CASE REPORT

A 28 year old woman with ventricular tachycardia and an abnormal chest radiograph

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A 28 year old white woman with no medical history presented to the emergency room with symptomatic non-sustained ventricular tachycardia. She was asymptomatic up to a few days before presentation. Her physical examination was essentially normal and hence did not help with the differential diagnosis of the problem. Bronchoscopic transbronchial biopsy led to the final diagnosis of cardiac sarcoidosis.

The following case report is presented and discussed by the authors.

CASE PRESENTATION

Michele Heath

A 28 year old woman with no medical history presented to the emergency room with complaints of five days of recurrent palpitations and occasional midepigastric chest discomfort. She had no associated symptoms of dyspnea, nausea, vomiting, diaphoresis, lightheadedness, or syncope.

Her review of systems was negative for fever, rash, cough, haemoptysis, myalgias, or arthralgias or for a history of cardiac, pulmonary, or renal disease. She reported normal exercise tolerance and played tennis regularly. She did report a 9 kg (20 lb) intentional weight loss over the previous three months.

The patient was originally from Moscow, Russia and had immigrated 21 years previously. She worked as a food handler, smoked half a pack of cigarettes a day, and did not use alcohol or injection drugs. She had no other HIV risk factors. She was taking no medications.

On physical examination, she was a young, fit appearing woman without distress. She was afebrile, with a blood pressure of 94/51 mm Hg, pulse of 80 beats/min, and oxygen saturation of 99% on room air. Sclera were anicteric and oropharynx was without lesions. Skin was without rash. No cervical, axillary, or inguinal lymphadenopathy was noted. Lungs were clear. On precordial examination, the rhythm was regular and no murmurs, gallops, or rubs were present. The cardiac point of maximal intensity was brisk and non-displaced. Abdominal examination was benign, without organomegaly. There was no clubbing or peripheral oedema. Neurological examination was intact. Admission laboratory results of creatinine, blood urea nitrogen, thyroid stimulating hormone, white blood cell count, haematocrit, platelets, and urinalysis testing were normal. Urine toxicology screen and β human chorionic gonadotropin were negative. A chest radiograph (fig 1) showed a diffuse interstitial infiltrative pattern. ECG (fig 2) showed sinus rhythm with left bundle branch block. During her evaluation in the emergency department palpitations recurred and ECG

Figure 1 Posteroanterior chest radiograph showing non-specific diffuse interstitial markings. No focal lung opacities, pleural effusions, or lymphadenopathy are noted. Cardiac silhouette is enlarged.

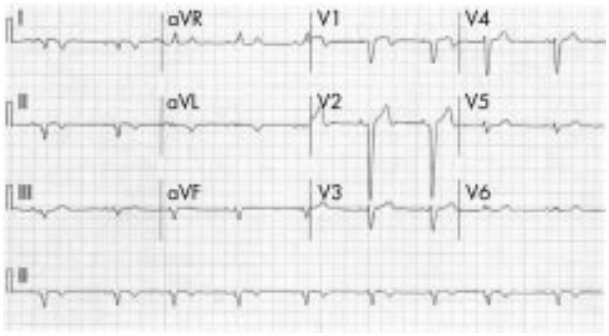

Figure 2 Presenting 12 lead ECG showing sinus rhythm with left bundle branch block. Note that the limb leads were inadvertently reversed on this tracing.

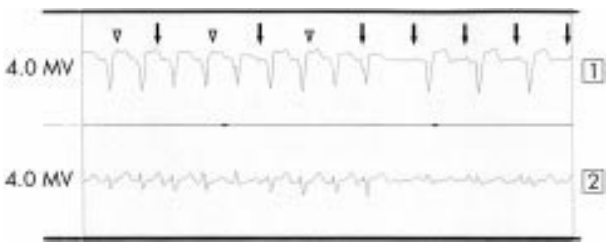

Figure 3 Rhythm strip recorded during subjective palpitations showing non-sustained ventricular tachycardia that was converted to sinus rhythm with left bundle branch block. Note the atrioventricular dissociation during ventricular tachycardia (black arrows). Retrograde P waves are also seen (white arrowheads).

