Tertiary Cardiovascular Syphilis, Including Aortic Regurgitation, Syphilitic Aortitis Complicated by Thrombus of the Ascending Aorta, and Coronary Artery Occlusion, Requiring Percutaneous Coronary Artery Intervention

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Patient: Male, 51-year-old
Final Diagnosis: Syphilis
Symptoms: Dyspena
Clinical Procedure: —
Specialty: Cardiology

Objective: Rare coexistence of disease or pathology
Background: Heart failure is caused by coronary artery disease, valvular disease, and arrhythmias and is highly treatable with recent technology. However, the incidence of syphilis is increasing worldwide. This case report describes tertiary cardiovascular syphilis, accompanied by aortic regurgitation, syphilitic aortitis complicated by thrombus of the ascending aorta, and coronary artery occlusion, requiring percutaneous coronary artery intervention.

Case Report: A 51-year-old Japanese man with no significant medical history was admitted to the hospital for worsening shortness of breath on exertion. On physical examination, there was no edema in either lower leg. Chest X-rays showed an enlarged heart and pulmonary congestion, and echocardiography showed a left ventricular ejection fraction of 18%, with full circumferential wall motion impairment. Heart failure was diagnosed, and the patient was found to have severe coronary artery disease and aortic regurgitation. He underwent percutaneous coronary intervention (PCI) for his coronary artery occlusion and was treated with medications for heart failure. Two months later, his condition improved, and PCI was performed for the revascularization of the remaining coronary artery. After PCI was completed, the patient was evaluated for vasculitis. The aortic wall lesion was likely a result of non-active syphilitic aortitis, and the results of serological tests of syphilis were positive. Therefore, we concluded that the diagnosis was cardiovascular syphilis.

Conclusions: This case report has highlighted the need for clinicians to be aware of the cardiovascular findings in syphilis, including syphilitic aortitis, particularly at this time, when the global incidence of syphilis is increasing.

Keywords: Aortic Valve Insufficiency • Heart Failure • Syphilis, Cardiovascular • Coronary Artery Disease

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Background

Heart failure is widespread globally and often encountered in daily clinical practice. Heart failure is caused by coronary artery disease, valvular disease, and arrhythmias and is highly treatable with recent technology [1]. On the other hand, syphilis is a sexually transmitted disease caused by *Treponema pallidum*, and its incidence increasing worldwide [2]. This report is of a 51-year-old man presenting with tertiary cardiovascular syphilis, including aortic regurgitation, syphilitic aortitis complicated by thrombus of the ascending aorta, and coronary artery occlusion, requiring percutaneous coronary artery intervention.

Case Report

A 51-year-old Japanese man with no remarkable medical history was admitted to our hospital with the chief concern of worsening shortness of breath on exertion for the past week. He had no family history of cardiovascular involvement and no history of radiation therapy. His vital signs were as follows: temperature, 36.7 °C; blood pressure, 94/66 mmHg; heart rate, 112 beats per min; SpO2, 97%; and respiratory rate, 18 breaths per min. His general appearance was good, aside from the low blood pressure and high heart rate, and there were no symptoms at rest. On physical examination, there was no edema in either lower leg, and no significant murmur was heard on auscultation. There was no evidence of skin rash or arthritis. Chest X-rays showed an enlarged heart and pulmonary congestion. Electrocardiography demonstrated mild ST segment elevations in aV_{6} and horizontal ST depression in leads V_{1} to V_{4} with sinus rhythm. A laboratory examination revealed blood counts were in the reference range. There were no electrolyte abnormalities, no dyslipidemia, and no renal dysfunction. The creatine kinase level was 1011 U/L, creatine kinase-MB was 182 U/L, and lactate dehydrogenase was 512 U/L. The level of N-terminal prohormone of brain natriuretic peptide was 1386 pg/mL.

Echocardiography showed a left ventricular ejection fraction (LVEF) of 18%, with full circumferential wall motion impairment. Although a quantitative evaluation was not performed, moderate aortic regurgitation was observed. The left atrial dimension in systole was 38 mm; the left ventricular internal dimension in diastole was 57 mm, and the left ventricular internal dimension in systole was 51 mm. Other valves were normal (Figure 1A).

We diagnosed heart failure and started the patient on diuretic therapy with intravenous furosemide, under careful observation. The next day, his respiratory condition suddenly worsened, and he was prepared for emergency tracheal intubation and coronary angiography, during which he suddenly went into cardiopulmonary arrest. Chest compressions were immediately initiated, and the patient resumed self-cardiac rhythm. Tracheal intubation was performed, and percutaneous cardiopulmonary support was initiated.

