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CASE REPORT / OLGU SUNUMU

Non-bacterial thrombotic endocarditis in long-standing primary hypoparathyroidism: A case report

Uzun süreli primer hipoparatiroidide nonbakteriyel trombotik endokardit: Olgu sunumu

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ABSTRACT

Non-bacterial thrombotic endocarditis is a rare condition characterized by the formation of thrombotic vegetations on heart valve leaflets, leading to valvular dysfunction, heart failure and thromboembolic events. It is known to be associated with other diseases and some cases remain undiagnosed or can be diagnosed in the postmortem analysis. Surgical excision of the mass may be necessary to prevent further embolic events and other complications. In this article, we report a young patient with non-bacterial thrombotic endocarditis, whose medical history was significant for primary hypoparathyroidism and a positive family history of coagulation disorders.

Keywords: Calcium, endocarditis, hypoparathyroidism, non-infective, thromboembolism.

ÖZ

Nonbakteriyel trombotik endokardit, kalp kapağı yapraklarında trombotik vejetasyonların oluşmasıyla karakterize, kapak disfonksiyonu, kalp yetmezliği ve tromboembolik olaylara yol açan nadir bir durumdur. Diğer hastalıklar ile ilişkili olduğu bilinmektedir ve bazı olgular tanı almadan kalmakta veya ölüm sonrası tanılanabilmektedir. Daha ileri embolik olayları ve diğer komplikasyonları önlemek için kitlenin cerrahi olarak çıkarılması gerekebilir. Bu yazıda, tıbbi geçmişinde primer hipoparatiroidi ve ailesinde pozitif koagülasyon bozukluğu öyküsü olan nonbakteriyel trombotik endokarditli genç bir olgu sunuldu.

Anahtar sözcükler: Kalsiyum, endokardit, hipoparatiroidizm, non-enfektif, tromboembolizm,

An uncommon disease, non-bacterial thrombotic endocarditis (NBTE), is characterized by the development of sterile, non-inflamed fibrothrombotic vegetations on heart valve leaflets. Although the exact etiology of NBTE is unclear, predisposing factors include malignancies, antiphospholipid syndrome, endothelial injury, hypercoagulable state, and a variety of other illnesses.[1] If untreated, NBTE can result in valvular dysfunction, heart failure, and thromboembolic events caused by friable vegetations. Many cases of NBTE are missed or detected postmortem cases.[1]

In this article, we report a rare case of NBTE in a young patient with a long history of primary hypoparathyroidism and a family history of coagulation disorders.

CASE REPORT

A 29-year-old female patient presented to the emergency department with a complaint of increased weakness in the left arm for one week. The patient was conscious and oriented, pupils were isochoric, the left nasolabial fold was flattened, and the speech was normal. She had left upper limb hemiplegia and the left lower limb had 1/5 of the predicted muscle strength and a positive Babinski sign on the left foot. Sensory evaluation and deep tendon reflexes were

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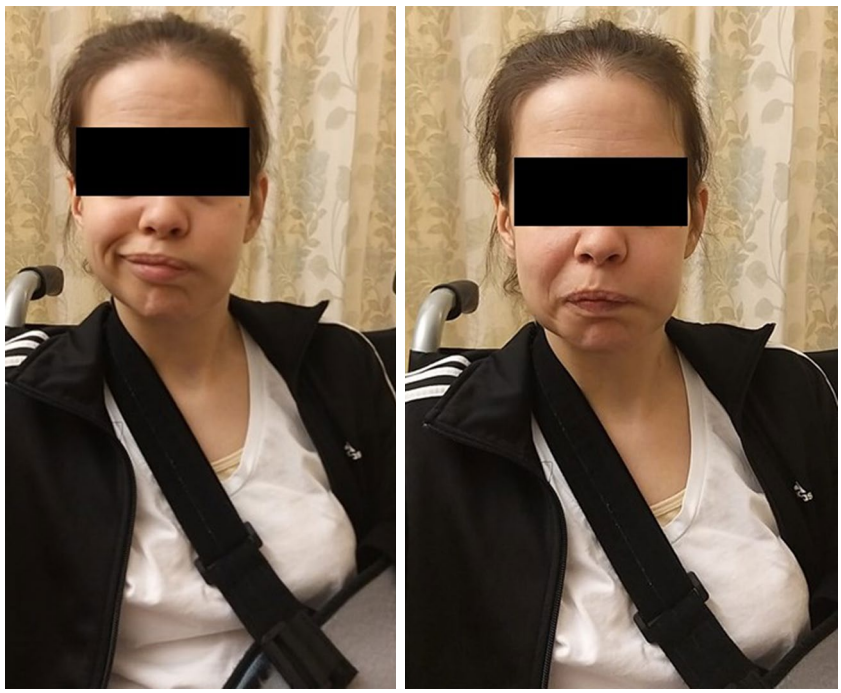


Figure 1. The initial presentation of the patient.

