JACC: CASE REPORTS VOL. 29, 2024

VASCULAR MEDICINE

CASE REPORT: CLINICAL CASE SERIES

Cardiology-Rheumatology Intersections in Aortitis and Aortic Aneurysms

Focus on Early Recognition and Management

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ABSTRACT

Aortitis is an uncommon cause of aortic aneurysms. Arterial inflammation can lead to irreversible vascular damage. Early recognition is necessary for treatment to prevent permanent consequences of vessel inflammation. (JACC Case Rep. 2024;29:102818) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Aortic aneurysms can be caused by both atherosclerotic and nonatherosclerotic processes. Aortitis is an inflammatory, nonatherosclerotic process that remains poorly understood with regard to early diagnosis and surveillance. Although causes of aortitis include trauma and infection, large-vessel vasculitis should be suspected in the absence of these findings, especially if there is involvement of the aorta and its branches. Here, we describe 3 cases of aortitis, and its underappreciated association with aortic aneurysms. We focus especially on advanced imaging techniques for diagnosis and various treatment options. Correct diagnosis of aortitis would lead to a change in management by modulating the underlying inflammatory condition. Special focus is given to giant cell arteritis (GCA).

TAKE-HOME MESSAGES

- Aortic aneurysm may be caused by nonatherosclerotic aortitis, which is linked to rheumatological conditions such as GCA and PMR.
- Screening and actively managing patients with GCA and PMR provides an opportunity for early treatment or intervention.

GCA is characterized by inflammation, likely immune-mediated, of medium- and large-sized arteries, including the aorta.[1] The diagnostic criteria for GCA include age ≥50 years, onset of headache, erythrocyte sedimentation rate ≥50 mm/h, and abnormal findings on artery biopsy.[2] Symptoms such as weight loss, low-grade fever, and jaw claudication can occur, and can be a precursor to the most feared complication: irreversible vision loss.[3,4] Treatment options include high-dose steroids and immunosuppressive agents. Recent findings indicate a 4-fold higher risk of myocardial infarction in patients with GCA than in those with other cardiac pathologies.[5]

Along with a lifetime risk of 0.5% in men and 1% in women, the incidence of GCA is 2.5 times higher in women.[3] Smoking and geography are also correlated—incidence is highest in North European regions. Around 40% to 60% of patients with GCA have polymyalgia rheumatica (PMR), whereas 16% to 21% of patient with PMR have GCA.[6] Additionally, studies

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

Manuscript received July 29, 2024; revised manuscript received October 7, 2024, accepted October 10, 2024.

ISSN 2666-0849 https://doi.org/10.1016/j.jaccas.2024.102818

ABBREVIATIONS AND ACRONYMS

CRP = C-reactive protein

CT = computed tomography

CTA = computed tomography angiography

FDG = (18)F-fluorodeoxyglucose

GCA = giant cell arteritis

IL = interleukin

PET = positron emission tomography

PMR = polymyalgia rheumatica

WBC = white blood cell

indicate a 17.3 times higher attribution of GCA to the onset of thoracic aortic aneurysms.[7] Furthermore, thoracic aneurysms caused by GCA increase the risk and incidence of mortality. Thoracic aneurysms in patients with GCA may develop due to aortic rupture, inflammation, or active aortitis.[8] GCA triggers systemic inflammation, possibly via its role in potentiating inflammatory biomarkers.