Coronary angiography revealed 99% stenosis in the left coronary artery (LCA) at the ostium of the left main coronary artery (LMT), and the right coronary artery (RCA) was occluded from the entrance (Figure 2A). Coronary spasm was ruled out, as the stenosis did not improve with nitroglycerin. Since the patient had bilateral coronary ostial lesions and moderate aortic regurgitation, surgical treatment was considered; however, since the patient was in cardiopulmonary arrest, the heart team decided that percutaneous coronary intervention (PCI) of the LMT would be preferable. Intravascular ultrasound showed relatively low-intensity plaque. A coronary stent was placed, and balloon dilation was performed before and after its placement. The final contrast-enhanced examination showed good stent dilation and no residual stenosis in the LCA (Figure 2B). Intra-aorta balloon pumping was added to the percutaneous cardiopulmonary support. One week later, cardiac catheterization confirmed a collateral blood channel from the LCA to the RCA (Figure 2C), and aortography showed degree II aortic regurgitation (Figure 2D). The patient was admitted to our hospital’s Intensive Care Unit.

The patient’s treatment course progressed well. The percutaneous cardiopulmonary support and intra-aorta balloon pumping were discontinued on day 6 of admission, and the patient was extubated on day 8 of admission. Fortunately, no neurological sequelae were observed. His vital signs stabilized, and treatment with enalapril, bisoprolol, spironolactone, and rosuvastatin was initiated. The diuretics were also changed from intravenous to oral administration. A cardiac computed tomography scan revealed a plaque-like aortic mural lesion in the ascending aorta near the beginning of the coronary artery (Figure 3A-3F). The patient was able to walk on his own and was temporarily discharged from the hospital before RCA revascularization and aortic regurgitation intervention.

Two months later, echocardiography showed that the patient’s LVEF had improved to 37% and his aortic regurgitation had slightly improved from moderate to mild, due to the medical therapy (Figure 1B). Transectional aortic echocardiography revealed that the aortic regurgitation was stronger at the gap between the coronary cusp and the aorta rather than at the apex of the valve (Figure 1C). Aortic wall lesions similar to those seen on CT were also observed on transectional aortic echocardiography (Figure 1D). Initially, because the RCA was completely occluded from the origin, the status of the patient’s aortic regurgitation was close to severe, and since the patient was relatively young at 51 years old, we speculated that 1-vessel coronary artery bypass graft surgery and aortic...
valve replacement would be better than PCI for revascularization of the RCA. However, because the aortic regurgitation was less severe than expected after re-evaluation, and because the ascending aortic wall lesion and the LCA stent protruded into the ascending aorta, surgical aortic valve replacement was considered a greater risk. PCI was therefore chosen for the revascularization of the patient’s RCA. A wire was passed from the LCA, using a retrograde approach through the bilateral radial arteries (Figure 4A). On intravascular ultrasound, the lesion appeared to be a series of relatively low-intensity plaques (Figure 4B). After balloon dilation, a drug-eluting stent was implanted, and the procedure was completed. The final contrast-enhanced examination detected no residual stenosis, including in the stent (Figure 4C).

After PCI was completed, the patient was evaluated for vasculitis. Diffusion-weighted imaging with background suppression was performed, and no abnormal high signal was detected, including wall-intact lesions in the ascending aorta.

Figure 1. (A) Echocardiography showed moderate or severe aortic regurgitation at the time of the patient’s admission. (B) Two months later, echocardiography showed that the patient’s left ventricular ejection fraction had improved to 37% and aortic regurgitation had improved from moderate to mild status. (C) Transesophageal echocardiography revealed that the patient’s aortic regurgitation was stronger at the gap between the coronary cusp and the aorta rather than at the apex of the valve (arrow). (D) Aortic wall lesions similar to those seen on computed tomography were also observed on transesophageal echocardiography (arrow).
Results of additional blood tests conducted later did not suggest collagen disease or coagulation abnormalities, and there were no elevations in erythrocyte sedimentation, ferritin, or C-reactive protein. However, the results of a serum rapid plasma regain test and a fixed *T. pallidum* latex agglutination test were positive. Therefore, we concluded that the diagnosis was cardiovascular syphilis.

