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Case Report

Infective Endocarditis Due to *Treponema pallidum*: A Case Diagnosed Using Polymerase Chain Reaction Analysis of Aortic Valve

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ABSTRACT

Syphilis is a sexually transmitted disease caused by *Treponema pallidum*. Syphilitic aortitis might coexist in a dysfunctional aortic valve, but the etiology remains unclear, because microbiological diagnosis is difficult. A 62-year-old man with low-grade fever was diagnosed with aortitis and infective endocarditis, due to *Treponema pallidum* infection, using polymerase chain reaction analysis. This case suggests that syphilis might cause infective endocarditis.

RÉSUMÉ

La syphilis est une infection sexuellement transmissible causée par *Treponema pallidum*. L'aortite syphilitique peut coexister dans une valve aortique dysfonctionnelle, mais l'étiologie demeure incertaine en raison de la difficulté du diagnostic microbiologique. Chez un homme âgé de 62 ans présentant une fièvre légère, un diagnostic d'aortite et d'endocardite infectieuse, attribuables à une infection à *Treponema pallidum*, a été posé grâce à une analyse par la technique de réaction en chaîne de la polymérase. Ce cas laisse à penser que la syphilis pourrait être une cause d'endocardite infectieuse.

Syphilis is caused by spirochete *Treponema pallidum*. The number of syphilis cases is increasing. However, microbiological diagnosis is difficult because it cannot be cultured and visualized in normal laboratories. In this case, we diagnosed infective endocarditis due to syphilis, using polymerase chain reaction analysis.

Case

A 62-year-old man with a 20-year history of intermittent low-grade fever that was never investigated, visited our hospital. His recent medical history included diabetes and anemia, with an earlier history of gonorrhea. Clinically, no skin abnormalities were noted. A diastolic murmur was heard, and transthoracic echocardiography showed vegetation on the aortic valve with severe aortic regurgitation (Fig. 1A and B). Laboratory findings indicated that C-reactive protein and B-type natriuretic peptide levels were slightly elevated at 1.45 mg/dL and 93.4 pg/mL (normal ranges: < 0.30 mg/dL and < 18.4 pg/mL), respectively. IE was suspected because of characteristic graphic findings and inflammatory signs. Blood culture tests yielded negative results, but rapid plasma reagin and *T pallidum* hemagglutination test results were positive, indicating syphilitic infection. Human immunodeficiency virus antibody test was negative. Computed tomography imaging revealed no coronary artery stenosis but highlighted a thickened aorta and left subclavian artery, which we believed were due to syphilis (Fig. 1C and D). The sinotubular junction was mildly dilated (Fig. 1E). On the basis of concerns regarding heart failure progression and cerebral infarction due to IE, an urgent aortic valve replacement was performed. During surgery, a thickened aorta, vegetation on the left coronary cusp, and injured aortic valve were found (Fig. 2A). Pathologically, we detected increased plasma cells and capillaries in aortic and vegetation sections, indicating chronic inflammation (Fig. 2B). *T pallidum* antibody test using an immunostaining method in the aortic section yielded positive results (Fig. 2C). *T pallidum* DNA was detected using a PCR

