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CASE REPORT

Probable recurrence of cardiac sarcoidosis in a transplanted heart

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Recurrence of cardiac sarcoidosis (CS) in post-transplant patients presents a rare but potentially life-threatening form of graft dysfunction and poses challenges due to varying clinical presentations, limited diagnostic modalities, and treatments based on anecdotal evidence. We discuss the case of a 46-year-old woman with CS, who developed cardiogenic shock necessitating orthotopic heart transplant. She subsequently developed likely recurrent CS in the transplanted heart. We discuss the rarity of this scenario as well as diagnostic modalities and management principles to consider.
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Recurrence of cardiac sarcoidosis (CS) post-transplant presents a rare but potentially life-threatening form of graft dysfunction. We present a case of a 46-year-old woman with a history of ocular inflammation presenting with subacute dyspnea, chest pain, and cough, who subsequently developed cardiogenic shock from severe dilated cardiomyopathy. Computed tomography chest imaging revealed mediastinal lymphadenopathy suspicious for sarcoidosis vs lymphoma. Cardiac magnetic resonance imaging subsequently showed transmural enhancement of the myocardium (Figure 1). Myocardial biopsy demonstrated noncaseating granulomas (Figure 2) with negative acid-fast bacilli staining, confirming CS. Despite the initiation of high-dose steroids and methotrexate, her clinical condition deteriorated, ultimately necessitating cardiac transplantation. As per our institutional protocol, 1,000 mg of methylprednisolone was given at the time of transplant and tapered as per standard. Mycophenolate mofetil (MMF) was initiated at 1,500 mg twice daily (BID) and tacrolimus was initiated at post operative day (POD) 1 reaching therapeutic level (trough 10-15 ng/ml) by POD 7. Biopsy at that time showed no evidence of inflammatory infiltrate. However, surveillance biopsy 2 weeks post-transplant showed granulomatous inflammation in a peri-vascular pattern with an appearance of invasion into the graft, concerning for recurrence of sarcoidosis (Figure 3). Alternate considerations, such as pre-existing donor granulomatous disease, were felt to be

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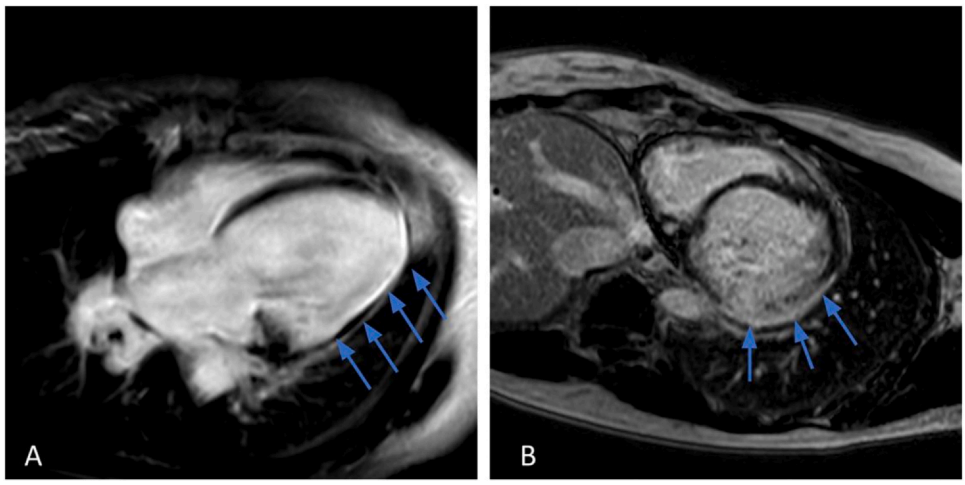

Figure 1 Cardiac MRI demonstrated near-transmural to transmural enhancement of the anterolateral, inferolateral, and inferior walls (blue arrows) with associated wall thinning and severe hypokinesis, in a pattern consistent with the diagnosis of cardiac sarcoidosis. MRI, magnetic resonance imaging.