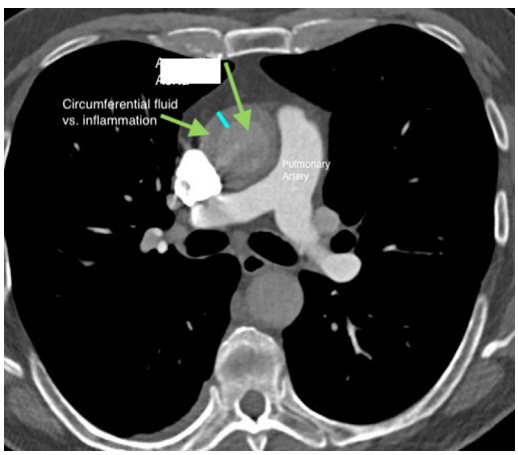
CASE 1

HISTORY OF PRESENTATION. A 64-year-old gentleman with a history of hypertension and chronic kidney disease presented to the emergency department due to acute onset of shortness of breath and chest pain radiating to his back. He was found to be in new-onset atrial fibrillation with rapid ventricular response in addition to laboratory data consistent with a non-ST-segment elevation myocardial infarction. He was afebrile, normotensive at 128/88 mm Hg, with a pulse of 152 beats/min and oxygen saturation of 98% on room air. While in the emergency department, a computed tomography (CT) angiography (CTA) pulmonary embolism protocol was performed that demonstrated wall thickening of the ascending aorta and the aortic arch (Figure 1). Contrast opacification was timed using a bolus-tracking nongated approach to the pulmonary arteries and fortuitously provided sufficient visualization of the aorta. Upon further questioning, it was discovered that this patient had a 30-pound unintentional weight-loss along with night sweats, diffuse muscle aches, and fatigue. His white blood cell (WBC) count was 6.5 $\times$ 10^3/μL with a sedimentation rate of 66 mm/h and C-reactive protein (CRP) of 27.5 mg/L. IgG4 levels were elevated, and pleural plaques were noted on imaging.

MANAGEMENT. The patient was started on a diltiazem drip with resulting rate control of his atrial fibrillation, ultimately converting into normal sinus rhythm. Due to his reported chest pain, a coronary angiogram was performed that showed multivessel coronary artery disease with significant left main disease. Given evidence of wall thickening in the ascending aorta, there was suspicion of both intramural hematoma and active vasculitis. The heart team opted for conservative management, given the concern that intervention may exacerbate an inflamed vessel and cause dissection. Cardiac surgery or coronary stenting was deemed greater risk at that time than monitoring. Advanced imaging was requested to further narrow the differential diagnosis.

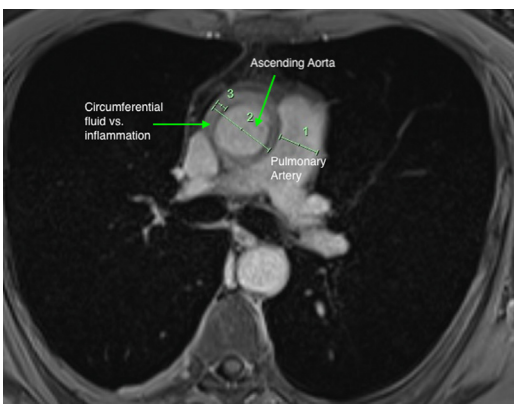
Magnetic resonance angiography of the chest and abdomen showed circumferential wall thickening of the aortic root and ascending aorta but also discovered wall thickening of the right common iliac artery (Figure 2). A nuclear medicine CT/positron emission tomography (PET) scan showed thickening of the ascending thoracic aorta, aortic arch, and bilateral

FIGURE 1 Computed Tomography Angiography Showing Thickening of the Ascending Aorta



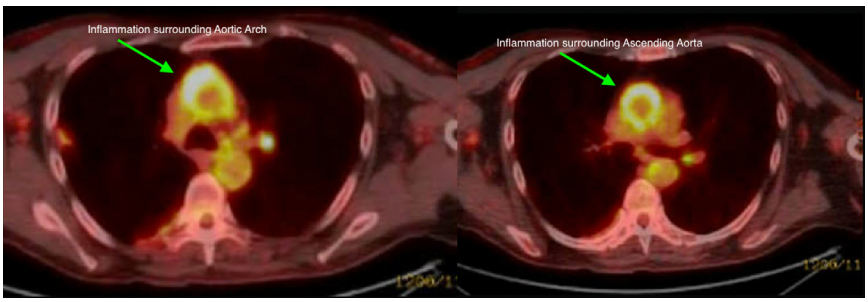
Computed tomography angiography showing thickening of the ascending aorta and aortic arch. The blue line represents the aortic wall thickening.

FIGURE 2 Magnetic Resonance Angiography Showing Thickening of the Ascending Aorta



Magnetic resonance angiography showing thickening of the ascending aorta that may represent circumferential fluid or inflammation.

FIGURE 3 Positron Emission Tomography Scan Confirming the Presence of Aortitis



Positron emission tomography scan with intense homogenous uptake along the ascending aorta and aortic arch confirming the presence of aortitis.