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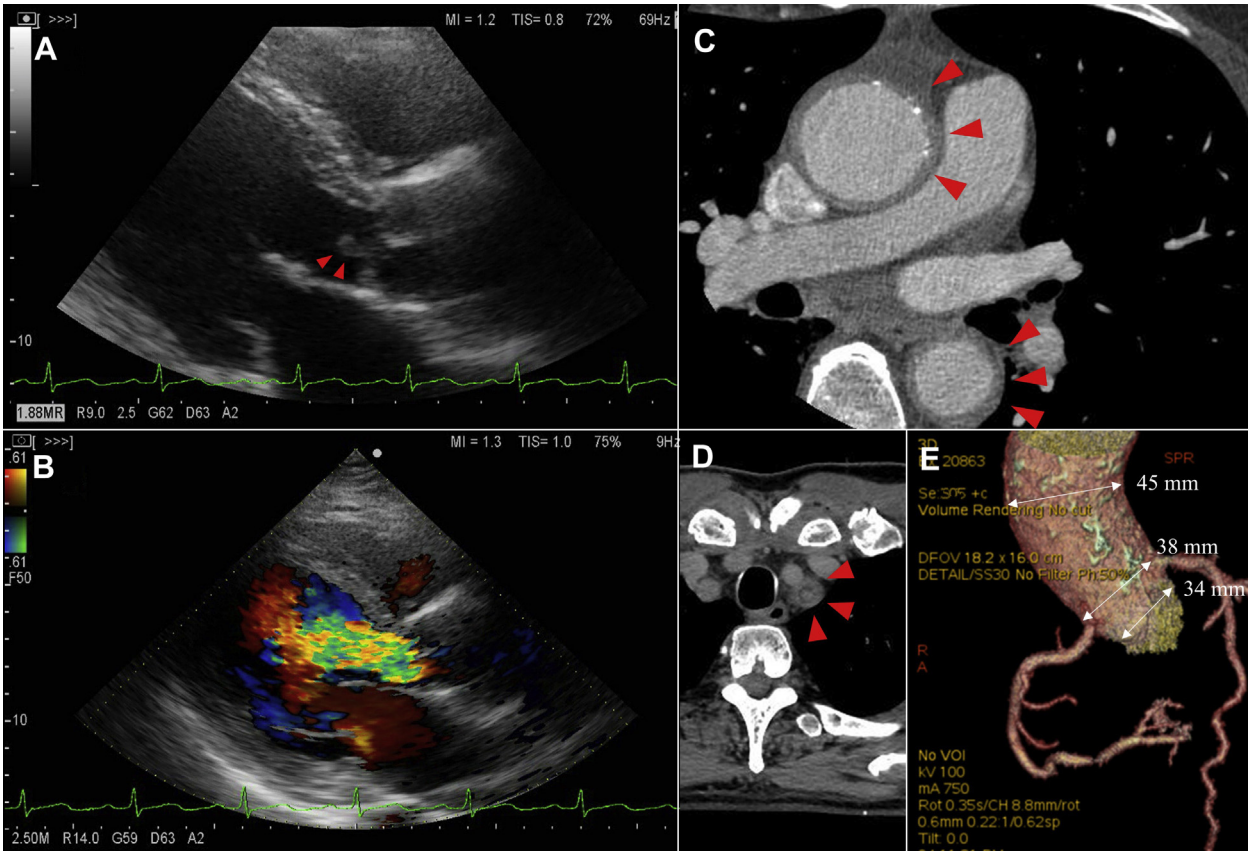

Figure 1. Transthoracic echocardiography revealed a mobile vegetation (8 × 4 mm) on the aortic valve (**A**) and severe aortic regurgitation (**B**). Computed tomography showed a thickened aorta (**C**) and the left subclavian artery (**D**). The ascending aorta was dilated in 3-dimensional computed tomography imaging (**E**).

