

A case of Takayasu arteritis with normal coronary arteries presenting as stable angina

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Abstract

Takayasu arteritis (TAK) is a type of large vessel vasculitis characterized by granulomatous inflammation involving the aorta and its main branches. Clinical presentation may vary from non specific symptoms such as fever, malaise, weight loss to manifestations of organ hypo perfusion. Cardiac involvement may take forms of valvular insufficiency, angina or heart failure. In this case, we report a 39-year-old woman with hypertension presenting with angina, who was found to have multiple arterial bruits, with blood pressure and pulse volume discrepancies, aortic regurgitation and renovascular hypertension. She was diagnosed with Takayasu arteritis with clinical and imaging criteria; managed with glucocorticoid and DMARDS, achieving good clinical response and planned for surgical intervention for valvular insufficiency.

Keywords: Takayasu arteritis, Stable angina, Aortic regurgitation, Renovascular hypertension

Introduction

Takayasu arteritis (TAK) is a type of large vessel vasculitis characterized by granulomatous inflammation involving the aorta and its main branches. It is a comparatively rare disease which is mainly seen in Asia, with a reported incidence of 1-2 per million in Japan. Earliest descriptions of TAK dates as far as 1830. It is a disease of young onset with a mean age of diagnosis between 20-30 years with a clear female preponderance.¹ Spectrum of clinical manifestations may range from non-specific constitutional symptoms to evidence of organ hypoperfusion. We report a case of TAK presenting with renovascular hypertension and angina pectoris.

Case presentation

A 39-year-old woman with hypertension was admitted with acute onset tightening type central chest pain. Chest pain followed moderate exertion and she had experienced sweating and nausea along with it. She gave a history of similar chest pain on exertion for three years with associated NYHA class 2 dyspnoea. She had been evaluated for these symptoms at a local hospital and was found to have iron deficiency anaemia and subsequent gastroscopy had confirmed a hiatus hernia. Her cardiac evaluation showed a normal resting ECG with left ventricular dysfunction grade 2 mitral regurgitation and grade 3 aortic regurgitation with an ejection fraction of 45%. She had been managed as stable angina and heart failure with reduced ejection fraction (HFrEF) with aspirin, carvedilol, GTN and diuretics. Anaemia had

been treated with iron supplements. At the time of the presentation, she denied any orthopnoea, paroxysmal nocturnal dyspnoea or lower limb swelling. She had no history of acute onset pulmonary oedema or acute coronary events. She denied any family history of premature coronary artery disease, hypertension or renal disease. She was afebrile, and not pale. Her blood pressure was elevated with wide pulse pressure, and a significant pressure discrepancy between the two arms was noted with a faint left radial pulse. Blood pressure on the right arm was 190/54 mmHg, whereas the left arm pressure was 174/50 mmHg. On further examination, she had bilateral carotid, subclavian and femoral bruits and a right-sided renal bruit. An early diastolic murmur compatible with aortic regurgitation was heard over the left sternal edge. Her ECG did not show any ischaemic changes, and high-sensitive troponin I level was not elevated.

A large vessel vasculitis was suspected in the background of the above findings. She denied any fever, fatigue, weight loss or limb claudication. There was no history of carotidynia, stroke or TIA, syncope/ light-headedness or any gastrointestinal symptoms. She had no history or significant contact history of tuberculosis and denied any high-risk sexual behaviour.

Her investigation panel showed a raised erythrocyte sediment rate (ESR) of 77 mm in 1st hour with a normal C reactive protein level. Her serum potassium level was in the low normal range with normal creatinine. Ultrasonic examination of the abdomen revealed an abdominal aortic aneurysm with fusiform dilatation of the suprarenal abdominal aorta, which extended to the thoracic aorta, the maximum diameter of which was 4cm. 2D echocardiogram showed grade 3 mitral regurgitation and moderate aortic regurgitation with an ejection fraction of 45-50%. Both the left ventricle and atrium were dilated with no left ventricular hypertrophy.

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She underwent a CT aortic angiogram which showed the previously seen abdominal aortic aneurysm with diffuse thickening of the aortic wall (maximum thickness 5mm). It also showed a dilated aortic root with a maximum diameter of 4.4cm and narrowing of multiple large arteries was noted. The right subclavian artery and left common carotid artery both showed narrowing just distal to its origin with distal dilatation, whereas the left subclavian and right common carotid arteries appeared normal. Coeliac, superior mesenteric and inferior mesenteric arteries showed stenosis at their origins, despite our patient being asymptomatic for mesenteric ischaemia. The right renal artery, which arose from the distal part of the aortic aneurysm, showed significant stenosis 7mm distal to its origin. CT findings suggested large and medium vessel vasculitis affecting all segments of the aorta. (figure 1)

A diagnosis of Takayasu arteritis was made based on the clinical picture and angiogram findings. This patient was managed in liaison with the rheumatology unit, and she was started on high-dose oral prednisolone and weekly methotrexate, along with folic acid supplementation and bone protection. Blood pressure was controlled with losartan and amlodipine.

She was followed up at the medical clinic, and a subsequent coronary angiogram failed to show any evidence of coronary arterial or ostial stenosis. She was continued on medical treatment for angina pectoris and was awaiting evaluation for valve replacement. At four-month review, it was noted that left radial pulse volume had improved with reduced intensity of vascular bruits and significant improvement in anginal symptoms. Her prednisolone dose was reduced to a tapering regimen, and a MR angiogram was planned to be done in 1 year.