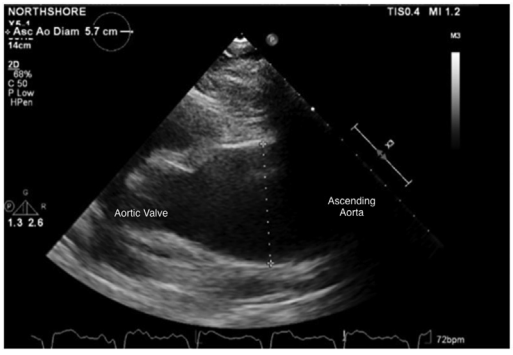
common iliac arteries with significant (18)F-fluorodeoxyglucose (FDG) uptake consistent with hypermetabolic activity (Figure 3). At this point, the multidisciplinary discussion expanded to also include cardiac imaging, radiology, and rheumatology who felt this patient's presentation was most consistent with aortitis. No site was amenable to biopsy, so there is uncertainty of the underlying diagnosis, though both IgG4 disease and GCA were considered. This patient was initiated on 50 mg/day prednisone with improvement of symptoms and reduced hypermetabolic activity on repeat nuclear medicine/CT PET scan. After a month of high-dose steroids, patient returned for planned revascularization of his triple-vessel coronary disease, which remained similar to before, and had successful percutaneous coronary intervention of his left main, left anterior descending, and left circumflex coronary arteries. Left main involvement prompted consideration of bypass surgery, however via heart team approach and shared decision-making, coronary stenting was chosen. The patient was recently seen in clinic and is asymptomatic without any limitations in his day-to-day life.

CASE 2

HISTORY OF PRESENTATION. A 75-year-old man with a history of combined ischemic and nonischemic cardiomyopathy, heart failure with reduced ejection fraction, and ventricular fibrillation status post-implantable cardioverter-defibrillator presented with an episode of acute decompensated heart failure and was incidentally found on echocardiogram to have an ascending aortic aneurysm measuring 5.7 cm (Figure 4). He was afebrile, normotensive at 114/80 mm Hg, with a pulse of 74 beats/min, and oxygen saturation of 97% on room air. Subsequent CTA of his chest scan demonstrated, instead of an ascending, a descending aortic aneurysm of 5.1 cm, including 0.8 cm of aortic wall thickening (Figure 5). His WBC count was 10.5 $\times$ $10^3/\mu L$ with a sedimentation rate of 5 mm/h and CRP of 6.3 mg/L.

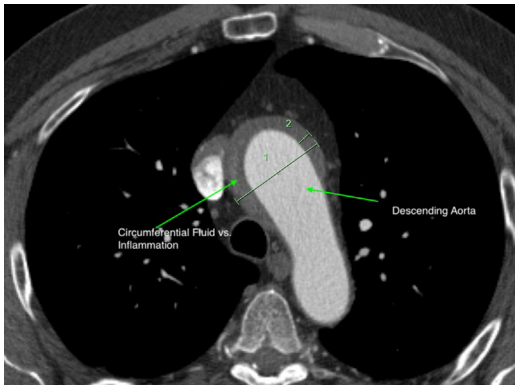
MANAGEMENT. Thoracic aortic aneurysm repair and coronary artery bypass grafting were performed successfully. Pathological findings of the aortic tissue revealed GCA (Figure 6). High-dose steroid therapy (prednisone 60 mg daily) was started to induce GCA remission. Subsequent imaging was performed for disease surveillance. CTA of the chest revealed moderate tortuosity in the ascending aorta. Magnetic resonance angiography of the chest revealed stable aortic tortuosity, no vessel wall enhancement, and no evidence of active aortitis. PET)/CT (Figure 7)

FIGURE 4 Transthoracic Echocardiogram Demonstrating a Dilated Ascending Aorta



Transthoracic echocardiogram demonstrating a dilated ascending aorta measuring 5.7 cm.

FIGURE 5 Chest Computed Tomography Angiography Demonstrating Descending Aortic Wall Thickening



Chest computed tomography angiography demonstrating descending aortic wall thickening suspicious for circumferential fluid or inflammation.

demonstrated mild heterogeneous hyper-metabolism in the thoracic aorta, which persisted on a repeat scan 4 months later with a slight increase in activity in the aorta in the setting of thoracic aortic aneurysm repair. A multidisciplinary team of cardiologists and rheumatologists is managing the patient.