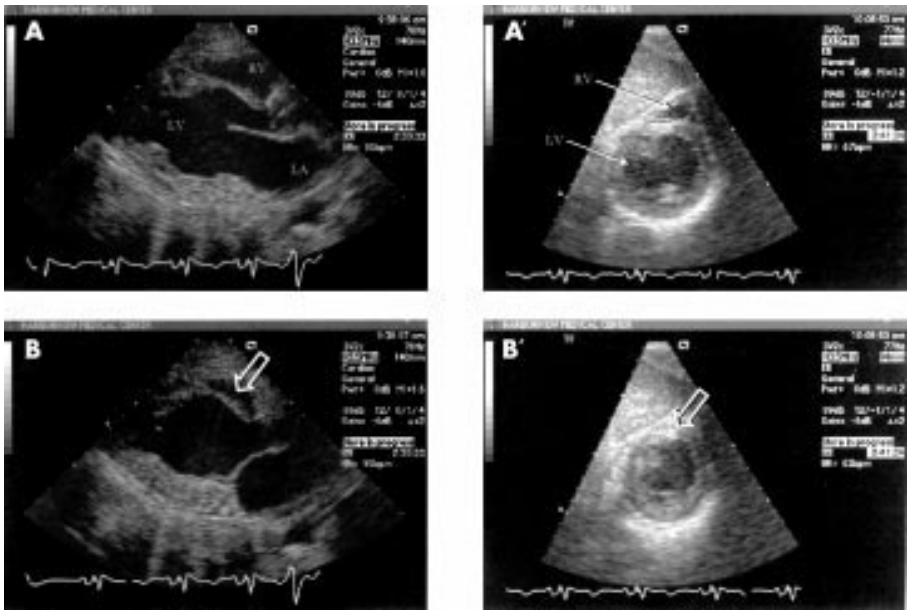

Figure 4 Echocardiograms of the left ventricle during diastole (parasternal long axis A and short axis A′ views) and during systole (parasternal long axis B and short axis B′ views). The left atrium (LA), left ventricle (LV), and right ventricle (RV) are labelled for clarity. Note the thin and dyskinetic septal wall (block arrow).

(fig 3) at that time showed non-sustained ventricular tachycardia.

The patient was admitted to the telemetry unit and metoprolol administration was started. An echocardiogram (fig 4) was obtained and showed mild mitral regurgitation, mild left ventricular dilatation, and an estimated left ventricular ejection fraction of 40%. The middle and basal portions of the anterior and inferior intraventricular septum were thin and dyskinetic. The right ventricle was normal and the pulmonary artery pressures were normal. Normal coronary arteries were seen on cardiac catheterisation.

During her hospital course she continued to have recurrent episodes of non-sustained ventricular tachycardia. She remained haemodynamically stable. On hospital day 4 she developed sustained ventricular tachycardia and was mildly symptomatic; the tachycardia resolved spontaneously and lasted slightly longer than 30 seconds.

Further diagnostic investigation found an erythrocyte sedimentation rate of 2 mm/h, negative rheumatoid factor, negative antinuclear antibody, and serum angiotensin converting enzyme (ACE) concentration of 38 U/l (normal range 14–87 U/l).

Chest computed tomography (CT), including high resolution images (fig 5), showed numerous very small nodular opacities throughout the middle and upper lungs in a perilymphatic distribution typical of an interstitial granulomatous process. There was no mediastinal or hilar lymphadenopathy.

A diagnostic procedure was performed.

