

Case Report

Antineutrophil Cytoplasmic Antibody (ANCA)-Associated Aortitis Presenting With Acute Dissection: Case Report and Comprehensive Literature Review

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Abstract

Description

Vasculitides are a group of diseases that produces vasculitis, which is characterized by inflammatory infiltrates within blood vessel walls and results in intimal injury as well as progressive mural destruction. Infiltrates are characterized per the Chapel Hill classification, into large, medium, and small-vessel vasculitides. ANCA-associated vasculitis (AAV) is a disease that has been described as involving small-sized vessels. However, some cases of large vessel disease involvement have been documented. ANCA-associated aortitis is a rare entity poorly described in the literature. Due to the rarity of this pathology, there is no Level I evidence available regarding diagnosis and treatment. We present the rare case of an 80-year-old male presenting with ANCA-associated aortitis complicated by acute dissection of the left common iliac artery. His case was successfully managed by corticosteroid therapy and endovascular stenting of the involved iliac artery. ANCA-associated aortitis is a rare entity that has not been described well in the current literature. We believe this case to be the first involving ANCA-associated aortitis presenting with an acute dissection.

Keywords

aortitis; antineutrophil cytoplasmic antibody; cANCA; aortic diseases; vasculitis; dissecting aneurysm; autoimmune diseases; aged

Introduction

Vasculitides are a group of diseases that produces vasculitis, which is characterized by inflammatory infiltrates within blood vessel walls and results in intimal injury as well as progressive mural destruction.^{1,2} Infiltrates are characterized per the Chapel Hill classification into large, medium, and small-vessel vasculitides. ANCA-associated vasculitis (AAV) is a disease that has been classically described as involving small-sized vessels.¹ However, some cases of large vessel disease involvement have been documented.^{3,4} ANCA-associated aortitis is a rare entity that has been poorly documented in the literature. Due to the rarity of this pathology, there is no Level I evidence available regarding diagnosis and treatment.

Case Description

An 80-year-old male with a past medical history of hypertension, controlled on amlodipine and metoprolol, presented to our facility complaining of left groin pain for the past 3 days. According to the patient, the pain began suddenly and did not abate. He also endorsed a history of fever, chills, and malaise for 2 months as well as a weight loss of 15 pounds. He denied having been previously screened for a colonoscopy or a history of illicit substance use. The patient also denied a history of visual disturbances, headache, jaw claudication, shortness of breath, epistaxis, hemoptysis, hematuria, skin rash, hematochezia, or melena. His vital signs during his initial examination were as follows: temperature of 98.2°F, heart rate of

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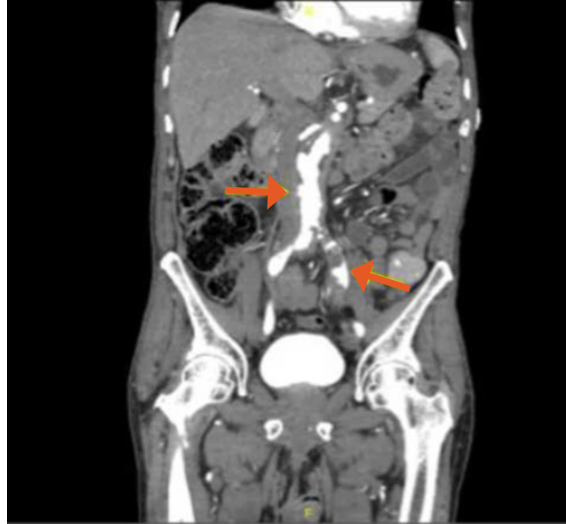


Figure 1. A coronal image from a CT abdomen and pelvis with contrast demonstrates mural thickening and extensive ulceration throughout the abdominal aorta and iliac arteries (arrows). Luminal narrowing of the left common iliac artery is also appreciated.

80 bpm, blood pressure of 127/77 mmHg, and a respiratory rate of 16 breaths/minute.

