

## Aspergillus endocarditis in a patient with acute lymphoblastic leukemia

### Akut lenfoblastik lösemili bir hastada aspergillus endokarditi

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*Aspergillus* endocarditis is a life-threatening condition. Establishment of the diagnosis and treatment remain highly challenging. *Aspergillus* endocarditis should be suspected in immunocompromised patients with negative blood cultures and vegetation on echocardiography. Definitive diagnosis is based on tissue histology and culture. The best treatment approach requires aggressive surgical debridement in combination with prolonged antifungal therapy. In this article, we report a 5.5-year-old boy with acute lymphoblastic leukemia in whom immunosuppression-related *Aspergillus* endocarditis developed. The patient underwent a Ross operation and excision of a large vegetation in the left ventricular outflow tract. However, he died due to possible intracerebral abscesses during follow-up.

**Key words:** Aspergilloma; *Aspergillus* endocarditis; infective endocarditis; Ross procedure.

*Aspergillus* has the ability to cause severe invasive infections in almost every major organ system, but it commonly infects immunocompromised hosts in the respiratory tract.<sup>[1]</sup> *Aspergillus* endocarditis (AE) is very rare and represents less than 1% of all cases of infective endocarditis.<sup>[2]</sup> Patients with conditions such as underlying cardiac abnormalities, prosthetic heart valves, malignancy, indwelling central venous catheters, prolonged use of broad-spectrum antibiotics, and intravenous drug use are predisposed to AE.<sup>[1,3]</sup> *Aspergillus* endocarditis is one of the most severe manifestations of invasive aspergillosis

*Aspergillus* endokarditi hayati tehlike oluşturan bir durumdur. Tanı ve tedavisi oldukça zordur. İmmün sistemi baskılanmış hastalarda alınan kan kültürlerinin negatif olması ve ekokardiyografide vejetasyon görülmesi durumunda *Aspergillus* endokarditinden şüphelenilmelidir. Bu hastalarda kesin tanı, doku histolojisi ve kültürü ile yapılır. Tedavide en iyi yaklaşım agresif cerrahi debridmanı ile birlikte uzun süreli antifungal tedavi uygulanmasıdır. Bu makalede immün yetersizlik nedeniyle *Aspergillus* endokarditi gelişen akut lenfoblastik lösemili 5.5 yaşında bir erkek olgu sunuldu. Hastaya Ross ameliyatı ile birlikte sol ventrikül çıkım yolundaki geniş vejetasyonun ekzizyonu uygulandı. Ancak, takip süresinde gelişen muhtemel intraserebral apselere bağlı olarak hasta kaybedildi.

**Anahtar sözcükler:** Aspergilloma; *Aspergillus* endokarditi; enfektif endokardit; Ross işlemi.

with an overall mortality rate of close to 70%.<sup>[4]</sup> Furthermore, the prevalence of AE is increasing in the hospital population.<sup>[5]</sup> Herein, we present a case of *Aspergillus fumigatus* endocarditis associated with immunosuppression in a patient with an underlying hematological malignancy and also describe the treatment modality that was used for the patient.

### CASE REPORT

A five and a half-year-old male who was referred to our clinic for the excision of a large aortic vegetation presented with left hemiplegia, left facial paralysis,



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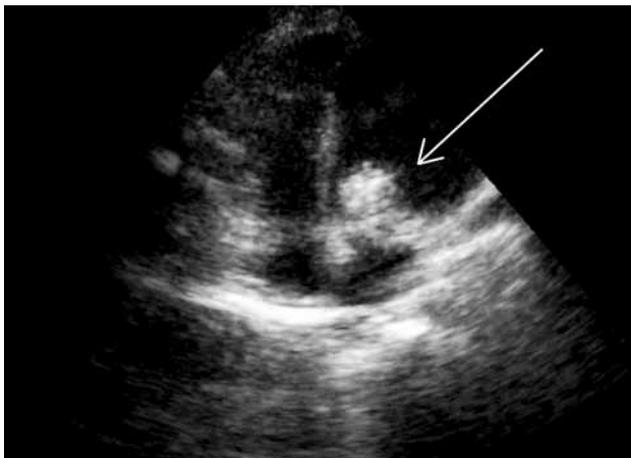
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keratitis, and asthma. He had been diagnosed with acute lymphoblastic leukemia (ALL) and had received several rounds of chemotherapy. Cranial magnetic resonance imaging (MRI) investigations had previously revealed multiple intracerebral abscesses, and the patient had undergone surgery to drain the worst ones. Fluid specimens were obtained at that time for microbiological cultures. However, the cultures failed to demonstrate the presence of any bacterial or fungal colonization. A repeat MRI investigation had revealed the persistence and/or progression of intracerebral abscesses; therefore the neurosurgeons had scheduled the patient for a new surgical procedure. Prior to the surgery, routine echocardiography had identified a large aortic vegetation which led to the diagnosis of infective endocarditis. This finding offered the most likely explanation for the source of the multiple intracranial abscesses. Empirical drug therapy for culture-negative endocarditis with intravenous meropenem (3x800 mg), vancomycin (4x240 mg), trimethoprim-sulphamethoxazole (4x80 mg), and caspofungin (1x40 mg) was then initiated.

The patient was then admitted to our facility to undergo the recommended surgical procedure. His temperature was 36.8 °C, and he had a pulse rate of 106 beats per minute, blood pressure of 90/50 mmHg, and a respiratory rate of 26 breaths per minute. His heart sounds were regular, and a grade 2/6 systolic murmur was audible on auscultation with a loud S1 and split S2. In addition, no evidence of peripheral or central cyanosis, clubbing, or peripheral stigmata of endocarditis was found during the physical examination. However, left hemiplegia and left facial paralysis were present.

