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Catastrophic Perforation in *Streptococcus Pneumoniae* Aortitis: Complications of Infective Endocarditis in the Current Antimicrobial Era

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Abstract

Infectious aortitis is an uncommon but life-threatening cause of aortitis. Given the lack of specific symptoms, establishing the diagnosis is often a challenge. When it is associated with an endovascular infection, such as infective endocarditis, blood cultures may be diagnostic although often limited by low positive predictive value. Imaging studies may reveal characteristic findings, with computerized tomography angiography being the most sensitive. Management includes prompt initiation of antimicrobial therapy followed by surgical intervention, keeping in mind that operative mortality is high due to weakened arterial wall integrity. Here we describe a 25-year-old woman without relevant medical history, who presented to the hospital with subacute onset of fever, back pain and malaise, and was found to have infectious aortitis secondary to *Streptococcus pneumoniae* endocarditis. Despite appropriate antimicrobial coverage and surgical repair attempts, she succumbed to aortic perforation after a complicated and prolonged hospitalization.

Keywords: Antimicrobials, Aortic perforation, Aortitis, Infectious aortitis, Infective endocarditis, Invasive pneumococcal disease, *Streptococcus pneumoniae*, Surgery

1. Introduction

Aortitis is defined as an inflammatory process within the arterial wall.¹ It can be dichotomized into non-infectious and infectious aortitis (IA).^{2,3} Common causes of non-IA are large vessel vasculitis such as giant cell and Takayasu arteritis.⁴ IA is infrequently encountered and diagnosis is usually post-mortem.^{5,6} Known culprits include salmonella and staphylococcal species, however, other microorganisms have also been reported.^{5,7–12} Aortitis secondary to gram-positive organisms, especially *Enterococcus* and *Streptococcus pneumoniae*, is strongly associated with infective endocarditis (IE).¹³ IE as the primary cause of IA has decreased from 90% in the pre-antimicrobial era to 14%.^{11,14,15}

2. Case report

A 25-year-old otherwise healthy African American woman presented to the hospital with a 2-week

history of fever. Associated symptoms were lower back pain, malaise and cough. Vitals were significant for fever (102.3 Fahrenheit) and tachycardia. Pertinent findings included diaphoresis and right-sided abdominal tenderness. Laboratory data revealed leukocytosis (28.9 [4.4–10.7 × 10E9/L]) with neutrophilia (87 [44–73%]), thrombocytopenia (20 [153–416 × 10E9/L]), elevated creatinine (1.2 from baseline of 0.7 [0.5–1.3 mg/dl]), elevated alanine transaminase (145 [13–61 U/L]) and aspartate transaminase (201 [5–40 U/L]) and hyperbilirubinemia (2.7 [0.2–1.0 mg/dl]). Chest X-ray reported bibasilar infiltrates and pleural effusions. Ceftriaxone and azithromycin were started for community-acquired pneumonia (Table 1).

Blood cultures turned positive for penicillin-susceptible *S. pneumoniae* at 6.5 h. Following the onset of acute encephalopathy and respiratory failure, patient was intubated. Vasoactive drugs were administered for shock. Transthoracic echocardiogram (ECHO) showed 1.3 × 1.8 cm vegetation with severe mitral

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regurgitation and left-to-right atrial septum bowing. Antimicrobials were adjusted to ceftriaxone and gentamicin for treatment of IE. Escalating oxygen requirements and transesophageal ECHO showing complete destruction of mitral valve warranted emergent valve replacement. One week after admission, patient underwent bilateral iliofemoral arterial thrombectomy with four compartment fasciotomies of bilateral lower extremities for acute limb ischemia with rhabdomyolysis. Postoperatively, right-sided hemiparesis due to left middle cerebral artery infarction was detected (Table 2).

Patient remained on ceftriaxone for 6 weeks alongside synergistic gentamicin for 2 weeks. At week 4, recurrence of fever and leukocytosis triggered vancomycin administration. Imaging showed occlusion of the aorta below the origin of inferior mesenteric artery with occlusion of right common iliac, internal and external iliac arteries. Findings during open aortoiliac thrombectomy were extreme peri-aortic inflammation and lymphadenitis, adjacent bleeding, chronic thrombus in the aorta and iliac arteries, and a large arterial thrombus plug in the proximal portion of the occlusion. Given multiple pre-existing infectious foci, arteriotomy was performed by primary closure as opposed to patching. Anticoagulation for mechanical mitral valve was resumed subsequently. Abdominal imaging obtained after development of hypotension and symptomatic anemia showed extensive ascites consistent with hemorrhage and probable retroperitoneal hemorrhage adjacent to the aorta. Patient underwent exploratory laparotomy, evacuation of intra-abdominal blood and retroperitoneal hematoma, and open thrombectomy of the left iliac artery.

