ESC European Society of Cardiology

European Heart Journal – Case Reports (2021) **5**(11), 1–5
https://doi.org/10.1093/ehjcr/ytab427

CASE REPORT
Other

An unusual presentation of non-infectious ascending aortitis: a case report of an asymptomatic murmur

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Received 24 February 2021; first decision 14 April 2021; accepted 11 October 2021; online publish-ahead-of-print 23 October 2021

Background Aortitis refers to pathologic inflammation of the aortic wall and is broadly categorized into inflammatory (or non-infectious) and infectious aortitis. While rare, isolated non-infectious ascending aortitis (I-NIAA) is a clinical entity that is becoming increasingly recognized but remains poorly understood.

Case summary A 72-year-old man presented with an asymptomatic murmur and was found to have severe aortic insufficiency second to a large ascending aortic aneurysm. He underwent surgical repair and pathology revealed isolated non-infectious ascending aortitis. Following successful surgical repair, he developed joint pains which were successfully treated with glucocorticoids.

Discussion Isolated non-infectious aortitis is a rare entity that warrants further investigation. This case highlights the importance of sending surgical specimens for histopathologic evaluation even when a systemic process is not evident at the time of surgical repair. The development of systemic symptoms following surgical repair in this patient emphasizes the importance of thorough rheumatologic evaluation in patients found to have I-NIAA. Isolated non-infectious ascending aortitis remains poorly understood, and further study is needed to evaluate both its existence as a distinct clinical entity and the role of immunosuppressive therapy.

Keywords Aorta • Autoimmune • Case report • Echocardiography • Three-dimensional imaging • Valve replacement

ESC Curriculum 2.1 Imaging modalities • 2.2 Echocardiography • 9.1 Aortic disease

Learning points

- This case reinforces the importance of understanding the different aetiologies of ascending aortitis and the importance of submitting all surgical specimens for histopathologic analysis.
- The case highlights that isolated non-infectious ascending aortitis is a distinct clinical entity that must be distinguished from other forms of ascending aortitis.

Introduction

Aortitis refers to pathologic inflammation of the aortic wall and is broadly categorized into inflammatory (or non-infectious) and infectious aortitis. Infectious causes are less common overall and vary in prevalence geographically. Aetiologies include bacterial infections (staphylococcus, streptococcus, salmonella, and Gram-negative rods), syphilis, and mycobacteria.[1] Non-infectious aortitis either occurs in isolation or in the presence of a systemic disorder such as vasculitis,

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Handling Editor: Francesco Giannini
Peer-reviewers: Marcelo Haertel Miglioranza and Andreas Mitsis
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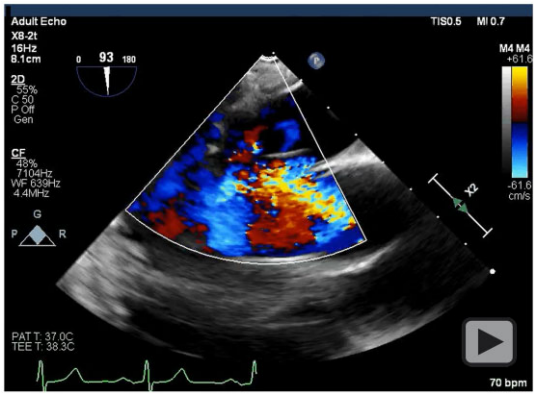
connective tissue disease, or other autoimmune diseases. With respect to ascending aortitis specifically, large-vessel vasculitis is the most common underlying process, specifically Giant Cell Arteritis and Takayasu Arteritis.[2] Other disease processes include Anti-neutrophil cytoplasmic antibody-positive vasculitides, sarcoidosis, Sjogren's syndrome, ankylosing spondylitis, systemic lupus erythematosus, rheumatoid arthritis, and Behcet's disease.[2] Isolated non-infectious ascending aortitis (I-NIAA) is a clinical entity that is becoming increasingly recognized but remains poorly understood. It refers to non-infectious ascending aortitis without evidence of an underlying rheumatologic process and is most commonly diagnosed on histopathology following repair of ascending aortic aneurysm or dissection.[3]

