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Breaking hearts and taking names: A case of sarcoidosis related effusive-constrictive pericarditis

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ABSTRACT

Introduction: Pericardial involvement of sarcoidosis is a rare cause for acute heart failure, and usually occurs as a result of the development of a pericardial effusion leading to cardiac tamponade. Even rarer still, is the manifestation of constrictive pericarditis. We report a case of sarcoidosis with lung, pleural, and pericardial involvement with effusive-constrictive pericarditis leading to cardiac tamponade.

Case presentation: A 34-year-old Caucasian man presented for evaluation of a history of worsening exertional dyspnea, edema, and weight loss. A high-resolution chest computed tomography showed diffuse pulmonary nodules with upper lobe predominance and in a perilymphatic distribution; large right pleural effusion; and large pericardial effusion with pericardial thickening. A transthoracic echocardiogram demonstrated early tamponade physiology for which a pericardial drain was placed. After removal of the drain he developed cardiogenic shock from cardiac tamponade attributed to the reaccumulation of a pericardial effusion and urgent pericardial window was performed. Serial echocardiography was concerning for organization and localization of the pericardial fluid. Cardiac magnetic resonance imaging demonstrated a significant reduction in pericardial slippage between the parietal and visceral layers around the heart collectively suggestive of constrictive pericarditis. Confirmation of effusive-constrictive pericarditis was noted on right heart catheterization. He then underwent pericardiectomy, which on histopathologic evaluation demonstrated non-necrotizing granulomas, thus confirming pericardial involvement of sarcoidosis.

Conclusions: We report a case demonstrating unique manifestations of sarcoidosis; effusive-constrictive pericarditis presenting with acute congestive heart failure.

1. Introduction

Constrictive pericarditis is a cardiac compressive syndrome caused by the progressive loss of elasticity of the pericardial sac. When there is coexisting pericardial fluid, it is known as effusive-constrictive pericarditis, and often presents with tamponade physiology. The etiology of constrictive pericarditis varies widely, of which sarcoidosis represents an extremely small percentage. We present a case of effusive-constrictive pericarditis caused by sarcoidosis.

2. Case

A 34-year-old Caucasian man presented for evaluation of a five-month history of worsening exertional dyspnea, productive cough, and lower extremity swelling. He reported associated fatigue, unintentional 50 pounds weight loss, and early satiety. His past medical history was notable only for hypertension, which was controlled with hydrochlorothiazide and carvedilol. He recently started taking furosemide for lower extremity swelling.

He is a never smoker. He has no history of recent travel or any relevant exposures. His vital signs were significant for an oxygen saturation of 92% on 2 L per minute of supplemental oxygen and mild tachycardia. Physical examination was notable for diaphoresis, pallor,

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Abbreviations

FVC	Forced vital capacity
DLCO	Diffusion capacity of the lung for carbon monoxide
BAL	Bronchoalveolar lavage
EBUS	Endobronchial ultrasound
LV	Left ventricle
RV	Right ventricle
TBNA	Transbronchial needle aspiration

diminished heart sounds, markedly decreased breath sounds over the right thorax, and 2+ pitting lower extremity edema.

Pulmonary function tests demonstrated an intrinsic restrictive ventilatory defect with a forced vital capacity (FVC) of 4.03 L (59% of predicted) and diffusion capacity of the lung for carbon monoxide (DLCO) of 23.3 mL/min/mmHg (55% of predicted). The partial pressure of oxygen on arterial blood gas was 60 mmHg. High resolution chest computed tomography showed diffuse pulmonary nodules with upper lobe predominance and in a perilymphatic distribution; diffuse partially calcified mediastinal and hilar lymphadenopathy; moderate to large right pleural effusion; and moderate to large pericardial effusion with pericardial thickening (Fig. 1). He subsequently underwent a transthoracic echocardiogram which demonstrated preserved left ventricular systolic function and a large circumferential pericardial effusion with evidence of mitral inflow/tricuspid inflow respiratory variation and paradoxical septal shift, concerning for early tamponade physiology. He was admitted to hospital and underwent an urgent pericardiocentesis with removal of 500 mL of serosanguinous fluid. Pericardiocentesis resulted in immediate clinical improvement. The fluid was monocyte-predominant, with negative cultures. The pericardial drain was removed after several days of minimal drainage.

