

CASE REPORT

Takayasu's arteritis: management of left main stem stenosis

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Takayasu arteritis is a chronic vasculitis involving the aorta and its main branches, the pulmonary arteries, and the coronary tree, and needs to be considered in a young patient with angina, in particular when pulses are absent. This case illustrates the limitations of exercise testing in diagnosing the extent of coronary artery disease and the risks associated with coronary angiography in patients with inflammatory disease in the left main stem coronary artery. It also highlights the novel use of non-invasive scanning with positron emission tomography using 18-fluorodeoxyglucose in assessing remission from this disease. Revascularisation was performed with percutaneous transluminal coronary angioplasty and stenting as an emergency procedure, but treatment of the restenosis with directional atherectomy was based on a review of the available literature. The lymphocytic alveolitis seen in this patient has not been previously described in Takayasu's disease.

A 27 year old white woman presented in 1994 with dyspnoea, a non-productive cough, and 14 lbs (6.36 kg) weight loss. There was reticulonodular shadowing on her chest radiograph and erythrocyte sedimentation rate was increased to 50 mm. Subsequent atypical pneumonia screen, avian precipitins, tests for acid fast bacilli, and autoantibody screens were negative. An open lung biopsy was performed, with histology showing a lymphocytic alveolitis. She was treated with intermittent oral steroids with some improvement in symptoms but not in the chest radiograph or transfer factor.

She continued clinic follow up and in 1999 appeared well, with mild exertional dyspnoea and a new chest pain occurring only on severe exertion. She also had a pain in her left arm unrelated to walking. She had stopped smoking in 1994, was premenopausal, did not have diabetes mellitus or hypertension, and had a total cholesterol concentration of 3.9 mmol/l. Blood pressure was 130/80 mm Hg supine in the right arm and not recordable in the left arm. Both the left radial and left brachial pulses were impalpable. Exercise testing showed 1 mm of horizontal ST segment depression after 7.5 minutes of exercising in the Bruce protocol in the lateral leads without chest pain. She was started on aspirin and diltiazem and, despite only a mildly positive exercise test, was referred for coronary angiography and arch aortography.

Left and right heart were catheterised through the right femoral approach. The right coronary artery was normal but there was a tight ostial stenosis of the left main stem (LMS) artery without distal disease (fig 1) The left subclavian artery was occluded and there was moderate pulmonary hypertension (pressure 66 mm Hg systolic). At the end of the procedure, while still on the angiogram table, she developed ST elevation anteriorly and had a cardiac arrest. The LMS artery was found to have occluded at repeat angiography but

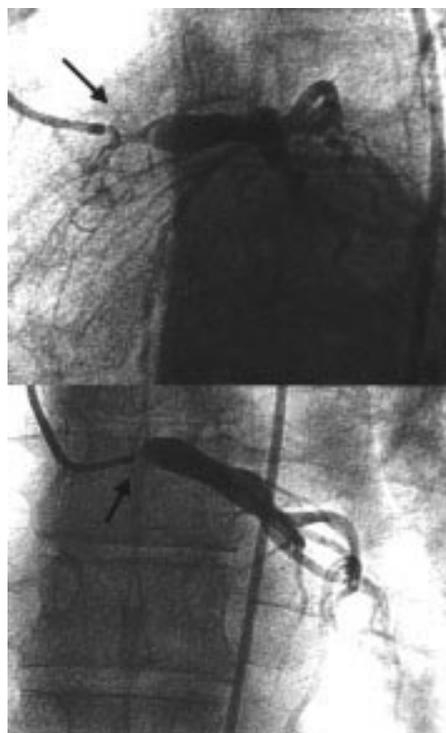


Figure 1 A tight stenosis is seen at the ostium of the left main stem (LMS) coronary artery at diagnostic coronary angiography (black arrows). The right coronary artery had no stenosis.

was rapidly reopened with the insertion of a coronary stent (fig 2) Her recovery was uncomplicated, with a creatine kinase peak concentration of 1000 IU/l.

A clinical diagnosis of Takayasu's arteritis was made since she had an absent major pulse with arm claudication, an abnormal aortogram, and ostial coronary disease at the age of 34 years.¹ Subsequent investigations showed a C reactive protein concentration of 980 mg/l, negative repeat autoantibody screen including antineutrophil cytoplasmic antibody, normal complement concentrations, and negative treponemal serology. An additional stenosis of the origin of the left common carotid artery was shown on magnetic resonance angiography (fig 3).

She was treated with oral prednisolone and monthly cyclophosphamide for six months. Her C reactive protein concentration returned to normal. Positron emission tomography using 18-fluorodeoxyglucose (FDG-PET) was used to assess

Abbreviations: FDG-PET, positron emission tomography using 18-fluorodeoxyglucose; LMS, left main stem; PTCA, percutaneous transluminal coronary angioplasty



Figure 2 The LMS was reopened with percutaneous transluminal balloon angioplasty and a 4.0 mm diameter \times 9 mm length stent was inserted after acute occlusion following diagnostic angiography. A good angiographic result was achieved.

