CASE REPORT

Refractory PMR with aortitis: life-saving treatment with anti-IL6 monoclonal antibody (tocilizumab) and surgical reconstruction of the ascending aorta

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SUMMARY

Aortitis is uncommon but well described in patients with polymyalgia rheumatica (PMR). While glucocorticoid remains the mainstay therapy for large-vessel vasculitis, there have been cases where tocilizumab therapy led to clinical and serological improvement in patients with relapsing or refractory disease. We report a case of life-threatening PMR with aortitis in the absence of manifestations related to giant cell arteritis, which, having failed to respond to corticosteroid therapy, was successfully treated with tocilizumab and emergency reconstruction of the ascending aorta. This case adds to the literature supporting the potential value of interleukin-6 inhibition in rare rheumatological conditions such as inflammatory aortitis.

BACKGROUND

Polymyalgia rheumatica (PMR) is an inflammatory disorder that usually affects adults over the age of 50 years.^{1–6} The diagnosis is made on clinical ground, based on certain diagnostic criteria and manifestations often overlap with those seen in giant cell arteritis (GCA), an associated inflammatory vasculopathy affecting large arteries. Even though non-infectious inflammatory aortitis is more commonly seen in GCA, Takayasu's arteritis (TA) or even human leucocyte antigen (HLA)-B-27-associated spondyloarthropathies, there have also been case reports of isolated PMR with aortitis in the absence of manifestations related to GCA.^{1–3}

Glucocorticoid has been the principal treatment in aortitis associated with large-vessel vasculitis. Besides numerous undesirable side effects and associated morbidity, some patients are also resistant to it and often relapse. In view of this, there is a need for a more specific treatment in patients with this spectrum of disease. More recently, there has been an interest in targeting more specific inflammatory mediators using biological therapies, and studies have shown that the interleukin (IL)-6 pathway is upregulated in GCA, TA and PMR.^{7–8} There have also been case reports where tocilizumab therapy led to clinical and serological improvements in patients with relapsing or refractory disease.^{4–6}

CASE PRESENTATION

A 62-year-old man presented with typical clinical and laboratory signs of PMR including a 3-month history of pain and stiffness in his neck, shoulders and proximal muscles followed by fatigue, weight loss, night sweats and fever. He was initially treated

with oral prednisolone in an outpatient setting (15 mg orally daily for 1 month then 10 mg orally daily) with some clinical improvement, but subsequently developed progressive worsening chest pain and shortness of breath which prompted his admission to hospital. He denied any jaw claudication, visual disturbances or headache.

Physical examination on admission revealed a blood pressure of 125/85 in both arms; radial pulse was present bilaterally and was irregularly irregular at 76 bpm. Shoulders and upper arms were mildly tender to touch. A bruit was heard at the right side of the neck. He had no scalp tenderness and his temporal arteries were palpable and pulsatile and did not show any local sign of inflammation.

INVESTIGATIONS

Haemoglobin was 10.9 g/dL, white cell count was $10.55 \times 10^9/L$, platelet count was $326 \times 10^9/L$, serum creatine was 72 $\mu\text{mol/L}$. His erythrocyte sedimentation rate (ESR) was 72 mm/h and C reactive protein (CRP) was 35 mg/L despite the ongoing corticosteroid therapy at 10 mg prednisolone orally daily. Rheumatoid factor (RF), HLA-B-27, antinuclear antibodies, anti-PR3 and anti-MPO IgG antibodies were all negative. His blood cultures were sterile, and his skin testing for tuberculosis and serological testing for syphilis were both negative.

Chest x-ray demonstrated aneurysmal dilation of the entire arch of the aorta (figure 1). ECG showed

Figure 1 Patient's chest x-ray shows aneurysmal dilation (red arrows) with calcific rim of the thoracic aorta (yellow arrow).

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Figure 2 Patient's precontrast thoracic CT image shows a thoracic aortic aneurysm with a calcified wall.

rate-controlled atrial fibrillation 84 bpm and further investigations included a transthoracic echocardiogram (TTE), which showed an aortic valve insufficiency and a thoracic aortic aneurysm. Temporal artery biopsy did not show any evidence of inflammation or vasculitis. Contrasted CT of the whole aorta was performed revealing an aortic aneurysm arising just proximal to the origin of the right brachiocephalic vessel that enlarged progressively around the aortic arch with maximal transverse diameter of 7 cm at the junction of aortic arch and descending aorta (figures 2 and 3).

TREATMENT

The patient was diagnosed as having isolated PMR based on Bird⁹ and American College of Rheumatology (ACR)/The European League Against Rheumatism (EULAR) 2012 classification criteria¹⁰ with aortitis, and was treated aggressively given the severity and rapid progression of the clinical and radiological features. Three daily pulses of intravenous methylprednisolone (total of 3 g) were given, followed by intravenous IL-6 inhibitor tocilizumab.

Given the severity of his cardiac symptoms and his TTE and CT findings, the patient was referred to the cardiology and cardiothoracic services for further evaluation. As the aneurysm was

Figure 3 Contrasted thoracic CT of the patient shows concentric low-attenuation ring of periaortic wall thickening at the aneurysmal ascending and descending aorta.

Figure 4 The graft of the ascending aorta, aortic arch and descending aorta.

deemed too large to be stented, an open aortic reconstruction was performed involving an aneurysmectomy and reconstruction of the aorta with replacement of the ascending aorta, aortic arch and descending aorta using a prosthetic graft (figure 4). The patient was discharged after a full recovery.

OUTCOME AND FOLLOW-UP

During his tocilizumab therapy, his clinical condition significantly improved and he continues to attend our day infusion unit for his monthly tocilizumab infusions. His inflammatory markers have been normal since the instigation of tocilizumab therapy, and his most recent ESR is 2 mm/h, CRP of <3 mg/L.

