

Syphilitic Aortitis and Coronary Ostial Stenosis: A Focused Review

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Abstract Cardiovascular syphilis is a manifestation of tertiary syphilis, and is one that can have many complications, including syphilitic aortitis. In this review article, we review the epidemiology and pathophysiology of syphilitic aortitis and focus in on one of its complication, coronary ostial stenosis. Next, we will discuss the diagnosis and treatment options for both cardiovascular syphilis as well as coronary ostial stenosis. Finally, we present the findings of case reports in patients who had syphilitic aortitis with coronary ostial stenosis and their outcomes.

Keywords: tertiary syphilis, cardiovascular syphilis, coronary ostial stenosis, aneurysmal dilatation, periaortic inflammation

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1. Introduction

Syphilis is an infection that can have a wide variety of outcomes, with the disease often occurring in sequential stages. It is usually transmitted during sexual contact and initially presents as a chancre, or a skin lesion, weeks to months after initially acquiring the disease. It usually occurs in the genital region and because it is painless and resolves on its own, some do not receive any medical treatment, allowing transmission to occur in the future. Secondary syphilis occurs in close to 25% of patients who had not treated the initial chancre, and is associated with prodromal symptoms, a maculopapular rash involving the palms and soles of the feet, and widespread lymphadenopathy. [1] Tertiary syphilis encompasses the most dangerous components of the disease and can occur anywhere from one to thirty years after initial infection. [2] These includes gummas, or nodular lesions throughout the patient’s body, central nervous system involvement, or cardiac manifestations, which is what will be discussed in this paper. As syphilis can sometimes go undiagnosed at the initial infection, it is important to understand that potential impact it can have later on. Cardiovascular syphilis can lead to increased morbidity and mortality in undiagnosed and untreated patient populations. In particular, coronary ostial stenosis is important to keep in mind as it can present as acute coronary syndrome in patients without any cardiovascular risk factors. Furthermore, if the syphilitic aortitis progresses to severe or complete coronary ostial stenosis, it can lead to myocardial infarction or even death in a rapid manner.

2. Epidemiology

Syphilis is an infectious disease that is still very prominent in today’s society, and a 2017 study conducted by the Center for Disease Control (CDC) confirmed this. The CDC, in its Sexually Transmitted Disease Surveillance, reported a 10.5% increase from 2016 to 2017 in the amount of confirmed primary and secondary syphilis cases. Furthermore, an increase of 72.7% was seen between 2013 and 2017. Confirmed cases of primary and secondary syphilis has increased every year since 2000, with the majority of cases reported in men who have sex with men (MSM). [3] It is also important to note that in the MSM population, 42% of confirmed primary/secondary syphilis cases also presented with human immunodeficiency (HIV) as well, per the CDC. [4] As mentioned above, one of the common complications of tertiary syphilis is cardiovascular syphilis, which has a predisposition to affect the aorta, known as syphilitic aortitis. Patients can present with aortic root dilatation, aortic aneurysm, aortic valve insufficiency or coronary ostial stenosis. [5]

Cardiovascular syphilis was actually quite common in the early 1900s. One report from the Philadelphia General Hospital noted a 6.93% prevalence of cardiovascular syphilis between 1927 to 1937. Another study reported a prevalence of cardiovascular syphilis of 0.76% from Kings County Hospital from 1950 to 1960. [5] “Before the discovery of penicillin, tertiary syphilis was the most common cause of thoracic aneurysms and accounted for 5-10% of all cardiovascular deaths” [6] However, there was a decline in syphilitic aortitis over the second half of the

1900s. [7] Syphilis is still present in society today, and there has actually been an increase in disease incidence in the US since 2000. Furthermore, Africa currently has the highest prevalence of syphilis in the world. In 2012, it was reported that 1.8% of the general population was infected. [6]