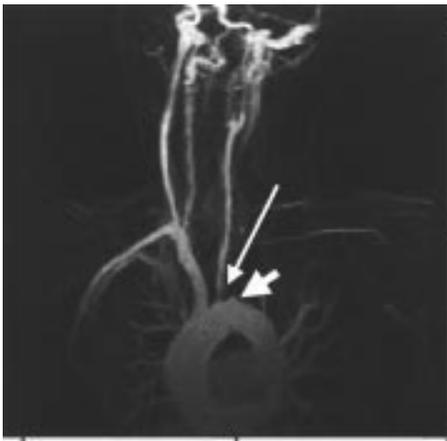


Figure 3 Magnetic resonance angiogram showing total occlusion of the left subclavian artery (wide arrow). In addition, there is a stenosis at the origin of the left common carotid artery (slim arrow).

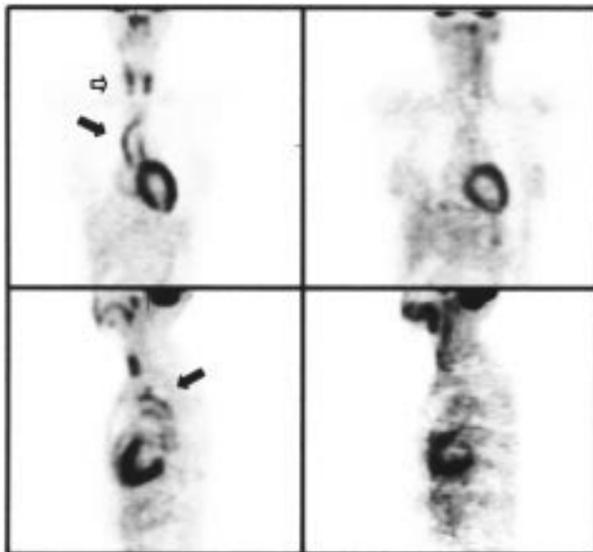


Figure 4 Positron emission tomography using 18-fluorodeoxyglucose (FDG-PET) was used to image the metabolic activity in the aorta (solid arrow) and head and neck vessels (open arrow) both before (left hand panels) and after (right hand panels) treatment with pulsed cyclophosphamide and prednisolone. Uptake in the heart and thyroid glands is similar but the aortic uptake has been dramatically reduced by treatment.



Figure 5 Follow up angiogram of the LMS stent showing severe in-stent stenosis three months after the initial procedure (black arrows).

inflammation in the aorta before and after treatment (fig 4). Following immunosuppressive treatment, there was a reduction in FDG uptake in the aortic wall, indicating a reduction in metabolic activity.

In view of the stent placed in the LMS, she was scheduled for repeat coronary angiography three months after stent placement despite being pain free (fig 5). This showed a tight in-stent stenosis in the LMS artery. It was not immediately treated, as inflammatory markers were still increased. She was kept in hospital to complete her course of immunosuppression. Following reduction in her inflammatory markers and the negative PET scan she underwent percutaneous revascularisation again. A cutting balloon was inserted to produce a tract for the directional atherectomy device. Three passages of the device retrieved a core of white glistening tissue with some stent struts obviously excised (fig 6). Histology showed smooth muscle cells with no significant inflammatory infiltrate. The end result was angiographically good (fig 7).

She remained free of symptoms and was discharged from hospital. A check angiogram was performed at a three month interval and showed no recurrence of the in-stent stenosis.



Figure 6 Core of tissue excised by the directional atherectomy device from the in-stent LMS restenosis. Stent struts are visible at either end of the specimen (black arrows).

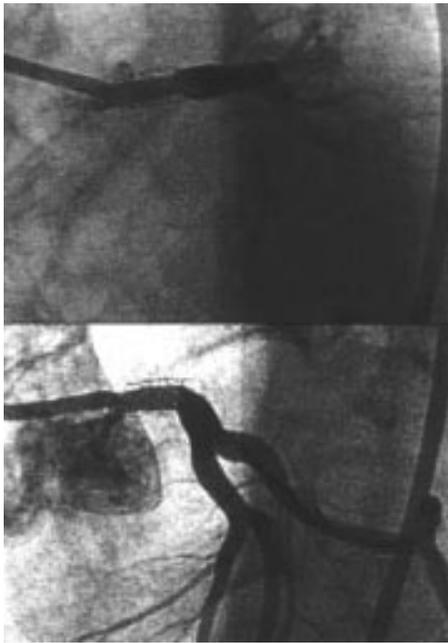


Figure 7 Result of directional atherectomy and balloon angioplasty to the in-stent stenosis of the LMS. There is now a good lumen within the LMS.

