Aortic dilatation in a patient with Takayasu arteritis treated with tocilizumab

In recent years there has been growing interest in the use of tocilizumab for the treatment of large vessel vasculitis. Although the primary endpoint (time to relapse) was not met in the first randomised, placebo-controlled trial evaluating the efficacy and safety of tocilizumab in patients with refractory Takayasu arteritis, the results suggested favour for tocilizumab over placebo without new safety concerns.[1] In this journal, three cases of Takayasu arteritis progression during tocilizumab treatment have been described.[2 3] We report one additional patient with disease progression despite tocilizumab therapy.

A 25-year-old woman presented with constitutional symptoms, anaemia of chronic inflammation, elevated erythrocyte sedimentation rate and C reactive protein levels, and imaging evidence of large vessel vasculitis. CT angiography showed vessel wall thickening of the carotid arteries, thoracic descending and infrarenal abdominal aorta and dilatation of the ascending aorta (40 mm). The patient was treated with glucocorticoids (prednisone 1 mg/kg/day) and methotrexate (20 mg/week). While on methotrexate and low-dose prednisone, low-grade fever recurred and inflammatory markers increased. A whole-body fluorodeoxyglucose positron emission tomography (FDG-PET)/CT scanning showed increased FDG uptake of the thoracic and abdominal aorta, prompting a switch to tocilizumab (8 mg/kg/month). With this, symptoms remitted and inflammatory markers normalised. After 6 months, FDG uptake of the aorta normalised as well. The disease remained stable over the following 18 months, when a magnetic resonance angiography showed development of ascending aorta dilation (54 mm) and descending thoracic and infrarenal abdominal aorta stenosis (figure 1). She underwent ascending aorta and proximal hemiarch replacement. Pathology from the surgical specimen demonstrated adventitial fibrosis and mural thickening (figure 2A) with adventitial small vessel vasculitis (figure 2B), consistent with Takayasu aortitis. Infliximab with high-dose steroids was promptly started. One year after surgery, the patient remains in remission on infliximab and prednisone 5 mg daily.

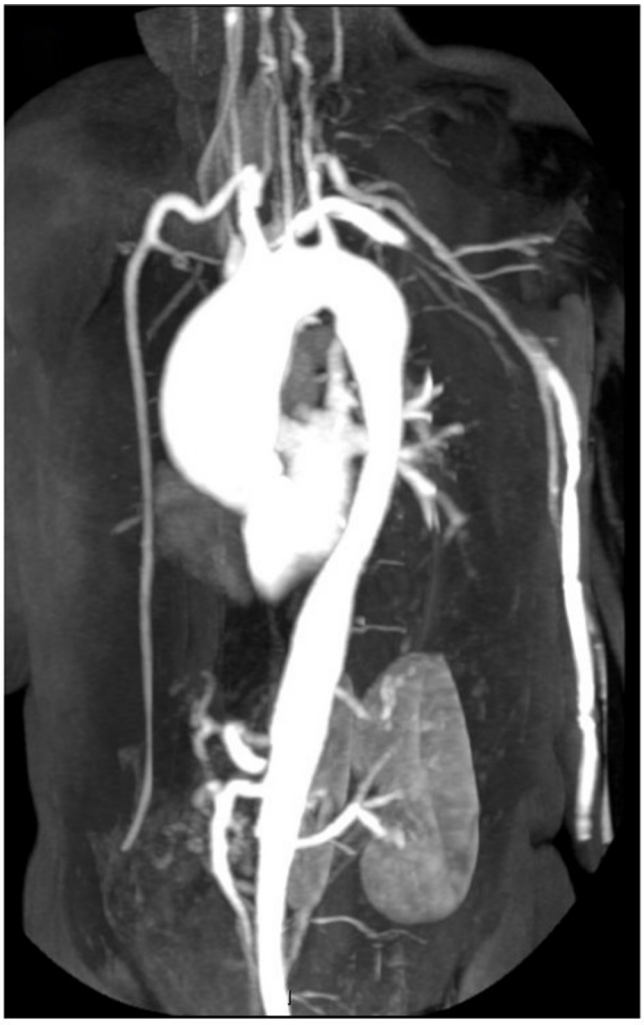

Figure 1 MR angiography showing ascending aorta dilation and descending thoracic and infrarenal abdominal aorta stenosis.

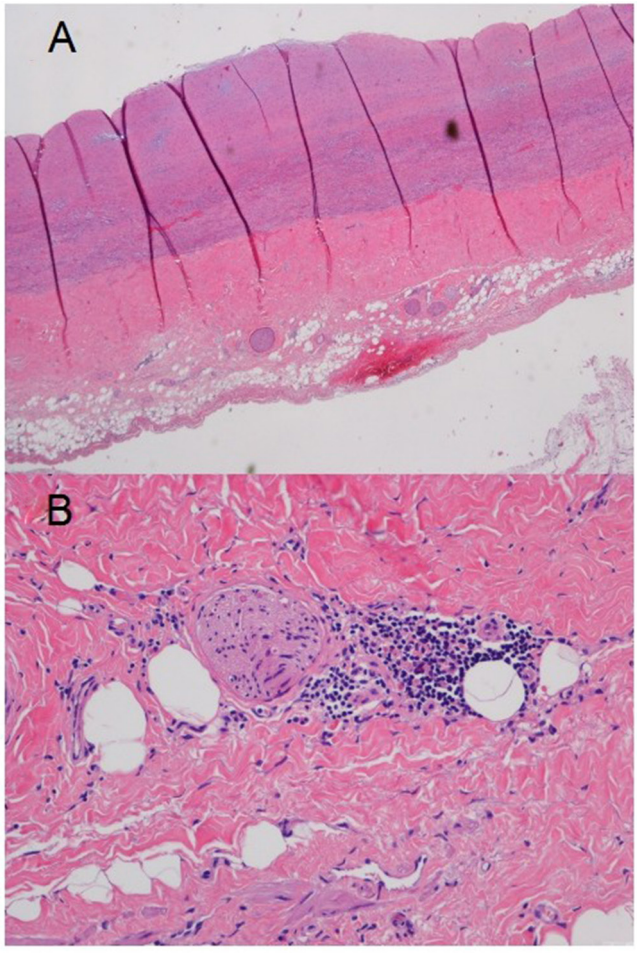

Figure 2 Histologic features of the ascending aorta showing adventitial fibrosis and mural thickening (A) and adventitial small vessel vasculitis (B).

Assessment of disease activity in Takayasu arteritis is challenging as inflammatory markers often do not correlate with disease activity. Moreover tocilizumab suppresses serum inflammatory markers even in the absence of a clinical response. This case clearly demonstrates that TAK can progress despite normal inflammatory markers, absence of symptoms and FDG uptake at PET/CT scanning, and despite treatment with tocilizumab. Assessment of disease activity in patients with Takayasu on tocilizumab should rely on a combination of clinical assessments and serial imaging studies.[4]

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