Thoracentesis and fiberoptic bronchoscopy with bronchoalveolar lavage (BAL), transbronchial biopsy, and endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA) of the mediastinal lymph nodes were also performed. Pleural fluid analysis showed monocytic predominant transudate (53% monocytes, 38% lymphocytes) with negative cultures, cytology, and flow cytometry. Adenosine deaminase level was normal. BAL of the right middle lobe was also predominantly monocytic, with negative cultures (including acid-fast bacilli) and cytology. Transbronchial biopsies yielded two non-necrotizing granulomas, and otherwise were negative for malignancy or infection. Mediastinal lymph node fine needle aspiration from the EBUS-TBNA was non-diagnostic.

Given the inconclusive nature of the results, the patient subsequently underwent video-assisted thoracoscopic surgery wedge biopsies of the right lung as well as pleural and pericardial biopsy. A pericardial window was attempted during the procedure but was not successful. A right chest tube was left in place with subsequent daily output of one liter or greater of transudative fluid. The pathology demonstrated lung tissue with florid non-necrotizing granulomas extending into the visceral pleura (Fig. 2). No fungi or acid-fast bacilli were identified on culture or tissue staining. The biopsy of the pericardium showed focal fibrosis but no granulomas were seen. He was diagnosed with sarcoidosis involving the lungs, pleura, and presumably the pericardium and was started on prednisone 30 mg daily.

Soon after, the patient's hospital course was complicated by re-accumulation of the pericardial effusion, and this time with cardiogenic shock, secondary to cardiac tamponade. He underwent an emergent pericardial window and mediastinal drain placement with resolution of shock but continued to have more than one liter of transudative drainage daily from both the chest and mediastinal tubes.

Further evaluation with cardiac magnetic resonance (CMR) imaging demonstrated a significant reduction in pericardial slippage between the parietal and visceral layers of the heart as well as prominent ventricular septal bounce consistent with enhanced inter-ventricular dependence; collectively suggestive of constrictive pericarditis (Fig. 3). Of note, there was no evidence of late gadolinium enhancement to support myocardial involvement with sarcoidosis. Confirmation of effusive-constrictive pericarditis was noted on right heart catheterization, which showed equalization of diastolic right ventricular (RV) and left ventricular (LV) pressures with evidence of a "square root sign", and RV/LV discordance (Fig. 4). He then underwent pericardiectomy, which on histopathologic evaluation demonstrated non-necrotizing granulomas, thus confirming pericardial involvement of sarcoidosis (Fig. 5).

The patient steadily improved clinically following his surgery and had complete resolution of the pleural effusion and lower extremity edema with diuretics. He was discharged in stable condition on 20 mg of prednisone. At one month follow-up he denied dyspnea and the echocardiogram demonstrated normal cardiac chamber size. Pulmonary function tests showed improvement with a FVC of 5.52 L (79% of predicted) and DLCO of 24.92 mL/min/mmHg (57% of predicted). Methotrexate was started as a steroid-sparing agent and prednisone was tapered off.

3. Discussion

Sarcoidosis poses a diagnostic challenge, as it not only affects different organ systems, but can manifest heterogeneously within each respective organ system. Our case highlights this point, as our patient not only presented with lung parenchymal findings classically seen with sarcoidosis but was also had less commonly encountered pleural and pericardial involvement.

Pleural effusion as a result of sarcoid pleural involvement is uncommon and has a prevalence of 1.1%–1.5% [1,2]. These effusions tend

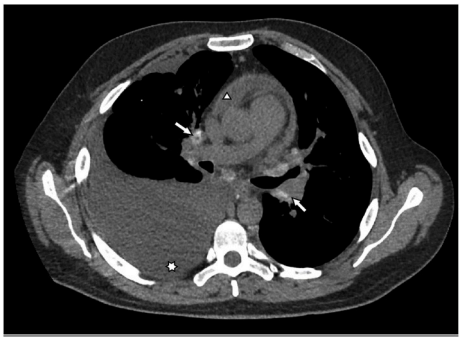

Fig. 1. Axial image of CT chest demonstrating calcified hilar lymphadenopathy (arrows), moderate to large pericardial effusion (triangle), and moderate to large right pleural effusion (star).