The epidemiology of aortitis is difficult to characterize, but non-infectious aetiologies predominate.[1,2] The Cleveland Clinic published a case series of 1204 surgical specimens from patients undergoing aortic surgery (mostly aneurysm repairs), and the prevalence of aortitis was 4.3%.[4] In almost 70% of the patients found to have aortitis, there was no evidence of underlying disease, and the inflammation was deemed to be an isolated non-infectious aortitis.[4]

The management of I-NIAA remains poorly understood and the role for immunosuppression is unclear. Some patients with a systemic disorder may initially present as an I-NIAA and subsequently develop other features of an underlying disorder later in the disease course. The recommendations regarding work-up for underlying rheumatologic disorders in patients found to have I-NIAA have not been well-defined. We present the case of a 72-year-old male who was diagnosed with I-NIAA following surgical repair of a large thoracic aortic aneurysm and subsequently developed clinical features suggestive of an underlying rheumatologic process.

Timeline

Day 1	72-year-old witd IV/VI diastolic murmur found to have severe aortic insufficiency on transtdoracic echocardiogram
Day 23	Computed tomography angiography demonstrated a fusiform aneurysm of the ascending thoracic aorta, measuring 5.7 cm × 6.5 cm in greatest dimension
Day 47	Transoesophageal echocardiogram demonstrated central aortic insufficiency jet occupying a width of 60% of the left ventricular outflow tract
Day 50	Patient underwent aortic valve replacement and supracoronary replacement of the ascending aorta.
Day 96	Patient evaluated in rheumatology clinic found to have elevated ANA and RF but otherwise negative work-up.
Day 159	Patient seen in rheumatology clinic and complained of shoulder pain and stiffness. He started prednisone for possible polymyalgia rheumatica.
Day 201	Pain resolved after 6 weeks of steroid therapy.
Day 278	Patient was seen in rheumatology clinic and reported continued resolution of joint pain.



Video 1 Initial evaluation by transthoracic echocardiography. Transthoracic echocardiography demonstrating a tricuspid aortic valve with severe aortic insufficiency.

Case presentation

A 72-year-old male presented to our cardiology clinic at the request of his primary care physician for an asymptomatic murmur. The patient reported a past medical history of well-controlled hypertension and diet-controlled type two diabetes mellitus. He denied family history of heart disease, aortic disease, or sudden cardiac death. He reported being physically active daily without chest pain or dyspnoea. Physical exam revealed a blood pressure of 160/59 and a heart rate of 59. He had prominent head nodding. There was a Grade IV/VI diastolic murmur heard loudest over the left upper sternal border. There were prominent carotid pulsations but no jugular venous distention or peripheral oedema. Lung auscultation revealed no abnormalities.

Aortic regurgitation was suspected given the characteristics of the murmur auscultated, wide pulse pressure, De Musset's sign, and prominent carotid pulsations. Transthoracic echocardiography revealed a tricuspid aortic valve with severe aortic insufficiency (*Video 1*). The ascending aorta was severely dilated. The left ventricular systolic function was preserved with a left ventricular ejection fraction of 60%. Left ventricular external end-diastolic dimension was 4.3 cm, and left ventricular external end-systolic dimension was 3 cm. Spiral computed tomography (CT) of the thorax was obtained with intravenous contrast, which demonstrated a fusiform aneurysm of the ascending thoracic aorta, measuring 5.7 cm × 6.5 cm in the greatest dimension (*Figures 1* and *2*). Transoesophageal echocardiography was obtained, which revealed a central aortic insufficiency jet occupying a width of 60% of the left ventricular outflow tract.