DISCUSSION

Aortitis can present in rheumatologic conditions especially large-vessel vasculitides : TA and GCA; however, there have also been documented cases of isolated PMR with aortic wall involvement.¹⁻³ We described a rare case of isolated PMR with aortitis in the absence of diminished pulse, or manifestations related to GCA. Our patient had classical symptoms of PMR; however, he did not have either jaw claudication or scalp tenderness. Furthermore, both his temporal arteries were pulsatile and palpable with no evidence of local inflammation and temporal artery biopsy was negative.

Our treatment choice was not the standard treatment for aortitis.⁵ We instigated an aggressive approach with three pulses of daily methylprednisolone (total of 3 g) followed by tocilizumab to rapidly downregulate inflammation, as the risk of aneurysmal rupture appeared great and there are case reports of successful treatment of methylprednisolone¹¹ and tocilizumab²⁻⁵ in patients with aortitis during the course of PMR or GCA. Our patient entered complete clinical remission, underwent the aortic reconstruction successfully and we were able to taper down his daily prednisolone dose to 10 mg, with his most recent bloods showing normal inflammatory markers.

Inflammatory aneurysmal formation occurs more commonly in the thoracic aorta, often being asymptomatic and usually discovered incidentally on plain chest x-ray or findings of a new aortic insufficiency murmur.¹² Open aortic reconstructive

surgery is generally the standard treatment for aortic aneurysms associated with aortitis, but more recently endovascular techniques have been successfully used.^{13–15} Strict control of systemic inflammation is essential in the perioperative stage as surgical repair of these lesions can be compromised with restenosis by the chronic inflammation of the aortitis.¹³

Our case highlights the use of IL-6 blockade as a therapeutic option in non-infectious aortitis. This case is in concordance with other small series and case reports showing positive outcome using tocilizumab for the treatment of inflammatory, non-infectious aortitis.

Learning points

- The case described here emphasises the importance and the need of evaluation of the aorta as a recommendation for patients with polymyalgia rheumatica presented with cardiac symptoms.
- Early diagnosis and treatment of aortitis is crucial for improving survival and preventing postoperative complications.
- This case adds to the literature supporting the potential value of interleukin -6 inhibition in rare rheumatological conditions such as in non-infectious inflammatory aortitis.

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Competing interests None.

Patient consent Obtained.

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REFERENCES

- 1 Narvaez JA, Nolla JM, Sirvent E, *et al.* Giant cell arteritis and polymyalgia rheumatica: usefulness of vascular magnetic resonance imaging studies in the diagnosis of aortitis. *Rheumatology (Oxford)* 2005;44:479–83.
- 2 Kataoka H, Atsumi T, Hashimoto T, *et al.* Polymyalgia rheumatica as the manifestation of unclassified aortitis. *Mod Rheumatol* 2008;18:105–8.
- 3 Milchert M, Brzosko M. Comment on 'Polymyalgia rheumatica as the manifestation of unclassified aortitis'. *Mod Rheumatol* 2008;18:427–8.
- 4 Schafer VS, Zwerina J. Biologic treatment of large-vessel vasculitides. *Curr Opin Rheumatol* 2012;24:31–7.
- 5 Nishimoto N, Nakahara H, Yoshio-Hoshino N, *et al.* Successful treatment of a patient with Takayasu arteritis using a humanized anti-interleukin-6 receptor antibody. *Arthritis Rheum* 2008;58:1197–200.
- 6 Unizony S, Arias-Urdaneta L, Miloslavsky E, *et al.* Tocilizumab for the treatment of large-vessel vasculitis (giant cell arteritis, Takayasu arteritis) and polymyalgia rheumatica. *Arthritis Care Res* 2012;64:1720–9.
- 7 Martinez-Taboada VM, Alvarez L, RuizSoto M, *et al.* Giant cell arteritis and polymyalgia rheumatica: role of cytokines in the pathogenesis and implications for treatment. *Cytokine* 2008;44:207–20.
- 8 Arnaud L, Haroche J, Mathian A, *et al.* Pathogenesis of Takayasu's arteritis: a 2011 update. *Autoimmun* 2011;11:61–7.
- 9 Bird HA, Esselinckx W, Dixon AS, *et al.* An evaluation of criteria for polymyalgia rheumatica. *Ann Rheum Dis* 1979;38:434–9.
- 10 Dasgupta B, Cimmino MA, Matteson EL, *et al.* 2012 Provisional classification criteria for polymyalgia rheumatica: a European League Against Rheumatism/American College of Rheumatology collaborative initiative. *Arthritis Rheum* 2012;64:943–54.
- 11 Cimmino MA, Macchioni P, Salvarani C, *et al.* Pulse steroid treatment of polymyalgia rheumatica. *Clin Exp Rheumatol* 2004;22:381–2.
- 12 Gornik HL, Creager MA. Diseases of the aorta. In: Topol EJ, ed. *Textbook of cardiovascular medicine*. 3rd edn. Philadelphia, PA: Lippincott, Williams & Wilkins, 2007:1474–92.
- 13 Shafii AE, Vivacqua A, Svensson LG, *et al.* Total arch replacement after a failed repair for Takayasu's ascending aortitis. *Ann Thorac Surg* 2012;93:300–2.
- 14 Zehr KJ, Mathur A, Orszulak TA, *et al.* Surgical treatment of ascending aortic aneurysms in patients with giant cell aortitis. *Ann Thorac Surg* 2005;79:1512–17.
- 15 Qureshi MA, Martin Z, Greenberg RK. Endovascular management of patients with Takayasu arteritis: stents versus stent grafts. *Semin Vasc Surg* 2011;24:44–52.

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