Native Aortic Valve Endocarditis in A Patient with Glucose-6-Phosphate Dehydrogenase Deficiency

GLUKOZ-6-FOSFAT DEHİDROGENAZ ENZİM EKSİKLİĞİ OLAN HASTADA NATİV AORT KAPAK ENDOKARDİTİ

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Abstract

Fatal opportunistic infections are seen in some variants of glucose-6-phosphate dehydrogenase deficiency and the responsible mechanism has been reported to be the failure of oxygen dependent bacterial lysis resulting from NADPH deficiency of granulocytes, as seen in the chronic granulomatous disease. However, to date, there is no similar case reported in the medical literature regarding the development of infective endocarditis on a native valve in a patient with glucose-6-phosphate dehydrogenase deficiency. In this paper, we report a native valve infective endocarditis in a patient with glucose-6-phosphate dehydrogenase deficiency.

Key Words: Glucose-6-phosphate dehydrogenase deficiency; endocarditis

Özet

Glukoz-6-fosfat dehidrogenez enzim eksikliğinin bazı varyantlarında fatal fırsatçı infeksiyonların görüldüğü bildirilmiştir ve mekanizmanın bir başka enzim eksikliği sonucu oluşan kronik granülomatöz hastalıkta olduğu gibi granülositlerde oksijen bağımlı bakteri lizisinin NADPH eksikliğinden dolayı gerçekleştirilememesi olarak ileri sürülmüştür. Fakat nativ kapakta infektif endokardit gelişen glukoz-6-fosfat dehidrogenez hastalıklı olgu literatürde bildirilmemiştir. Bu yazıda herhangi bir kapak hastalığı olmadan enfeksiyona eğilimin artması nedeniyle gelişen aort kapak enfektif endokardit olgusu sunulmuştur.

Anahtar Kelimeler: Glukoz-6-dehidrogenaz enzim eksikliği; endokardit

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The hexos monophosphate pathway (HMP) plays a key role in the protection of erythrocytes against oxidative stress. HMP shunt is the only way for the production of NADPH, as erythrocytes lack nuclear material and mitochondria. NADPH, which is formed by the activity of glucose-6-phosphate dehydrogenase enzyme, plays a role in the regeneration of glutathione which protects membrane phospholipids against oxygen radicals that are produced when erythrocytes are exposed to infection, acidosis and to some drugs. NADPH acts as an important cofactor that plays a role in oxygen dependent phagocytosis of granulocytes and hence its deficiency can lead to serious oppurtunistic infections.[1]

Case Report

A 17-year-old male was admitted to our center with fever and shivering. He had a history of jaundice and fatigue after aspirine ingestion at the age of 7 years. In the pediatric clinic where he was investigated, a diagnosis of glucose-6-phoshate dehydrogenase deficiency was established. The patient underwent a second hemolytic attack 4 years later and was asymptomatic since then. On physical examination, a 2/6 systolic murmur was audible at aortic region and splenomegaly were detected. He had deep anemia (Hb: 6.9 g/dL), leucocytosis and increased erythrocyte sedimentation rate (ESR: 72 mm/h). On blood cultures, enterococci resistant to gentamicin

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and sensitive to ampicillin, teicoplanin and vancomycin was grown.

Transthoracic echocardiography revealed a 3 x 0.6 cm mass on ventricular side of aortic valve and moderate to severe aortic regurgitation (Figure 1). With the diagnosis of infective endocarditis, intravenous 12g/24 hours ampicillin was continuously initiated (12 g per 24 h iv 6 equally divided). Because the patient with native valve endocarditis had destruction in his aortic valve, his treatment with antibiotics was extended to four weeks before and two weeks after the operation. During antibiotherapy, the clinical and laboratory symptoms improved.

The control echocardiography which was applied four weeks later showed the persistence of aortic vegetation with a diameter of 1.2 cm and moderate aortic regurgitation and hence aortic valve replacement was decided. Patients with a vegetation diameter greater than 10 mm have a significantly higher incidence of embolization and have poor outcomes on medical treatment alone.[2]

In the operation, a stentless CryoLife-O'Brian no: 21 bioprosthetic valve (CryoLife, Inc., Kennesaw, GA) was implanted in order to reduce the mechanical trauma over the succeptible erythrocytes so as to minimalise hemolysis. The native valve underwent microbiological and pathological examinations (Figure 2) and enterococci had grown on cultures. On pathological examination;

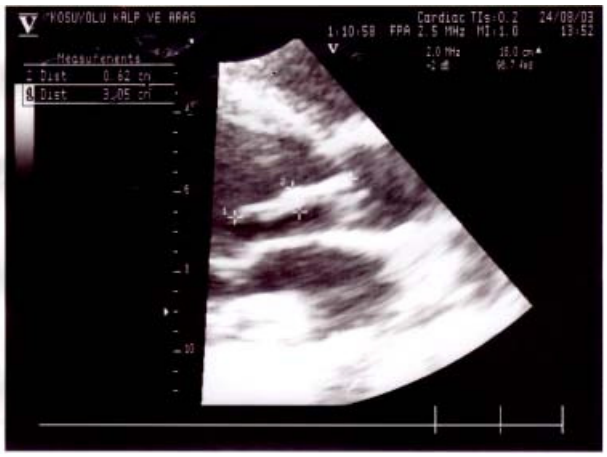

Figure 1. Parasternal long axis view showing the 3.1 x 0.6 cm mobile mass on the left ventricular site of the aortic valve.