He had no symptoms to suggest an underlying infectious aetiology. He had no risk factors for tuberculosis or syphilis. He had no symptoms or clinical features suggestive of an underlying vasculitis, connective tissue disease, or autoimmune disorder. He had no family history of autoimmune disease. His labs demonstrated a normal complete blood count with differential, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP).

The patient was referred to cardiothoracic surgery for evaluation. Pre-operative left heart catheterization revealed angiographically

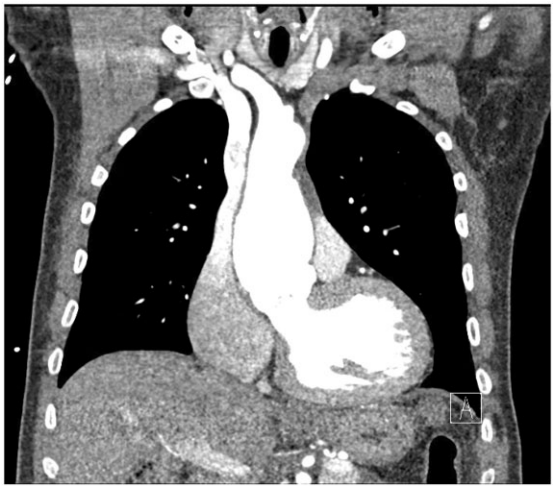


Figure 1 Computed tomography demonstrating fusiform aneurysm of the ascending thoracic aorta. Electrocardiogram-gated computed tomography of the thorax with intravenous contrast demonstrating fusiform aneurysm of the ascending thoracic aorta, measuring up to 5.7 cm × 6.5 cm in greatest dimension.

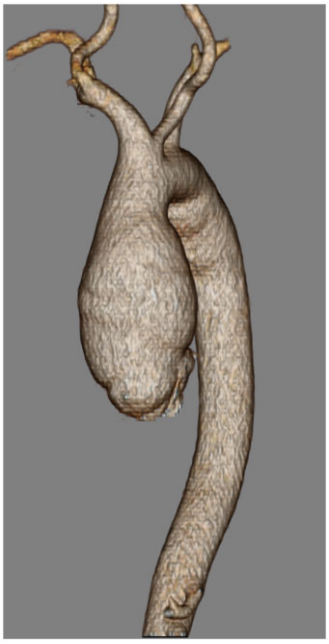


Figure 2 Three-dimensional reconstruction demonstrating ascending thoracic aortic aneurysm. Advanced three-dimensional post-processing of spiral computed tomography of the thorax re-demonstrating fusiform aneurysm of the ascending thoracic aorta, measuring up to 5.7 cm × 6.5 cm in greatest dimension. There is an additional fusiform aneurysm of the distal aortic arch/proximal descending aorta.

normal coronary arteries with a left ventricular ejection fraction of 60% by ventriculogram. He underwent aortic valve replacement with Carpentier-Edwards pericardial valve and supracoronary replacement of the ascending aorta with a Gelweave graft. The post-operative transthoracic echocardiogram revealed a normally functioning biological aortic prosthesis with trace aortic insufficiency and a mean gradient of 14.2 mm of mercury.

The intra-operative pathology revealed fibrosis and myxoid degeneration of the aortic valve leaflets. Biopsy of the ascending aorta demonstrated lymphoplasmacytic inflammation with some fibrosis, consistent with non-infectious ascending aortitis (*Figures 3*, *4*, and *5*). He was referred to rheumatology for further evaluation. Several months after his initial presentation, he developed morning stiffness and shoulder pain. His initial rheumatologic work-up was non-diagnostic. His ESR and CRP remained within normal limits. He was found to have a positive anti-nuclear antibody and rheumatoid factor. He was started on an oral steroid taper for a possible rheumatologic component in the setting of known aortitis. The patient's joint pain and morning stiffness responded well to steroid therapy. He continues to follow-up in both rheumatology and cardiology clinics. He will require follow-up on at least an annual basis to ensure no interval changes.