normal. Her arrival at the clinic is depicted in Figure 1. She was prescribed calcitriol due to a diagnosis of hypoparathyroidism at the age of 17. She had never smoked, never used oral contraceptives, and had no known condition predisposing to hypercoagulability. Her father experienced a clotting issue at the age of 40. Magnetic resonance imaging (MRI) with 3T diffusion-weighted imaging revealed a diffusion limitation at the right frontoparietotemporal region with a size of 70×45-mm area coherent with acute ischemia, which affected the basal ganglion and internal capsule. Cranial MRI angiography revealed a right middle cerebral artery (MCA) in the M1 segment occlusion-related acute infarction. The patient was admitted to the neurology service with acetylsalicylic acid of 300 mg once daily and enoxaparin sodium of 4,000 IU once daily. The patient had a normal sinus rhythm and the transthoracic echocardiography revealed vegetation on the mitral valve. On the same day, the patient developed fever (37.2°C); however, no growth was detected on blood culture. On the 48-h rhythm Holter, the patient was in sinus rhythm and no paroxysmal atrial fibrillation was detected. On transesophageal echocardiography, the size of the heart chambers and both ventricular functions were within normal limits. At the atrial side of the posterior leaflet

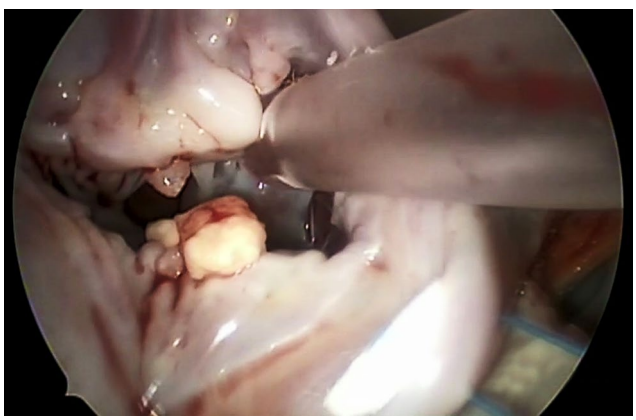
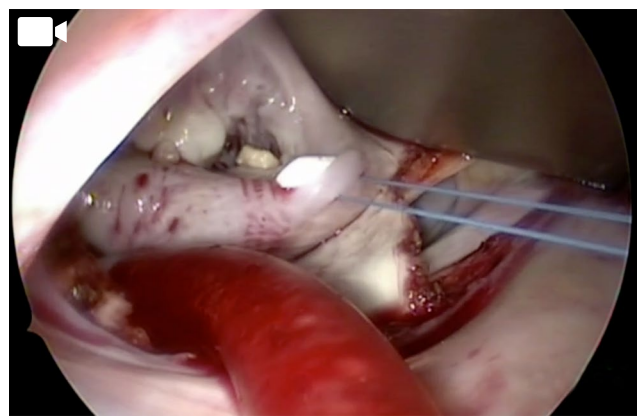


Figure 2. Endoscopic views of the masses on the atrial side of the mitral valve.



Video 1. Intraoperative video. Minimally invasive mass excision.

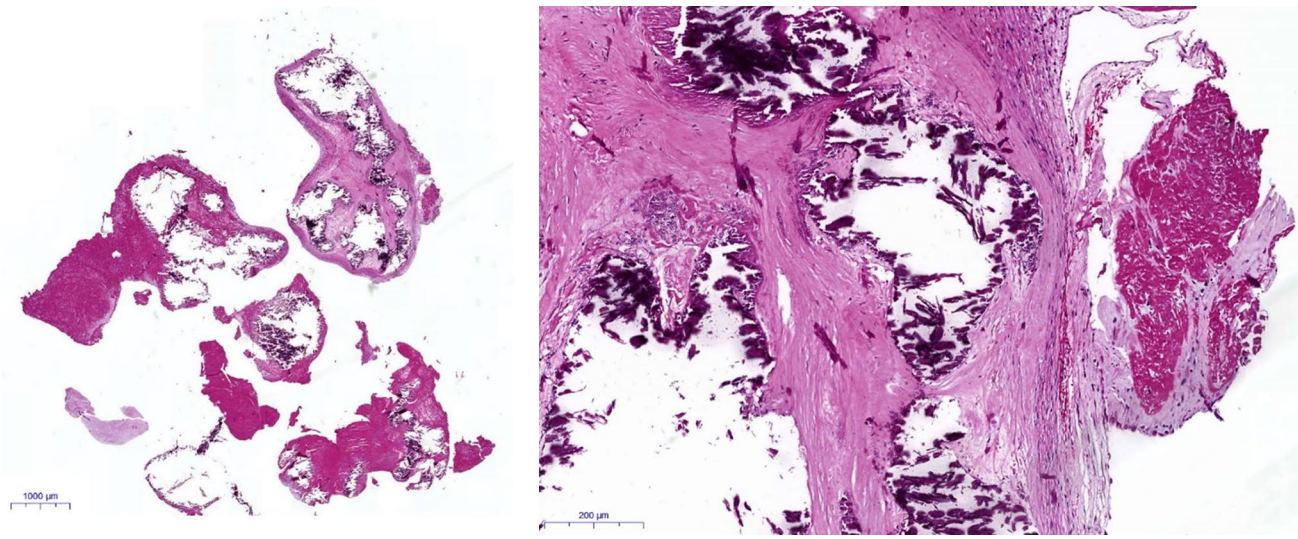


Figure 3. The microscopy of the extracted fibrinoid-thrombotic mass. (H&E, ×0.9 and ×7.8).