Discussion

This case is of a 51-year-old man presenting with tertiary cardiovascular syphilis, including aortic regurgitation, syphilitic aortitis complicated by thrombus of the ascending aorta, and coronary artery occlusion, requiring percutaneous coronary artery intervention.
Syphilis is a sexually transmitted disease caused by *T. pallidum*, and the incidence of syphilis is increasing worldwide despite a falling mortality rate [2]. Tertiary syphilis is late symptomatic syphilis that can manifest months or years after the initial infection as cardiovascular syphilis, neurosyphilis, or gummatous syphilis [3]. Cardiovascular syphilis can occur 10 to 30 years after the initial infection [4]. The treponemes initially infect the adventitial vasa vasorum of the aorta, inducing perivascular lymphoplasmaacytic inflammation and leading to endarteritis obliterans, median destruction, and intimal thickening and wrinkling [5]. Syphilitic aortitis can thus also cause aortic regurgitation and coronary artery ostial narrowing, related to aortic wall thickening [6]. Our patient was later revealed to be positive for syphilis antibodies. Active vasculitis was negative, but his coronary ostial stenosis was probably the result of a syphilis infection incurred more than 10 years ago. Although no aortic root dilatation was seen, it is reasonable to speculate that the weakening of the aortic wall caused
the aortic regurgitation [6]. Cardiovascular syphilis can cause aortic aneurysm, aortic regurgitation, and coronary artery ostial stenosis [7-9]. Based on these reports, our patient’s case aligned with cardiovascular syphilis.

We initially suspect that the patient’s myocardial ischemia and aortic regurgitation were caused by a lesion in the wall of the aorta, and the wall lesion was plaque. The etiology of aortic regurgitation is broadly classified as either leaflet abnormalities or aortic root abnormalities, congenital or acquired [10]. His history, physical examination results, and blood laboratory results showed no findings suggestive of collagen or connective tissue disease, and active vasculitis was negative, except for syphilis.

Could the mural lesion in the ascending aorta have been an atherosclerotic plaque? Plaque is formed by the infiltration of macrophages, in addition to intimal thickening and lipid deposition in blood vessels, and vascular inflammation thus plays an important role in plaque development [11]. Imakita et al reviewed autopsy cases of young Japanese patients to examine atherosclerotic lesions in 1066 aortas [12]. They reported that the lesion area of aortic atherosclerosis was correlated with serum cholesterol and was also related to age and systolic blood pressure. Our patient’s blood pressure values before the onset of his heart failure are not known, but his serum cholesterol levels were not high, and there was no evidence of atherosclerosis (including in the coronary arteries) other than in the ascending aorta. Two reports of severe aortic regurgitation due to atherosclerotic lesions in the aortic valve annulus gap are available [13,14]. Although it cannot be ruled out that fluidic stimulation by the aortic regurgitation may have formed the plaque in our patient’s case, it is not typical for plaque to be localized in a portion of the ascending aorta. In addition, in patients with syphilis and atherosclerosis, coronary ostial stenosis in normal coronary vessels can occur in patients with disorders such as Kawasaki disease, Takayasu’s arteritis, iatrogenic stenosis including intramural aortic hematoma caused by cardiopulmonary resuscitation, thymic carcinoma, sinus of Valsalva aneurysm, and anomalous origin of the right coronary artery [15,16]. None of these were observed in our patient’s case.

Notably, we did not perform an urgent coronary artery evaluation at our patient’s arrival. Electrocardiography and blood test results did not rule out acute coronary syndrome. The patient had no symptoms of chest pain, including chest pain on exertion, the onset of myocardial ischemia was unknown, and his general condition was relatively good. Considering the possibility that catheter stimulation might induce worsening of the patient’s heart failure, conservative treatment was chosen. However, the patient had heart failure and low systolic blood pressure, and his circulation was not stable; an urgent coronary evaluation should thus have been performed [17].

We speculated that our patient’s myocardial ischemia and aortic regurgitation were the cause of his heart failure, with reduced LVEF. The pathogenesis of the mural lesions of the aorta in his case is not certain, but it is reasonable to conclude that the lesions were caused by non-active syphilitic aortitis.
A question remains regarding how our patient’s aortic regurgitation improved after heart failure treatment. In general, aortic regurgitation flow appears to increase as heart failure resolves and the left ventricular end-diastolic pressure decreases. In our patient’s case, it is possible that more aortic valve regurgitation would have been depicted due to fluid volume overload during the acute phase of heart failure. This may be because the coronary stent was placed into the weakened aorta damaged by inflammation (eg, syphilitic aortitis), resulting in smaller dehiscence at an aortic valve commissure.

**Conclusions**

This case report has highlighted the need for clinicians to be aware of the cardiovascular findings in syphilis, including syphilitic aortitis, particularly at this time, when the global incidence of syphilis is increasing.

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**References:**