Postprint of a Case of Occult Cardiac Sarcoidosis

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Abstract

Sarcoidosis is a multisystem disease characterized by non-caseating granulomas, with commonly affected organs including the lungs, heart, eyes, skin, and other organs. Approximately 2%–5% of sarcoidosis patients exhibit cardiac involvement, while autopsy studies have demonstrated that the incidence of cardiac involvement in sarcoidosis patients may reach as high as 25%–58%. However, the condition is insidious, lacking cardiac clinical symptoms, which predisposes to missed or delayed diagnosis and severely impacts patient prognosis. This article reports a case of occult cardiac sarcoidosis, analyzing its clinical characteristics, laboratory findings, and diagnostic and therapeutic course, to alert clinicians to the importance of evaluating vital organ involvement in sarcoidosis patients.

Full Text

A Case of Sarcoidosis with Asymptomatic Cardiac Involvement

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Abstract

Sarcoidosis is a multi-system inflammatory disorder characterized by non-caseating granulomas, commonly involving the lungs, heart, eyes, skin, and other organs. Symptomatic cardiac involvement occurs in approximately 2%–5% of patients. However, autopsy studies have detected asymptomatic cardiac involvement in 25%–58% of sarcoidosis patients, often leading to delayed diagnosis and poor prognosis. We report the clinical manifestations, laboratory findings, diagnostic approach, and treatment course of a sarcoidosis patient with latent cardiac involvement.

Keywords: Cardiac, Sarcoidosis

Case Report

Sarcoidosis is a multi-system disease characterized by non-caseating granulomas with an incidence of 4.7–64 per 100,000, more common in women[1]. Common organ involvement includes the lungs, heart, eyes, and skin. Approximately 2%–5% of sarcoidosis patients exhibit cardiac involvement, which can manifest as various clinical presentations depending on the location, extent, and activity of the disease, including conduction block, ventricular arrhythmia, congestive heart failure, pericardial effusion, and sudden death[2]. Cardiac sarcoidosis can be clinically silent, with autopsy studies revealing cardiac involvement in up to 25%–58% of patients, though some show no clinical manifestations of cardiac disease[3,4].

A 54-year-old female presented to the Department of Respiratory Medicine at Peking Union Medical College Hospital in May 2013 with a six-month history of cough, without sputum production, hemoptysis, fever, night sweats, dry eyes, arthralgia, or weight loss. Her personal, family, and reproductive histories were unremarkable. Physical examination revealed no palpable cervical lymphadenopathy, and no abnormal findings in the heart, lungs, or abdomen.

Laboratory investigations showed: white blood cell count $7.29\$\times10^{\{9\}/L, hemoglobin137g/L, plateletcount273\times10}\{9\}/I$ $convertingenzyme(ACE)51U/L(normalrange12–68U/L); andnegativeT -$ $SPOT.TB.ChestCTrevealedmultiplenodulesofvaryingsizesinbothlungswithbilateralhilarandmediastinally$ $FVC2.43L(107.5\_\{1\}\$$ 2.03 L (107.1%), FEV_1/FVC 83.55%, TLC 3.98 L (100%), and DLCO SB 79.3%.

Bronchoscopy showed multiple small nodules in the right middle lobe bronchial mucosa. Bronchoalveolar lavage fluid (BALF) cytology revealed a total cell count of $6.4\$\times10\hat{}\{6\}\$$ cells, with macrophages 59%, lymphocytes 41%, and no neutrophils or eosinophils. BALF T-cell subsets showed: T cells 61.8%, CD4 45.1%, CD8 14.3%, and CD4/CD8 ratio 3.2 (normal range 0.9–2.0). Brush cytology was negative for malignant cells, and acid-fast staining was negative. Pathology from the right middle lobe mucosal nodules showed epithelioid granulomas

without necrosis in the submucosa. Right lower lobe lung tissue pathology revealed chronic inflammation. Based on these findings, a diagnosis of pulmonary sarcoidosis, stage II, was established, and the patient was started on inhaled corticosteroids (Pulmicort Turbuhaler, 2 inhalations twice daily).

