Fungal Endocarditis: Review of Our Cases over a Four-Year Period

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Abstract

Over a 4-year period, we studied six cases of fungal endocarditis, four of which were caused by *Aspergillus sp.* and the other two were candidal in origin. Both sides of the heart showed involvement by these infections. The vegetations of infective endocarditis tend to vary in size, but fungal lesions are often large. Our youngest patient was four months old and the oldest one was 62 years old. A high index of clinical suspicion, together with histopathological and microbiological studies, can be used as tools to diagnose and treat such patients in due course. It is important to send fresh specimens for tissue culture studies in sterile normal saline and not in fixatives such as formaldehyde. Pathologically, not only are the special staining methods such as Periodic acid-Schiff useful in the demonstration of fungal elements in tissue or vegetation sections, but also the routine hematoxylin and eosin stain is capable of showing these structures clearly ***(Iranian Heart Journal 2010; 11 (1):34-37).***

Key words: endocarditis ■ fungus ■ Candida ■ Aspergillus

Apergillus endocarditis is rare in patients who have a normal immune system. Therefore, the most significant factor that alters the host defense is the surgical operation itself.

Aspergillosis may become symptomatically evident even months after the surgical operation, while blood culture studies are negative in most if not all such cases.[1]

Embolic involvement of the legs is a relatively uncommon occurrence as a presenting sign; however, it has been previously reported by other authors.[2]

A yet rarer presentation of candidal endocarditis is a cardiac mass resembling a tumor.

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chemotherapy.

Case reports

I. A 49 year-old man was referred to us with fever, dyspnea, malaise, anorexia, weight loss and left leg pain of three months' duration.

He had undergone coronary artery bypass grafting some 2.5 years previously. Also, there were two episodes of arterial embolic events, for which he had received vascular surgery in another center, but no definite pathology or culture results were obtained.

His physical findings included a low grade fever and a holosystolic cardiac murmur.

The laboratory results showed a hemoglobin level of 9.5g/dL, leukocytosis, eosinophilia, an increased erythrocyte sedimentation rate (ESR) as well as a positive C-reactive protein test. All the routine blood culture results were negative.

Echocardiography revealed a bulky mobile vegetation on the aortic valve with ring abscess formation and valvular regurgitation.

The patient underwent a surgery, during which the vegetation was removed together with the aortic valve. Multiple soft and fragile pieces of vegetation were delivered to the pathology ward, and histopathology examinations showed acute-angle branching septate hyphae consistent with *Aspergillus sp*. The vegetations were also sent for culture studies, which further substantiated our pathological findings.

Despite the extensive antifungal treatment, the patient's condition deteriorated and a second operation to replace the implanted prosthetic valve was performed. Seven weeks after the second operation, the endocarditis still persisted and the patient finally died in an abrupt episode of sudden and severe chest pain. In the post-mortem examination, valve thickening, ring abscess formation, and bulky masses of vegetation were the striking features.

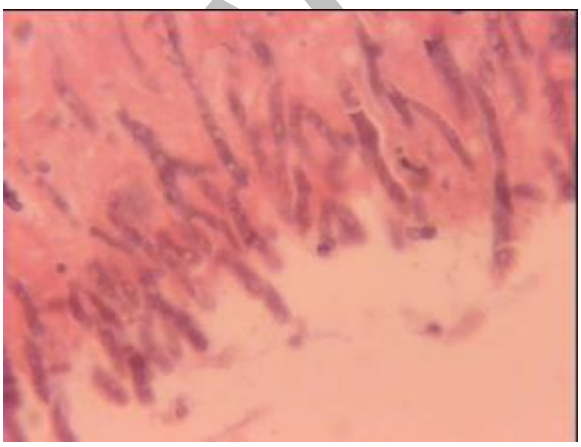

Fig. 1. Acute-angle branching septate hyphae, consistent with *Aspergillus sp* (H & E, X 400).

II. A 4 month-old male infant who had a history of low birth weight with several hospital admissions elsewhere was referred to our hospital. In his past medical history, prior instances of umbilical and femoral catheterization were of note.

He was mildly anemic, and his blood culture results were positive for *Candida sp*.

Echocardiography showed a bulky mass in the right atrium as well as a membranous VSD with a patent ductus arteriosus (PDA). Workup of the patient for possible immune deficiency states proved unyielding. The infant underwent an operation in which his right atrial vegetation was removed and the defects were repaired.