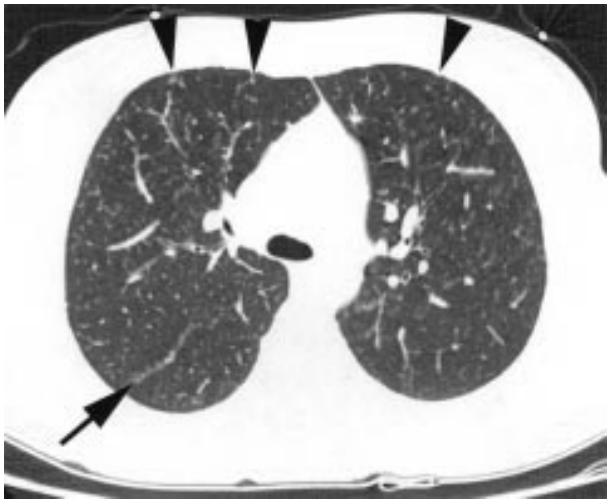

Figure 5 High resolution computed tomographic images show numerous very small nodular opacities throughout the lungs in a perilymphatic distribution typical of an interstitial granulomatous process. Note the subpleural nodules (arrowheads) and the string of nodules along the right major fissure (arrow).

DISCUSSION

Edward A Gill

The patient is a young white woman who presented with symptomatic non-sustained ventricular tachycardia. She was asymptomatic up to a few days before presentation. Her physical examination was essentially normal and hence did not help with the differential diagnosis of the problem. Although not mentioned, the patient should have had, based on the conduction defect, a paradoxically split second heart sound. The ECG is helpful in that it shows a conduction defect of the left bundle branch type. The combination of the conduction defect, the septal wall motion abnormality on the echocardiogram, and the interstitial pattern on her chest radiograph suggests a systemic disease.

Ventricular tachycardia is always a worrisome rhythm. Sustained ventricular tachycardia can be life threatening, regardless of its cause. Except for unusual causes of ventricular tachycardia, such as would be seen in a re-entrant tachycardia involving the right ventricular outflow tract, ventricular tachycardia is associated with and caused by structural heart disease. Structural heart disease is most commonly caused by myocardial infarction and subsequent scar formation.

The presence of a septal wall motion abnormality consisting of paradoxical motion and thinning on the echocardiogram suggests an old myocardial infarct. However, a myocardial infarct secondary to atherosclerotic coronary artery disease would be distinctly unusual in a 28 year old woman, unless risk factors such as familial hypercholesterolaemia were present. She had no family history of hypercholesterolaemia or myocardial infarction occurring at a young age. Other causes of myocardial infarction in a young woman would include cocaine use, Kawasaki disease with subsequent coronary aneurysm formation, and spontaneous dissection of a coronary artery. The patient denied cocaine use and a

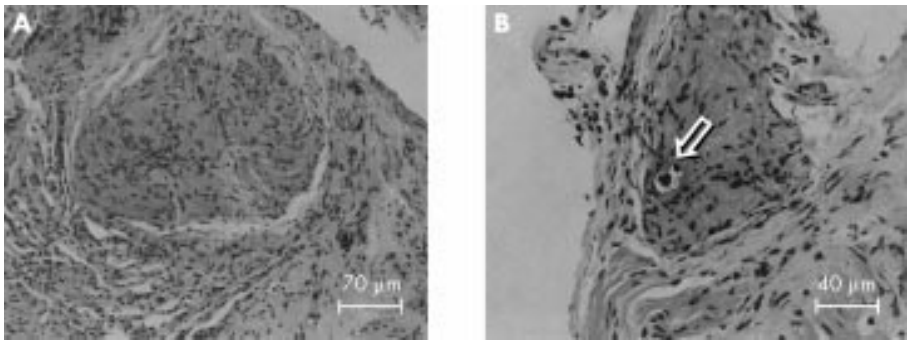

Figure 6 Bronchoscopic transbronchial biopsy images: (A) Peribronchial connective tissue with compact granuloma. (B) Granuloma with Schaumann body (arrow).

toxicological screen for cocaine was negative. There was no clinical history to suggest Kawasaki disease. The coronary angiogram did not show the characteristic aneurysm formation that would be seen in Kawasaki disease. Dissection of the coronary arteries has its highest incidence in young women who are pregnant. The patient had no history of pregnancy and a β human chorionic gonadotropin test was negative.