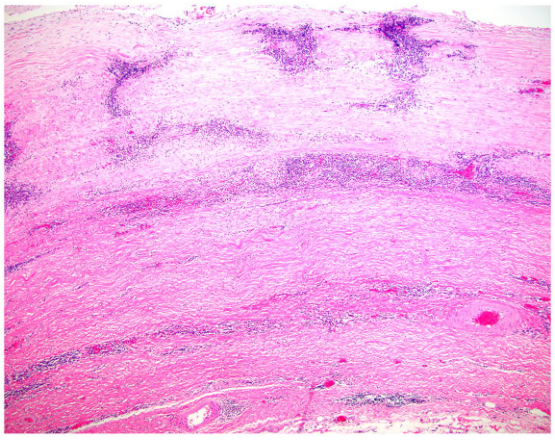


Figure 3 Histopathology of full-thickness ascending aorta. Histopathology of the full-thickness ascending aorta, demonstrating moderate patchy chronic inflammation with increased number of plasma cells. The intima is thickened.

Discussion

Isolated non-infectious ascending aortitis is most commonly diagnosed on histopathology following repair of thoracic aortic aneurysms in patients without systemic signs of illness, which highlights the importance of sending all aortic surgical specimens for histopathologic analysis. In inflammatory aortitis, most specimens are characterized by an inflammatory cellular infiltrate, often including multinucleated giant cells and areas of necrosis. There are some features that help distinguish an aetiology when present, such as intimal/adventitial fibrosis or scarring due to Takayasu's arteritis, medial

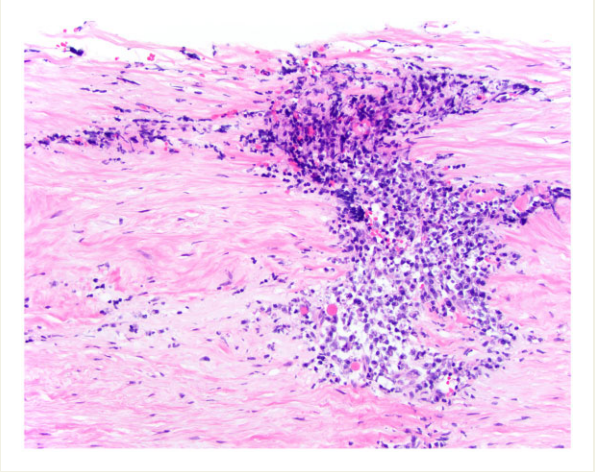


Figure 4 Higher power histopathology demonstrating chronic inflammation of ascending aorta. Re-demonstration of the moderate patchy chronic inflammation of the ascending aorta with a higher power view of the increased number of plasma cells. The vasa vasorum shows thickened media without classic obliteration.

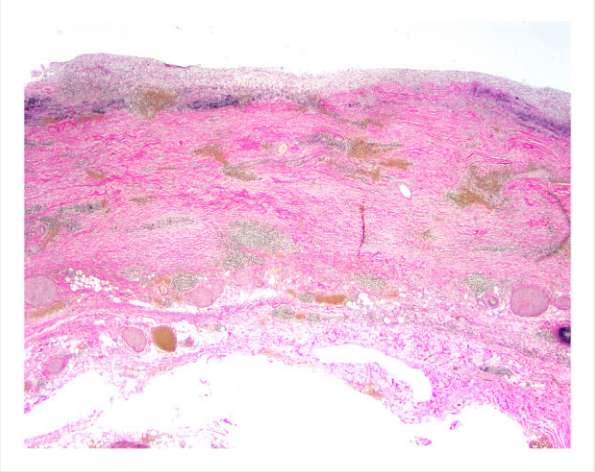


Figure 5 Elastic stain of ascending aorta. Elastic staining of the full-thickness ascending aorta demonstrating significant fibrosis of the adventitia. The media is markedly altered by fibrosis with disruption of the regular elastic fibres.