Cardiovascular syphilis is one of the manifestations of tertiary syphilis, and typically occurs 10-30 years after the initial infection. [6,9] One of the most common complications of cardiovascular syphilis is syphilitic aortitis. There have been reports that syphilitic aortitis occurs in 70-80% of all untreated infections. [6] However, it is usually only clinically evident in 10-15% of cases. [8] Patients can either present with pain in the thoracic region or can have no symptoms at all, with findings noted incidentally on a chest X-ray. Occasionally, patients may present with a fatal rupture of the aneurysm. [10,11] It is important for all clinicians to consider this diagnosis as mortality rate within one year is close to 80% if no

surgical intervention is performed, as these aneurysms can rupture. [12] Furthermore, there is involvement of the Coronary Ostial Arteries in 20-26% of patients with syphilitic aortitis. [13,14] Another article reported that, according to two separate studies, Coronary Ostial Stenosis was seen in 20 and 26% of cases. [15]

3. Pathophysiology

Cardiovascular Syphilis, which is essentially the cardiovascular complications of tertiary syphilis, can have various clinical manifestations. Cardiovascular syphilis often leads to syphilitic aortitis, which most often affects the ascending aorta. In turn, this can present as asymptomatic aortitis, aortic regurgitation due to aortic valve insufficiency, aneurysm or coronary ostial stenosis. [13,16]

