

## Active aortitis in relapsing polychondritis

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### Abstract

**Relapsing polychondritis (RP) is a rare inflammatory multiorgan disorder affecting cartilaginous structures and other connective tissues. Serious cardiovascular complications have been reported in patients with RP, the most frequent being aortic or mitral regurgitation and aortic aneurysms. Aortitis is a very rare complication. An unusual case of active aortitis in a patient with RP, despite intensive immunosuppressive treatment, is described with a special emphasis on the pathological findings.**

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Relapsing polychondritis (RP) is an uncommon multisystem disease characterised by episodic or progressive inflammation of cartilaginous tissues. All types of cartilage can be involved, including the elastic cartilage of the ears and nose, the hyaline cartilage of peripheral joints, the fibrocartilage at axial sites, and the cartilage in the tracheobronchial tree. RP can also involve other proteoglycan rich structures, such as the eye, heart, blood vessels, and inner ear.

Cardiovascular complications appear in about 25% of patients with RP and include aortic and mitral regurgitation, aortic aneurysm, aortic dissection, myocarditis, pericarditis, atrioventricular block, and systemic vasculitis. These complications are the second most frequent cause of mortality after pneumonia in patients with RP.<sup>1</sup> Aortitis has been rarely reported in patients with RP and there has been little description of the pathological changes.<sup>1</sup> An unusual case of aortitis in a patient with RP who was under intensive immunosuppressive treatment is described, with special emphasis on the pathological findings

### Case history

A 54 year old woman was diagnosed with relapsing polychondritis in 1996; she had involvement of the cartilage of the ears and nose, with nasal bridge collapse and recurrent episodes of scleritis. She was of normal height and weight with no family history of Marfan's syndrome, other skeletal abnormalities, or collagen vascular diseases. An echocardiogram in 1996 showed mild aortic regurgitation. In late 1999 she had a flare up of her disease, with a further episode of scleritis, a rise in erythrocyte sedimentation rate (ESR) to 90 mm/hour, and signs of considerable aortic regurgitation. She was treated by increased immunosuppression with azathioprine (150 mg/day) and prednisolone (30 mg twice daily) from March



Figure 1 Spino-echo image of the aortic root and the ascending thoracic aorta acquired in a coronal plane. The ascending aorta, beyond the sinotubular junction, is dilated (arrow), with a maximum diameter of 6.0 cm.

2000. Echocardiography showed severe aortic regurgitation, with dilated aortic root, and a possible aneurysm; therefore, it was decided to change her immunosuppression to intravenous cyclophosphamide. The first pulse of 750 mg was given in June 2000 and a second pulse was given in July 2000; the prednisolone dose was reduced to 20 mg, twice daily. In September 2000, her ESR was 24 mm/hour and the prednisolone dose was further reduced to 17.5 mg once a day. A cardiac magnetic resonance imaging (MRI) scan (fig 1) showed a dilated ascending aorta (maximum 6 cm), extending from the sinotubular junction to beyond the right innominate artery. Moderate aortic regurgitation and a dilated left ventricle were also noted. In October 2000, aortic root and aortic valve replacement was performed. During the operation, the aorta was found to be thick walled and dilated and the aortic valve ring was dilated with no other abnormality of the valve. The aortic valve was replaced with a 23 mm St Jude's mechanical valve and the ascending aorta was replaced with a 38 Gel seal interposition graft. The aorta was sent for pathological examination.

### Pathological findings

On macroscopic examination, the aortic wall was thickened, measuring 5 mm, with pronounced intimal surface irregularity (fig 2). Histologically, the aorta showed intimal fibrosis and infiltration with admixed acute and chronic inflammatory cells. There was destruction and replacement of most of the medial elastic tissue with vascular granulation tissue and focal areas of necrosis. There was an increase in the vasa vasorum, which showed endothelial swelling, and was surrounded by

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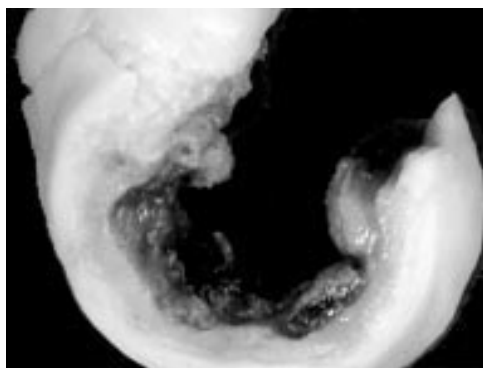


Figure 2 Transverse section of opened ascending aorta showing thickening of all layers of the wall and intimal irregularity.