inflammation and necrosis with giant cell arteritis, and rheumatoid nodules in the aortic wall with rheumatoid arthritis.[2] However, there is often significant overlap and a diagnosis of a specific aetiology for non-infectious aortitis cannot be made with histopathology alone.[5] Infectious aortitis is typically easier to distinguish on histopathology, as there is often bacterial seeding via the vasa vasorum.[2]

The presentation of aortitis varies widely, including isolated findings of thoracic aortic aneurysms.[2] When the diagnosis of aortitis is suspected based on clinical presentation, patients should undergo imaging of the entire aorta.[2] Computed tomography angiogram is classically used, as it is widely available and simultaneously evaluates for pathologies like dissection. Magnetic resonance angiography (MRA) or positron emission tomography (PET) should be considered, especially in patients who present with clinical features of an underlying infectious or rheumatologic process, as the sensitivity for detecting inflammation is higher than in CT alone.[2,6] The exact role of MRA and PET requires further study and should be considered on a case-by-case basis.

In all patients with suspected ascending aortitis, ESR, CRP, blood cultures, complete blood count, and the comprehensive metabolic panel should be obtained to investigate for the possibility of underlying infection. Testing for syphilis and tuberculosis is typically reserved for high-risk groups based on clinical suspicion.[2] Further testing for rheumatologic disease, including anti-nuclear antibodies, anti-neutrophil cytoplasmic antibodies, and rheumatoid factor, can be considered on a case-by-case basis (*Figure 6*).

The appropriate course of management in I-NIAA with respect to immunosuppression is unclear, but glucocorticoid therapy is considered on a case-by-case basis.[5] Typically, therapy is reserved for patients with extensive inflammation on imaging following surgical repair. In this case, the subsequent development of joint symptoms suggestive of an underlying inflammatory process informed the decision to pursue immunosuppressive therapy.

Interval imaging of the entire aorta should be considered, as there have been case series that describe an increased risk of aneurysm formation in other vascular beds over time in patients with I-NIAA.[2] The exact timing of interval imaging has not been well-defined and requires further study.

This case highlights the importance of a thorough review of systems and consistent follow-up for patients found to have I-NIAA. This patient developed systemic symptoms after receiving a diagnosis of I-NIAA based on surgical pathology, raising the suspicion for a secondary rheumatologic process. The longitudinal follow-up revealed symptomatology that suggested that I-NIAA in this patient was the presenting feature of an underlying rheumatologic process, although the patient's presentation does not neatly fit a single rheumatologic diagnosis. Isolated non-infectious ascending aortitis is becoming an increasingly common diagnosis and can be the initial presentation for an underlying rheumatologic process. As a result, these patients require close follow-up, as missing an underlying autoimmune process could be devastating. Further study is needed to evaluate both its existence as a distinct clinical entity, the role of immunosuppressive therapy, and the timing of interval follow-up.

Lead author biography

Avery Calhoun is a third year internal medicine resident at Emory University in Atlanta, Georgia. She is going to pursue a cardiology fellowship and ultimately plans to practice in academic medicine.

