

Sarcoidosis Presenting With Complete Atrio-Ventricular Block and Cranial Nerve Palsy

Dear Editor,

Sarcoidosis is a multi-system disease. Cardiac sarcoidosis is a major cause of death in patients with systemic sarcoidosis and should be suspected in young patients with AV block, ventricular dysrhythmias or unexplained heart failure. A high index of suspicion is required as these patients can present initially only with arrhythmias and with no pulmonary involvement. An accurate and early diagnosis is essential to enable the prompt administration of immunosuppressants.

Case Report

A 43-year-old Malay man presented to a large tertiary hospital with 2 weeks' history of vague chest pain and recurrent episodes of syncope. A month earlier, he was seen in the out-patient ophthalmology department with a blurring of vision and diplopia and had clinically an isolated right 6th cranial nerve palsy. A computed tomography (CT) scan of the brain showed a small right cerebellar calcified lesion with no mass effect or evidence of raised intracranial pressure. There were also multiple small cervical lymph nodes.

He denied any constitutional symptoms of fever, night sweats, malaise or lethargy. There were no respiratory symptoms of cough or dyspnoea. He had hypertension and hypercholesterolaemia and was on aspirin, perindopril and simvastatin.

A clinical examination revealed palpable bilateral rubbery and non-tender cervical lymph nodes. He was bradycardic with a heart rate of 35. He was unable to gaze laterally to the right but maintained the ability to converge his eyes. His pupils were reactive to light and accommodation and the rest of the neurological system was normal.

Laboratory investigations showed normal full blood count, serum biochemistry, calcium and cardiac markers. The erythrocyte sedimentation rate was 15 mm/hr. His anti-nuclear antibody, double stranded DNA and rheumatoid factor were normal. The thyroid function test showed sub-clinical hypothyroidism. Mantoux test was normal with <5 mm induration after 48 hours. Serum angiotensin converting enzyme assay was not available.

His electrocardiogram (ECG) showed complete heart block with documented long ventricular standstill on telemetry (Fig. 1). The patient subsequently underwent a dual chamber permanent pacemaker insertion.

The chest X-ray (CXR) did not show any evidence of bilateral lymphadenopathy. Spirometry and lung diffusing capacity were normal (Fig. 2).

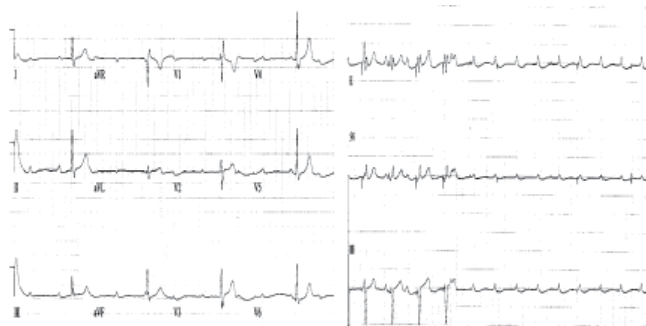


Fig. 1. ECG showing complete AV dissociation and a long ventricular standstill.

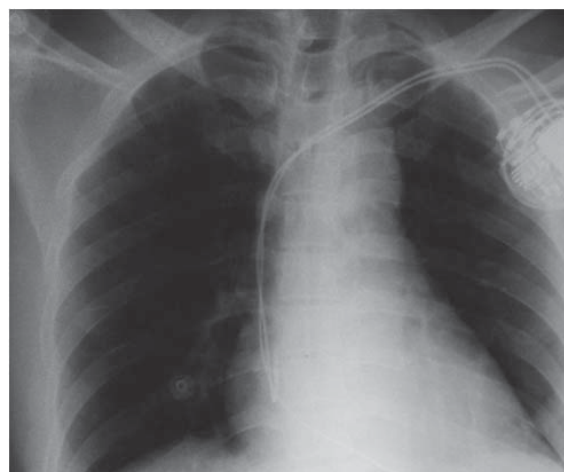


Fig. 2. Chest X-ray after a dual chamber pacemaker implantation. There was no evidence of pulmonary sarcoidosis.

An echocardiogram showed mild left ventricular hypertrophy with good systolic function but tissue doppler showed restrictive pattern associated with diastolic dysfunction.

Repeat brain CT confirmed the initial findings and thoracic CT scan showed no evidence of pulmonary sarcoidosis. A cervical lymph node biopsy showed chronic inflammatory infiltration of hyalinised material with occasional non-caseating granulomata consistent with sarcoidosis.

The patient was treated with prednisolone 1 mg/kg/day which was gradually tapered down and titrated against

his symptoms. On follow-up 3 months later, he reported no new symptoms and his ophthalmoplegia had improved. Brain MRI scan was not done because of the indwelling permanent pacemaker.