In February 2016, the patient' s cough worsened. Repeat investigations showed erythrocyte sedimentation rate 5 mm/h and ACE 84 U/L. Cardiac enzymes were negative. Arterial blood gas analysis revealed pH 7.476, pCO_2 31.3 mmHg, and pO_2 82.9 mmHg. Pulmonary function tests showed: FVC 2.26 L (98.1%), FEV_1 1.84 L (95.6%), FEV_1/FVC 81.64%, TLC 3.68 L (89.5%), and DLCO SB 92.9%. High-resolution chest CT demonstrated decreased size and number of pulmonary nodules and mediastinal/hilar lymph nodes compared to previous imaging [Figure 1: see original paper].

Twenty-four-hour Holter monitoring revealed frequent premature ventricular contractions, occasional premature atrial contractions with brief atrial tachycardia episodes, and ST-T segment depression. Echocardiography showed LVEF 51%, global cardiac enlargement predominantly affecting the right heart, mild tricuspid and mitral regurgitation, decreased left ventricular diastolic function, and small pericardial effusion. Estimated pulmonary artery systolic pressure was 39 mmHg (1 mmHg = 0.133 kPa). ^{18}F-FDG PET demonstrated hypermetabolic lymph nodes in the right neck, mediastinum, and bilateral hilar regions, hypermetabolic pulmonary nodules, heterogeneous cardiac metabolic uptake, and multiple hypermetabolic nodules in the liver and spleen [Figure 2: see original paper]A. ^{13}N-$NH_3 \cdot H_2O$ cardiac PET-MRI showed heterogeneous myocardial ammonia uptake without obvious perfusion defects [Figure 2: see original paper]B, 2C. Based on these findings, cardiac sarcoidosis involvement was suspected, and the patient was started on oral prednisone 40 mg daily with regular follow-up, showing stable disease.

Discussion

The 2016 European Heart Rhythm Association expert consensus on cardiac sarcoidosis diagnosis established two main criteria[5]: (1) Histopathological diagnosis from cardiac tissue showing non-caseating epithelioid granulomas with exclusion of other diseases (microbiological staining negative when feasible); and (2) Clinical diagnostic criteria requiring: (a) extrathoracic organ pathology confirming sarcoidosis, and (b) at least one of the following: (1) response of cardiomyopathy or conduction block to corticosteroids or immunosuppressive therapy; (2) unexplained reduced left ventricular ejection fraction (<40%); (3) unexplained sustained (spontaneous or induced) ventricular tachycardia; (4) second- or third-degree atrioventricular block; (5) PET showing heterogeneous myocardial metabolic uptake; (6) cardiac MRI showing delayed gadolinium enhancement; or (7) positive ^{67}gallium myocardial uptake; plus (c) exclusion of other cardiac disease etiologies. This patient met the clinical diagnostic criteria with pulmonary sarcoidosis pathology and heterogeneous cardiac metabolic uptake on ^{18}F-FDG PET, without other cardiac diseases.

Endomyocardial biopsy remains the gold standard for diagnosing cardiac sarcoidosis but is an invasive procedure with poor sensitivity, yielding positive results in less than 30% of cases[3]. This low yield stems from two factors: first, cardiac sarcoid lesions typically involve the left ventricle, while biopsy is performed via jugular or femoral venous access to obtain right ventricular tissue; second, cardiac involvement is often focal, making it difficult to obtain representative non-caseating granulomatous tissue[6].

Recent studies show that combined PET or cardiac magnetic resonance (CMR) imaging can increase biopsy yield to approximately 50%[7]. The most common PET finding in cardiac sarcoidosis is focal metabolic uptake, often with mild diffuse uptake, resting perfusion defects, or wall motion abnormalities[8]. Studies evaluating ^{18}F-FDG PET for sarcoidosis diagnosis demonstrate 89% sensitivity (95% CI: 79%, 96%) and 78% specificity (95% CI: 68%, 86%)[9]. The 2014 expert consensus also recommended PET and CMR for cardiac sarcoidosis evaluation[10]. This patient' s ^{18}F-FDG PET showed heterogeneous cardiac metabolic uptake, while myocardial perfusion imaging demonstrated heterogeneous ammonia uptake, consistent with inflammatory cell infiltration.