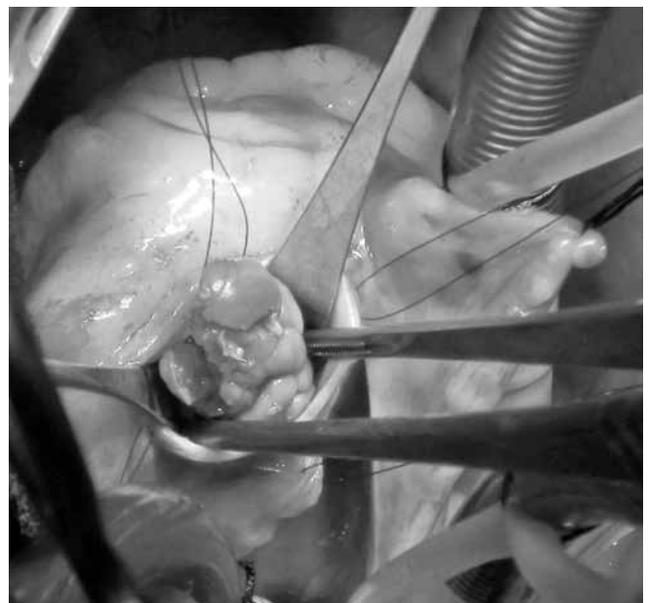


**Figure 1.** A transthoracic echocardiogram demonstrating a 19x14 mm vegetation in the subaortic position.

A laboratory evaluation revealed normal chemistry and liver enzyme levels. The white blood cell count was slightly elevated ( $12.7 \times 10^9$  cells/l) and demonstrated a left shift (78% neutrophils and 16% bands). Low hemoglobin (9.8 g/dl) and platelets ( $5 \times 10^4$  ml) were noted, and the C-reactive protein was negative. A chest X-ray and an electrocardiogram also demonstrated no abnormalities. Three sets of blood cultures were obtained from the patient at that time.

A transthoracic echocardiogram revealed a 19x14 mm vegetation on the aortic valve in the subaortic position which was causing left ventricular outflow obstruction (Figure 1). Color Doppler echocardiography revealed moderate aortic stenosis with a 40 mmHg systolic gradient. Additionally, the patient's ejection fraction (EF) was 59.6% and his fractional shortening was 30.8%.

The patient underwent surgical extraction of the large aortic vegetation, and a solitary mass measuring approximately 15x20 mm was observed in the subaortic position intraoperatively (Figure 2). The stiff mass was tightly adhered to the highly degenerated left coronary cusp and could not be resected without excising this. Consequently, the Ross procedure was performed in which the excised aortic valve was replaced with an autologous pulmonary root. This was followed by the insertion of a 19 mm xenograft valve. The patient was taken to the intensive care unit with stable hemodynamics and no inotropic support. He was extubated on the first postoperative



**Figure 2.** A solitary mass measuring approximately 15x20 mm was observed in the left ventricular outflow tract.



**Figure 3.** *Aspergillus fumigatus* colonies on a Sabouraud dextrose agar plate inoculated with the patient's excised vegetation.

day and began oral feeding. Intravenous antibiotic and antifungal therapy was begun with the same protocol that had been performed preoperatively. The early postoperative period was uneventful, and all blood cultures remained negative. At the end of the second postoperative day, a generalized convulsion began which was followed by pulmonary arrest and bradycardia. Resuscitation was initiated, but the patient failed to respond and died. A culture of the intraoperatively excised mass grew pure cultures of *Aspergillus fumigatus* (Figure 3).

## DISCUSSION

*Aspergillus* is the source of approximately 20-30% of all fungal endocarditis cases.<sup>[3,5]</sup> The main clinical features associated with AE are fever, a changing heart murmur, the embolization of the major arterial vessels, a large valve vegetation, and negative blood culture results.<sup>[6]</sup> Most patients with AE are male and possess a predisposing condition.<sup>[3]</sup> However, among children, congenital heart disease is the most common risk factor.<sup>[7]</sup> The diagnosis of AE requires a high index of suspicion. Barst et al.<sup>[8]</sup> reported that the diagnosis had been established postmortem in 21% of reported cases, but the blood cultures were usually negative and the vegetations were frequently large (96%). Optimal management of AE remains a challenging issue, and a combined medical and surgical approach is normally proposed.<sup>[9]</sup> However, despite advances in surgical procedures and the development of new antifungal agents, the mortality rate remains dramatically high. Two cases of AE were reported in a recent paper by Nikolousis and Velangi.<sup>[10]</sup> In the first case, liposomal amphotericin B along with voriconazole resolved the AE in a

month without the need for surgical intervention, but the second case required urgent resection of the Aspergilloma together with a combined antifungal therapy due to the cardiocirculatory compromise. Despite this patient's need for intensive care treatment, the outcome was good.

The major predisposing conditions exhibited by our patient were the evolving ALL and the central venous catheter used for his chemotherapy treatments. He had received several doses of immunosuppressive therapy and did not have congenital heart disease.

## Conclusion

The treatment modality for patients with infective endocarditis due to *Aspergillus* includes surgery as an adjunct to medical treatment. The radical debridement of the necrotic tissue combined with valve replacement using autologous tissue is the preferred surgical procedure. However, the results have been disappointing with only a limited number of reported survivors in the literature. Therefore, a multidisciplinary approach is warranted for the primary prevention of the disease.

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