A rare life-threatening presentation of Takayasu arteritis

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Case presentation

A 22-year-old lady born in India, presented with a 1-month history of fever, weight loss of 2.5 kg, symptoms of left arm claudication, episodes of central chest pain, palpitations and paroxysmal nocturnal dyspnoea. On admission she was febrile with a blood pressure in the right arm of 190/95 mmHg. There were absent left radial and brachial pulses.

Blood tests showed elevated inflammatory markers, cardiac biomarkers and an acute kidney injury; CRP 38 g/l, ESR 47 mm/h, troponin 88 ng/l (normal <32 ng/l), Brain natriuretic peptide (BNP) 165.3 ng/l (normal <89 ng/l), creatinine 115 μmol/l and eGFR 53 ml/min. There was a microcytic anaemia; haemoglobin 99 g/l and mean cell volume 65.9 fl. Autoimmune serology showed a positive anti-nuclear antibody with a homogeneous pattern, titre 1 : 640 with negative extractable nuclear antigens. There were negative double-stranded DNA, anti-phospholipid and anti-neutrophil cytoplasmic antibodies (ANCA), with normal complement and immunoglobulin levels.

Chest X-ray showed small effusions at both lung bases. An echocardiogram demonstrated a dilated left ventricle with a left ventricular ejection fraction (LVEF) of 24% and antero-septal regional wall motion abnormalities. Coronary CT angiogram showed non-obstructed coronary arteries. Cardiac MRI confirmed a dilated left ventricle with severe global left ventricle systolic impairment in keeping with a non-ischaemic dilated cardiomyopathy. There was poorly defined delayed enhancement in the anterolateral wall consistent with myocarditis.

Given the absent upper limb pulses an MRI aorta was carried out, which showed an occluded left subclavian and right renal artery, a small ischaemic right kidney and significant focal narrowing within the left renal artery (Fig. 1A). In addition, 18F-FDG-PET-CT showed metabolically active mediastinal and right supraclavicular lymph nodes (Fig. 1B).

Diagnosis and management

The clinical picture and investigations were in keeping with a large-vessel vasculitis in the form of Takayasu arteritis complicated by inflammatory myocarditis. There was concern regarding the aetiology of the PET avid lymph nodes particularly for tuberculosis (TB) or lymphoma. Ultrasound and fine-needle aspiration of the enlarged supra-clavicular lymph nodes revealed granulomatous inflammation with evidence of central necrosis. There were no acid-fast bacilli seen on initial culture.

The findings posed a clinical therapeutic challenge with high clinical suspicion of active tuberculosis along with evidence for active Takayasu arteritis with organ-threatening myocarditis requiring immunosuppression. The decision was made to proceed with immunosuppressive treatment with prednisolone 80 mg (1 mg/kg/daily) and pulsed i.v. cyclophosphamide (15 mg/kg monthly) alongside...
quadruple anti-TB therapy. A steroid dose of 1 mg/kg/daily was chosen to compensate for the liver enzyme-inducing effect of the anti-TB treatment. In addition, she received an ovarian protection regimen with the cyclophosphamide. This was followed by treatment with oral prednisolone and mycophenolate mofetil. TB culture subsequently showed acid-fast bacilli consistent with TB infection. Treatment led to improved symptoms with no further fevers and resolution of chest pain and palpitations. The elevated acute phase response and cardiac biomarkers normalized. It was felt that the anti-nuclear antibody was non-specifically positive due to the coexisting TB infection.

Treatment led to improved symptoms with no further fevers and resolution of chest pain and palpitations. The elevated acute phase response and cardiac biomarkers normalized. It was felt that the anti-nuclear antibody was non-specifically positive due to the coexisting TB infection. Once the vasculitis was in clinical remission, left renal artery angioplasty was performed to good effect (Fig. 1C). Repeat serial echocardiograms showed significant improvement in cardiac function and the most recent LVEF, 6 years after initial presentation, was 63% with resolution of the regional wall motion abnormalities. Renal function has improved with creatinine now 86 μmol/l and eGFR 80 ml/min. The prednisolone was weaned over 54 months and the patient remains in remission on mycophenolate mofetil 750 mg twice a day.

Discussion

Myocarditis is a rare but life-threatening complication of Takayasu arteritis with case series estimating the prevalence at 2.8% [1]. However, cross-sectional studies of cardiac MRI in Takayasu arteritis suggest subclinical myocarditis is far more common, with previous unrecognized myocardial injury being demonstrated in 27% of patients [2]. Endomyocardial biopsies demonstrate an inflammatory infiltrate consisting of natural killer cells and γδ T lymphocytes [3]. More common causes of cardiac failure in Takayasu arteritis include aortic regurgitation secondary to aortic root dilatation, coronary artery disease or systemic hypertension [4].
Cardiac MRI (CMR) alongside Doppler echocardiogram is a sensitive, non-invasive method used to aid the diagnosis of myocarditis [5]. CMR sensitivity is optimal during the first 2 weeks of symptoms and current protocols offer sensitivity of 76% and specificity of 95% for identifying myocardial inflammation [5, 6]. Signs suggestive of active disease include myocardial oedema, regional vasodilatation due to hyperaemia and myocardial necrosis with subsequent fibrosis [5].

Treatment of life-threatening disease in Takayasu arteritis, including myocarditis, usually involves prednisolone and i.v. cyclophosphamide [1, 7]. Following cyclophosphamide treatment our practice is to switch to a disease-modifying anti-rheumatic drug with either methotrexate, mycophenolate mofetil, azathioprine or leflunomide alongside a weaning course of prednisolone. IL-6 inhibition with tocilizumab should be considered in those in whom cyclophosphamide is contraindicated or ineffective [1].

Serial follow-up imaging with echocardiogram is used to evaluate the response to treatment and in this case demonstrated an improving left ventricular ejection fraction. CMR is of additional value, particularly in those with an insufficient response to treatment and the suspicion of persistent myocarditis.

Renal artery angioplasty was undertaken to treat a significant short, proximal arterial stenosis with the aim of improving renal function. Renal arterial involvement in Takayasu arteritis commonly leads to short, ostial lesions that are more amenable to endovascular intervention when compared with longer more irregular lesions, which may require open repair [8]. Surgical outcomes are markedly improved in patients with clinically inactive disease due to periprocedural immunosuppression [7].

**Acknowledgements**

The authors would like to thank the patient for her consent to publish this manuscript for educational purposes.

**Funding:** The authors wish to acknowledge support from the Imperial College, National Institute for Health Research, Biomedical Research Centre scheme. This paper forms part of the supplement entitled ‘EUVAS Cambridge Vasculitis Course Case-Base Supplement’.

This supplement is supported by the University of Cambridge.

**Disclosure statement:** The authors declare no conflict of interest.

**Data availability statement**

The data underlying this article will be shared on reasonable request to the corresponding author.

**References**