Cardiac Sarcoidosis Diagnosed on Explant Pathology Following Heart Transplantation

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Introduction

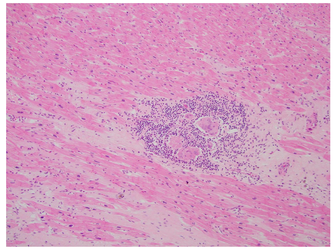
Cardiac sarcoidosis (CS) is a rare and likely underrecognized manifestation of sarcoidosis. CS typically occurs in the context of systemic sarcoid, but isolated cases may exist. We present two cases of patients with nonischemic cardiomyopathy (NICM) and end-stage heart failure who underwent heart transplantation (HT) and were subsequently found to have evidence of CS on explant pathology.

Case Descriptions

Patient 1

A 58-year-old woman presented with symptoms of exertional dyspnea and was diagnosed with complete heart block requiring permanent pacemaker implantation. Four years later, she developed new heart failure symptoms:

- LVEF 20-25%
- Diagnosed with NICM
- Despite upgrade to a biventricular system, the patient experienced progression to end stage heart failure, eventually requiring transplant
- Explant pathology demonstrated noncaseating granulomas and extensive fibrosis
- Patient maintained on tacrolimus and long-term low dose steroids.



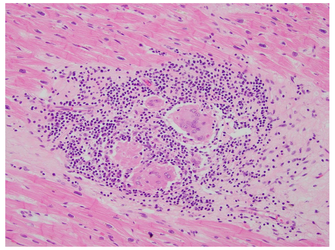
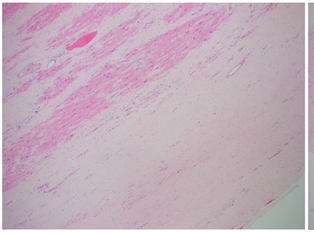
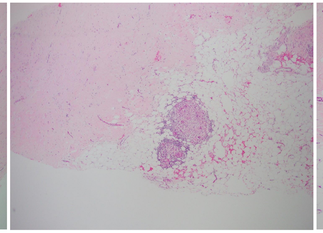


Figure 1: Noncaseating granulomas from the lateral wall of the left ventricle. **L:** 40x; **R:** 100x; H&E stain





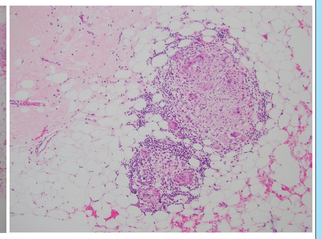


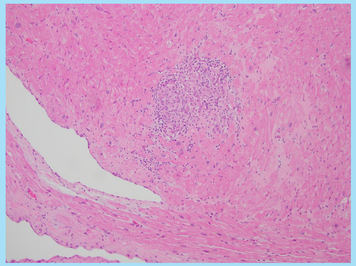
Figure 2: Sections showing extensive fibrosis, indicative of healed or "burnt out" sarcoidosis with no active inflammation. **L:** 40x, posterior wall of left ventricle; **M, R:** 40x, 100x, right ventricular infundibulum; H&E stain

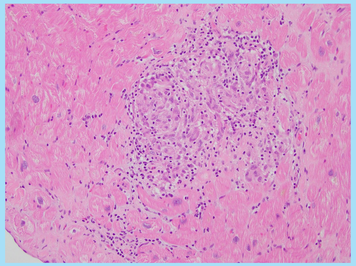
Case Descriptions Continued

Patient 2

A 61-year-old man with a history of NICM secondary to severe mitral regurgitation (MR) underwent surgical mitral valve repair. Following discharge, the patient had progressive symptoms of end stage heart failure. Cardiac MRI demonstrated:

- LVEF 10% and small, focal, mid-wall LGE along the basal inferior RV insertion site
- Patient ultimately underwent transplant
- Explant pathology demonstrated noncaseating granulomas of the LV and interventricular septum.
- Patient maintained on tacrolimus and long-term low dose steroids.





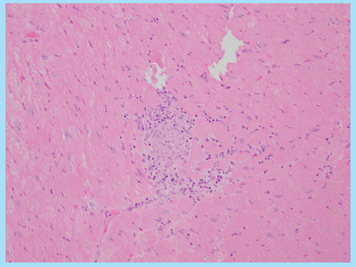


Figure 3: Noncaseating granulomas from the left ventricular free wall. **L:** 40x; **R:** 100x; **B:** 100x; H&E stain

Discussion

- Patient 1
  - Did not undergo advanced cardiac imaging.
  - The awareness of the heterogeneity of NICM and the emphasis on further work-up has evolved in the recent past, although up to 66% of patients may be initially misdiagnosed (Cheng et. al). This has culminated in the European Society of Cardiology providing a Class I recommendation in 2023 to utilize Cardiac MRI in the evaluation of new cardiomyopathies, and a class IIa recommendation to repeat Cardiac MRI every 2-5 years to monitor disease (Arbelo et. al).
  - This case is an excellent example of the necessity of advanced cardiac imaging in further evaluating NICM. Retrospectively, this patient met 2 major criteria according to the 2016 Japanese Circulation Society criteria for isolated CS (Cheng et. al). Further evaluation with advanced cardiac imaging may have strengthened the suspicion of CS.
- Patient 2
  - Likely represents a perplexing case of mixed cardiomyopathy due to both CS and valve disease
  - The minimal LGE on the patient CMR is a non-specific finding and did not raise suspicion of an underlying infiltrative disease process. However, with progressive heart failure symptoms, a repeat CMR 2-5 years after diagnosis as recommended by the ESC may have been beneficial in revealing an infiltrative process (Arbelo et. al).
- Interestingly, neither patient exhibited evidence of extra-cardiac sarcoidosis. The presence of isolated CS is exceedingly rare and requires further heightened level of suspicion to make the diagnosis.
- Overall, the outcomes of patients diagnosed with CS who receive advanced therapies are similar to those without a diagnosis of CS (Cheng et. al).
- Finally, these incidental findings highlight the outcomes and immunosuppressive considerations of patients with CS discovered post-transplant. Although there is minimal data on the best management of these patients, expert consensus is to continue immunosuppressive therapy with both calcineurin inhibitors and corticosteroids (Cheng et. al).

Conclusion

- CS remains an insidious disease process that requires a heightened level of suspicion, especially in patients with NICM.
- Multi-modality, advanced cardiac imaging is important in the evaluation of NICM.
- Although data on the management of patients with CS post-advanced therapies is limited, expert consensus is to continue immunosuppressive regimens.

References

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