of the mitral valve, a 9-10×2-3-mm sized, mobile vegetation leading to 1-2+ mitral regurgitation was identified with calcification. In the genetic analysis, Factor V Leiden factor II variations were not detected; however, angiotensin-converting enzyme (ACE) gene D/D genotype was identified. The patient was consulted to the endocrinology department and the calcitriol dose was increased to 0.5 µg b.i.d. and calcium and vitamin D3 were added.

The patient received enoxaparin sodium, until the resection of the vegetation. Via right mini-thoracotomy, the masses (Figure 2), one at the anterior leaflet, and two at the posterior leaflet were minimally invasively resected (Video 1). Postoperatively, mitral valve functions returned to normal. The masses were 1×0, 7×0, and 5 mm, rough, white-yellow fibromyxoid tissue pieces that were calcified and organized fibrinoid vegetations (Figure 3). Gram staining revealed no leukocytes or microorganisms and the culture result was negative. Based on these findings, the preliminary diagnosis of NBTE was confirmed. Postoperatively, the patient was scheduled for 15 sessions of left upper and lower extremity range of motion, proprioceptive neuromuscular facilitation, and muscle strengthening exercises. Her neuromotor functions improved and she still continues to take calcitriol and calcium without any complaints.

DISCUSSION

Non-bacterial thrombotic endocarditis is a rare condition characterized by the formation of sterile thrombi on heart valves, without the presence of bacterial growth in blood cultures. Although the pathogenesis of NBTE has not been fully understood, it is believed to be caused by the migration of inflammatory mononuclear cells to form thrombi containing platelets, fibrin, and immune complexes.[1] The most common symptoms of NBTE are caused by systemic thromboembolic events, such as stroke, which occurs in up to 50% of patients.[2]

The diagnosis of NBTE can be difficult, as it often presents with similar symptoms to other conditions such as infective endocarditis and atherosclerotic disease. Transesophageal echocardiography can be used to evaluate valve lesions and determine the underlying etiology, if there is a clinical suspicion.[1] However, imaging tools are unable to distinguish between sterile and infective vegetations. A definitive diagnosis can be made through a histological examination.[3]

There is a known association between NBTE and hypercoagulable states, such as primary antiphospholipid syndrome, malignancy, burns, and sepsis.[2] The antinuclear antibodies (ANA), extractable nuclear antigens (ENA), anti-double stranded deoxyribonucleic acid (anti-dsDNA), rheumatoid factor, and anticardiolipin antibodies were also investigated to rule out any underlying autoimmune disease.[1] To assess hypercoagulable state, an extended coagulation screening and clotting factor assay should be performed, including prothrombin time, partial thromboplastin time, fibrinogen, thrombin time, D-dimer, and cross-linked fibrin degradation products.[1] In our case, the patient

had a history of thrombosis in the family and was found to have the ACE gene D/D genotype, which is associated with an increased risk of thrombotic events.[4] A total body computed tomography (CT) scan revealed no evidence of cancer.

Hypercalcemia is also thought to be a potential contributing factor to NBTE. Calcium is known to cause vasoconstriction, activate multiple clotting factors, and increase platelet aggregation, all of which can lead to thrombosis.[5] The patient had hypoparathyroidism and received calcium and vitamin D supplements. Calcium therapy itself, however, is not thought to predispose thromboembolism.[6]

The primary treatment for NBTE is addressing the underlying condition. Long-term anticoagulation therapy, specifically unfractionated or low-molecular-weight heparin, has shown efficacy and low risk of intracerebral hemorrhage in previous studies.[1] Frequent monitoring is necessary to rule out recurrent embolism and ensure an adequate anticoagulation. Factors such as the patient's age, comorbidities, valvular dysfunction, and recurrent thromboembolic events should be considered for making decision for surgery. Our patient underwent surgery due to recurrent embolism, despite anticoagulation and an unknown etiology.

In conclusion, non-bacterial thrombotic endocarditis is a rare condition and difficult to diagnose due to its similarity to other conditions. The presence of hypercoagulable state and calcium disorders should be considered as potential contributing factors. Further research is needed to better understand the pathogenesis of non-bacterial thrombotic endocarditis and to develop effective diagnostic and treatment strategies.

Patient Consent for Publication: A written informed consent was obtained from the patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Idea/concept, control/supervision: Ş.Ş., C.A.; Design, data collection and/or processing: T.E.; Analysis and/or interpretation, literature review, writing the article: T.E., N.D.; Critical review, references and fundings: G.A.

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