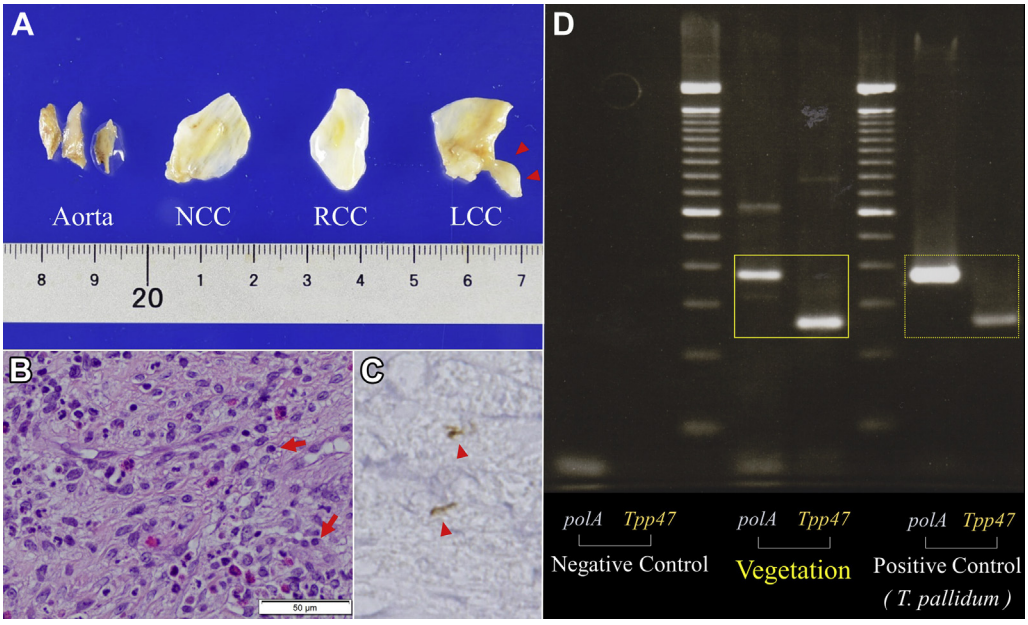

Figure 2. Findings in tissues extracted during surgery. (**A**) Vegetation adhered to the left coronary cusp. (**B**) Plasma cells (**arrow**) and capillaries were seen in the vegetation and in the aortic sections (hematoxylin and eosin staining), indicating chronic inflammation. (**C**) The *Treponema pallidum* antibody was positive in the aortic section. (**D**) In polymerase chain reaction analysis, the vegetation result matched that of the positive control. LCC, left coronary cusp; NCC, non-coronary cusp; RCC, right coronary cusp.

analysis of the vegetation section (Fig. 2D). Therefore, we diagnosed aortitis and syphilis-related IE. Treatment comprised intravenous antibiotics, namely, gentamicin and vancomycin for the first 7 days, and sulbactam/ampicillin over the following 5 weeks. C-reactive protein levels decreased to the normal range. Rapid plasma reagin value decreased from 184.0 to 68.2 units. The patient was subsequently discharged with no symptoms.

Discussion

Although the number of reported cases of syphilis have been increasing, tertiary syphilis remains extremely rare.[1] One autopsy case report of syphilitic aortitis revealed destruction of aortic valve due to vegetation.[2] However, the relationship between syphilis and vegetation remains unknown. PCR for syphilis was developed in recent years; its sensitivity and specificity using swab specimen were reported to be 95%.[3] Our literature search revealed no reports of IE due to *T pallidum* diagnosed using PCR. After DNA extraction, we amplified the *polA* and *Tpp47* genes with TaKaRa Mighty Amp DNA Polymerase Ver 2 (Takara Bio Inc, Kyoto, Japan) and these were positive. Blood contamination could not be totally excluded; however, the possibility is extremely low because of the following reasons. First, we cleaned the vegetation with saline (Fig. 2A). Second, sensitivity of PCR was very low at 0-14% using 200-μL blood specimen in latent syphilis.[3,4] Less than 20 μL vegetation was used for extraction; it was too little to detect *T pallidum* DNA of contaminated blood. Finally, there were no positive results in other bacterial tests, and similar pathological changes were detected in the aorta and the vegetation. Therefore, there was an overwhelming probability of *T pallidum* having infected the aortic valve.

Previous reports showed that PCR of resected valve was useful for the diagnosis of IE caused by culture-negative or slow-growing bacteria.[5] Using PCR for detection of syphilis is advantageous over serological tests, because the former enables detection of real-time infections.

The sinotubular junction was dilated; however, two-thirds of the LCC was affected by inflammation, and the regurgitation jet was mildly directed toward the septal wall. Therefore, both mechanisms of malcoaptation and flail were found to be related to aortic regurgitation in this case.

In conclusion, syphilis can cause IE as well as aortitis, and this is a remarkable new finding.

Disclosures

The authors have no conflicts of interest to disclose.

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