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INVITED REVIEWS

# What is isolated / idiopathic / non-syndromic aortitis? What is not?

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This manuscript was peer-reviewed by Assoc. Prof. Dr. Berkan Armağan

**Definition:** Aortitis is a non-specific inflammation that affects any of the aorta wall layers, regardless of the underlying etiology [1]. The causes of aortitis are evaluated under two main headings infectious and non-infectious causes. The main infectious causes include; salmonella, staphylococcus aureus, syphilis, hepatitis B and C, HIV, histoplasmosis, and tuberculosis. The main non-infectious causes include; large vessel vasculitis such as giant cell arteritis (GCA) and Takayasu arteritis (TA), sarcoidosis, IgG4-RD, Behçet's disease, Cogan syndrome, Erdheim-Chester disease, connective tissue disease, and idiopathic aortitis (IA) [2]. Idiopathic aortitis, which is a diagnosis of exclusion, is defined by an aortic wall thickening >2 mm on computed tomography/magnetic resonance (CT/MR) and/or aortic aneurysm associated with an unexplained inflammatory syndrome (C-reactive protein (CRP) or fibrinogen elevation).

**Clinical Features:** Although idiopathic aortitis clinic is mostly asymptomatic, nonspecific constitutional symptoms such as fever, malaise, weight loss, myalgia, resistant blunt back and chest pain, abdominal pain, vascular insufficiency, and progressive cough may occur.

***Diagnosis (Radiology & Histopathology):*** The initial evaluation of a patient with all aortitis requires rapid differential diagnosis of the infectious etiology because of its rapid progression, complications, and high mortality [3]. Radiological and nuclear imaging (CT/MR and positron emission tomography scan) evaluated along with clinical, histopathologically, and laboratory findings increase diagnostic accuracy. Apart from diagnostic evaluation, radiological and nuclear imaging is also helpful in measuring disease activity, treatment plans, and post-treatment follow-up [4]. Vessel aneurysm, ectasia, wall thickening, dissection, stenosis, and thrombosis are the most common radiological findings. Histopathologically, aortitis classification is divided into 4 groups;

1. **Granulomatous/giant cell pattern of inflammation;** Idiopathic aortitis, GCA, TA, rheumatoid vasculitis, sarcoidosis, granulomatous polyangiitis, a mycobacterial and fungal infection.
2. **The lymphoplasmacytic pattern of inflammation;** (lymphocytes and plasma cells without a granulomatous/giant cell component); IgG4-related disease, syphilis, ankylosing spondylitis, systemic lupus erythematosus.
3. **Suppurative pattern of inflammation;** Gram positive cocci, pseudomonas, salmonella.
4. **Mixed inflammatory pattern;** (lymphocytes, plasma cells, macrophages, neutrophils, mast cells, and eosinophils); Behçet disease, Cogan syndrome, relapsing polychondritis.

**Differential diagnosis:**

– **Takayasu arteritis;** luminal narrowing or occlusion, discrepant blood pressure between arms, arterial bruit, limb claudication, carotidynia, absent or diminished peripheral pulses, hypertension.

- **Temporal arteritis;** Isolated aortitis demonstrates a granulomatous/giant cell pattern histopathologically. It cannot be distinguished histopathologically. Headache, abrupt onset of visual disturbances, jaw claudication, limb claudication, and temporal artery abnormalities such as tenderness to palpation.
- **Relapsing polychondritis;** inflammation in cartilaginous structures and other tissues throughout the body, particularly the ears, nose, eyes, joints, and respiratory tract.
- **Erdheim -Chester disease;** multifocal sclerotic lesions of the long bones demonstrating sheets of foamy histiocytes on biopsy.
- **Cogan syndrome;** clinical hallmarks are interstitial keratitis and vestibulo auditory dysfunction.
- **Sarcoidosis;** bilateral hilar adenopathy, pulmonary reticular opacities, skin, joint, and/or eye lesions, ACE↑, urine calcium↑.
- **IgG4-related disease;** tumor-like swelling of involved organs.