Fifty six days after admission, patient went into pulseless electrical activity. Point-of-care ultrasound revealed a large volume of free fluid in the abdomen. After return of spontaneous circulation, patient underwent an emergent exploratory laparotomy which identified perforation in the left anterior aspect of the distal aorta and proximal left iliac artery. The integrity of the aorta was very weak, causing sutures to tear. The procedure was completed with pledgetted sutures of 3-0 prolene with follow up by 5-0 prolene due to oozing between aortic pledgets. Post-operatively, patient went into asystole and postmortem examination showed distal focal aortitis with full wall thickness necrosis and tunica media dissection, status post repair of distal aorta and left iliac artery (Table 3).

3. Discussion

The tunica intima of the aorta is highly resistant to infections.^{1,13} When an infection does occur, the

proposed mechanism involves bacterial seeding of the aorta from distant sources including IE, urinary tract infection, cellulitis, pneumonia, osteomyelitis or intravenous access-associated infection.⁸ Intimal weakening by pre-existing atherosclerosis, inflammation, aneurysm, old aortic dissection and endovascular aortic stents are likely contributing factors.^{6–8,16} Other mechanisms involve traumatic inoculation of the vessel wall, contiguous infectious processes and bacterial emboli from vasa vasorum.^{4,8,9,13,17} Associated risk factors for abdominal and thoracic IA include old age, male sex, congenital abnormalities of the aorta, corticosteroid use, immunosuppressive agents, alcoholism, tobacco dependency, hypertension, dyslipidemia, chronic kidney disease and diabetes.^{8,10,16,18} In this case, it is perceived that a combination of delay in seeking medical attention, severity of the infection and multiorgan involvement contributed to poor outcomes.

Clinical manifestations of abdominal and thoracic aortitis, in descending order of prevalence, include fever, back pain, abdominal and testicular pain as well as signs of a pulsatile abdominal mass.^{8,16} Laboratory findings may include leukocytosis, raised inflammatory markers and anemia of inflammation.⁸ Due to poor sensitivity and specificity of the above manifestations and findings, a high index of suspicion is warranted. Blood cultures should be obtained in all cases as positivity is seen in 40–60% of cases. Due to low bacterial inoculum, use of antimicrobials, and vascular wall microabscesses not directly in contact with the bloodstream, in about 10–75% of cases the microorganisms is detected primarily from surgical cultures.¹⁰ In case of prior antimicrobial use, molecular diagnostic techniques such as polymerase chain reaction (PCR) may be beneficial. The most sensitive imaging modality is computerized tomography (CT) angiography.^{6,8,19} Radiologic findings of aortitis include a thin aortic wall with rim enhancement, eccentric wall thickening, increased wall diameter, sacciform aneurysm, perivascular inflammation, peripheral lymphadenopathy, fat stranding, thrombus formation, and periaortic air or fluid or both.^{7–9} Presence of air in the aorta is uncommon but highly suggestive of IA.^{8,19} Other studies to consider include magnetic resonance imaging, positron emission tomography-CT and aortography.⁸

Development of IA with *S. pneumoniae* bacteremia has been previously reported.^{5,6,8,18–21} Polymicrobial infections have been detected through intraoperative aortic tissue cultures.^{7,9} Interestingly, one case developed despite pneumococcal vaccination.⁹ Another case reported early diagnosis of IA due to positive urinary pneumococcal antigen, followed by confirmation via surgical specimens¹⁰

(Table 4). Once IA is suspected, prompt management is essential. IA may form pseudoaneurysms or mycotic aneurysms leading to rupture, associated with mortality of 14%–100%.^{7,22} More virulent bacteria may cause rupture without dilatation.¹¹ Broad-spectrum antimicrobials should be initiated while awaiting culture data. The duration of therapy is debatable, but 6–12 weeks after surgery and clearance of blood culture is favored. Depending on the microorganism, treatment may even be lifelong.²³ Since antimicrobial treatment or surgical management alone is associated with high mortality, a combination of both is recommended.^{8,13,17,24,25}

Surgical management of IA comprises of wide and extensive debridement or resection of the infected portion, followed by revascularization via in situ versus extra-anatomic grafting.¹⁹ The former is preferred due to more favorable outcomes and long term results.²⁶ Operative mortality is lower in patients with involvement of infrarenal aorta as compared to suprarenal or thoracic aorta.⁸ At present, however, there are no recommendations regarding the timing of surgery or aortic reconstruction with or without prosthetic material.²⁴

4. Limitations

In the presence of *S. pneumoniae* bacteremia and IE, intraoperative tissue specimen was deferred. Molecular diagnosis of IA, although useful in identifying different microorganisms and possibly a polymicrobial infection, was not obtained in light of positive blood cultures.²⁷ In our case, definitive surgical resection was performed emergently after aortic perforation, leaving the impact of an earlier surgical intervention unknown.