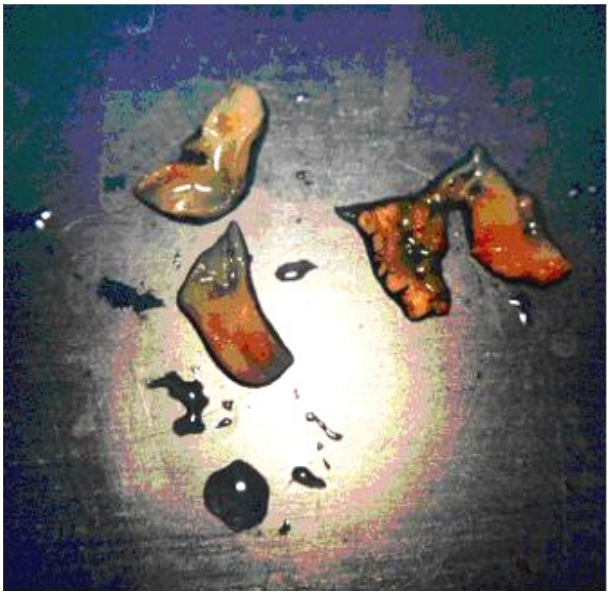

Figure 2. Macroscobic view of the resected material demonstrating focal myxomatous dejenaration, fibrous exudation, and dystrophic calcification.

fibrosis, focal myxomatous degeneration, dystrophic calcification, small foci of microabscesess in fibropurulent exudates with surrounding active inflammatory granulation tissue adherant to valve and acute and chronic nonspecific inflammation were detected (Figure 3).

There was no sign of Aschoff nodule. The patient was discharged on the 7th postoperative day without complication. On 6th and 12th months follow-up the prosthetic valve was normofunctional and there was no biochemical sign of active hemolysis, however the patient died due to recurrent infective endocarditis of the bioprosthetic aortic valve and subsequent acute renal failure on the postoperative 15th month.

Discussion

The hexos monophosphate pathway (HMP) is the only source of NADPH in mitochondria deficient erythrocytes. NADPH, which is formed by the activity of glucose-6-phosphate dehydrogenase (G6PD) enzyme is essential for the integrity of erythrocyte membrane by increasing the levels of glutathione that protects the cells against oxidative stress. Individuals with an inherited defect in HMP are unable to maintain an adequate level of reduced glutathione. As a result, the sulfhydryl groups of

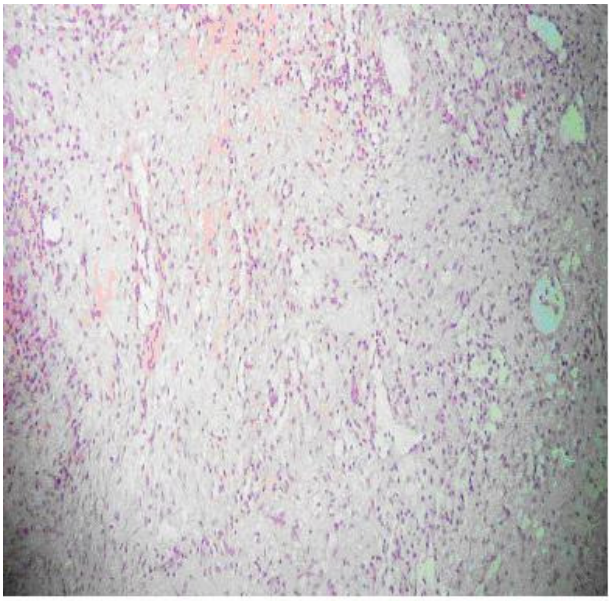

Figure 3. Histopathological examination of the resected material demonstrating small foci of microabscesses in fibrinopurulent exudate surrounded by active inflammatory granulation tissue that adheres to valvular tissue and lack of Aschoff nodules.

hemoglobin become oxidized and hemolysis occurs.[3] Among the congenital defects, G6PD deficiency is by far the most common one and over 400 variants are described.

The G6PD gene is located on the X chromosome and thus the G6PD deficiency is seen in hemizygous males. The G6PD deficiency is restricted to erythrocytes, because they lack the ability of protein synthesis after being released from the bone marrow, thus the instability of G6PD is seen first in erythrocytes.[4]

Severe G6PD deficiency may cause symptoms of chronic granulomatous disease (CGD) such as recurrent bacterial and fungal infections.[4–7] Normally, CGD occurs because of a defect in one of the constituents of NADPH oxidase. This enzyme catalyzes the superoxide formation in phagocytes. This superoxide production is used by the phagocytes to kill the microorganisms. In G6PD deficiency, phagocytosis is defective and this is the reason for the increased susceptibility to infections in these patients.

Our patient had a diagnosis of G6PD deficiency. As mentioned, the histopathological examination of the resected material revealed no underlying predisposing valvular disease. A G6PD deficiency case with a native valve endocarditis as observed in our patient has not been reported before. Because of the risk of embolization of the remaining vegetation and the aortic regurgitation, the patient underwent aortic valve surgery. In operation, a stentless bioprosthetic valve implantation was preferred in an aim to decrease hemolysis.

Homograft and valve replacement are preferred because the risk of reinfection following native or prosthetic valve endocarditis is lower.[8] The homograft valves are taken out 24 hours after the death of the donor and they are sterilised in antibiotics and cryoprespitant. The aorta root with aortic valve until the sinotubular junction is removed from the donor to be placed in the left ventricular outflow track. Because of the area that the annulus takes in, the homograft placed at the outflow track, leads to a smaller valve area and faster antegrade velocity. In order to reduce the mechanical trauma which will cause an intravascular hemolysis in our patient due to his blood disease, a stentless bioprosthetic valve with has a larger surface area has been used. This strategy seemed to be beneficial during the 12 months follow-up without any clinical or biochemical evidence of hemolysis.

This case states that the patients with G6PD deficiency may benefit from infective endocarditis prophylaxis and also that the bioprosthetic valves can be used in patients with a high risk of hemolysis. This subject merits further investigation.

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