CLINICAL VIGNETTE

Cardiac Sarcoidosis: Clinical Presentation and Diagnosis Using Extra-Cardiac Biopsy and Multimodality Cardiac Imaging

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Case

A 59-year-old man with history of metastatic germ cell tumor 8 years prior presented for evaluation of lymphadenopathy found incidentally on CT scan of the chest after a motor vehicle accident with chest trauma. In addition to a clavicular fracture, the Chest CT scan demonstrated mediastinal lymphadenopathy. His metastatic germ cell tumor included pulmonary metastasis and was treated with orchiectomy and adjuvant chemotherapy with complete remission. Given concern that the enlarged mediastinal lymph nodes represented recurrent disease, he underwent PET-CT. In addition to increased uptake corresponding to the recent left clavicular fracture, the scan identified lymphadenopathy in cervical, mediastinal and abdominal areas. Multiple subcentimeter lung nodules were also noted. The myocardium also had significant nodular FDG uptake (Figure 1). The patient underwent endobronchial biopsy of the mediastinal lymph nodes, demonstrating non-caseating granulomas consistent with sarcoidosis.

At follow-up the patient reported increasing exertional dyspnea and orthostatic lightheadedness. Pulmonary function tests showed normal spirometry, lung volumes and diffusing capacity. ECG showed complete heart block, right bundle branch block and left anterior fascicular block. Echocardiogram:noted normal wall motion, with echogenic foci seen in the septum, lateral and inferior walls (Figure 2). Cardiac MRI demonstrated patchy delayed contrast enhancement of the septum and inferior wall, consistent with cardiac sarcoidosis (CS) (Figure 3). The patient was started on prednisone 60 mg daily and underwent implantable cardiac defibrillator placement (ICD). Within two days of starting steroids, he felt better and showed improvement in his ECG from complete heart block to normal sinus rhythm with first degree AV block.

Discussion

Sarcoidosis is a systemic condition characterized by the presence of non-caseating granuloma. Cardiac involvement of sarcoidosis is common, with electrical disturbances and heart failure causing significant mortality. Electrical disturbances including conduction system delays or blocks, as well as ventricular arrhythmias, can lead to sudden cardiac death (SCD). Patients may also present with congestive heart failure from myocardial involvement. Involvement of valvular or subvalvular structures may cause valvular regurgitation. An autopsy series of 84 consecutive patients with known sarcoidosis identified 23 (27%) with CS.[1] Seven of these 23 patients had a history of sudden cardiac death (SCD). Of the 61 patients without findings of CS on autopsy, 8 had a clinical history of SCD, suggesting poor recognition of CS at autopsy. In an autopsy series of 42 Japanese patients with fatal CS, 16/42 (38%) had a clinical history of SCD[2]. Given the concern for the electrophysiologic consequences of CS, there is a low threshold for ICD placement. In addition, complete heart block is seen in 25-30% of patients with CS and may be the presenting illness in patients with sarcoidosis. These patients have a high risk of fatal cardiac events and consideration can be given to ICD placement, as opposed to pacemaker placement.[3]

Diagnosis of CS is challenging. Due to the patchy nature of myocardial involvement, endomyocardial biopsy is insensitive due to sampling error, although this is improved with the use of voltage-mapping guided biopsy.[4] 18F-FDG-PET allows evaluation of pulmonary sarcoidosis as well as CS. Focal or focal-on-diffuse myocarditis is characteristic of CS.[5] MRI is previously reported to have sensitivity greater than 92% and specificity greater than 86%, although this may have improved due to enhancements in imaging techniques.[6] MRI appearance varies with stage of cardiac sarcoid involvement. Acute inflammation results in edema (seen on T2-weighted imaging), focal myocardial thickening and focal early hyper-enhancement (first pass perfusion imaging) with or without delayed contrast hyper-enhancement. This is likely due to variable accumulation of gadolinium chelates from differences in contrast distribution volume. Post-inflammatory replacement scarring is characterized by regional myocardial thinning and hypokinesis with delayed gadolinium enhancement (DGE) of the mid-myocardium and epicardium. This differs from the pattern seen in myocardial infarction which shows delayed enhancement beginning in the endocardium and moving out to the epicardium.[7] Echocardiogram may reveal echogenic focus and regional hypokinesis corresponding to granulomatous infiltration.

