

## Syphilis aortitis in the differential diagnosis of aortitis: When should we suspect?

Berivan Bitik<sup>1</sup> 

<sup>1</sup> Başkent University, Department of Internal Medicine, Division of Rheumatology, Ankara, Türkiye.

Corresponding Author: Berivan Bitik • E-mail: berivanbitik@hotmail.com  
This manuscript was peer-reviewed by Prof. Dr. Sedat Kiraz

Syphilis is a systemic disease caused by *Treponema pallidum*. It is most commonly transmitted by sexual contact, rarely by transplacental/perinatal and blood transfusion, and can cause serious morbidity and mortality [1]. Syphilis can be divided into four stages according to clinical signs and symptoms.

**a) Primary Syphilis:** It occurs as a painless, round, initially shiny ulcer in the genital area. Enlargement is detected in lymph nodes close to the ulcer site. Syphilis is very contagious during this period. The ulcer, called chancre, heals spontaneously within 6 weeks [1].

**b) Secondary Syphilis:** Approximately 25% of individuals with untreated primary infection develop symptoms that can mimic any skin disease in the following 2 years. Diffuse, symmetrical macular or papular rashes involving the whole trunk and extremities, systemic symptoms such as fever, headache, malaise, anorexia, sore throat, myalgia, weight loss, renal pathologies such as diffuse lymphadenopathy, hepatitis, acute renal failure, nephrotic syndrome, acute nephritis, neurological abnormalities and ocular abnormalities such as uveitis (most often posterior), retinal necrosis, optic neuritis can be seen during this period. Ocular abnormalities may also be a manifestation of neurosyphilis [1].

**c) Latent Syphilis:** It is the serological infection period without any signs of disease. There is no contagiousness.

**d) Tertiary Syphilis:** The period observed after approximately 15 years in untreated patients. This period is rare nowadays. Involvement of the ascending aorta, which classically presents with an aneurysm in the cardiovascular system, may rarely cause dissection. In tertiary syphilis, granulomatous-nodular lesions are observed in the skin, bone, and visceral organs. Central nervous system involvement may occur at any stage of syphilis, tabes dorsalis and paresthesia may be seen [1]. All cases of syphilis should also be screened for HIV virus serology.

### Diagnosis of Syphilis

Serological tests are the main diagnostic method in the diagnosis of syphilis. Treponemal tests and non-treponemal tests are used as serological tests. Both tests can be used initially as screening tests. It is confirmed by a non-treponemal antibody test followed by the more specific treponemal test. In the presence of clinical suspicion, the diagnosis of syphilis is made after the two tests are found to be reactive. More than a single test is required for diagnosis. However, both tests have limitations. For

Non-treponemal Tests	Treponemal Tests
Venereal Disease Research Laboratory (VDRL)	T. pallidum hemagglutination testi (TPHA)
Rapid Plasma Reagin (RPR)	Microhemagglutination Assay T.pallidum (MHA-TP)
Toluidine Red Unheated Serum Test (TRUST)	Fluorescent treponemal antibody absorption (FTA-ABS)
	T. pallidum enzyme immunoassay (TP-EIA)

example, non-treponemal tests may be positive in rheumatological diseases (e.g. SLE) [2].

### Treatment for Syphilis

A single dose of benzathine penicillin G (2.4 million units intramuscularly) is standard therapy for primary, secondary, and early latent syphilis. Doxycycline, tetracycline, and ceftriaxone are alternative treatment agents [1].

### Syphilis Aortitis

Frequency data for cardiovascular involvement in patients with untreated syphilis were obtained from two major studies: the Oslo study and the controversial Tuskegee study. The Oslo study first analyzed native Oslo patients hospitalized for primary syphilis from 1890 to 1910 and followed for 40-60 years. Cardiovascular syphilis (with or without saccular thoracic aortic aneurysm, aortic regurgitation, or coronary ostial stenosis) was diagnosed in 45 (15%) of 303 men and 47 (8%) of 584 women.

Tuskegee study began in 1932 and continued until 1972. It included 408 African-American men hospitalized for primary syphilis. Patients included in the study were followed without treatment with penicillin, which was introduced in the United States in 1943. The study subsequently caused great ethical debates. In 1952, approximately 1/3 of the patients died and 89 had autopsy findings. Fusiform aneurysm of the thoracic aorta was detected in 40 patients (45%), saccular aneurysm of the thoracic aorta in 7 patients (8%), and aortitis (by histological examination) in 41 patients (46%). Of the 89 patients examined at autopsy, 60 (67%) had positive serological test findings for syphilis when last tested; suspicious test results were found in 3 and negative results in 24. The clinical diagnosis of cardiovascular syphilis was made at autopsy in 88% of the patients (3). Of the 69 hearts (with existing weights), 48 (70%) weighed >400 g.