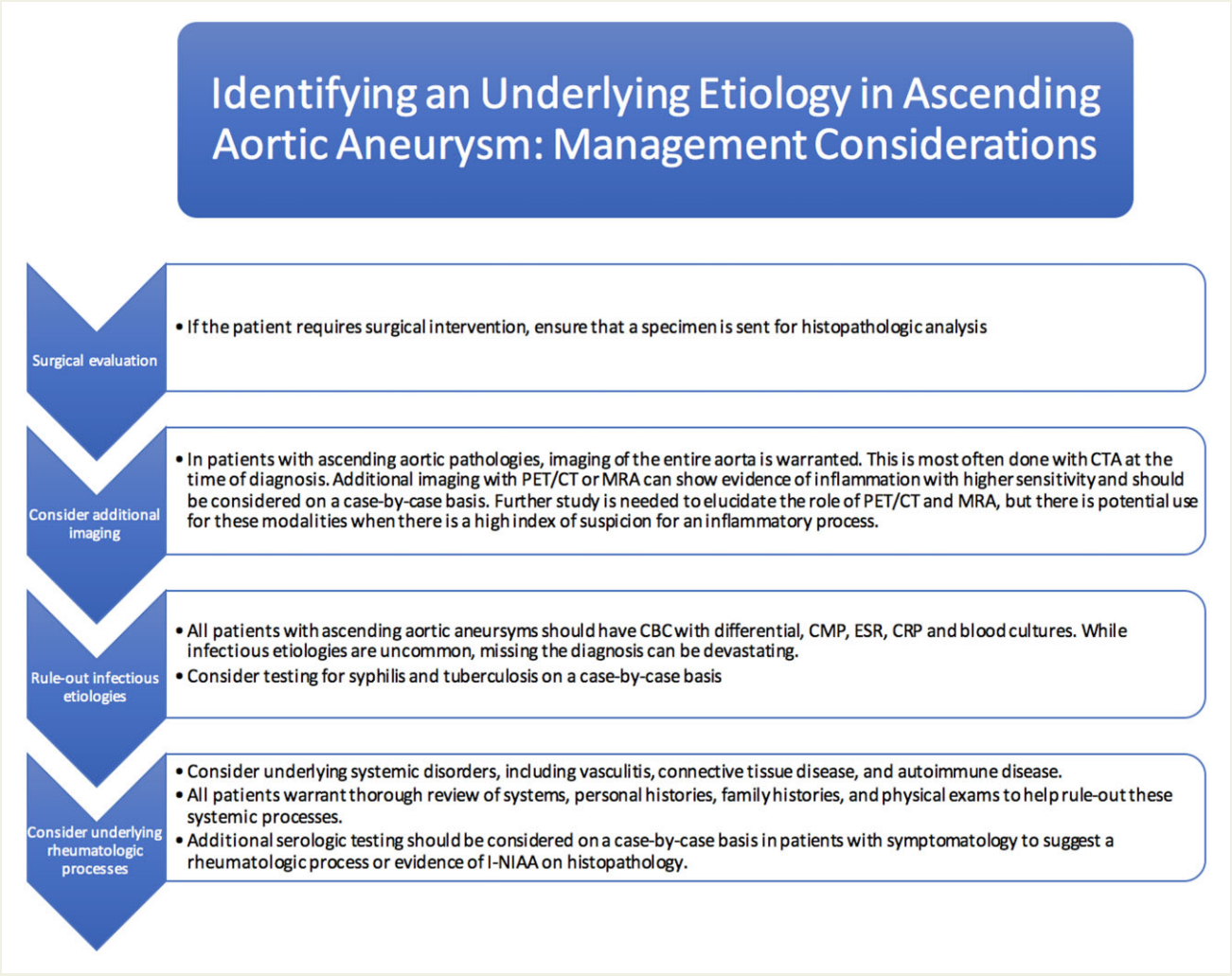


Figure 6 Identifying an underlying aetiology in ascending aortic aneurysm: management considerations. This figure details the general considerations relevant to all patients who present with ascending aortic aneurysms. The timing of this work-up will depend on the urgency of surgical intervention. In cases that do not require emergent surgical intervention, it is reasonable to initiate this work-up in this order in the pre-operative period. Whatever is not completed prior to surgical intervention can be completed post-operatively and tailored to the pathology results.

Patient privacy statement

All patient information included in this case is presented accurately without identifying information.

Data availability

The data underlying this article are available in the article and in its Supplementary material online.

Supplementary material

Supplementary material is available at *European Heart Journal—Case Reports* online.

Slide sets: A fully edited slide set detailing these cases and suitable for local presentation is available online as Supplementary data.

Consent: The authors confirm that written consent for submission and publication of this case report, including images and associated text, has been obtained from the patient in line with COPE guidance.

Conflict of interest: None declared.

Funding: None declared.

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