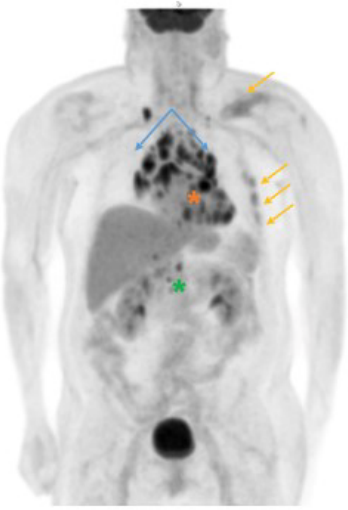
The treatment of CS is multifaceted and requires a multi-disciplinary approach. The rhythm disturbances of CS may require pacemaker or ICD placement. Guideline-directed medical therapy is the standard of care in patients with CS with congestive heart failure, although further information is needed to determine if this represents optimal treatment. The treatment of systemic sarcoidosis is also important to reduce granuloma formation and the subsequent inflammatory response. Steroids are the mainstay of therapy, although steroid-sparing medications can be used for long-term maintenance.[8] Response to treatment can potentially be monitored using 18F-FDG PET. Further data is needed on the optimal medical regimen and long-term prognosis in patients with recognized CS.

Conclusion

The diagnosis of CS is challenging, requiring a high level of clinical suspicion. While myocardial biopsy can provide a definitive diagnosis, a negative result does not exclude disease. In the appropriate clinical setting, multimodality imaging can demonstrate characteristic findings of CS with extra-cardiac biopsy providing supporting evidence for a diagnosis. This case demonstrates the characteristic findings of CS on multimodality imaging (Figure 4), as well as diagnosis without the use of endomyocardial biopsy.

Figures

Figure 1. Thick slab maximum intensity projection reconstruction from FDG-PET demonstrates multifocal increased FDG-activity in the myocardium (orange *) and multistation mediastinal lymph node activity (blue arrows) corresponding to site of biopsy proven caseating granulomas. Left clavicle and rib activity (yellow arrows) the result of healing left clavicular and rib fractures. Retroperitoneal lymph node activity (green *).



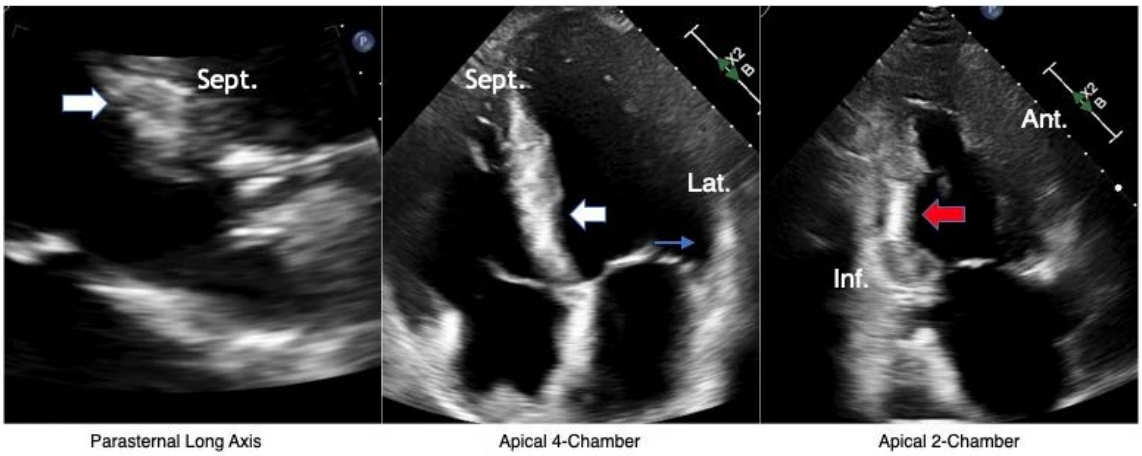


Figure 2. Echocardiographic images demonstrating echogenic foci consistent with focal infiltrate of sarcoidosis seen in the basal septum (white arrow), basal lateral wall (blue arrow) and basal inferior wall (red arrow).