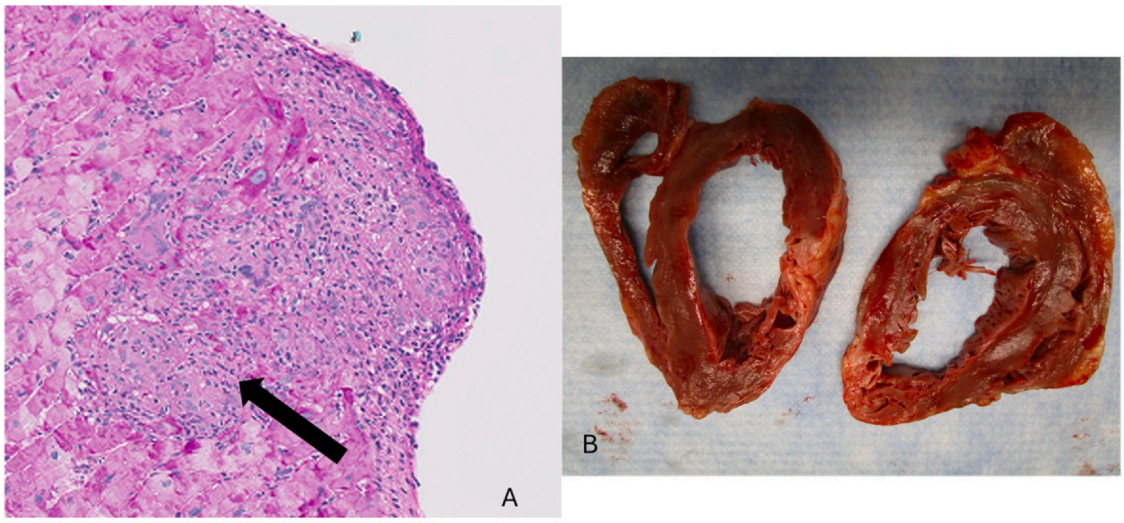

Figure 2 (A) Pretransplant myocardial biopsy revealing non-necrotizing granuloma consistent with a diagnosis of cardiac sarcoid (black arrow). Additional stains ruled out any underlying infection. (B) Gross anatomy of the heart explant showing areas of dense fibrosis in the inferolateral walls consistent with the cardiac MRI findings. MRI, magnetic resonance imaging.

unlikely. Pulse-dose steroids were administered again and prednisone was tapered very slowly over 6 months. MMF was increased to 2,000 mg BID. Follow-up biopsy 2 weeks later showed scant persistent granulomas but all subsequent biopsies were negative. Donor-derived cell-free DNA assays remained negative at 12 months post-transplant but began to climb at 24 months. Cardiac magnetic resonance imaging at that time showed normal graft function without late gadolinium enhancement and computed tomography scan of the chest did not show evidence of any extracardiac sarcoidosis.

CS is a less frequent cause of cardiomyopathy sparsely reported in literature, for which immunomodulatory therapy is the mainstay of management. Recurrence after transplant is exceedingly rare, and outcomes after transplant for CS are generally equivalent to other populations.[1] In a single-center review of 411 cardiac transplants with only 5 due to CS, none demonstrated recurrence.[2] Another review of 19 heart transplants for sarcoid demonstrated no recurrence of sarcoid in the allograft, but 3 patients exhibited extracardiac recurrence.[3] Of the previously published case reports of recurrence, incidence was typically 6 months to several years post-transplant, making our case of early recurrence particularly unusual.[4,5]

Diagnosis of recurrent CS can be challenging, given the low sensitivity of myocardial biopsy.[2] Management relies on expert opinion and centers around augmented immunosuppressive therapy. Despite lack of consensus, prednisone at 30 to 60 mg/day, tapered over months, is suggested as first-line treatment. Additional agents, including MMF, methotrexate, and/or TNF-alpha antagonists, can be considered. Immunosuppression during the acute post-transplant period is a predicament, balancing risk of rejection and recurrence with that of infection. In our patient, the combination of high-dose MMF and prolonged steroid taper proved successful.