Upon examination, the bilateral upper and lower extremities appeared normal and without any skin abnormalities/rash. His motor and sensory functions were preserved. There was a presence of palpable bilateral femoral and dorsalis pedis pulses. There were no signs of acute limb ischemia in the bilateral lower extremities, and his capillary refill was preserved with less than 3 seconds in bilateral lower extremities. Bilateral carotid artery pulses were present, and bruit was not auscultated. Bilateral brachial and radial pulses were also present and symmetric. Labs were significant

for microcytic anemia with hemoglobin of 7.4 g/dL and a mean corpuscular volume (MCV) of 76. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels were elevated at 84 mm/hr and 14.6 mg/L, respectively. Blood and fungal cultures were negative, and venereal disease research laboratory/rapid plasma reagin (VDRL/RPR) testing was non-reactive for syphilis. Serology for autoimmune vasculitides demonstrated positive rheumatoid factor and perinuclear anti-neutrophil cytoplasmic antibodies (p-ANCA) or Anti-myeloperoxidase (MPO). Antineutrophil cytoplasmic antibodies (c-ANCA), antinuclear antibody (ANA), hepatitis B/C serology, and human immunodeficiency virus (HIV) testing were all negative.



Figure 2. An axial image from a CT abdomen and pelvis with contrast demonstrates anterior and posterior aortic ulcerations as well as circumferential aortic wall thickening (arrow).

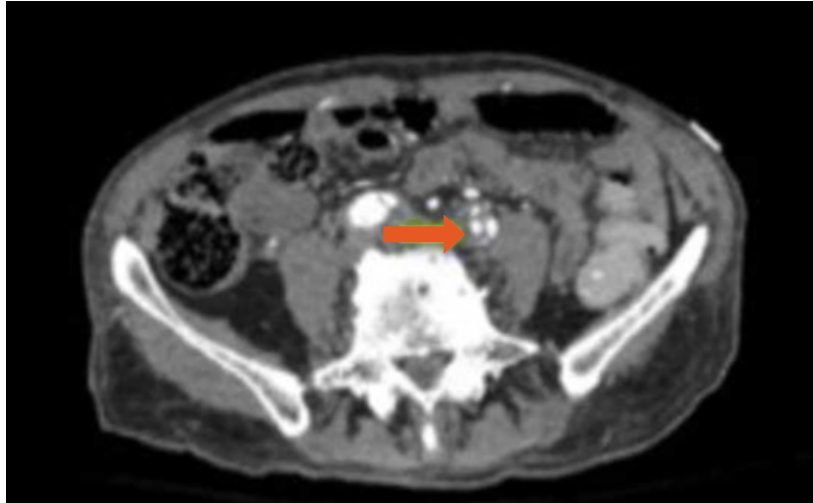


Figure 3. An axial image demonstrates the dissection lumen (arrow) and the adjacent true lumen of the left common iliac artery. Associated mural thickening and peri-arterial inflammation can also be appreciated.

A computed tomography (CT), with contrast, of the chest, abdomen, and pelvis demonstrated penetrating ulcers along the posterior and anterior walls of the abdominal aorta with mural wall thickening circumferentially throughout the length of the abdominal aorta and bilateral iliac arteries (**Figures 1 and 2**). No perforation was detected. Mural thrombus with multiple penetrating ulcers and dissection were observed in the left common iliac artery, with the dissection resulting in greater than 50% lumen stenosis (**Figure 3**). Penetrating ulcers and a non-occlusive thrombus were also noted in the right common iliac artery.

The patient was subsequently placed on 81 mg aspirin and underwent a colonoscopy and an esophagogastroduodenoscopy (EGD), which failed to identify any masses or lesions. The patient was placed on prednisone 20 mg daily and underwent a left common iliac artery stent placement for the dissection with coil embolization of the left internal hypogastric artery (**Figures 4 and 5**). A left temporal artery biopsy was also performed to rule out giant cell arteritis.

The patient's postoperative course was uneventful, and he reported resolution of his



Figure 4. An angiogram of aortic bifurcation demonstrates luminal stenosis secondary to dissection. Ulceration of the vessel wall can also be seen. The left internal hypogastric artery has already been coil embolized.



Figure 5. An angiogram of the aortic bifurcation following stenting of the diseased arterial segment demonstrates that the dissection and adjacent ulceration of the artery are no longer appreciated, and a normal lumen diameter has been restored.

left groin pain. He was discharged in stable condition on postoperative day 2. The temporal artery biopsy was negative for giant cell arteritis or any other vasculitis during the final pathology.