CASE 3

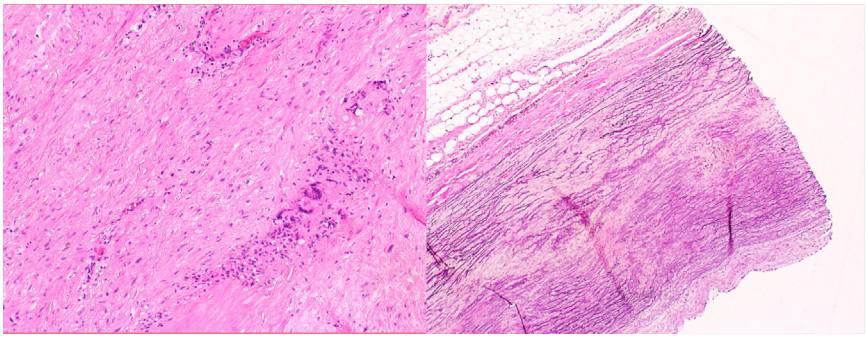
HISTORY OF PRESENTATION. A 70-year-old gentleman with a history of PMR presented as an outpatient with worsening joint symptoms. He received steroids starting a year before and was weaned off 4 months prior to presentation. He was afebrile, normotensive at 132/81 mm Hg, with a pulse of 64 beats/min, and an oxygen saturation of 95% on room air. His WBC count was 5.2 $\times$ 10^3/μL with a sedimentation rate of 66 mm/h and CRP that increased from 6.5 to 32.5 mg/L. A low-dose chest CT scan to monitor previously observed pulmonary nodular opacities revealed a new aneurysmal dilation of 5.2 cm at the sinus of Valsalva, which was promptly followed by a coronary CTA).

MANAGEMENT. Chest CTA with and without contrast revealed peri-aortic wall thickening surrounding the ascending aorta and aortic arch, with a 5.1-cm aneurysmal dilatation of the ascending aorta and a 1.1-cm thickened wall (Figure 8). GCA was suspected given the clinical history of PMR with new evidence of aortitis. A PET scan showed evidence of FDG uptake in the ascending aorta, consistent with aortitis (Figure 9). Ultimately, a multidisciplinary approach was used with a decision to initiate 50 mg/day prednisone and tocilizumab infusions. Tocilizumab is an interleukin-6 (IL6) inhibitor and a steroid-sparing therapy for both GCA and PMR. The patient tolerated both treatments well, and his CRP subsequently normalized to 0.3 mg/L after treatment.

DISCUSSION

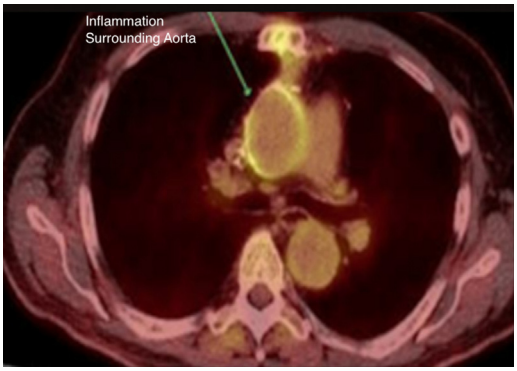
Aortitis is rarely the top of the differential, and it is more often incidentally suggested via echocardiogram or chest CT imaging for other indications. Cardiac and aortic imaging demonstrating aortic aneurysm or aortic wall thickening may prompt

FIGURE 6 Staining of the Aorta



(Left) Artery shows transmural inflammation with interspersed giant cells and intimal layer thickening on hematoxylin and eosin. (Right) Elastin stain highlights elastic lamina disruption.