Non-ischaemic causes of a wall motion abnormality on echocardiography would include myocarditis, infiltrating cardiomyopathy, metabolic related cardiomyopathy such as that secondary to thyroid disease or pheochromocytoma, and an early idiopathic cardiomyopathy. The patient did not describe a recent viral illness to suggest a viral mediated myocarditis, although the lack of such history certainly does not exclude the diagnosis. Viral serologies were not performed, but these rarely establish a diagnosis. The patient's thyroid stimulating hormone concentration was normal. Idiopathic cardiomyopathy is a diagnosis of exclusion. With regard to infiltrating cardiomyopathy, the two most likely causes of this uncommon condition are amyloidosis and sarcoidosis. I will dismiss amyloidosis at this point, as there was no plasma cell dyscrasia and no evidence of a chronic inflammatory process that would cause amyloidosis. In addition, the patient's young age makes amyloidosis unlikely.

The findings on echocardiography are compelling for the diagnosis of sarcoidosis. Cardiac sarcoidosis should always be considered in a young patient with ventricular tachycardia and a conduction disorder. Sarcoidosis is a granulomatous disease of unknown cause that is relatively rare. The incidence is 10–40/100 000 in the USA and Europe. There is of course a remarkable diversity in the prevalence of sarcoidosis between racial groups, with African Americans being particularly affected. In the USA the ratio of affected African Americans to affected whites ranges from 10:1 to 17:1. In Europe, however, the disease affects mainly whites.[1] Although infiltration of the lungs, reticuloendothelial system, and skin dominate its clinical presentation, virtually any tissue can be involved, and the heart is no exception. Despite this, only 5% of patients have clinical manifestations of cardiac disease.[2 3]

Conduction defects and ventricular arrhythmias are frequent clinical manifestations of cardiac sarcoidosis. However, conduction defects are considerably more common than ventricular tachycardia. Indeed, sarcoidosis is a relatively rare disease and ventricular tachycardia is a rare presentation of sarcoidosis.[2–5] Conduction system disease varies from first degree atrioventricular block to bundle branch block to complete heart block.[4] At necropsy, cardiac involvement has been shown in 20–30% of cases, most of which were cases of generalised sarcoidosis.[5] Interestingly, myocardial sarcoidosis often affects young or middle aged patients without sex predilection.[5] Particularly relevant to the present case is that the granulomatous infiltration of sarcoid can be patchy but it preferentially involves the upper septum,[6] as seen in this case.

Ventricular arrhythmias caused by cardiac sarcoidosis can be serious and even fatal. Roberts and colleagues[7] found that sudden death is the terminal event in 67% of sarcoid heart disease deaths. The risk of sudden death has been related to the extent of cardiac involvement.[8] In a series by Winters and colleagues,[9] seven patients with cardiac sarcoid, ejection fraction $< 45\%$, and inducible ventricular tachycardia on programmed stimulation were studied. There was no improvement in arrhythmia with corticosteroids. In this era, antiarrhythmic treatment was more frequently used for malignant ventricular arrhythmias than today when implantable defibrillators have become standard of care. In this series, two patients had sudden cardiac death and four had recurrence of ventricular tachycardia on medical treatment. Four patients had an automatic cardioverter-defibrillator placed and received appropriate shocks.

Chest radiography and CT findings are consistent with pulmonary sarcoidosis. As far as can be discerned, the patient had no respiratory symptoms. Of note is that the serum ACE concentration was normal. However, serum ACE concentrations are not highly sensitive for sarcoidosis[10] and may be even less sensitive for cardiac sarcoidosis.[11 12]

Several diagnostic procedures could have been considered, as well as further imaging studies. Perfusion defects have been noted in cardiac sarcoidosis using thallium 201.[12] Positron emission tomography has recently been advocated to diagnose cardiac sarcoidosis.[13 14] An endomyocardial biopsy might have been considered, especially since the interventricular septum appeared to be involved, the area where endomyocardial biopsy specimens are taken. Having said this, the rate of a false positive biopsy still would have been substantial, as the area of involvement was the proximal septum and endomyocardial biopsy specimens are more frequently taken from the mid to distal septum. In addition, the diagnostic rate achieved with endomyocardial biopsy is said to be low even in the setting of a high suspicion of cardiac sarcoidosis.[15] A transbronchial biopsy would probably yield diagnostic results, given the radiological evidence of pulmonary involvement.