After a multidisciplinary assessment between vascular surgery, internal medicine, and hematology-oncology teams, the patient was diagnosed with ANCA-associated aortitis, due to other causes of vasculitis being ruled out. An aorta biopsy was not pursued due to its invasiveness and risk of perforation. The patient was continued on corticosteroid therapy of prednisone 20 mg daily for 6 months. During a 3-month follow-up visit, the patient reported the resolution of the aforementioned symptoms. He was prescribed long-term corticosteroid therapy and remanded for follow-up imaging at 6 months postoperatively. The patient, however, was lost to follow-up, and no further assessment of the patient's disease could be performed.

Discussion

Vasculitides are a group of diseases defined by inflammatory cell infiltration within vessel walls resulting in damage and destruction of the vessel wall as well as surrounding structures. This inflammation results in progressive vessel wall damage and destruction, leading to the loss of vessel integrity. This mural destruction can subsequently result in local complications such as bleeding, aneurysmal degeneration,

mural dissection, and thrombosis, as well as downstream tissue ischemia and necrosis. The pathophysiology of vasculitis can occur either as a primary process only involving the vessels or stem from secondary underlying or inciting disease processes.^{1,2}

Vasculitides are classically defined by the vessel type, size, and location they involve. The Chapel Hill Consensus Conference Classification System (CHCC) classifies vasculitis according to vessel size and characteristic clinical and histo-pathological features.¹ This classification was further revised in 2012 to include cutaneous vasculitides.²

Large vessel vasculitis involving large vessels (eg, the aorta) has been characterized per the Chapel Hill Classification as being seen to occur in giant cell arteritis (GCA) and Takayasu's arteritis.¹ Large vessel vasculitis can also occur as part of the broad spectrum of disease with medium and small-vessel vasculitides, though these presentations are rarely reported in the literature.^{3,4}

AAV are a group of vasculitides that have been classically associated with small-vessel vasculitis. The 2012 CHCC formally adopted the term antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) for the group of 3 disorders that include microscopic polyangiitis (MPA), granulomatosis with polyangiitis (GPA), and eosinophilic granulomatosis with

polyangiitis (EGPA). AAV can also occur in an isolated organ with the most common type being renal-limited AAV. Aortic-limited AAV, also known as ANCA-associated aortitis, however, is a poorly elucidated entity that has rarely been described in the literature. This type of aortitis can occur in isolation or may precede a more systemic presentation of vasculitis.¹⁻³

ANCA-associated aortitis involves both thoracic and abdominal segments of the aorta and large branching vessels, such as the brachiocephalic, subclavian, renal, and iliac arteries.⁴⁻⁶ These inflammatory changes can consist of mural thickening, saccular aneurysmal degeneration, ulceration, and stenosis.⁶ As with many other types of vasculitides, ANCA-associated aortitis is also associated with elevated inflammatory markers such as ESR and CRP. ANCA-associated aortitis has been described with both p-ANCA (Anti-MPO) and c-ANCA (Anti-Proteinase 3).^{3,6} P-ANCA associated aortitis has been described in a cohort of 3 cases in which all of them demonstrated stenosis or occlusion of subclavian arteries.⁵ Two of these cases demonstrated thickening of the aortic wall, and the third case presented with irregular stenosis of both common iliac arteries.⁵

The pathogenesis behind ANCA-associated aortitis is unknown. Several theories have been made regarding the pathological process behind this entity. One theory proposes that intimal injury is the initial insult, which then progresses to inflammation of the medial layer of the aorta and, subsequently, the adventitia.⁴ Another postulates that the large vessel changes seen in aortitis occur as a result of vasculitis of the vasa vasorum within the aortic wall.^{3,6}

Aortitis associated with positive ANCA serology may be associated with an underlying, and yet undiagnosed, small vessel vasculitis that is classically associated with ANCA seropositivity. It is, therefore, important to rule out the involvement of other organ systems with a thorough clinical exam, imaging modalities, and laboratory testing, such as hepatic and renal function testing. Mycotic (infectious) aortitis should also be ruled out with blood and fungal cultures, as well as VDRL/RPR testing since treatment for this form of aortitis is vastly different than for ANCA-associated aortitis and other non-infectious inflammatory aortitis

syndromes. Treatment with immunosuppressive therapy could further exacerbate cases of mycotic aortitis. Temporal artery biopsies should also be performed if there is a suspicion of GCA.