Discussion

Sarcoidosis is rare in Asians, except in the Japanese population (where the estimated incidences are 3.8 and 5.6 per 100,000 for males and females, respectively).¹ Common sites involve the lungs (95% with hilar lymphadenopathy and infiltrative disease), skin (20% with erythema nodosum and lupus pernio), renal (nephrocalcinosis with abnormal calcium metabolism), eyes (12% with uveitis) and parotid/salivary glands (5% with swelling). Our patient presented with a single cranial nerve palsy which could be a manifestation of neurosarcoidosis but the diagnosis was not entertained until he developed myocardial involvement. Although isolated neurosarcoidosis without systemic involvement is rare, it had been reported mimicking neurosurgical entities of non-vascularised space occupying lesions in the brain.² His ophthalmoplegia certainly improved with the administration of corticosteroids. Unfortunately with the indwelling pacemaker, we could not perform a brain magnetic resonance imaging (MRI) to monitor the progression of the disease.

Cardiac sarcoidosis is present in about 5% of cases in clinical series with mainly rhythm problems ranging from conduction disturbances (43%) to ventricular arrhythmia (46%).³ Sudden cardiac death can present in about 20% of cardiac sarcoidosis with the terminal rhythm being atrioventricular block or ventricular tachycardia/fibrillation.³ Anti-arrhythmics such as amiodarone or beta-blockers can be helpful in controlling the tachycardia although amiodarone should be given cautiously in view of its potential side-effects of lung fibrosis and thyroid disturbances. The implantation of permanent pacemakers or automatic intra-cardiac defibrillators should be considered although this might restrict the use of MRI scanning as an imaging modality in the future monitoring of the disease.³

Heavy infiltration of myocardium by sarcoid granulomata can cause intractable congestive cardiac failure and should be suspected in young patients. Echocardiogram findings include both systolic and diastolic dysfunction. A stress thallium perfusion scan may be useful in which any perfusion defect due to sarcoidosis will reduce in size as opposed to enlargement in coronary artery disease. This phenomenon is called reverse distribution.⁴ The definite diagnosis of cardiac sarcoidosis is made by endomyocardial biopsy. However the biopsy yield is only positive in about 25% of patients because of the patchy distribution of the disease with a preferential localisation in the left ventricle or septal.⁵ Therefore authorities have suggested combining results of

echocardiography, perfusion imaging, MRI and obtaining multiple biopsy samples for a more definite diagnosis.³

The prognosis of symptomatic cardiac sarcoidosis is not well defined, but 5-year mortality rates may exceed 50%.³ Steroid therapy is usually initiated in the absence of definite histological proof. However in view of the lack of controlled studies, diagnostic specificity and adequate follow-up, the ability of corticosteroids to modify the course of myocardial sarcoidosis remains uncertain. Infliximab, a tumour necrosis factor antagonist, has shown early promise in small groups of patients with aggressive extra-pulmonary sarcoidosis who are intolerant or resistant to steroid therapy.^{6,7} However the findings are still inconclusive and moreover one of the side-effects of infliximab is the potential reactivation of latent tuberculosis which is endemic in Asia.⁷

Conclusion

The incidence of cardiac sarcoidosis may be higher than anticipated in patients presumed to have idiopathic atrioventricular block. Reaching a correct diagnosis early in the course of the disease is difficult unless sarcoidosis is also present in other organs. An accurate and early diagnosis is essential to enable prompt administration of immunosuppressant. Close monitoring of disease progression requires input from both cardiologists and chest physicians.

REFERENCES

1. Yamaguchi M, Hosoda Y, Sasaki R, Aoki K. Epidemiological study on sarcoidosis in Japan. Recent trends in incidence and prevalence rates and changes in epidemiological features. *Sarcoidosis* 1989;6:138-46.
2. Walid MS, Ajjan M, Grigorian AA. Neurosarcoidosis – the great mimicker. *J Natl Med Assoc* 2008;100:859-61.
3. Chapelon-Abrie C, de Zuttere D, Duhaut P, Veyssier P, Wechsler B, Huang DL, et al. Cardiac sarcoidosis: a retrospective study of 41 cases. *Medicine* 2004;83:315-34.
4. Okayama K, Kurata C, Tawarahara K, Wakabayashi Y, Chida K, Sato A. Diagnostic and prognostic value of myocardial scintigraphy with thallium-201 and gallium-67 in cardiac sarcoidosis. *Chest* 1995;107:330-4.
5. Uemura A, Morimoto S, Hiramitsu S. Histologic diagnostic rate of cardiac sarcoidosis: evaluation of endocardial biopsies. *Am Heart J* 1999;138:299-302.
6. Uthman I, Touma Z, Khoury M. Cardiac Sarcoidosis responding to monotherapy with infliximab. *Clin Rheumatol* 2007;26:2001-3.
7. Judson MA, Baughman RP, Costabel U, Flavin S, Lo KH, Kavuru MS. Efficacy of infliximab in extrapulmonary sarcoidosis: results from a randomised trial. *Eur Respir J* 2008;31:1189-96.

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