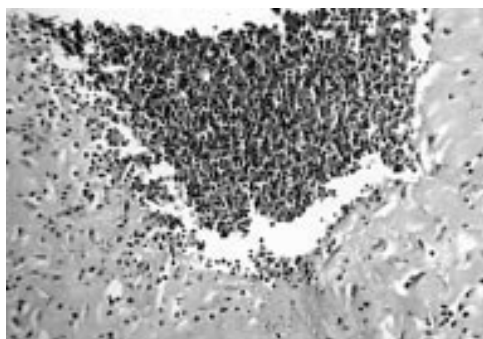


Figure 3 Medial layer of aortic wall showing microabscess formation containing neutrophils and cellular debris.

inflammatory cells, mainly lymphocytes. The vasa vasorum extended throughout the full thickness of the aortic wall. There were localised aggregates of neutrophil microabscesses within the media and intima (fig 3). The adventitia showed focal lymphoid aggregates and fibrosis. Special stains for bacteria (Gram and Ziehl Neelsen stains) and fungi (Grocott stain) were negative. No giant cells, granuloma formation, or eosinophils were seen. In summary, the aortic wall showed a florid acute and chronic aortitis with pronounced destruction of the media and intimal fibrosis.

### Discussion

RP is a rare disease with only approximately 600 cases being reported in the literature.<sup>1</sup> Most have been reported as single case reports. There are no epidemiological data on its incidence in the UK. It is thought to have an immunological basis, with serum autoantibodies to type II collagen in up to two thirds of cases.<sup>1</sup> According to a literature review, the most frequent aortic lesion in RP is aortic insufficiency (occurring in 4–9% of patients), as a result of aortic root dilatation rather than primary involvement of the valve, as in our patient. In a few cases, aortic regurgitation is caused by exclusive cusp involvement without dilatation of the aortic root. When regurgitation is a result of valvular involvement, thickening, fraying, loss of elastic tissue, and cystic degeneration of the aortic valve cusps are described.<sup>2</sup>

Various histological features have been described with RP affecting the aortic wall.

The main findings are lymphocytic infiltration around the vasa vasorum of the outer media, with fragmentation or total loss of elastic tissue, and fibrous replacement with hyalinisation.<sup>3</sup> Leucocyte infiltration, pronounced neovascularisation, and necrotising inflammation have been mentioned in only one previous report, and then only in the aortic valve, with no mention of the aortic wall.<sup>2</sup> Aneurysm of either the thoracic or abdominal aorta occurs in 4% of patients with RP and is caused by the disruption of elastic fibres.<sup>3,4</sup>

Our case is interesting in that the patient had florid acute and chronic aortitis involving all three layers of the aortic wall, with prominent microabscesses, despite immunosuppressive treatment and a fall in inflammatory serological markers. Her aortic regurgitation progressed despite this treatment, highlighting that cardiological follow up is essential in patients even with clinically quiescent disease.

The histopathological appearances of the aortic lesion in RP can easily be distinguished from those seen in cystic medial necrosis, in which there is accumulation of Schiff positive material in the media with no inflammation.<sup>5</sup> It is important to distinguish it from other cases of aortitis, including syphilitic aortitis and giant cell aortitis. In syphilitic aortitis, the inflammation is usually chronic with plasma cells. In giant cell aortitis, the primary abnormality appears to be panaortitis with giant cells. Giant cell aortitis can be seen in a variety of conditions including rheumatoid arthritis, systemic lupus erythematosus, ankylosing spondylitis, and Reiter's syndrome. Our patient lacked giant cells and these have not been reported with polycondritis. The prominent vasa vasorum lymphocytic inflammation that has been reported occurs early in the disease and may be related to the cell mediated immunological abnormality that is thought to be responsible for this disease.<sup>1</sup>

In RP, 86% of the patients embark on a relapsing and 14% on a progressive clinical course.<sup>4</sup> Corticosteroids and cyclophosphamide can decrease the frequency, duration, and severity of recurrences, but might not be able to stop the disease progression. In particular, the aortitis can become refractory,<sup>6</sup> as in our case. Successful surgical replacement of heart valves and aneurysm resection have been reported, but inflammation can recur adjacent to grafts.<sup>7</sup> Therefore, regular clinical follow up of all patients is essential. Estimated five and 10 year survivals are 74% and 55%, respectively.<sup>8</sup> By assessing the aorta using MRI, aortic involvement may be diagnosed early before the onset of aortic rupture, dissection, or valve regurgitation, and early treatment can be planned.

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