Syphilis aortitis manifests clinically 10-40 years after primary syphilis as aortic regurgitation, coronary ostial stenosis, or aortic aneurysm. In the pre-antibiotic era, up to 10% of untreated syphilis patients developed symptomatic cardiovascular complications, but nowadays the late form of syphilis is rarely seen in developed countries. Aortic

regurgitation due to direct syphilitic involvement of the aortic valve or dilatation of the aortic ring affects 20-30% of patients with syphilitic aortitis. It is reported that 20-26% of the patients have coronary ostial stenosis. Although ostial involvement can cause symptoms of angina, it rarely results in myocardial infarction, as the slow process of stenosis allows the formation of collateral vessels. The prevalence of coronary ostium lesions with aortic regurgitation in patients with syphilitic aortitis has been reported as 14%. Aortic aneurysms are clinically detected in only 5-10% of patients, and 50% are seen in the ascending aorta [4]. CT, MRI, and echocardiography are diagnostic imaging modalities used in aortitis. The specificity of CT scans for syphilitic aortitis has not been defined [5].

It is important to differentiate the involvement of the aorta from atherosclerosis. While the media and adventitia layer of the vessel is normal in atherosclerosis, fibrosis and inflammatory cells are seen in the media and adventitia layer in syphilis, and the vessel wall is thickened. The thickening results from extensive scarring of the adventitia and less dense fibrous tissue in the intima with or without calcium. The media layer is not thickened and thinner than normal, elastic fibers and smooth muscle cells may be completely absent in scar areas with fibrous tissue. Therefore, despite the thickening, the associated arterial wall is weaker than normal due to the disruption of the media's elastic fibers and smooth muscle cells. While widespread involvement is observed in syphilis, focal vessel involvement is observed in atherosclerosis, except for familial hyperlipidemia patients. The syphilitic process appears to involve only arteries with vasa vasorum. Vasa vasorum is found in the entire thoracic aorta but not in the abdominal aorta, and their absence in this part of the aorta seems to explain the absence of syphilitic involvement in the abdominal aorta [3].

If syphilitic aneurysms are not treated, the 2-year mortality rate is more than 80%. Obliterative endarteritis of vasa vasorum leads to an intense inflammatory reaction that may result in rupture of the aorta or fistulization to adjacent structures [6]. Antimicrobial pharmacotherapy and surgical treatment are recommended for the treatment of syphilis aortitis.

REFERENCES

- [1] Golden MR, Marra CM, Holmes KK. Update on syphilis: resurgence of an old problem. *JAMA*. 2003;290(11):1510
- [2] Park IU, Chow JM, Bolan G, et al. Screening for syphilis with the treponemal immunoassay: analysis of discordant serology results and implications for clinical management. *J Infect Dis* 2011; 204:1297.
- [3] William Clifford Roberts, Jong Mi Ko, Travis James Vowelsa. Natural History of Syphilitic Aortitis. *The American Journal of Cardiology*. Volume 104, Issue 11, 1 December 2009, Pages 1578-1587. <https://doi.org/10.1016/j.amjcard.2009.07.031>
- [4] Ryota Nomura, Fumio Yamazaki, Yuki Egawa. Syphilitic aortitis: chronic left coronary ostial occlusion and aortic regurgitation with aortitis. *General Thoracic and Cardiovascular Surgery* (2021) 69:736–739. <https://doi.org/10.1007/s11748-020-01523-y>
- [5] John A Chadwick, Anita MacNab, Jaydeep Sarma, Simon Ray, Isaac Kadir, Eavan G Muldoon. Secondary syphilis presenting with aortitis and coronary ostial occlusion. *Sex Transm Infect* 2016 92: 108-109. <https://doi.org/10.1136/sextrans-2015-052247>
- [6] Leonard N. Girardi. Syphilitic aortitis: The bigger Picture. *Journal of Thoracic and Cardiovascular Surgery*, The, 2017-08-01, Volume 154, Issue 2, Pages e27-e28. <https://doi.org/10.1016/j.jtcvs.2017.04.052>