This case highlights that the possibility of recurrence of CS after transplant, while rare, still warrants lifelong

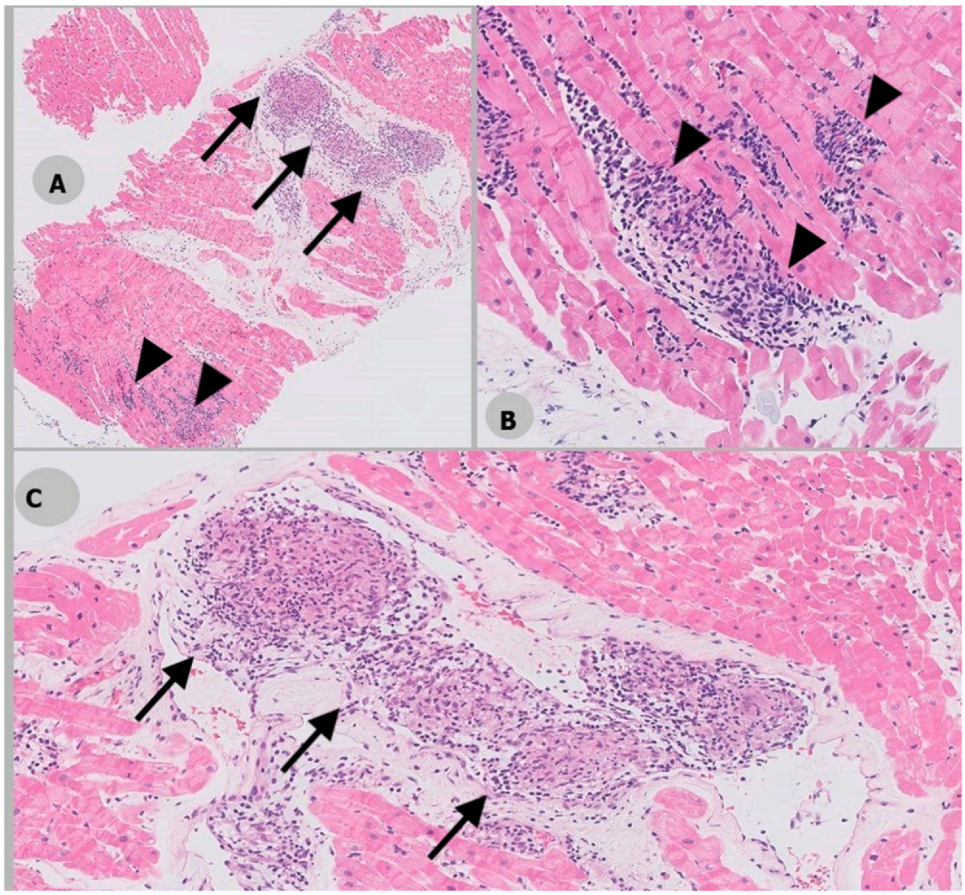

Figure 3 Post-transplant biopsy 2 weeks post OHT demonstrating multiple, well-formed non-necrotizing granulomas with inflammation mostly within the blood vessels (A and C—arrows) with single focus in the myocardium (A and B—arrowhead). OHT, orthotopic heart transplant.

surveillance. Lacking consensus guidelines, modalities such as biopsy, donor-derived cell-free DNA, and repeat imaging should be considered.

Patient consent

Informed consent was obtained from the subject of this case report before the preparation and publication of this manuscript.

Author contributions

Matthew Seplowe: Writing – Original Draft, Writing – Review and Editing, Visualization, Project administration. Shazli Khan: Writing – Review and Editing, Visualization, Project administration. Lakshmisree Vemulakonda: Visualization. Fouzia Shakil: Visualization. Liana Michaud: Writing – Review and Editing. Chhaya Aggarwal-Gupta: Supervision. Gregg Lanier: Supervision. Avi Levine: Supervision. Suguru Ohira: Supervision. David Spielvogel: Supervision. Alan Gass: Supervision. Stephen Pan: Writing – Review and Editing, Conceptualization.

Disclosure statement

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