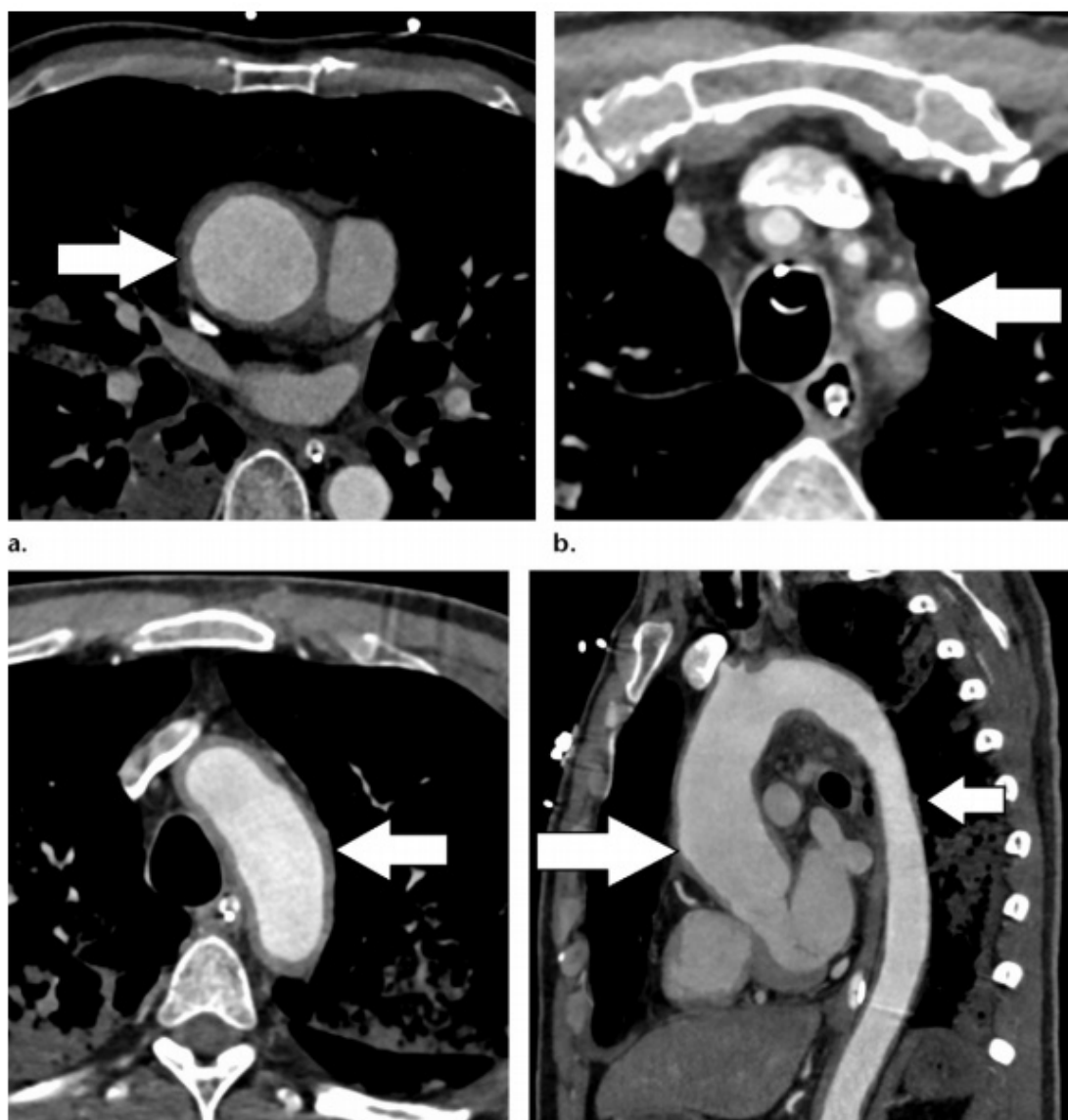


Figure 1. (a) Axial CT angiogram obtained at the level of the ascending aorta shows aneurysmal dilatation with circumferential wall thickening and periaortic inflammatory changes (arrow). (b) Axial CT angiogram obtained at the level of the great vessel origins shows circumferential wall thickening and perivascular inflammatory changes involving the brachiocephalic, left common carotid, and left subclavian arteries (arrow). (c) Axial CT angiogram obtained at the level of the aortic arch demonstrates aortic wall thickening and periaortic inflammatory changes (arrow). (d) Sagittal CT angiogram of the thoracic aorta shows aneurysmal dilatation of the entire ascending aorta (large arrow). There is circumferential wall thickening involving the ascending aorta, aortic arch, and proximal descending thoracic aorta. The remainder of the descending thoracic aorta (small arrow) is spared. Used with permission RadioGraphics 2017; 37: 407-412

Syphilitic aortitis is an inflammatory response to the bacteria infecting and invading the aortic wall. [6] As the treponemes invade the aortic adventitia, they begin to disrupt the vasa vasorum, or the blood supply of the vasculature. This leads to perivascular lymphoplasmacytic inflammation and infiltration of the aortic adventitia. This results in obliterative endarteritis, adventitial scarring and medial necrosis of the elastic fibers. [5,6,8,17,18,19] This also causes the intimal thickening and wrinkling, which causes the 'tree bark' appearance that has been linked to syphilitic aortitis. [8,17] The now weakened structure of the vasculature leads to the complications seen in this disease, including the aforementioned aortic aneurysm, aortic root dilation, aortic valve insufficiency and coronary ostial stenosis. [6] Furthermore, it is believed that the ascending aorta and the aortic arch is the area that is most commonly affected due to the larger number of vasa vasorum in this area. [8] See [Figure 1](#).

While Coronary Ostial Stenosis is one of the complications of cardiovascular syphilis, it only occurs in a minority of cases. [17] While the pathophysiology of aortic aneurysms and aortic valve insufficiency is linked to the weakening of the aortic wall, the pathophysiology of coronary ostial stenosis is more unique. Coronary Ostial Stenosis is often caused by the fibrosis of the aortic media that leads to aortic wall thickening [6,20] This fibrosis and formation of scar tissue can progress to the level of the Coronary Ostium and lead to Coronary Ostial Stenosis. [5]

Jackman JD et al. reported the case of a 82 year old woman who had postmortem findings that were classic for syphilitic aortitis. "Microscopic examination revealed an inflammatory infiltrate within the adventitia consisting of lymphocytes and plasma cells distributed predominantly around the vasa vasorum throughout the thoracic aorta. The media was remarkable for areas of elastic fiber degeneration in a lamella fashion with disruption by irregularly shaped scars." [5]

4. Diagnosis/Treatment

Cardiovascular syphilis can be difficult to diagnose. As mentioned above, the effects of tertiary syphilis often manifests years after the original infection. Because of this gap in time between initial infection and possible onset of symptoms from cardiovascular syphilis, it can be difficult to connect the two points in time. However, it has been shown, that when cardiovascular syphilis is part of the differential diagnosis, CT angiogram is the preferred imaging method. CT angiogram allows for "unparalleled spatial resolution" when assessing for aortitis and can be used to assess for aortitis-associated coronary ostial stenosis as well. [6]