## CASE PRESENTATION

A 51-year-old female patient who had a history of hypertension, Hashimoto's disease, and migraine presented to our clinic in 2017 with non-productive progressive cough, myalgia, subfebrile fever, back and chest pain, bilateral proximal arm pain for the last one year. There were no remarkable findings on physical examination. Blood tests revealed elevated CRP (26.3 mg/dl, ULN>5) and erythrocyte sedimentation rate 78 mm/h (ULN>20 mm/h), leukocyte (6624/mm3), neutrophil (2500/$mm^3$) with negative serology of RF (IU/ml), CCP (U/ml), ANA .

Since the patient's symptoms and acute phase reactant elevation continued for 1 year, malignancy screening was initially performed. A peripheral blood smear, mammography screening, and the fecal occult blood test were negative. Thorax CT; A few parenchymal nodules, the largest of which is 6 mm, in ACs, soft tissue increase measuring 1 cm in the thickest part around the ascending aorta. The soft tissue augmentation begins at the root of the aorta just superior to the level of the valsalva and extends superiorly along the ascending aorta (aortitis?) (Figure 1).

Infectious tests were requested first because of an aortitis report on thorax CT. HBV, HCV, anti-HIV, Toxo IgM, anti-rubella IgM, CMV IgM VDRL, Brucella, Grubal widal , IGRA results were all negative. Echocardiography was normal (ejection fraction 65%, pulmonary artery pressure normal ) and no pathology was detected in pelvic X-ray. The patient was diagnosed with non-infective isolated aortitis and prednisolone (20 mg/day) plus oral methotrexate (10 mg/week )were started. One month later, both clinical improvement and normalization at acute phase levels were seen. Prednisolone was gradually tapered and completely discontinued at 6 months. However, radiological and clinical progression was detected first year MR imaging (wall thickening in isolated ascending aorta and increased anteroposterior diameter of the ascending aorta (dilatation << progression). SC certolizumab (200 mg /ml/ 2 weeks) treatment was started due to disease progression. Due to itching and clinical unresponsiveness after certolizumab,

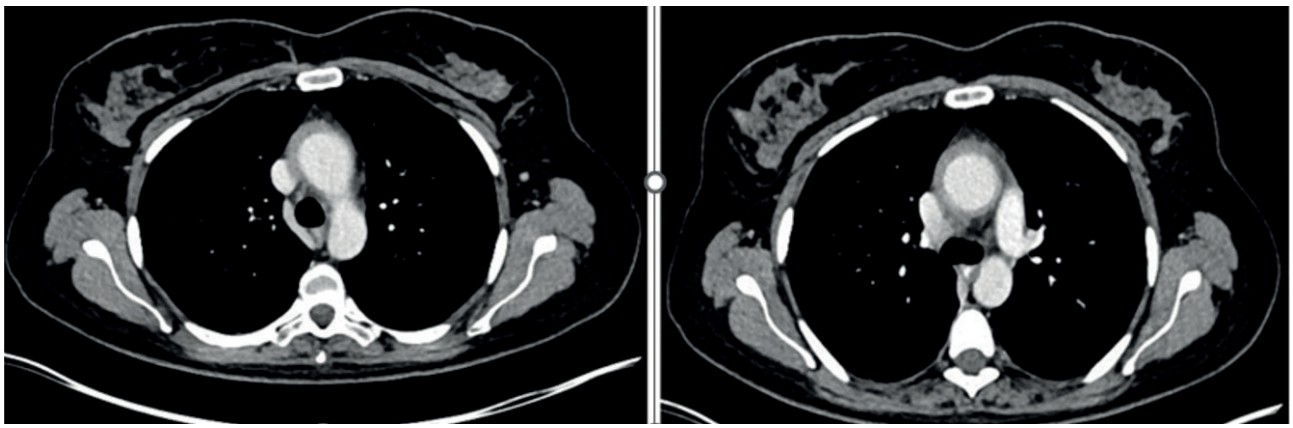

**Figure 1.** Axial CT scans acquired during the venous phase show concentric wall thickening of the aorta characterized by an internal hypoattenuating ring.