Discussion

Classification criteria for Takayasu arteritis were updated in 2022, and these include age < 60 years, evidence of vasculitis on imaging as absolute requirements, and additional clinical and imaging criteria. A score has been allocated to each of these components, and a score of 5 or more has been validated to classify TAK with a sensitivity of 93.8% and a specificity of 99.2%.² Our patient has a cumulative score of 13 points in the above criteria and therefore falls well within the classification of TAK. Differential diagnosis of TAK includes giant cell arteritis and other types of inflammatory large vessel vasculitides, infectious aortitis secondary to tuberculosis or syphilis, Behcet's disease, IgG4 disease and widespread atherosclerosis. Perhaps, the most difficult to differentiate would be giant cell arteritis, as both show similar histological features. However, GCA

is a disease presenting exclusively after 50 years of age, they typically involve external carotid vessels rather than aorta and renal artery involvement is rare. Most of the other differentials also have distinct extra-aortic manifestations which were absent in our patient, helped in differentiating TAK from them. Another important differential is tuberculous aortitis as tuberculosis has also been implicated as a trigger of TAK. Our patient did not have a history or a clinical picture suggestive of tuberculosis and her imaging findings were typical of TAK rather than tuberculous aortitis. However, tuberculous aortitis may mimic TAK on imaging and therefore needs exclusion³

In Takayasu arteritis clinical manifestations may vary from asymptomatic disease to non-specific symptoms to significant vascular stenosis causing complications related to organ hypoperfusion. Characteristic features include diminished pulses leading to limb claudication and blood pressure discrepancies, hypertension owing to renal artery stenosis, neurological symptoms related to hypertension, ischaemia or subclavian steal, Takayasu retinopathy, pulmonary artery involvement and cardiac involvement.⁴ Multiple non-specific symptoms such as fever, loss of weight, malaise and arthralgia have been commonly reported.⁵ Clinically apparent, mesenteric angina is rare, as in our patient where she had radiological evidence of stenosis in mesenteric arteries without any symptoms.⁶

Cardiac involvement in TAK may take the form of valvular insufficiency, angina or heart failure. Heart failure can result from hypertensive heart disease, valvular insufficiency, myocardial ischaemia or pulmonary arteritis causing pulmonary hypertension. A rare type of granulomatous myocarditis causing dilated cardiomyopathy and, congestive cardiac failure has also been described⁵. Myocardial ischaemia in TAK can be due to the involvement of coronary arteries or hypoperfusion due to markedly widened pulse pressure with or without aortic regurgitation. Coronary arterial involvement may vary from ostial stenosis to diffuse stenosis and aneurysmal dilatation. In our patient normal coronary angiogram ruled out any of the above lesions. However, she had significant aortic regurgitation, wide pulse pressure with low diastolic pressure. Therefore, in this case, the cause for the angina was the supply-demand mismatch created due to low diastolic pressures causing reduced coronary perfusion during diastole⁵. She also had renal artery stenosis giving rise to secondary hypertension, which may have contributed.

In a study analysing long-term outcomes and related prognostic factors in 120 patients with TAK, presence of hypertension, retinopathy, aortic regurgitation and aneurysm formation, were found to be predictors of worst prognosis. The same study showed early intensive medical therapy and interventions can alter disease

outcomes in such patients.⁶ Index patient fell into this category as she had already developed several major complications listed above.

Management of TAK is challenging due to its frequent relapsing course, lack of indicators of disease activity, and presence of active disease despite clinical quiescence. The cornerstone of medical management is steroids. Currently, there are no RCTs evaluating glucocorticoids' role or comparative studies on the efficacy of DMARDs in achieving disease remission. Data from observational studies have shown about a 50% remission rate with steroids alone, albeit with a higher relapse rate when attempts were made at tapering.⁷

Methotrexate (MTX), Cyclophosphamide, Azathioprine, mycophenolate mofetil, leflunomide and biological DMARDs (tocilizumab, anti -TNF α) are being used as steroid-sparing adjuncts, and a meta-analysis showed approximately 60% remission rate with non-glucocorticoid agents although with significant relapse rates.⁸

Other aspects of management include surgical intervention, which is indicated in the presence of critical ischaemia due to arterial stenosis,⁹ Early revascularization is recommended as opposed to conservative management in the presence of coronary artery disease. In TAK, coronary artery bypass graft (CABG) has lower rates of MACE (major adverse cardiac events) and coronary restenosis than percutaneous coronary interventions.¹⁰

Aortic regurgitation (AR) is the most common valvular lesion encountered in TAK, and cardiac failure due to AR is the most common cause of mortality in TAK. Our patient had a significant aortic regurgitation with left ventricular dysfunction and therefore referred to the cardiothoracic team for further evaluation. As her blood pressure was adequately controlled with ACE inhibitors and calcium channel blockers with normal renal function, she did not require any interventions in view of ameliorating renal artery stenosis.

Monitoring of patients with TAK is demanding as there are no defined markers of disease activity. Acute phase reactants such as ESR and CRP have not consistently reflected the disease activity limiting their use as reliable markers to monitor.¹¹

Vessel wall imaging is an objective way of monitoring these patients, and current practice is at least annual MR or CT angiography in TAK patients.¹²

Conclusion

Index case angina is probably due to wide pulse pressures leading to decreased myocardial perfusion. Early recognition and treatment of cardiovascular

complications is important as they predict poor prognosis.

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