Symptoms of ANCA-associated aortitis are very similar to those in other types of aortitis. Patients can present with fever, night sweats, malaise, weight loss, and back or groin pain.⁶⁻⁸ Patients presenting with aortitis complicated by dissection may present with a severe 'tearing' pain of the back or groin, depending on the location of the dissection, though these cases are rarely present to medical attention due to high mortality.^{9,10} Diagnosis is typically obtained with CT-angiography, which is considered the gold standard and is widely available. The CT-angiography allows for delineation of the aortic lumen and any abnormalities and also demonstrates mural and peri-aortic inflammatory changes. Magnetic resonance imaging (MRI) may be required if patients have renal dysfunction and are unable to handle a contrast load.^{11,12} Even without gadolinium enhancement, vessels can still be assessed with Magnetic resonance angiography (MRA) techniques. ¹⁸F-fluoro-2-deoxy-D-glucose (¹⁸F-FDG)-positron emission tomography (PET)/CT is beginning to play an increasing role in assessing the inflammatory changes seen in vasculitis.^{13,14} FDG does not accumulate in normal vascular structures. Therefore, any uptake of ¹⁸F-FDG in the aortic wall can be considered to be secondary to an inflammatory or infectious process.¹¹⁻¹⁴ Both MRI and PET-CT are limited in their utility by both expense as well as scarce availability at many medical institutions. Aortography can also be utilized in the diagnosis of aortitis. However, it is limited since it only captures luminal characteristics and abnormalities and is unable to demonstrate the mural abnormalities and inflammation seen with aortitis. Aortography is better utilized when there is suspicion of dissection, stenosis, or perforation, as it can be performed in conjunction with therapeutic modalities such as endovascular stenting.^{7,12}

Treatment of ANCA-associated aortitis mirrors the treatment for other AAV, with immunosuppression being the cornerstone of therapy. Immunosuppressive therapies commonly include glucocorticoids and cyclophosphamide, which have been proven in the treatment of

AAV.⁴⁻⁷ Cases of ANCA-associated aortitis being treated successfully with monoclonal antibodies, including rituximab and tocilizumab, have also been reported.^{6,15} Due to the need for long-term corticosteroid therapy and the potential for steroid-related adverse effects such as osteoporosis, gastric ulceration, and *Pneumocystis jiroveci* pneumonia, medications to prevent such side effects should be prescribed for patients with aortitis receiving long-term corticosteroids.^{7,16}

Surgical intervention is typically not required unless complications such as aneurysmal degeneration, dissection, critical stenosis, or rupture are present.⁷ Both open and endovascular approaches to the treatment of aortitis and its complications have been described.^{6,7} No randomized trials exist comparing one modality to another in regards to ANCA-associated aortitis, and therapy should, therefore, be tailored towards the patient with regards to the extent of the disease process, the acuity of complications, and the ability to tolerate surgery. Due to our patient's dissection being in the left common iliac artery and the remaining diseased aorta being uncomplicated, we determined that the best course of action was endovascular stenting of the dissecting portion of the vasculature.

There are no clear guidelines regarding follow-up for patients with ANCA-associated aortitis. It has been recommended that patients who are receiving immunosuppressive therapy have CT-angiography or MRA imaging done depending on age and renal function.^{3,17} Regular ANCA serology is also recommended to monitor treatment response and disease relapse, as ANCA titers have been associated with disease relapse in ANCA-associated aortitis.^{3,5,6,15}

Conclusion

After an exhaustive literature review, we determined that this is the first reported case of ANCA-associated aortitis presenting with acute dissection. Dissection has been associated with other types of aortitis, most commonly in association with GCA.^{18,19} A single case report describing aortitis secondary to systemic lupus erythematosus complicated by dissection has also been reported.⁹ Mortality rates with aortitis complicated by dissection are high, with patients succumbing in many cases

within hours of dissection onset.^{10,18,19} A high suspicion for dissection in patients with known or recently diagnosed aortitis presenting with suggestive symptoms, such as acute limb pain and signs of ischemia, should be maintained to reduce the risk of mortality. CT-angiography is the preferred imaging modality for diagnosis and other types of vasculitis, including infectious forms, and must be ruled out with appropriate diagnostic testing. Corticosteroid therapy forms a cornerstone for the management of ANCA-associated aortitis, as it is autoimmune in nature. Surgical management of ANCA-associated aortitis should be aimed at complications that arise in association with this vasculitis, such as dissection, thrombosis, or vascular leak, and can be approached via open and endovascular methods.

Conflicts of Interest

The authors declare they have no conflicts of interest.

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