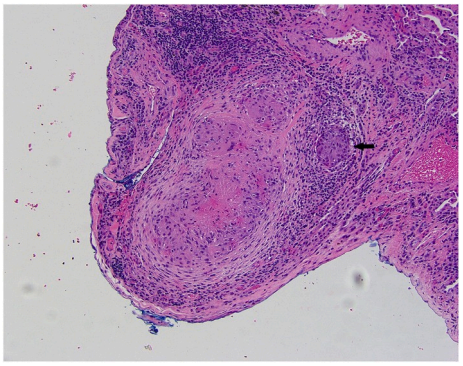

Fig. 2. (10x H&E) Right lung demonstrating multiple non-necrotizing granulomas involving the lung and extending into the pleura, with surrounding multinucleated giant cells (black arrow).

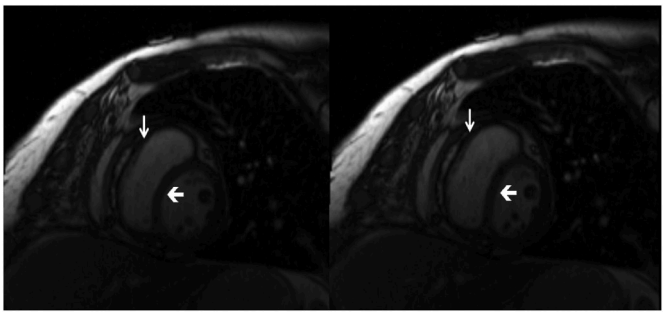

Fig. 3. Cardiac MRI Septum (thick arrow) is bowed during systole and flattened during diastole, representing the "septal bounce", a paradoxical interventricular septal movement during early diastole where the septum first moves toward the left ventricle (left panel) and then away from the left ventricle (right panel), a finding consistent with constrictive pericarditis. Also seen is the thickened pericardium (thin arrow).

to be lymphocyte predominant and exudative by protein criteria alone on Light's criteria [1]. To recall, our patient had a transudative effusion with evidence of sarcoidosis affecting the pleura, mirroring a recently published case which the authors report to be the first to show a transudative effusion as the initial presentation of sarcoidosis [3].

Pericardial sarcoidosis is uncommon, can mimic congestive heart failure, and is most often encountered as asymptomatic pericardial effusions [4,5]. In rare instances, it can present with large, and recurrent, pericardial effusions with or without tamponade physiology. Only a handful of cases in the English-language literature describe large pericardial effusions with associated cardiac tamponade attributed to sarcoidosis [6–13]. The role of immunosuppression for the management of large pericardial effusions is not clear, but several case reports have reported resolution with corticosteroid therapy [6,10,12–16].

Constrictive pericarditis is an even rarer manifestation with only three reported cases in the literature [17–19]. Two pathophysiological mechanism have been described: fibrous constrictive or effusive-constrictive. Our patient had effusive-constrictive pericarditis, which is an increasingly recognized clinical syndrome characterized in patients with tamponade with associated diastolic heart failure who continue to have elevated intracardiac pressure after the removal of pericardial fluid [20]. The disorder is due to pericardial inflammation causing scarring and constriction in conjunction with the presence of pericardial fluid under pressure, leading to hemodynamic disturbances and ultimately reducing myocardial transmural pressure and filling [20,21]. The diagnosis requires right heart catheterization to demonstrate persistently elevated right atrial pressure once intrapericardial pressure is normalized via pericardiocentesis or pericardial window. Our patient had elevated pressures despite pericardial window.

To emphasize the novelty of our case, a review of 42 published cases of effusive-constrictive pericarditis from 2000 to 2014 showed only one to be caused by sarcoidosis [19,20]. Of the three previous cases of constrictive pericarditis attributed to sarcoidosis, only two had adequate data to review regarding how the diagnosis was made. Both patients had effusive-constrictive physiology and underwent pericardiectomy, but neither case demonstrated granulomas in the pericardial tissue. Both had concomitant myocardial involvement as diagnosed by either CMR or endomyocardial biopsy [17,19].