In summary, I believe this patient suffered from cardiac sarcoidosis and the diagnostic procedure was a transbronchial biopsy. If sarcoidosis were confirmed by transbronchial biopsy, the involvement of the heart with sarcoidosis would be essentially certain given the findings on echocardiography and the malignant ventricular arrhythmia, both characteristic of cardiac sarcoidosis.

RADIOLOGICAL FINDINGS

Eric J Stern

In the case presented, the studding of the pleural surfaces is compelling evidence of granulomatous involvement of the subpleural lymphatics and is typical of sarcoidosis, despite the lack of lymphadenopathy. In a patient with no respiratory symptoms, the high resolution CT features are very strongly suggestive of sarcoidosis.

In the lung, sarcoid granulomas are distributed primarily along the lymphatics and therefore in the peribronchovascular

interstitial space, the interlobular septa, and subpleural interstitial space. Radiographically, nodules are coalescent non-caseating granulomas, usually have irregular margins, and are typically 2–10 mm in diameter. Parenchymal opacities commonly involve the upper and middle lung zones but can also involve the lower lung zones. Other CT features are mass-like confluent nodules, fibrosis with lung architectural distortion, and traction bronchiectasis, thickening of the pleural surfaces, ground glass opacities, and air filled cavities or cysts. In other words, sarcoidosis can have many different appearances, even within the same patient. Many of the parenchymal findings on high resolution CT can be considered to be representative of both reversible and irreversible disease. Irregularly marginated nodules and alveolar or pseudoalveolar consolidation are inflammatory lesions that may be reversible with or without treatment, whereas septal thickening, parenchymal bands, and lung distortion are fibrotic lesions that are typically irreversible.

PATHOLOGICAL FINDINGS

Heike Deubner

The diagnostic procedure was a bronchoscopic transbronchial biopsy. The specimen consisted of eight pieces of tan coloured, soft tissue measuring up to 0.1 cm in greatest dimension. Haematoxylin and eosin stained sections showed benign peribronchial and pulmonary tissue. A few compact non-caseating granulomas composed of epithelioid histiocytes and occasional multinucleated giant cells were present (fig 6A), and a single Schaumann body was identified (fig 6B). There were only a few scattered lymphocytes. Gomori methenamine silver stain for fungi and acid fast stain for mycobacteria showed no diagnostic pathogens. No refractile material suggestive of a foreign body reaction was evident. The uninvolved portions of pulmonary parenchyma had normal, thin alveolar septa and occasional alveolar macrophages.

The histopathological findings are compatible with the clinical impression of sarcoidosis. Schaumann bodies are laminated calcific concretions characteristic of sarcoidosis but they are not specific and can be seen in other granulomatous processes, such as beryllium granulomatosis. Furthermore, the negative fungal and acid fast stains do not entirely exclude infectious aetiologies, as the sensitivity of histological evaluation is not absolute compared with microbiological culture. Complicating matters further, sarcoid-like granulomas can also be seen in association with malignancies—for example, Hodgkin's disease. Correlation of the histopathology with clinical findings, occupational history, microbiological culture, and radiological results is therefore required for definite diagnosis of sarcoidosis.

CLINICAL FOLLOW UP

Despite evidence in the literature that steroid treatment does not seem to prevent ventricular arrhythmias, the data are somewhat anecdotal and the patient was treated with prednisone 60 mg/day for one month followed by tapering. The patient had an implantable cardioverter defibrillator placed before discharge. As was predicted by the literature, the prednisone did not seem to affect the arrhythmias. Sotalol was added to help suppress the arrhythmias. At last follow up one month after hospitalisation, the patient continued to have non-sustained episodes of ventricular tachycardia that are short and have not required use of the implantable cardioverter defibrillator.

FINAL DIAGNOSIS

The final diagnosis was cardiac sarcoidosis.

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