Sustained response to tocilizumab in a patient with relapsing polychondritis complicated by aortitis

Sirs,

Relapsing polychondritis (RP) is a multisystem autoimmune disease characterised by episodic or progressive inflammation of the cartilaginous tissues. All types of cartilage may be involved, including the elastic cartilage of the ears and nose, the hyaline cartilage of peripheral joints and the tracheobronchial tree, the fibrocartilage of axial sites and proteoglycan-rich structures like the eye, heart, blood vessels and inner ear.

Cardiovascular complications are present in 24–52% of patients, aortic regurgitation being the most common. Aortic aneurysms, aortitis, cardiac ischaemia, cardiac conduction abnormalities, pericarditis and thrombophlebitis have also been reported (1).

A 38-year-old man was diagnosed with RP in 2014 after presenting recurrent auricular chondritis, nasal chondritis and episcleritis since 2007. In late 2014 he had a flare of disease with bilateral auricular chondritis, episcleritis, fever, hoarseness, dysphonia, hearing loss, fatigue and effort dyspnea.

Clinical examination revealed a bilateral swollen tender ear and right episcleritis. There was no lymphadenopathy or visceromegaly. Heart and breath sounds were normal, as was the scan locomotor system. Laboratory tests revealed haemoglobin 9.5mg/dL, haematocrit 29%, iron 13ug/dL, transferrin 164mg/dL, ferritin 642ng/mL, white blood cell count 15,900, platelet count 721,000, erythrocyte sedimentation rate (ESR) 120 mm/h, and normal liver and kidney function. C-reactive protein (CRP) was 218 mg/dL and immunoglobulins were normal. Antinuclear antibodies, aDNA, antineutrophil cytoplasmatic antibodies, rheumatoid factor and HLA B27 were negative. Complement C3 and C4 tests were normal, as was urinary sediment. Viral hepatitis serology was negative and plain chest radiograph was normal.

The patient was initially treated with prednisone 0.5 mg/kg/day and with topical glucocorticoids for episcleritis and auricular chondritis.

Spirometry showed a mild small airway obstruction with a positive bronchodilator test result. Laryngoscopy was normal. Computed tomography of the thorax demonstrated no tracheal or bronchial abnormality; however, it revealed a dilated ascending aorta and aortic arch of 43 mm and a thickened aortic wall. Echocardiogram showed aortic root dilation and aortic regurgitation.

We raised the prednisone dose to 1 mg/kg/day and introduced oral methotrexate (titrated up to 20mg weekly) but the auricular chondritis persisted and serum inflammatory markers increased.

A fasting positron emission tomography-CT (PET-CT) was performed and showed increased F-18 fluorodeoxyglucose accumulation in the ascending aorta and aortic arch. Relapsing polychondritis with secondary aortitis was diagnosed.

Treatment with the anti-IL6 receptor monoclonal antibody tocilizumab (8 mg/kg) administered intravenously once a month was started. After the first infusion there was complete resolution of symptoms as well as normalisation of serum inflammatory markers, and the dose of prednisone could be lowered. Twelve months after initiating treatment, the PET-CT showed persistent inflammation but at a reduced intensity.

RP is a rare disease. The most common manifestation of cardiovascular involvement is valvular heart disease. The aortic valve is the most affected site (4-10%), resulting in aortic root dilation and aortic regurgitation. RP patients may present vasculitis in any vessel, and the condition may be local or systemic.

A literature search yielded 12 cases of RP and aortitis (2-12). Initially, three patients were asymptomatic, five suffered non-specific abdominal or chest pain, one presented heart failure and in three no symptoms were described. Most patients had elevated serum inflammatory markers. The aortic lesions comprised six isolated aortitis, four aortitis with aortic regurgitation and two aortitis with aortic regurgitation and coronary ostium stenosis (the last one presenting ischaemic heart disease). Six were located in the thoracic aorta, three in the thoracic and abdominal aorta, and in the last three the location was not described.

The treatment of large-vessel vasculitis is based on high-dose glucocorticoids and methotrexate as a steroid sparing agent. If the classical immunosuppressive drugs fail, recent studies of the pathogenesis of large-vessel vasculitis suggest that IL-6 is an important mediator. They found high levels of IL-6 in the wall of the artery and serum which correlated with disease activity. Therefore, tocilizumab, an IL-6 antagonist, may provide effective treatment (13).

Of the 12 cases of RP and aortitis, five were refractory to classical immunosuppressive therapy and so biological treatment was used. Four started TNF-alpha inhibitors (infliximab and adalimumab) and one tocilizumab (TCZ). In three patients receiving TNF-alpha inhibitors, the drug proved inefficient and was withdrawn, and two of them started TCZ. At the time of publication the three patients with TCZ were in remission.

We report a sustained response to tocilizumab in a patient with refractory RP with aortic involvement. Our description corroborates previous reports of the potential role of IL-6 antagonists to treat large-vessel vasculitis and RP resistant to standard therapies (14).

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Competing interests: none declared.

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