The optimal treatment of constrictive pericarditis is unclear, particularly regarding the role of immunosuppression. In acute constrictive pericarditis of any etiology, there is a role for anti-inflammatory therapy if imaging shows evidence of pericardial inflammation [22]. Pericardiectomy is the treatment of choice in most cases of constrictive pericarditis. The role for continued immunosuppression following pericardiectomy is less clear, particularly for those patients with isolated

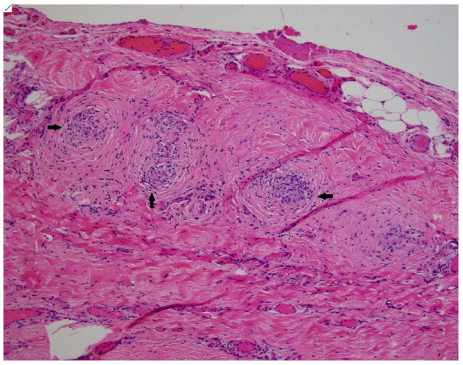

Fig. 5. (10x H&E) The pericardium demonstrating multiple non-necrotizing granulomas (arrows).

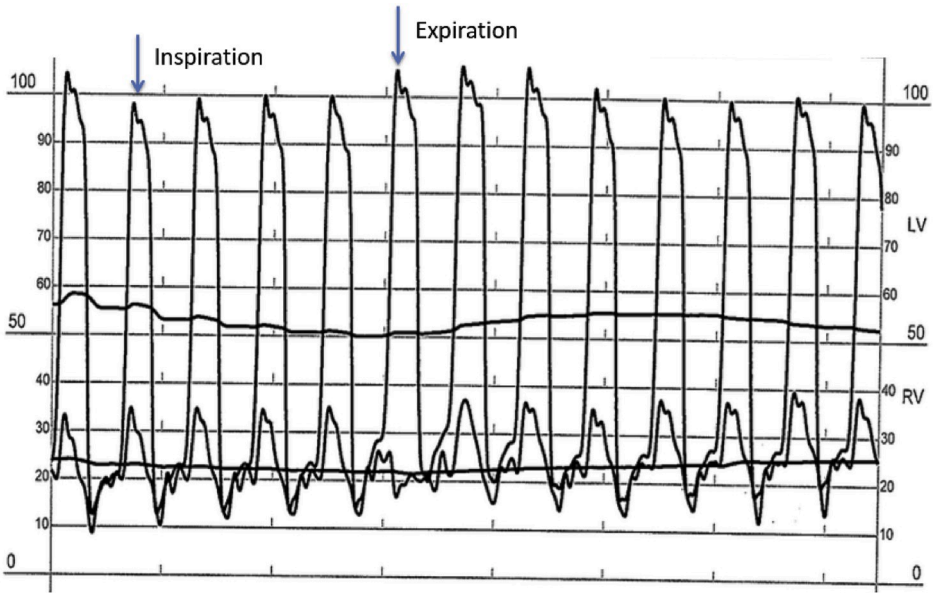

Fig. 4. Elevated and equalized end diastolic LV and RV pressures resulting in the "square root sign". Intraventricular interdependence is demonstrated by a decrease in LV pressure and increase in RV pressure during inspiration (arrow), and an increase in LV pressure and decrease in RV pressure during expiration (arrow).

pericardial disease and no myocardial involvement. This is important to note, as there may be a link between higher corticosteroid exposure and poorer patient-reported health-related quality of life [23]. Given our patient's concomitant lung and pleural involvement, we believe there is a present role for corticosteroid therapy, with close follow-up to determine opportunities for tapering of immunosuppression.

4. Conclusion

This case demonstrates that sarcoidosis can manifest in a multitude of ways including, in this case, life-threatening pleural and pericardial effusions, and should be considered in the differential of patients presenting with acute heart failure with preserved ejection fraction and normal myocardium by MRI imaging.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Ramon Valentin: Conceptualization, Visualization, Writing - original draft. **Ellen C. Keeley:** Resources, Data curation, Writing - review & editing. **Ali Ataya:** Conceptualization, Writing - review & editing. **Diana Gomez-Manjarres:** Conceptualization, Writing - review & editing. **John Petersen:** Resources, Data curation, Writing - review & editing. **George J. Arnaoutakis:** Writing - review & editing. **Peter Drew:** Resources, Data curation, Writing - review & editing. **Matt Barnes:** Resources, Data curation. **Divya C. Patel:** Conceptualization, Project administration, Supervision, Visualization, Writing - original draft, Writing - review & editing.

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