The treatment for cardiovascular syphilis includes addressing both the initial infection as well as the cardiac manifestations associated with the disease. The best way to address cardiovascular syphilis, is properly treating the initial syphilis infection with penicillin. However, the primary syphilis infection is not always detected and can often go untreated. If the syphilis

infection progresses to cardiovascular syphilis, the treatment is also with penicillin as well as addressing the complications of cardiovascular aortitis. Along with CT angiogram, clinicians can obtain electrocardiograms (ECG), echocardiogram and cardiac catheterization to determine the impact of the treponeme on the cardiovascular system. In the case of coronary ostial stenosis, it has been shown that the current best treatment is coronary artery bypass grafting. [6,20,21] In fact, a recent 4-year retrospective study showed that patients treated with CABG had significantly lower incidence of restenosis at 6 months after surgery when compared to patients treated with PCI. [22]

5. Discussion

Syphilis is an infectious disease that can lead to many complications. After initial infection, patients infected with syphilis can soon-after experience painless chancres, rashes or wart-like lesions. However, if the disease is not treated properly, syphilis can lead to more serious complications. One of those feared complications is cardiovascular syphilis, which often presents 10-20 years after the initial infections. [6] One of the main complications of cardiovascular syphilis is syphilitic aortitis. Syphilitic aortitis can then lead to other complications, including aortic root dilation and aneurysm formation, aortic insufficiency and coronary ostial stenosis. [5] Coronary Ostial Stenosis is often due to the inflammation and fibrosis of the aortic wall that leads to aortic wall thickening. [6,20] This fibrosis can eventually extend to the coronary ostium where it can lead to Coronary Ostial Stenosis. [5]

The symptoms and complications of Coronary Ostial Stenosis can be quite severe. As mentioned throughout this paper, presentation can vary and is easy to miss from a clinician's standpoint. Some patients can remain asymptomatic for years while others can develop symptoms such as angina and present similarly to Acute Coronary Syndrome. For that reason, we will present various case studies of Coronary Ostial Stenosis in patients with confirmed cardiovascular syphilis. The patient's age/sex, clinical presentation and imaging findings are noted below and can be utilized by clinicians if there is clinical suspicion of this disease. See [Table 1](#) for summary of all case reports discussed.

In summary, syphilitic aortitis can have various presentations with associated devastating manifestations. Most of the patients reported in this article presented to the hospital with signs or symptoms of acute coronary syndrome, despite predominantly having little to no cardiovascular risk factors. In patients like these, it is very important to obtain a thorough history and to include cardiovascular syphilis in the differential. As we have seen, one of the complications from cardiovascular syphilis is coronary ostial stenosis. This stenosis can lead to myocardial ischemia and even death in extreme cases. However, with earlier detection and appropriate treatment, morbidity and mortality associated with cardiovascular syphilis can improve.

Table 1. Patients with cardiovascular manifestations of tertiary syphilis

Age, Sex	Symptoms	ECG	2D-echo	Cath	CT Angio	Source
58, M	Angina	Anterior ST-segment depression	-	90% ostial stenosis of the LAD, dilated ascending aorta	Aortitis	Fergus et al. [23]
44, M	Unstable Angina	Anterolateral/Inferior ST-segment depression ST-segment elevation in aVR	Dilated ostial right coronary artery	-	Critical stenosis of left main coronary shaft	Tewari et al. [24]
35, F	Acute confusion, Psychosis	Lateral ST-segment depression & T wave inversion	Dilated left ventricle with severe aortic regurgitation	-	Severe bilateral ostial disease with left mainstem and right coronary artery stenosis	Chadwick et al. [25]
46, M	Aggravating chest pain	-	-	Severe left main coronary artery ostial stenosis and tight stenosis of right coronary artery ostium	Diffuse thickening of thoracic aortic wall and significant ostial stenosis of both arteries Stenosis of left common carotid and left subclavian artery	Kim et al. [26]
58, M	Angina for three days duration, worsening chest pain dyspnea, syncopal episode	Inferolateral & anterolateral ST-segment depression	-	>90% obstruction of left coronary artery ostium Dilated & irregular ascending aorta	Aortitis	Lian et al. [6]
M (No age)	Angina	NSTEMI	Aortic regurgitation 90% focal stenosis of left main ostium and right coronary artery ostium	-	-	Choon et al. [27]
37M	Exertional chest pain	STEMI	Mildly dilated proximal ascending aorta Aortic regurgitation	-	Sub-occlusions of right and left main coronary arteries Coronary ostial stenosis	Zvirblyte et al. [20]
37, M	Severe chest pain upon exertion	Normal	Severe aortic regurgitation Enlarged left ventricle	Severe right and left main coronary ostial stenosis Severe aortic valve incompetence	Dilated ascending aorta & thickened wall	Feier et al. [17]
36, M	Chest pain complicated by cardiogenic shock	ST-segment elevation in precordial leads	-	Severe ostial left main stenosis Enlarged ascending aorta with mild aortic regurgitation	-	Predescu et al. [13]
32, F	Chest pain	-	(Discovered on autopsy) Marked thoracic aortic thickening involving aortic root Near-total stenosis of both coronary artery ostia	-	-	Kennedy et al. [8]
59, M	Congestive heart failure	-	-	Severe aortic insufficiency Severe bilateral coronary ostial stenosis	-	Frank et al. [28]
50, M	Angina Congestive heart failure	-	-	Aortic insufficiency with dilation of ascending aorta Complete stenosis of right coronary artery ostium 75% stenosis of left coronary artery ostium	-	Aizawa et al. [29]