The most common manifestations of cardiac sarcoidosis include atrioventricular block and ventricular arrhythmias. Atrioventricular block results from granulomatous lesions and scar tissue involving the conduction system (sinoatrial node, interventricular septum)[11]. Ventricular arrhythmias, including premature ventricular contractions and ventricular tachycardia, arise from re-entrant circuits caused by focal granulomatous lesions and represent the leading cause of mortality[12]. Atrial arrhythmias are also common, possibly related to inflammation or atrial scarring, though some suggest they result from ventricular dysfunction or pulmonary parenchymal involvement causing atrial dilation[10].

Approximately 46% of patients with cardiac sarcoidosis have myocardial damage with decreased left ventricular diastolic function, possibly related to granulomatous infiltration of the myocardial interstitium or coronary microvascular ischemia[13]. Pulmonary hypertension occurs in 5%–20% of sarcoidosis patients, associated with pulmonary fibrosis destroying distal capillary beds, chronic hypoxia, extrinsic compression of large pulmonary arteries, granulomatous involvement of small pulmonary vessels, and left ventricular dysfunction from myocardial involvement[14]. About 20% of patients develop pericardial effusion, typically small, related to granulomatous pericardial involvement[15]. Other cardiac manifestations include mitral valve prolapse and mitral/tricuspid regurgitation, mostly related to papillary muscle involvement or left ventricular dilation rather than direct valvular involvement[16]. Aortic regurgitation or aneurysm can also occur from granulomatous involvement of the aortic root[17].

This patient' s serial echocardiograms showed decreased left ventricular diastolic function, small pericardial effusion, mild tricuspid and mitral regurgitation, right heart enlargement, and estimated pulmonary artery systolic pressure of 36–39 mmHg, without overt pulmonary hypertension. The absence of lower extremity edema, hepatic congestion, significant hypoxia, or pulmonary hypertension

suggests right heart dilation was likely due to sarcoid myocardial involvement.

Studies indicate that left ventricular dysfunction severity and sustained ventricular tachycardia correlate with survival in cardiac sarcoidosis[5]. Recent research shows that even in patients with normal ejection fraction, delayed gadolinium enhancement on CMR and myocardial inflammation on ^{18}F-FDG PET/CT predict poor outcomes[18]. Prognosis in asymptomatic cardiac sarcoidosis remains uncertain[5].

Treatment decisions in sarcoidosis depend on the risk of irreversible organ damage, functional impairment, mortality risk, and impact on quality of life. Most experts recommend treatment when sarcoidosis involves the heart, nervous system, kidneys, eyes refractory to local therapy, or causes hypercalcemia[1]. Oral prednisone 20–40 mg daily for 1–3 months, followed by maintenance dose of 10–15 mg daily for 6–9 months, is recommended[19]. Cardiac sarcoidosis may require higher initial doses of 40–60 mg daily[20]. Despite over 50 years of corticosteroid use, no evidence-based data demonstrate improved prognosis. Inhaled corticosteroids are considered for mild disease to reduce systemic side effects[21], though studies show no significant improvement in cough symptoms[22]. The benefit-risk ratio of long-term corticosteroids in asymptomatic patients remains unclear. This patient with confirmed cardiac involvement received oral corticosteroids and remains stable on follow-up.

Cardiac involvement is a poor prognostic factor in sarcoidosis, with nonspecific clinical manifestations and low diagnostic yield from invasive biopsy. Asymptomatic cardiac sarcoidosis poses particular diagnostic challenges, often leading to missed or delayed diagnosis and severely impacting survival. This case highlights the importance of systematic evaluation in sarcoidosis patients and demonstrates that PET imaging serves as an effective diagnostic tool to facilitate early diagnosis and treatment, thereby improving patient outcomes.

Figures and Legends

Figure 1. Chest CT in 2013 showing scattered nodules and mediastinal lymphadenopathy (A, B). Chest CT in 2016 demonstrating decreased size and number of nodules and lymph nodes (C, D).

Figure 2. ^{18}F-FDG PET in 2016 showing hypermetabolic lymph nodes in the right neck, mediastinum, and bilateral hila; hypermetabolic pulmonary nodules; heterogeneous cardiac metabolic uptake; and hypermetabolic nodules in the liver and spleen (A). ^{13}N-$NH_3 \cdot H_2O$ cardiac PET-MRI demonstrating heterogeneous myocardial ammonia uptake without obvious perfusion defects (B, C).

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Note: Figure translations are in progress. See original paper for figures.