DISCUSSION

Takayasu arteritis is a chronic vasculitis involving the aorta and its main branches, the pulmonary arteries, and the coronary tree. It may lead to stenosis with obstruction caused by fibrosis and thrombus formation or aneurysm formation due to weakening of the vessel wall. It was first described in 1908 in a Japanese patient with retinal artery abnormalities but was later characterised as a more generalised arterial disease.^{2,3} The pathology is of a “panarteritis”, with intimal fibrous thickening and typical atheromatous lesions, medial smooth muscle and elastic lamina destruction, and medial and adventitial cell infiltration and fibrosis. With earlier diagnosis, fatality in the acute phase has been reduced and thus the problem of atherosclerosis has become more prominent.

The estimated worldwide incidence is 2.6 cases per million per year, with women more commonly affected than men. They usually have no risk factors for atherosclerosis and yet have atheromatous aortae, suggesting the importance of inflammation in atherosclerosis.⁴ The disease has been mainly studied in Japan but western series have also been published suggesting an older population at risk.^{1,5–10}

No serological test is available for diagnosis of Takayasu's disease.¹¹ Therefore, diagnosis rests on clinical criteria (table 1).^{1,8,12,13} Cardiac features are present in up to 40% of cases. Aortic regurgitation secondary to aortic root dilatation may occur in 20% of cases. Hypertension may occur in a third of patients, usually related to renal artery stenosis.^{6,14} Angina pectoris is rarely a presenting feature but has been reported in 6–16% of cases.^{6,15,16} More rarely, pericarditis, palpitations, and congestive cardiac failure may occur. Pulmonary involvement occurs in 15–17% of cases.^{17–21} Pulmonary hypertension is well recognised.²² The lymphocytic alveolitis seen in our patient has not been previously described in Takayasu's disease.

First line treatment of Takayasu's arteritis is immunosuppression, primarily with corticosteroids. With glucocorticoid treatment, remissions occur in 40–60% of all patients. About 40% of all steroid resistant patients respond to the addition of cytotoxic agents. Approximately 20% of all patients are resistant to any kind of treatment.^{8,15,23} Methotrexate is an alternative immunosuppressive agent to cyclophosphamide and may induce remission if other treatments have failed.²⁴

Table 1 Takayasu's arteritis: the American College of Rheumatology's 1990 diagnostic criteria¹³

- Patient below 40 years of age at initial diagnosis
- Claudication of extremities
- Reduced brachial pulse
- Difference in blood pressure between right and left arms >10 mm Hg
- Bruit above subclavian artery, aorta, or both
- Arteriographic appearance

At least three criteria must be present for a diagnosis. Characteristic angiographic appearances are described.¹

Angina pectoris is usually caused by premature coronary disease, in particular involving the ostia of the coronary arteries,²⁵ but may be related to extrinsic compression of the coronary tree or a steal phenomenon.^{26,27} In addition, acute inflammation and the related oedema may be important, as highlighted by two cases where regression of an LMS stenosis was reported with administration of steroids.^{28,29}

Treatment of the coronary disease is problematic, since arterial inflammation is persistent in over 40% of cases even after treatment.⁸ This would jeopardise the insertion sites of new grafts.³⁰ Surgery may involve coronary bypass with venous rather than arterial conduit (coronary artery bypass graft) or endarterectomy through the aorta. In addition, patches may be used to enlarge diseased segments of the arterial tree.^{31–33} Studies of surgical series have reported an in-hospital mortality of 7.9–8.7%.^{25,34} Surgery may have been even more hazardous in our patient in view of her pulmonary hypertension.

Percutaneous transluminal coronary angioplasty (PTCA) has been reported previously in isolated cases of Takayasu's disease.^{35–38} The use of intracoronary stents has also been reported.^{39–43} The largest series had only two cases, and the literature on management of in-stent restenosis in Takayasu's disease is limited. We chose to use directional atherectomy to reduce the plaque burden before treating the in-stent LMS restenosis. Although some stent struts were excised, the final angiographic result and the clinical outcome three months later were excellent. Although rotational atherectomy (Rotablator rather than directional atherectomy) was described in a previous report on coronary revascularisation in Takayasu's disease, this was not performed within the LMS artery.⁴⁰

FDG-PET uptake has been used previously to image other forms of aortitis. Uptake can be reduced within two weeks of initiation of treatment in giant cell arteritis.⁴⁴ FDG-PET uptake was increased acutely in a previously reported case of Takayasu's arteritis but follow up data were not provided.⁴⁵ Residual activity in Takayasu's disease is difficult to detect based on plasma markers or clinical signs. We have shown that FDG-PET may allow the disease to be monitored non-invasively.

Summary

Takayasu's arteritis needs to be considered in a young patient with angina, in particular when pulses are absent. This case illustrates the limitations of exercise testing in diagnosing the extent of coronary artery disease and the risks associated with coronary angiography in patients with inflammatory LMS disease. It also highlights the novel use of non-invasive scanning with FDG-PET in assessing remission from this disease. Revascularisation was performed with PTCA and stenting as an emergency procedure, but treatment of the restenosis with directional atherectomy was based on a review of the available literature.

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