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AUTOMATED IMPLANTABLE CARDIAC DEFIBRILLATOR AND BIVENTRICULAR THORATEC ASSIST DEVICE AS BRIDGE TO TRANSPLANTATION IN A PATIENT WITH SARCOIDOSIS

H. J. Ankersmit, MD,[a] G. A. Wieselthaler, MD,[a] B. Moser, MD,[a] S. Taghavi, MD,[a] M. Grimm, MD,[a] G. Roth, MD,[a] M. Gorlitzer, MD,[a] H. Tschernich,[c] R. Horvat, MD,[b] and E. Wolner, MD,[a] *Vienna, Austria*

Sarcoidosis of the heart is an unusual but previously reported indication for transplantation. Sarcoidosis is a systemic disease that can manifest itself with arrhythmias and cardiomyopathy. The case presented here is that of a 30-year-old man in whom an implantable cardioverter and a biventricular assist device (BIVAD) were used to bridge the time to heart allograft transplantation.

Noncaseating granulomas were first autopsy proven in 1929, indicating heart involvement in sarcoidosis.[1] In 1935 Salvesen[2] described a patient with known sarcoidosis and bundle branch block on electrocardiogram that was believed to be clinically consistent with the diagnosis of cardiac sarcoidosis. Since that time, a large number of reviews has shown that the combination of arrhythmias and sudden death, seen in about 50% to 60% of patients with cardiac sarcoidosis, constitutes the most prevalent and lethal complication of the disease.[3] This led to the prophylactic implantation of implantable cardioverter-defibrillators in this patient population with documented success in bridging to transplantation.[4] We are reporting in this article the first successful implantation and bridging to transplantation with a BIVAD (Thoratec Corporation, Pleasanton, California) in a patient with medically intractable cardiac failure.

Clinical summary. A 30-year-old man with lung biopsy–proven sarcoidosis was admitted to our intensive care unit in cardiac shock. The disease was diagnosed when he was 17 years old, when he had symptoms of dyspnea, fatigue, weight loss, and fever. Signs of Loefgren's syndrome were absent. A diagnostic thoracotomy and lung biopsy with detection of characteristic granulomas confirmed the diagnosis of sarcoidosis. After treatment with steroids, he recovered and remained in stable condition with low-dose immunosuppression. Ten years after this first manifestation, chest pain and palpations were reported, and he was monitored with a Holter electrocardiogram and echocardiography. The echocardiogram revealed an enlarged 4-chamber view and the electrocardiogram documented Lowen grade IV arrhythmia. This led to the prophylactic implantation of an implantable cardioverter-defibrillator, modification of the immunosuppression, and initiation of cardiomyopathy treatment (angiotensin-converting enzyme inhibitors and digitalis) with normalization of angiotensin-converting enzyme levels. At the time of admittance with signs of cardiac shock, his cardiac output was evaluated to be 1.5l with an ejection fraction of 12%. We implanted a pneumatically driven BIVAD (Thoratec) and the patient was bridged to transplantation for 90 days (Fig 1). His intensive course was complicated by an initial general blood-borne septic event with cultured *Staphylococcus aureus* and *Candida albicans.* This was treated by broad-spectrum antibiotics/mycotics (vancomycin, cefuroxime, and fluconazole). Moreover, on day 50 the patient had a spleen infarction verified by computed tomography. No therapeutic consequence was drawn. Anticoagulation was initially maintained with heparin and was switched after 10 days to phenprocoumon (Marcoumar). The patient recovered well and was transferred to the normal ward on day 86. After 90 days of mechanical assisted support, an appropriate donor heart became available and bicaval heart transplantation was performed. The recipient's heart was histologically evaluated and characteristic sarcoidosis granulomas were documented (Fig 2). After heart

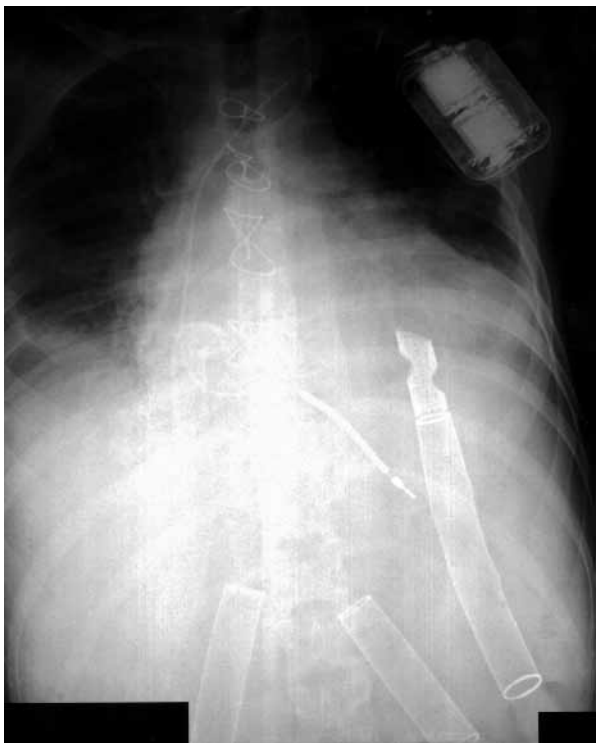

Fig 1. Transthoracic x-ray film showing enlarged heart with biventricular Thoratec inflow and outflow conduits and automated cardiac defibrillator.