Age, Sex	Symptoms	ECG	2D-echo	Cath	CT Angio	Source
48, M	Chest pain Dyspnea	-	Moderate aortic regurgitation Ectasia of ascending aorta and diffuse hypokinesis of left ventricle	-	70% ostial stenosis of left coronary artery 60% ostial stenosis of right coronary artery along with aortic insufficiency and stenotic lesion of left subclavian artery	Croti et al. [30]
40, M	Exertional chest pain	ST-segment depression	-	95% ostial stenosis of left coronary artery 75% ostial stenosis of right coronary artery	-	Cohen et al. [31]
46, M	Exertional chest pain	ST-segment depression	-	95% ostial stenosis of left coronary artery 50-70% ostial stenosis of right coronary artery	-	New England Journal of Medicine [32]
37, M	Unstable angina	Anterolateral ST-segment depression with T wave inversions	-	95% ostial stenosis of left coronary artery	-	Shah et al. [15]
39, M	Chest pain Shivers	-	Left ventricular dilatation Dilation of aorta at sinus of Valsalva	Ostial stenosis of right coronary artery	-	Levasseur et al. [12]
48F	Abdominal pain Chest tightness	Q-waves in the anterior leads along with elevated troponin levels.	Aortic regurgitation Left ventricular wall motion abnormalities Increased size of the left atrium and left ventricle Decreased aortic elasticity	-	Occlusion of ostium of the left main artery as well as severe stenosis of the right coronary artery ostium	Li et al. [9]
69M	Sudden shortness of breath	-	Severe aortic regurgitation	-	Complete obstruction of the left coronary ostium with collaterals from the right coronary artery Irregular thickening of the aortic wall without aneurysm formation.	Nomura et al. [14]

6. Conclusion

Syphilis is a complex disease that can lead to a myriad of symptoms and clinical conditions, ranging from a rash to cardiovascular syphilis and syphilitic aortitis. Syphilitic aortitis can lead to complications, including aortic root dilatation, aortic aneurysm, aortic valve insufficiency and coronary ostial stenosis. Coronary ostial stenosis can cause myocardial ischemia and even death, in severe cases. Given that younger patients without any history of cardiovascular risk factors can be affected, it is important to keep syphilitic aortitis on the differential diagnosis in cases resembling acute coronary syndrome. The diagnosis of syphilitic aortitis and coronary ostial stenosis should include syphilis serology and CT angiography and severe coronary ostial stenosis requires coronary artery bypass graft to restore patency. The recognition of syphilis as the etiology of cardiovascular disease can prevent the development of more serious complications related to syphilitic aortitis.

Acknowledgements

Figure 1 a, b, c, d was used with permission Lian K, Lee L, Machan L., MD Syphilitic Aortitis with Coronary Ostial Involvement1 RadioGraphics 2017; 37: 407-412.

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