Autopsy Case Reports

Image in Focus

Non-infectious thrombotic endocarditis

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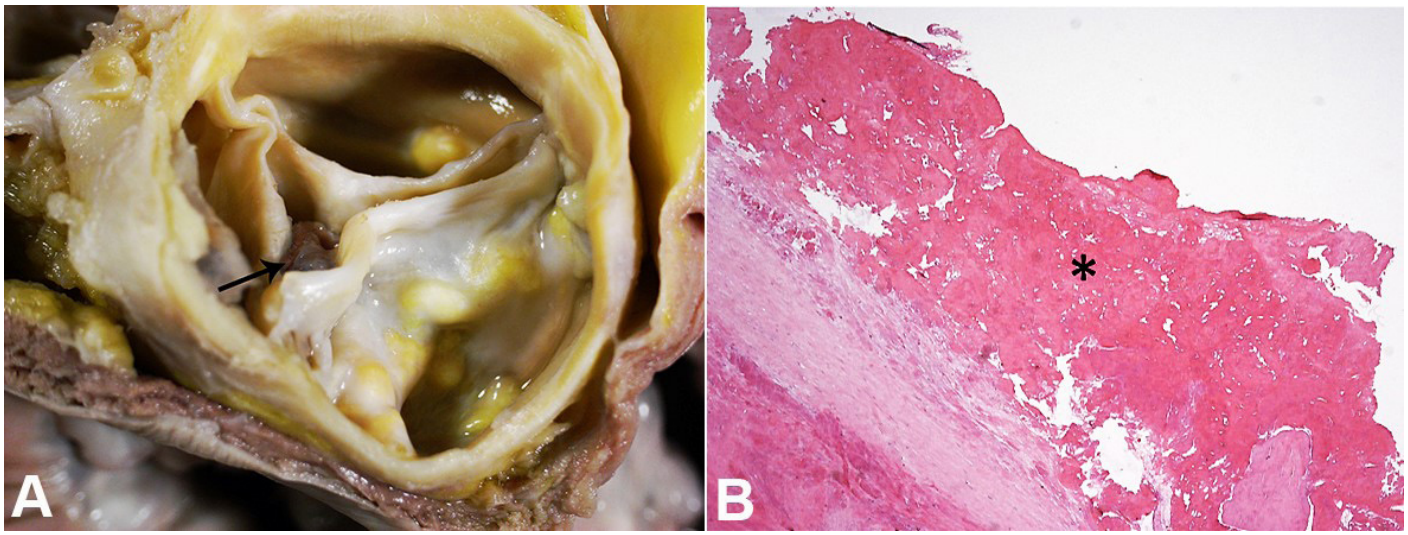

Figure 1. A- Gross view of the three-leaflet aortic valve showing calcific aortic stenosis and vegetation (arrow) measuring 9 × 6 mm attached to the ventricular surface of the one of the aortic cusps. Note the calcium nodules recovered by lipid deposits projecting outwards to the aortic surface and the 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 Trousseau[1] first characterized the association of thromboembolic events and malignancy. Then, in 1888, Ziegler[2] 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 Sacks[2] 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 Sacks[5] included this kind of endocarditis in the group of "indeterminate endocarditis," which also included the so-called "terminal" or "cachectic" endocarditis. Originally

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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 Friedberg[6] 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.

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