

INFLAMMATORY DISEASES ASSOCIATED WITH THORACIC AORTIC DISEASE

Definitions

Aortitis refers to inflammatory disorders of the aorta, which may result in wall thickening, stenosis, aneurysm, and dissection. Inflammatory aortitis is most often caused by large vessel vasculitis, including giant cell arteritis, Takayasu's arteritis, immunoglobulin G4-related aortitis, and isolated aortitis (Table 1).¹ Immunoglobulin G4-related disease (IgG4-RD) is increasingly recognized and may be as common as LVV.² Infected thoracic aortic aneurysms due to bacterial infections may also be seen as a complication of endocarditis or cardiac surgery or due to contiguous spread from adjacent thoracic structures. Aortitis and large-vessel arteritis are characteristics of Takayasu's arteritis, and giant-cell (temporal) arteritis.^{1,3,4}

TAKAYASHU ARTERITIS

Definition

Takayasu arteritis, also known as pulseless disease, is an idiopathic arteritis involving the aorta and its branches.

Epidemiology

It mainly affects women (10 times more than men) and is usually but not invariably diagnosed in the third decade of life. In the US its prevalence is 2.6 cases/million.⁵

Pathophysiology

Takayasu is a T-cell-mediated panarteritis the pathogenesis of which remains poorly defined. The disease proceeds from adventitial vasa vasorum involvement inward with resultant tissue destruction that yields aneurysms and inflammatory infiltrates that causes stenosis. Coronaries are affected in <10% with the development of aneurysms. In the Japanese type, the thoracic aorta and great vessels are most commonly affected. In the Indian type, the disease most commonly affects the abdominal aorta and the renal arteries.

Presentation

Fatigue, night sweats, anorexia, malaise, and weight loss characterize the acute phase of the disease. Chronic symptoms are aortic valve regurgitation, hypertension due to involvement of the renal arteries, upper extremity claudication, and cerebrovascular insufficiency (vision loss, lightheadedness, stroke, carotid artery pain). The proportion of male patients or patients with later onset has been found increased in recent reports. Female patients, particularly young patients, show a tendency to have localized vascular involvements in the aortic arch and/or its major branches. Male patients often have extensive aortic lesions or aneurysm, as well as localized abdominal lesions.⁶

Diagnosis

The diagnosis of Takayasu arteritis is traditionally made by identifying at least three of the 1990 American College of Rheumatology criteria (Table 2).⁷ ESR and CRP are elevated in 50-70% of patients depending on the disease phase. The most recent European League Against Rheumatism (EULAR) recommendations present simplified criteria for the definition of active disease, combining clinical signs and symptoms, imaging or biopsy, and elevated inflammatory markers.⁸

Takayasu arteritis is classified by angiographic findings: type I (branches of the aortic arch-the most common type), type IIa (ascending aorta, aortic arch, and its branches), type IIb (IIa lesions with the thoracic descending aorta), type III (thoracic descending aorta, abdominal aorta, and renal arteries), type IV (abdominal aorta and/or renal arteries), and type V (type IIb + IV, ascending aorta, aortic arch, and its branches, and the thoracic descending aorta as well as the abdominal aorta and/or renal arteries).⁹ Pulmonary artery involvement and pulmonary hypertension are not rare in Takayasu arteritis.¹⁰

Therapy

The first-line therapy is based on steroids, but one-half of TA patients have steroid-resistant or relapsing diseases for which the addition of other immunosuppressive agents to steroid therapy may be required to achieve remission.¹ Immunosuppression with steroids or agents such as methotrexate, azathioprine, and antitumor necrosis factor-alpha agents such as infliximab or adalimumab are used for 1-2 years (Figure 1). Remissions occur in 40-60% of patients on steroids, and 40% of them respond to cytotoxic agents.^{5,11} Male sex, elevated CRP and carotidynia are factors associated with relapse, while progressive disease course, thoracic aorta involvement, and retinopathy are associated with vascular complications that may occur ≤ 10 years from diagnosis.¹²