5. Conclusion

Over the last two decades, the etiology of aortitis has shifted towards non-infectious causes, possibly due to vaccination and antimicrobial usage. Our patient, despite lack of prior medical history and coverage with appropriate antimicrobial therapy, succumbed to a very aggressive and invasive strain of *S. pneumoniae*. Valuable learning points include: limitations in reaching a preoperative diagnosis, need for intraoperative culture data, early surgical resection of infected segment of aorta, role of serial abdominal imaging in assessing postoperative disease progression and stratifying risk of spontaneous rupture, and anticipated increase in incidence of IA with development of antimicrobial resistance.

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Conflicts of interest

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None.

Abbreviations

- CT computerized tomography
- ECHO echocardiogram
- IA infectious aortitis
- IE infective endocarditis
- PCR polymerase chain reaction

Supplemental Material

Table 1. Additional investigations performed on index patient.

Investigation	Interpretation
Hematology and Chemistry	
Peripheral Blood Smear	Negative for schistocytes
Lactate Dehydrogenase (LDH)	High - 660 [100–200 U/L]
Haptoglobin	Normal - 100 [30–200 mg/dl]
Fibrinogen	Normal - 305 [200–400 mg/dl]
Prothrombin Time (PT)	High - 13.8 [9.5–11.6 s]
International Normalized Ratio (INR)	High - 1.4 [0.9–1.1]
Urine Qualitative HCG	Negative
Microbiology	
HIV 1/2 Antibody and p24 Antigen	Non-reactive

(continued on next page)

Table 1. (continued)

Investigation	Interpretation
Sputum Culture, Influenza A and B PCR, Respiratory Syncytial Virus PCR	Negative
Urine <i>Streptococcus pneumoniae</i> & Legionella Antigen	Negative
Mononucleosis Qualitative Screen	Negative
Human Granulocytic Ehrlichiosis IgM/IgG Serology	Negative
Hepatitis A Antibody IgM & Hepatitis C Antibody Screen	Non-reactive
Hepatitis B Core Antibody IgM and Hepatitis B Surface Antigen	Non-reactive
CSF Analysis	Colorless clear cerebrospinal fluid, otherwise unremarkable
CSF HSV-1 & -2 PCR, CSF West Nile Virus IgM & IgG	Negative
Plasma Rapid Plasma Reagin (RPR) and CSF Venereal Disease Research Laboratory (VDRL)	Negative
Pathology	
Resected mitral valve	Endocarditis with fibrinoid necroinflammatory material
Autoimmune	
Anti Nuclear Antibody (ANA)	Negative
Anti double stranded DNA (dsDNA)	Normal - <1 [0.0-9.0 IU/ml]
Glomerular Basement Membrane Ab	Negative - 6 [0.0-20 Units]
Anti-myeloperoxidase (MPO) Ab	Negative - <9 [0.0-9.0 U/ml]
Anti-proteinase-3 (PR-3) Ab	Negative - <3.5 [0.0-3.5 U/ml]
Ribonucleoprotein Antibody (RNP)	Negative - <0.2 [0.0-0.9 AI]
Smith (Extractable Nuclear Antigen - ENA) Antibody	Negative - <0.2 [0.0-0.9 AI]
Sjogren's Antibody (SS-A and SS-B)	Negative - <0.2 [0.0-0.9 AI]

Abbreviations: Ab - antibody, CSF - cerebrospinal fluid, DNA - deoxyribonucleic acid, HCG - human chorionic gonadotropin, HIV - human immunodeficiency virus, HSV - herpes simplex virus, Ig - immunoglobulin, PCR - polymerase chain reaction.

Table 2. Radiological studies performed on index patient.