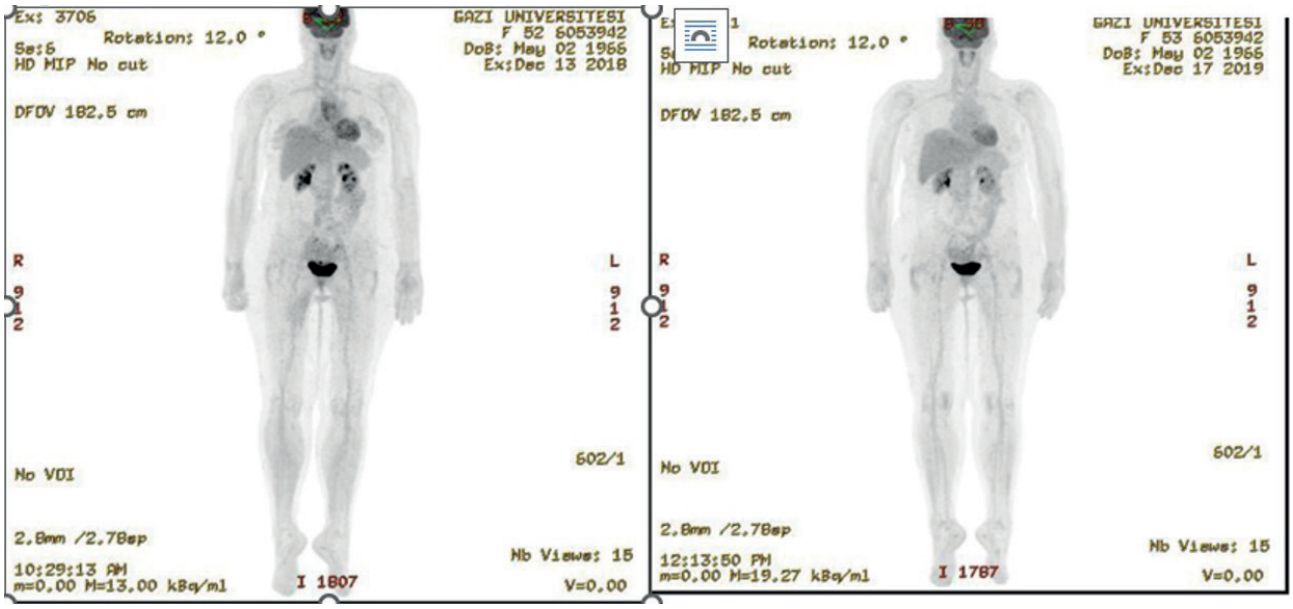


**Figure 2.** Increased FDG uptake in the aorta and disappearance of aortic involvement (2022) after tocilizumab treatment in 2019.

it was switched to SC tocilizumab (162 mg/week) treatment. After the SC tocilizumab treatment, she has no clinical complaints or radiological regression for about three years (Figure 2).

## Key messages

- The initial evaluation of a patient with aortitis requires rapid differential diagnosis of the infectious etiology because of its rapid progression, complications, and high mortality.
- Location of aortic involvement; ascending, arc us, and descending aorta, suprarenal abdominal aorta, subrenal abdominal aorta, or entire aorta. Tobacco use, older age, connective tissue disease, diabetes mellitus, heart valve disorder, and family history of aortic aneurysm are among the risk factors.
- To prevent the development of life-threatening complications of IA, corticosteroids should be initiated.
- Apart from steroids, methotrexate, azathioprine, cyclophosphamide, mycophenolate mofetil, and TNF inhibitors (in refractory cases) are preferred.
- In medical treatment failure or severe aortic regurgitation , surgical procedures may need to apply such as aneurysmectomy, arterial reconstruction or aortic valve operation.
- The 5-year event-free survival for patients with IA is 38%.

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