Sarcoidosis, microvascular angina and aortitis: New dimensions of the 'Takayasu syndrome' – A case report

Isma Rafiq MD, Vidya Nadig MD, Leisa J Freeman MD

I Rafiq, V Nadig, LJ Freeman. Sarcoidosis, microvascular angina and aortitis: New dimensions of the 'Takayasu syndrome' – A case report. *Int J Angiol* 2007;16(3):113-114.

A case of Takayasu aortitis associated with sarcoidosis presenting with recurrent angina is reported. This association has been called 'Takayasu syndrome', which reflects what is likely a shared etiology. Myocardial perfusion abnormalities have recently been documented in sarcoidosis, but this case clarifies for the first time that the angina

in Takayasu syndrome is likely due to small vessel coronary arteritis. Corticosteroids and cytotoxic therapy have been shown to be beneficial in all forms of sarcoidosis related to vasculitis. Initiation of steroid therapy may provide relief of angina in patients with evidence of reversible ischemia in normal coronary arteries.

Key Words: *Microvascular angina; Reversible ischemia; Sarcoidosis; Takayasu aortitis*

Sarcoidosis is a multisystemic granulomatous disease of unknown etiology that may affect most organ systems. Granulomatous infiltration of the heart, causing conduction abnormalities and infiltrative cardiomyopathy, is well known. Systemic vasculitis is an unusual complication of sarcoidosis that may affect small- and large-calibre vessels. We present a case of small and large vessel vasculitis suggestive of Takayasu arteritis associated with sarcoidosis. The association of two rare conditions has previously been noted and labelled 'Takayasu syndrome' (1). Myocardial perfusion abnormalities have recently been documented; the present case clarifies that this is likely due to small vessel coronary arteritis.

CASE PRESENTATION

A 41-year-old woman was admitted as an emergency with left-sided, severe chest pain associated with shortness of breath. The pain was not relieved by sublingual glyceryl trinitrate, and had occurred spontaneously while she was working at a supermarket checkout. There were no new acute electrocardiogram changes, but troponin I was elevated at 0.44 µg/L. She was treated conservatively with clopidogrel, low-molecular-weight heparin and oral nitrates in addition to her antihypertensive medications (bisoprolol, lisinopril, doxazosin, candesartan and bendrofluzide). During this admission she continued to complain of typical chest pain, but subsequent coronary angiography demonstrated completely normal, smooth-walled coronary arteries without ectasia or aneurysm formation. She had a small aortic root with extensive aortic calcification. Echocardiographic assessment of left ventricular function was normal. Four years earlier, coronary angiography had also been normal despite a strong history of anginal pain

and exercise-induced inferior segment depression of 2 mm at 6 min associated with pain (modified Bruce protocol). Of relevance in her medical history, a patent ductus arteriosus was closed surgically at two years of age. At 28 years of age, in her second pregnancy, she had predominant systolic hypertension in the third trimester, which proved very resistant to treatment. Subsequent renal angiography was normal, but arch aortography documented extensive calcification of the ascending and descending aorta, consistent with aortitis. A focal supraceliac stenosis with a 50 mmHg withdrawal gradient was surgically resected. Unfortunately, the histological specimens were lost.

At this most recent admission, bihilar lymphadenopathy was noted on her chest x-ray, and a thoracic computed tomography scan confirmed additional mediastinal lymphadenopathy, subsequent biopsy of which confirmed typical granulomatous changes of sarcoidosis. Treatment with prednisolone produced good symptom resolution, including angina relief. Her hypertension became better controlled, and her plasma renin fell dramatically from 1613 mU/L to 10 mU/L. Reduction of steroids provoked a recurrence of angina, and a diagnosis of microvascular angina was considered. Resting magnetic resonance imaging showed no focal wall abnormalities or wall thinning, nor focal necrosis with gadolinium enhancement (Figure 1). However, with adenosine infusion, the patient experienced chest pain, inferior and lateral T wave inversion, and there were widespread subendocardial perfusion abnormalities (Figure 2) consistent with microvascular angina. Reintroduction of low-dose steroids and treatment with calcium channel blockers, nitrates and angiotensin-converting enzyme inhibitors allowed her discharge, and at follow-up her symptoms were once again well controlled.

