm of the left pulmonary artery of 3 cm in diameter at the bronchial bifurcation of the upper and lower lobes (Figure 1). Additional aneurysms, including those in the right lower lobe branches, were also observed. The surgical

Figure 1. Computed tomographic scan demonstrating aneurysm of the left pulmonary artery at the bronchial bifurcation of the upper and lower lobes.

procedure is discussed and described as a new lung parenchyma-sparing technique.

Methods

A 26-year-old patient with confirmed Behçet disease and a week-long history of hemoptysis was admitted to our hospital. The patient had previously undergone treatment for uveitis and oral and genital ulceration. A portion of the small intestine had also been

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