Disease progression of Takayasu arteritis in two patients treated with tocilizumab

INTRODUCTION

In recent years there has been growing interest in the use of tocilizumab for the treatment of large vessel vasculitis, particularly giant cell arteritis. Nakaoka et al recently suggested that tocilizumab may be of therapeutic benefit in patients with relapsing Takayasu arteritis (TAK). In this journal, a case of aortic ulceration in a patient with TAK while on tocilizumab was described. We report two additional patients who had disease progression despite tocilizumab therapy.

Case 1

A 44-year-old woman with a 20-year history of seropositive rheumatoid arthritis in clinical remission on adalimumab presented with new-onset right upper extremity claudication. A diagnosis of TAK was made after angiography demonstrated arterial thickening of the aorta and arch branches with multifocal narrowing of the subclavian and common carotid arteries. Mycophenolate mofetil and prednisone were added to adalimumab resulting in symptomatic improvement.

A year and a half later the patient experienced worsening upper extremity claudication, paresthesias and jaw discomfort. Erythrocyte sedimentation rate was 87 mm/1 hour and C-reactive protein (CRP) was 37.8 mg/L. Mycophenolate mofetil was continued while adalimumab was switched to tocilizumab 8 mg/kg monthly and prednisone was restarted. Inflammatory markers and symptoms subsequently improved.

After 2 years of tocilizumab therapy, a new diastolic heart murmur was detected. Imaging demonstrated interval progression of the carotid stenosis (figure 1) and development of aortic root dilation and severe aortic valve regurgitation. She underwent ascending aorta, proximal hemiarch and aortic root replacement. Pathology from the surgical specimen demonstrated smouldering aortitis with prominent adventitial fibrosis and mural thickening, consistent with TAK aortitis. Mycophenolate mofetil and tocilizumab were discontinued. She was placed on high-dose glucocorticoids with taper and a 6-month course of cyclophosphamide. One year after surgery, the patient remains in remission on azathioprine 150 mg daily and prednisone 5 mg daily.

Case 2

A 25-year-old woman who presented with vision changes, carotidynia and constitutional symptoms was found to have an absent left radial pulse and elevated inflammatory markers. MR angiography demonstrated bilateral carotid artery stenosis and occlusion of left subclavian artery with mural thickening, consistent with TAK. The patient was treated with glucocorticoids and azathioprine. While on azathioprine, carotidynia recurred and inflammatory markers increased, prompting a switch to tocilizumab (8 mg/kg/month). With this, symptoms remitted and inflammatory markers normalised. Fifteen months following treatment with tocilizumab the patient developed recurrent, transient vision loss. A CT angiogram revealed diffuse and severe narrowing of the right common carotid artery, moderate stenosis of the right vertebral and occlusion of the left common carotid, left vertebral and bilateral subclavian arteries. Comparison of repeat angiography to that obtained 1 year prior showed clear evidence of disease progression.

The patient required an ascending aorta to bilateral carotid bypass with transposition of the right vertebral artery. Postoperatively her vision symptoms markedly improved. Currently she remains on azathioprine and low-dose prednisone.

DISCUSSION

Assessment of disease activity in TAK is challenging as inflammatory markers often do not correlate with disease activity. Moreover, tocilizumab directly decreases the synthesis of CRP by inhibiting the biologic activity of interleukin-6, making it difficult to interpret the values of the acute phase reactants. These two cases clearly illustrate that TAK can progress significantly despite normal inflammatory markers, and despite treatment with tocilizumab. Indeed, the study by Nakaoka et al may have underestimated the risk of progression on treatment as standardised imaging was not required in the trial. In summary, monitoring disease activity in TAK with both clinical evaluation and serial imaging studies is of utmost importance.

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Handling editor Josef S Smolen

Contributors All authors were involved in the preparation of the manuscript and have approved the manuscript and this submission.

Conflict of interest None declared.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; internally peer reviewed.

Accepted 28 October 2018

Published Online First on 8 December 2018. Downloaded from http://ard.bmj.com/ on August 11, 2022 by guest. Protected by copyright.
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