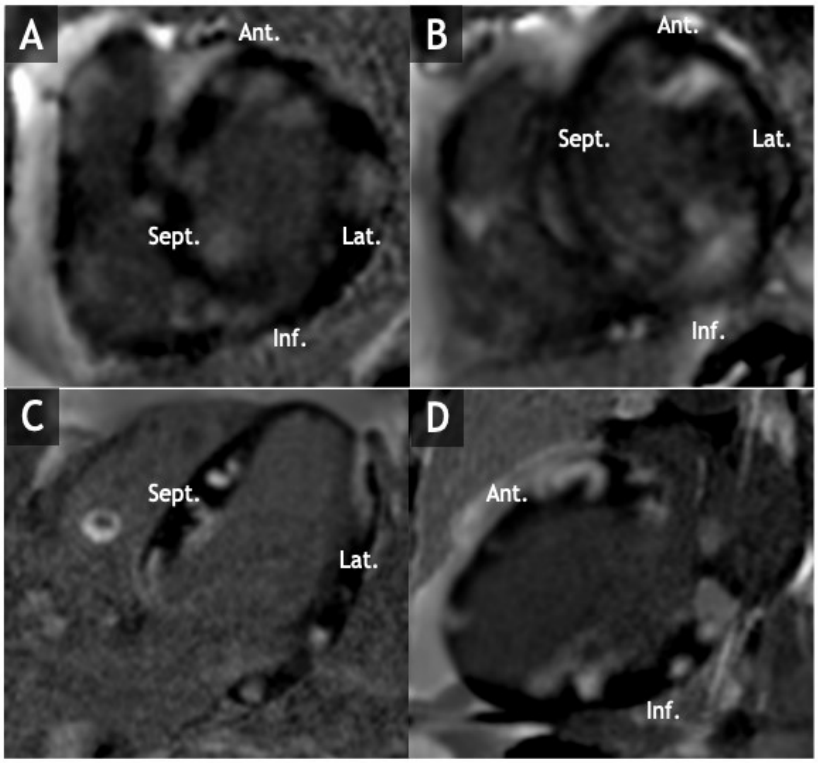


Figure 3. Post-contrast phase sensitive inversion recovery imaging demonstrates multifocal patchy delayed enhancement throughout the left, and to a lesser extent, the right ventricles in a non-vascular territory of distribution. A) Basal short axis B) Mid ventricular short axis C) Horizontal long axis D) Vertical long axis.

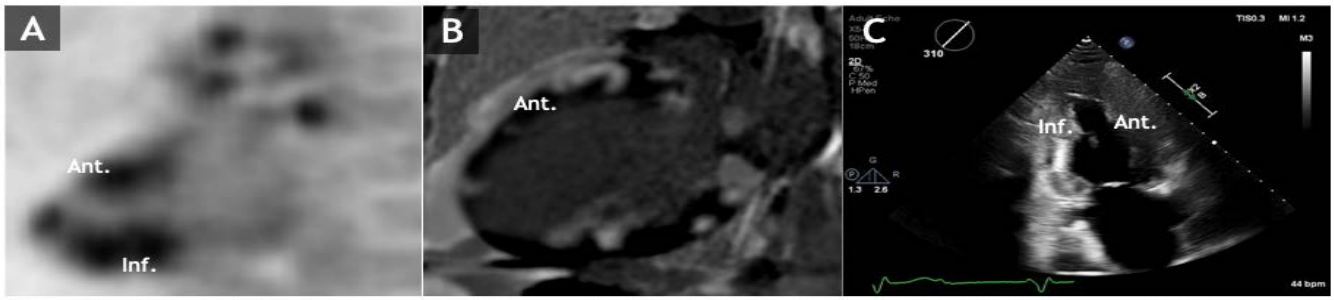


Figure 4. Multimodality imaging in cardiac sarcoidosis. A) Attenuation corrected PET in the vertical long axis (VLA) plane with multifocal FDG-avid foci involving the anterior and inferior left ventricular myocardium, B) Post-contrast phase sensitive inversion recovery (PSIR) MRI in VLA with corresponding foci of multifocal delayed hyperenhancement and C) Transthoracic echo images in the apical 2-chamber view with corresponding foci of increased echogenicity in the inferior LV wall.

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