



Autopsy and Case Reports

ISSN: 2236-1960

Hospital Universitário da Universidade de São Paulo

Ferraz de Campos, Fernando Peixoto; Takayasu,
Vilma; Kim, Elizabeth Im Myung; Benvenuti, Luiz Alberto
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Autopsy and Case Reports, vol. 8, no. 2, e2018020, 2018, April-June
Hospital Universitário da Universidade de São Paulo

DOI: <https://doi.org/10.4322/acr.2018.020>

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Non-infectious thrombotic endocarditis

Fernando Peixoto Ferraz de Campos^a, Vilma Takayasu^a,
Elizabeth Im Myung Kim^a, Luiz Alberto Benvenuti^b

How to cite: Campos FPF, Takayasu V, Kim EIM, Benvenuti LA. Non-infectious thrombotic endocarditis. Autops Case Rep [Internet]. 2018;8(2):e2018020. <http://dx.doi.org/10.4322/acr.2018.020>

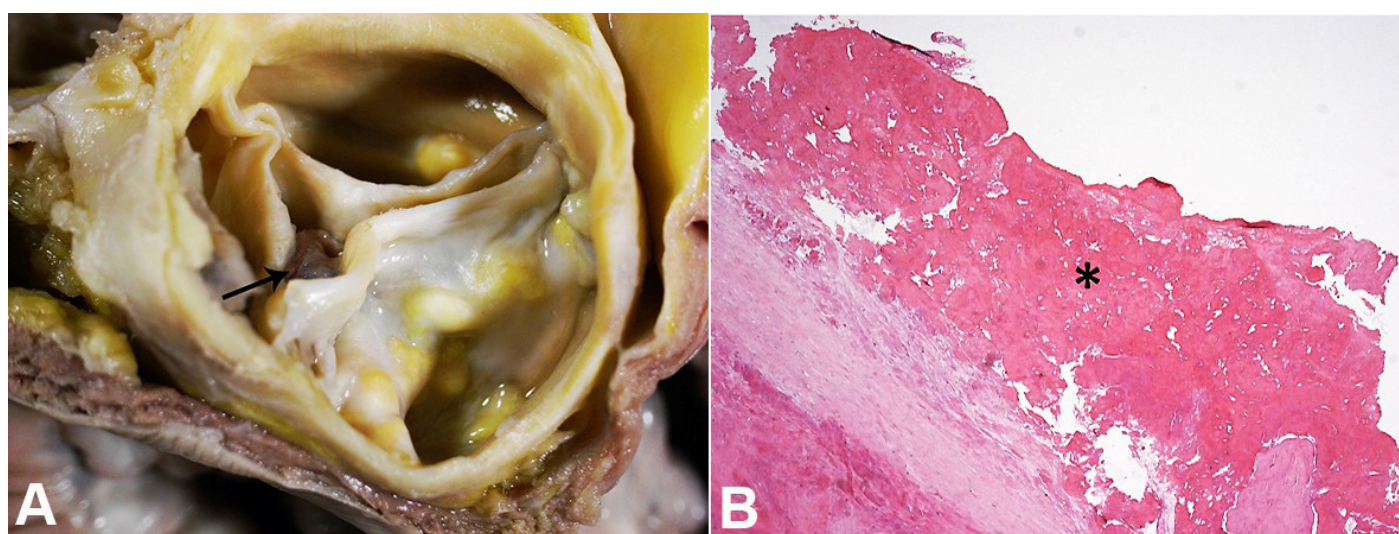


Figure 1. A- Gross view of the three-leaflet aortic valve showing calcific aortic stenosis and vegetation (arrow) measuring 9 × 6 mm attached to the ventricular surface of the one of the aortic cusps. Note the calcium nodules recovered by lipid deposits projecting outwards to the aortic surface and the thickened aortic leaflets; **B-** Histopathology of the vegetation (asterisk) disclosed fibrin with no inflammatory cells; the histochemical search for bacteria and fungi was negative.