From the Departments of Cardiothoracic Surgery,[a] Pathology,[b] and Cardiothoracic Anesthesia,[c] General Hospital of Vienna, Vienna, Austria.

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transplantation, induction therapy was initiated with antithymocyte globulin (2 mg/kg) for 5 days and triple therapy with steroids, azathioprine, and cyclosporine (INN: ciclosporin). However, the patient had International Society for Heart and Lung Transplantation grade II/III rejection rates in 2 consecutive weeks after allograft transplantation, which were steroid resistant. Therapy was switched to mycophenolate and high doses of FK506. With this therapy regimen, endomyocardial biopsy tissue normalized and the patient was discharged after 3 weeks. His postoperative course has since been uneventful.

Discussion. Sarcoidosis is a systemic disease and the clinical manifestation may be generalized or focused on one or more organs. Because the lung is almost always involved, however, most patients have symptoms referable to the respiratory system. Independent of the site, the clinical manifestations relate directly to inflammation and organ dysfunction caused by the granulomatous disease process. The frequency of clinical heart involvement in patients with systemic sarcoidosis is extremely low and in one series was reported to be less than 2%.[5] Most of the patients with cardiac sarcoidosis who have clinical manifestations present with conduction disturbances or arrhythmias or, less commonly, with pump failure. Those with primary heart involvement do, however, have a high incidence of sudden cardiac death.[6] There have been case reports of patients with cardiac sarcoid undergoing heart transplantation, and sarcoidosis was advocated to be a relative indication for allograft transplantation.[7] Reports have documented recurrence of sarcoidosis in a cardiac allograft after transplantation.[8] One article even showed that transmission of sarcoidosis via cardiac transplantation was possible.[9] These observations supported the observation by Mitchell and Rees[10] that the disease was transmissible with human sarcoid tissue, thus being an infectious agent.

At the time of this report and in contrast to the literature, bridging to transplantation with a BIVAD had not been reported with regard to this disease. There are several aspects of this case that deserve comment. First, to our knowledge, this is the first report that bridging with a BIVAD is possible in this type of patient. Second, in this case, postimplantation severe sepsis was present, indicating BIVAD-induced susceptibility to blood-borne germs and decreased immune competence.[11] Third, despite aggressive anticoagulation (international normalized ratio 2.5-3.5), a spleen infarction with hyperthermia developed. Finally, at least in this patient, there was a clear hyperimmune response as indicated by steroid-resistant rejection episodes, thus indicating that aggressive immune suppression should be initiated after support with a cardiac assist device.

It has not yet been determined that this particular systemic disease can be controlled long term with appropriate immunosuppression. Thus, we contend that this patient was saved by implanting a BIVAD to bridge to transplantation for sarcoidosis, hence indicating a new experimental therapy.

This article is dedicated to my colleague K.H.

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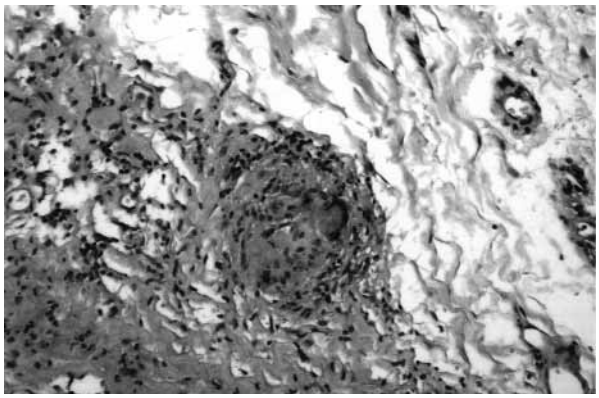

Fig 2. After being sampled, the heart was formaldehyde fixed, paraffin embedded, and histologically evaluated. All blocks presented interstitial edema, mild-to-moderate perivascular lymphohistocytic infiltrate, and small numbers of noncaseating granulomas composed of aggregated epithelioid cells containing Langerhans-type multinucleated giant cells including an asteroid body within the cytoplasm as shown in the photomicrograph (hematoxylin and eosin; original magnification ×400).

Address for reprints: Hendrik Jan Ankersmit, MD, Department of Cardiovascular Surgery, AKH Wien, Währinger Gürtel 18-20, 1090 Vienna, Austria (E-mail: hjankersmit@hotmail.com).

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