Radiological Studies	
Day 01 - CT abdomen and pelvis with contrast	3 cm left ovarian cyst and free pelvic fluid, and bilateral small pleural effusions with atelectasis
Day 01 - MRI brain with and without contrast	Mild T2/FLAIR signal abnormality within the medial temporal lobes bilaterally. Questionable finding due to the presence of motion artifact on post contrast images
Day 01 - MRI of cervical, thoracic and lumbar spine with and without contrast	Unremarkable
Day 01 - ECHO	Severe mitral regurgitation with a 1.3 × 1.8 cm mobile vegetation and markedly dilated left atrium with left-to-right atrial septum bowing
Day 04 - Bilateral LE Venous Duplex	No evidence of deep or superficial venous thrombosis or insufficiency
Day 04 - Ankle Brachial Index (ABI)	Right - 0.28, left - 0.27
Day 04 - Bilateral LE Arterial Doppler	Patent right and left common femoral artery with very low velocity monophasic flow suggestive of possible severe inflow (aortoiliac) disease, and absent left dorsalis pedis doppler waveform, absent left dorsal pedal artery doppler waveform
Day 13 - CT head without contrast	Edema within the left frontal and temporal lobe and the left basal ganglia with a 2 mm left-to-right midline shift
Day 31 - CT chest with contrast	Changes of recent cardiac surgery, large pericardial effusion, bilateral pleural effusions with compressive atelectasis, several subcentimeter peripheral pulmonary nodules, pulmonary vascular congestion and evidence of pulmonary hypertension
Day 31 - ECHO	Pericardial effusion without tamponade physiology
Day 32 - CT abdomen and pelvis with contrast	Occlusion of the aorta below the level of origin of inferior mesenteric artery, occlusion of right common iliac and internal and external iliac arteries, new right renal infarct involving the upper pole, large left gluteal abscess measuring 1.5 × 7.7 × 12.2 cm and myositis ossificans in the right gluteal muscle
Day 46 - CT abdomen and pelvis with contrast	Extensive dense ascites, consistent with hemorrhage and probable retroperitoneal hemorrhage adjacent to the aorta. The aorta and right common iliac artery were found to be patent but the right external iliac artery, left common and left external iliac artery remained occluded

Abbreviations: cm - centimeter, CT - computerized tomography, ECHO - echocardiogram, FLAIR - fluid attenuated inversion recovery, LE - lower extremity, mm - millimeter, MRI - magnetic resonance imaging.

Table 3. System-based list of diagnoses in index patient.

Diagnoses
<i>Streptococcus pneumoniae</i> bloodstream infection
Neurological
Acute toxic metabolic encephalopathy
Acute left middle cerebral artery cerebrovascular accident
Cardiac
Mitral valve endocarditis with severe regurgitation necessitating mechanical valve replacement
Mixed shock: distributive septic and cardiogenic
Arrhythmias: atrial fibrillation, torsades de pointes, ventricular fibrillation status post cardioversion
Pulmonary
Acute hypoxemic respiratory failure necessitating ventilatory support
Pneumococcal pneumonia
Bilateral pleural effusions with compressive atelectasis
Vascular
Aortitis and periaortic lymphadenitis with aortic perforation
Occlusion of aorta necessitating open aortoiliac thrombectomy
Occlusion of right common iliac and internal and external iliac arteries
Occlusion of left common iliac artery necessitating open thrombectomy
Critical lower limb ischemia necessitating bilateral iliofemoral arterial thrombectomy
Compartment syndrome necessitating bilateral lower extremity four-compartment fasciotomy
Renal
Sepsis-related acute kidney injury
Renal infarction of right upper pole
Rhabdomyolysis
Hematological
Sepsis-related severe thrombocytopenia necessitating platelet transfusion
Musculoskeletal
Left gluteal abscess necessitating debridement
Myositis ossificans of right gluteal muscle

Table 4. Medical and surgical treatment strategies adopted for pneumococcal aortitis.

Paper	Treatment	Outcome
Postema et al. ¹	Penicillin + replacement of aorta by Dacron graft and placement of gentamicin sponges around prosthesis and native aorta	Died
Brouwer et al. ²⁴	Amoxicillin followed by ceftriaxone x 6 weeks + excision of infected portion of aorta	Survived
Teng et al. ⁷	Replacement of aorta by rifampin-soaked polyester graft + graft excision with reconstruction of aortoiliac system with autologous femoral veins after detection of polymicrobial aortitis + intravenous antibiotics x 6 weeks	Survived
Cartery et al. ⁸	Intravenous amoxicillin + aortobiliac bypass with arterial allograft for ruptured mycotic aneurysm	Died
Rondina et al. ⁹	Gatifloxacin x 6 weeks + resection of aneurysm with placement of rifampin-soaked Dacron graft	Survived
Mangioni et al. ²⁰	Ceftriaxone + aorto-aortic homograft substitution	Survived
Abraud et al. ¹⁰	Cefotaxime x 4 weeks and gentamicin x 6 weeks followed by amoxicillin x 3 months + aorto-aortic bypass with cryo-conserved aortic allograft	Survived
Maclennan et al. ¹¹	Cefazolin with addition of vancomycin x 6 weeks + resection of infrarenal aorta and replacement by Dacron tube graft	Survived
Hoogendoorn et al. ⁶	Penicillin x 8 weeks followed by lifelong clindamycin after surgery was declined	Survived
Mlynski et al. ¹⁶	Penicillin x 2 weeks followed by oxacillin x 4 weeks + removal of aortoiliac stent and extra-anatomic revascularization	Survived
Melzer et al. ²¹	Benzylopicillin x 4 weeks + elective endovascular repair of aorta after 9 months	Survived

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