In 1865, Armand Trousseau¹ first characterized the association of thromboembolic events and malignancy. Then, in 1888, Ziegler² identified vegetation in the cardiac valves, but this time they were associated with chronic inflammatory states. In 1920, Dr. Emanuel Libman recognized a subset of endocarditis, which he could not categorize according to the available classification, due to the lack of an apparent cause.³ Four years later, he and Dr. Benjamin Sacks² published

four cases of a peculiar valvular and mural cardiac vegetating lesion, which was examined clinically and during the postmortem examination, and proved to be free from demonstrable microorganisms that were first designated as “atypical verrucous endocarditis.”⁴ At that time, Libman and Sacks⁵ included this kind of endocarditis in the group of “indeterminate endocarditis,” which also included the so-called “terminal” or “cachectic” endocarditis. Originally

^a University of São Paulo (USP), Hospital Universitário, Internal Medicine Division. São Paulo, SP, Brazil.

^b University of São Paulo (USP), Heart Institute (InCor), Hospital das Clínicas da Faculdade de Medicina, Laboratory of Pathology. São Paulo, SP, Brazil.

described as valvular masses (mulberry-like clusters of verrucae) mostly involving the mitral and aortic valves, accompanied by leaflet thickening and valvular dysfunction—frequently stenosis—this entity was later named marantic (from the Greek—*marantikos*—which means “wasting away” due to the wasting state of most of the patients), and in 1936 Gross and Friedberg⁶ named the lesion non-bacterial thrombotic endocarditis (NBTE). However, considering the negative results in the pursuit of all infective agents, the lesion is more appropriately named “non-infectious thrombotic endocarditis.” Since the first descriptions, NBTE has been associated with malignancy, chronic inflammatory states (e.g. infectious diseases and autoimmune disorders), and, more recently, sepsis and burns.⁶⁻¹² The entity has been reported in a wide range of age, with no sex predilection. It involves any cardiac valve, but predominates in the aortic followed by the mitral valve.¹³ Vegetations generally are found in previously healthy valves and vary in size from microscopic to large, which can detach and cause distant infarctions. They occur characteristically in the coaptation edge of the leaflets and are constituted by degenerating platelets intermingled with fibrin. The local inflammatory response is feeble, which can explain the high frequency (average 42%) of detachment and embolization.^{7,13} The above figure also depicts the calcific aortic stenosis (CAS), indeed, the most common cause of aortic stenosis worldwide, and the second most frequent cardiovascular disease after coronary artery disease and hypertension. The prevalence of CAS is 0.4% in the general population and 1.7% among those over 65 years. In addition to age, the congenital abnormality (bicuspid valve), metabolic syndrome, and elevated plasma level of lipoprotein are risk factors for the development of CAS. Nearly half of the aortic valves that are surgically removed due to CAS, are bicuspid. This entity represents a progressive remodeling of the native valvular tissue into fibro-calcification. Initially, the valve becomes thickened or sclerotic (without hemodynamic derangement) but gradually over the years, the calcification superimposes, causing obstruction to the blood flow. Instead of a degenerative process, as previously considered, current histopathologic and clinical data suggest an active process involving lipoprotein deposition, chronic

inflammation, osteoblastic transition of the valve interstitial cells, and active leaflet calcification.¹⁴

The above image refers to an autopsied case of a 66-year-old woman hospitalized due to marked asthenia, dyspnea, edema, and jaundice. She had a past medical history of hypertension and hypothyroidism, and recently she had been diagnosed with a combined lesion of the aortic valve (predominantly stenosis) and heart failure. A laboratory work-up revealed a peak systolic pressure gradient across the aortic valve of 110 mm Hg, concentric ventricular hypertrophy, and a mobile and filamentary vegetation attached to the atrial surface of the mitral valve measuring 15 × 10 mm, elevated bilirubin, hepatic enzymes, and altered coagulation tests. The patient was screened for viral hepatitis and autoantibodies, which resulted in a positive ANA titer 1/320 speckled pattern. The patient was referred to a tertiary cardiology center with the working diagnosis of infective endocarditis. Blood cultures were repeatedly negative. The outcome was unfavorable with worsening of the respiratory function then death.

The autopsy showed an extensive venous thrombosis of the right iliac vein accompanied by great vessel pulmonary embolism with extensive infarction areas. The authors infer the possibility of a thrombophilia associated with an indeterminate autoimmune disease, which could explain the thromboembolic phenomena and the presence of NBTE. It is possible that the mitral valve's vegetation detected on the Doppler examination detached by the time the autopsy was done and could not be found.