Biological-targeted treatments with TNF- α antagonists and tocilizumab (anti-IL-6 receptor), have been found safe and effective in drug-refractory disease.¹³ Surgical revascularization is implemented when needed in the non-acute phase but at an increased risk of anastomotic aneurysms. Percutaneous intraluminal angioplasty of the carotid, subclavian, renal arteries and pulmonary arteries is feasible.¹⁴ Surgical or percutaneous revascularization is associated with a 44% 5-year rate of complications, particularly when it is performed at time of prominent biological inflammation.¹⁵

GIANT CELL (TEMPORAL) ARTERITIS

Definition

Giant cell arteritis involves the aorta and its secondary and tertiary branches, and especially the external and internal carotids, and shares the same pathology with Takayasu arteritis.

Epidemiology

It mainly affects patients above 50 years (with a peak at 75-85 years, women: men in a 3:2 ratio), and has a predilection for northern Europeans. Its incidence in the US is 20/100000.¹⁶

Pathophysiology

This also a T-cell-mediated arteritis that mainly involves the extracranial branches of the aorta, and spares intracranial vessels. In medium-sized arteries inflammation results in narrowing and obstruction of vessels, but in the thoracic aorta aneurysm formation and rupture may be caused.

Presentation

It is variable. Half of the patients report malaise, fever, night sweats, weight loss and depression. Headache, scalp tenderness, abnormal temporal arteries are present in most patients with biopsy-proven disease. Jaw claudication is common (50%) visual changes and or neurologic symptoms and stroke develop in one third of patients. Diplopia, amaurosis fugax, or blurriness are important to notice since if left untreated permanent blindness may occur. Up to 30% of patients develop large artery complications such as aortic aneurysm/dissection, and stenosis of the vertebral, subclavian and brachial arteries.¹⁷

Approximately 40% of patients also have polymyalgia rheumatic which has the same genetic risk factors and acute-phase responses.¹⁶

Diagnosis

It is established by at least three of the 1990 American College of Rheumatology criteria:

1) age older than 50 years, 2) recent-onset localized headache, 3) temporal artery pulse attenuation or tenderness, 4) erythrocyte sedimentation rate greater than 50 mm/h, and 5) an arterial biopsy demonstrating necrotizing vasculitis. With intracranial disease, temporal artery biopsies (performed within 7 days of steroid initiation) are diagnostic in up to 80% of cases. The most recent EULAR recommendations present simplified criteria for the definition of active disease, combining clinical signs and symptoms, imaging or biopsy, and elevated inflammatory markers.⁸

Therapy

Immunosuppression with steroids and aspirin for 1 or 2 year are the treatment of choice. Steroids as essential to prevent blindness although exacerbations of the disease may be seen in 30-59% of patients. In 2017, subcutaneous tocilizumab, an anti-IL-6 receptor monoclonal antibody, was approved by the U.S. Food and Drug Administration for use in combination with glucocorticoids for the treatment of GCA (Figure 2).¹ Upadacitinib, an oral and selective Janus kinase (JAK)-1 inhibitor, has the potential to block multiple pathogenic pathways in giant-cell arteritis. In the SELECT-GCA phase 3 trialIn patients with giant-cell arteritis, upadacitinib at a dose of 15 mg with a 26-week glucocorticoid taper showed efficacy superior to that of placebo with a 52-week glucocorticoid taper.¹⁸

INFECTIOUS AORTITIS

MYCOTIC ANEURYSMS

INFECTED GRAFTS

Infected native aortic aneurysms, also referred to as mycotic aortic aneurysms, are rare, life-threatening microbial infections leading to degradation of the aortic wall. Non-typhoidal *Salmonella* accounts for 60% of cases, followed by *S. aureus* (16%) and *Streptococcus* species (7%).¹⁹ Endovascular treatment of mycotic aneurysms is now feasible and for most patients a durable treatment option (Table 3). Late infections do occur, are often lethal, and warrant long-term antibiotic treatment and follow-up. Surgical repair is associated with significantly more favourable post-discharge survival compared with EVAR.¹⁹ Patients with non-Salmonella positive blood cultures were more likely to die from late infection.²⁰ Recommendations for infections of native aorta, and prosthetic graft infection are provided in Table 3.

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