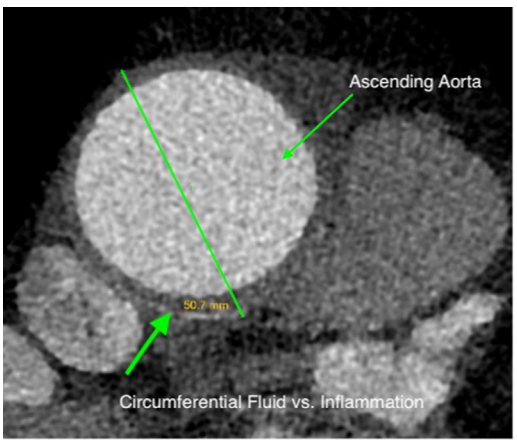
FIGURE 7 Positron Emission Tomography Demonstrating Aortitis



Positron emission tomography/computed tomography imaging demonstrating heterogeneous uptake along the thoracic aortic wall, representing aortitis in this patient with history of giant cell arteritis.

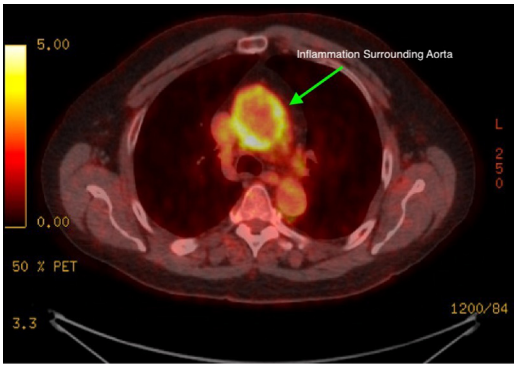
suspicion of aortitis, and in the right clinical setting, GCA or other forms of aortitis may be suspected, as occurred with these 3 patients. Ultimately, advanced imaging via PET-CT can provide convincing evidence of inflammation. Still, even PET-CT may be difficult to interpret in the setting of postsurgical changes as seen in Case 2, highlighting the difficult nature of diagnosis. The presence of FDG uptake is an imperfect marker for thoracic aortitis in this case because aneurysm repair is itself associated with chronic FDG uptake and associated changes; however, the heterogeneous appearance may hint toward residual GCA disease. Although the second case provided definitive biopsy evidence of GCA, clinicians often have to empirically treat aortitis if biopsy proves challenging or not possible. Case 1 provides such a diagnostic dilemma, where uncertainty remains of the underlying diagnosis.

FIGURE 8 Chest Computed Tomography Angiography Demonstrating Ascending Aortic Wall Thickening



Ascending aorta surrounded by circumferential fluid or inflammation raising suspicion for aortitis.

FIGURE 9 Positron Emission Tomography Scan Confirming the Presence of Aortitis



Positron emission tomography (PET) scan confirming evidence of aortitis in the ascending aorta.

Given that as many as 20% of patients with PMR develop GCA, as was suspected in Case 3, patients with PMR provide an opportunity for early screening of aortic manifestations of GCA.[6] Although there is some evidence of ultrasound and PET imaging in helping to diagnose PMR itself, there are no documented guidelines on imaging for the monitoring of possible manifestations of GCA. Routine imaging via echocardiogram or cardiac CTA may be useful in accurately triaging patients with PMR by screening for thoracic aneurysms and aortic wall thickening, which are some of the possible manifestations of aortitis. Emerging technologies of dynamic CT may prove especially useful in screening for and characterizing aneurysmal structures.

In these clinical cases, immune-modulating medications were initiated with subsequent improvement in patient status. An incomplete understanding of GCA immunopathology makes early diagnosis and management challenging. The role of IL-21 and IL-17 in GCA depends on their increased production by T cells (TH21 and TH17), which are activated inside the adventitial layer by dendrocytes.[3] The management of GCA with high-dose steroids helps minimize the accumulation of IL17 and Th17; however, it does not

affect the activities of gamma interferon and Th1.[9] IL6 has had a known correlation to PMR and GCA for over 30 years and may be useful for early diagnosis and screening for degree of inflammation, as well as being a target for treatment.[10]

Aortitis, with special consideration for GCA, may represent an underdiagnosed cause of aortic aneurysm. Advanced imaging provides special utility in making this diagnosis with subsequent treatment altering progression of the disease. Further research is needed to understand the natural history of aortitis and best practices for surveillance and management in patients with known aortitis and associated rheumatologic conditions.

CONCLUSIONS

Clinical acumen is required for early diagnosis and treatment of aortitis. Multimodal imaging is important for diagnosis and management.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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KEY WORDS aortitis, giant cell arteritis, thoracic aneurysm