Keywords

Endocarditis, Non-Infective; Pulmonary Embolism; Aortic Valve Stenosis; Heart Failure.

REFERENCES

1. Trousseau A. Clinique médicale de l'Hôtel-Dieu de Paris. Paris: Ballière; 1865.
2. Ziegler E. Ueber den Bau und die Entstehung der endocarditis chen Efflorescenzen. Ver Kong Inn Med. 1888;7:339-43.
3. Libman E. Section of medicine. BMJ. 1920;304(28):3014. PMID:20769818.
4. Libman E, Sacks B. A hitherto undescribed form of valvular and mural endocarditis. Arch Intern Med

- (Chic). 1924;33(6):701-33. <http://dx.doi.org/10.1001/archinte.1924.00110300044002>.
5. Xiushui R, Foster E, Ryan EW, Lange RA. Libman sacks endocarditis. New York: Medscape; 2018 [cited 2018 Mar 24]. Available from: <https://emedicine.medscape.com/article/155230-overview>
 6. Gross L, Friedberg CK. Nonbacterial thrombotic endocarditis. Classification and general description. Arch Intern Med (Chic). 1936;58(4):620-40. <http://dx.doi.org/10.1001/archinte.1936.00170140045004>.
 7. el-Shami K, Griffiths E, Streiff M. Nonbacterial thrombotic endocarditis in cancer patients: Pathogenesis, Diagnosis, and Treatment. Oncologist. 2007;12(5):518-23. <http://dx.doi.org/10.1634/theoncologist.12-5-518>. PMID:17522239.
 8. Ferrans VJ, Rodriguez ER. Cardiovascular lesions in collagen-vascular diseases. Heart Vessels Suppl. 1985;1(S1):256-61. <http://dx.doi.org/10.1007/BF02072405>. PMID:3916476.
 9. Wada H, Sase T, Yamaguchi M. Hypercoagulant states in malignant lymphoma. Exp Oncol. 2005;27(3):179-85. PMID:16244577.
 10. Hughson MD, McCarty GA, Sholer CM, Brumback RA. Thrombotic cerebral arteriopathy in patients with the antiphospholipid syndrome. Mod Pathol. 1993;6(6):644-53. PMID:8302806.
 11. Deppisch LM, Fayemi AO. Non-bacterial thrombotic endocarditis: Clinicopathologic correlations. Am Heart J. 1976;92(6):723-9. [http://dx.doi.org/10.1016/S0002-8703\(76\)80008-7](http://dx.doi.org/10.1016/S0002-8703(76)80008-7). PMID:998478.
 12. Sharma S, Mayberry JC, Deloughery TG, Mullins RJ. Fatal cerebroembolism from nonbacterial thrombotic endocarditis in a trauma patient: Case report and review. Mil Med. 2000;165(1):83-5. <http://dx.doi.org/10.1093/milmed/165.1.83>. PMID:10658436.
 13. Lopez JA, Ross RS, Fishbein MC, Siegel RJ. Nonbacterial thrombotic endocarditis: A review. Am Heart J. 1987;113(3):773-84. [http://dx.doi.org/10.1016/0002-8703\(87\)90719-8](http://dx.doi.org/10.1016/0002-8703(87)90719-8). PMID:3548296.
 14. Lindman BR, Clavel MA, Mathieu P, et al. Calcific aortic stenosis. Nat Rev Dis Primers. 2016;2:16006. <http://dx.doi.org/10.1038/nrdp.2016.6>. PMID:27188578.

Authors contributions: Takayasu V. and Kim EIM. were responsible for the patient's medical care and the report of the case. Campos FPF. wrote the manuscript together with Benvenuti LA., who was the Pathologist in charge of the autopsy examination.

Conflict of interest: None

Financial support: None

Submitted on: March, 24th, 2018

Correspondence

Fernando Peixoto Ferraz de Campos
Internal Medicine Division - Hospital Universitário (USP)
Av. Prof. Lineu Prestes 2565 - Butantã - São Paulo/SP, Brazil
CEP: 05508-000
Phone: +55 (11) 30919275
fpfcampos@gmail.com