Department of Cardiology, Norfolk and Norwich University NHS Trust, Norwich, United Kingdom

Correspondence: Dr Isma Rafiq, Department of Cardiology, Norfolk and Norwich University NHS Trust, Colney lane, Norwich NR4 7UY, United Kingdom. Telephone 44-01603-286286, fax 44-01603-286363, e-mail leisa.freeman@nnuh.nhs.uk

Figure 1) Resting magnetic resonance imaging showing no focal wall abnormalities or wall thinning, nor focal necrosis with gadolinium enhancement

Figure 2) Magnetic resonance imaging with adenosine infusion (stress perfusion): low signal in the subendocardial region post adenosine

DISCUSSION

Cardiac involvement in sarcoidosis commonly presents with ventricular ectopy or arrhythmias, atrioventricular conduction disturbances (including complete heart block), congestive heart failure or even sudden death (2). Myocardial involvement is usually focal and scattered, with a predilection for the left ventricular free wall, the papillary muscles (that may be completely replaced by granulomatous tissue) and the interventricular septum (that may be thin or aneurysmal from fibrosis). Myocardial infarction is uncommon, although there have been reports of granulomas externally occluding epicardial coronary arteries. However, in active sarcoidosis there may also be microvascular vasoconstriction caused by local release of vasoactive mediators (histamine, serotonin, prostaglandin D_2 , and leukotrienes C_4 and D_4) (3). Tellier et al (4) have demonstrated reversible myocardial ischemia with isotope scintigraphy, using dipyridamole, in nine patients with sarcoidosis. They have suggested that such provokable ischemia is unlikely to represent scar fibrosis or extensive confluent granulomas as a mechanism for ischemia; improvement with corticosteroids and relapse on withdrawal has suggested that the problem is microvascular. Sarcoidosis with large-calibre vessel vasculitis has predominantly been reported in African American patients, while small-calibre vessel vasculitis is more frequently observed in white patients (5).

Takayasu arteritis (also called aortic arch syndrome) involves mainly the aorta, but frequently involves the pulmonary, subclavian, carotid and renal arteries as well. It is characterized by a marked thickening of the arterial wall. Aneurysm and stenosis are generated by fibrosis of the intima and mainly of the adventitia with a fibrous ring where inflammation may have disappeared. Coronary arterial involvement in Takayasu arteritis is usually ostial and proximal, and occurs in 10% of cases, but diffuse lesions or aneurysm may rarely

occur. Revascularization with angioplasty or surgery may be required (6). It is rare in Western Europe but presents more commonly in women younger than 40 years of age.

There have been seven case reports to date of an association of sarcoidosis and large vessel disease. Weiler et al (1) have argued that Takayasu arteritis in the presence of sarcoidosis suggests a common etiology, and they have proposed the term 'Takayasu syndrome'. The present case fulfils the criteria for Takayasu syndrome, which has not previously been associated with microvascular angina. Moreover, it clearly documented that the ischemia was related to the small vessels rather than the epicardial coronary arteries. Corticosteroid and cytotoxic therapy is palliative for all forms of sarcoidosis-related vasculitis. The present case suggests that this therapy may provide relief from angina, although we suspect that reversible ischemia, in the presence of a normal coronary angiogram, should precede the initiation of steroids.

REFERENCES

1. Weiler V, Redtenbacher S, Bancher C, Fischer MB, Smolen JS. Concurrence of sarcoidosis and aortitis: Case report and review of literature. *Ann Rheum Dis* 2000;59:850-3.
2. Dorfman T, Canales J, Farukhi I, McGuire DK. Sarcoidosis masquerading as an acute coronary syndrome. *Cardiol Rev* 2005;13:256-9.
3. Chapelon-Abrie C, de Zuttere D, Duhaut P, et al. Cardiac sarcoidosis: A retrospective study of 41 cases. *Medicine (Baltimore)* 2004;83:315-34.
4. Tellier P, Paycha F, Antony I, et al. Reversibility by dipyridamole of thallium-201 myocardial scan defects in patients with sarcoidosis. *Am J Med* 1988;85:189-93.
5. Fernandes SR, Singen BH, Hoffman GS. Sarcoidosis and systemic vasculitis. *Semin Arthritis Rheum* 2000;30:33-46.
6. Kerr GS, Hallahan CW, Giordano J, et al. Takayasu arteritis. *Ann Intern Med* 1994;120:919-29.