Histopathological examinations of the mass, which was first presumed to be tumoral, revealed yeast forms and pseudohyphae, consistent with Candida sp. The post-operative course was uneventful.

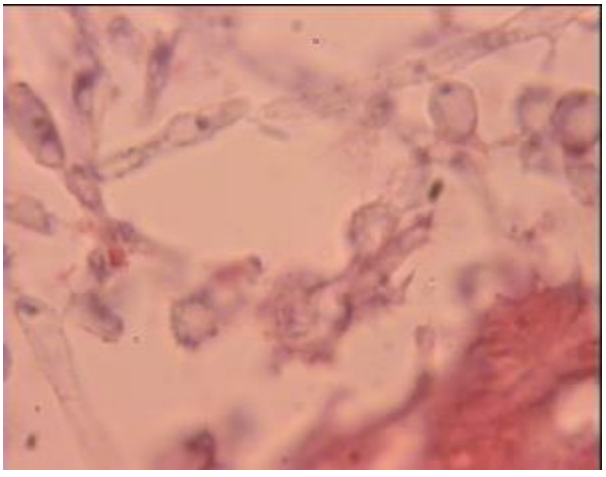

Fig. 2. Multiple yeast forms and pseudohyphae, consistent with *Candida sp* (H & E, X 400).

III. A 62 year-old woman who had a prior aortic valve replacement presented with vegetations on her prosthetic valve. The patient underwent an operation and received antifungal therapy. In this case again, the histopathological and tissue culture findings were compatible and showed *Aspergillus sp.* Fortunately, she left the hospital in good clinical condition, and her follow-up has not so far been indicative of recurrence of the lesion.

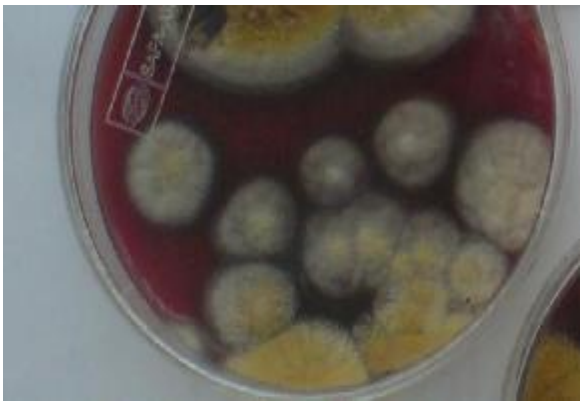

Fig. 3. Multiple fungal colonies that grew after incubation on sheep blood agar.

IV. A 3 year-old girl who was receiving chemotherapy for acute lymphoblastic leukemia (ALL) was referred to our center with signs and symptoms of endocarditis.
Further workup of the patient revealed vegetations on her tricuspid valve.
The lesion was excised and the vegetation fragments were sent to the pathology and microbiology laboratories. Again, we recovered fungal elements that were consistent with *Candida albicans*. The patient was discharged after the surgical operation.

V**.** A 2 year-old girl who had undergone a total correction operation for tetralogy of Fallot some four months before her recent symptoms was found to have huge vegetations on the anterior leaflet of the tricuspid valve with no response to antibiotics earlier in her course.
She died a few hours post-operatively. No tissue sample was sent to the microbiology laboratory for culture studies, but the main lesion proved to be Aspergillus endocarditis pathologically.
VI**.** A 37 year-old man who had undergone aortic and mitral valve replacement about a month before was referred to our hospital. Echocardiography showed bulky vegetations on the left-sided cardiac valves.
As a high index of suspicion existed clinically, antifungal therapy was begun immediately. Not long after, the patient showed signs and symptoms of ischemia in his lower limbs. Emboli were excised from the bilateral femoral arteries. Histological examinations showed fungal elements in the clots removed, but again no sample was sent for tissue culture.
Deterioration of the patient's condition prompted a surgical intervention to remove the huge vegetation and the prosthetic aortic valve. This time again, we found fungi that were compatible with *Aspergillus sp*. This was a finding also proved by culture studies.

Discussion

The vegetations of infective endocarditis tend to vary in size on heart valves, with fungal lesions often causing large masses.[1] Aspergillus endocarditis is rare in those who have a normal immune system. Therefore, the most significant factor that alters the host defense is the surgical operation itself.[2,5]
Fungi cause up to 12% of infectious endocarditis cases in children.[4]
Aspergillosis may become symptomatically evident even months after the surgical operation, while blood culture studies are negative in most, if not all, such cases.
Embolic involvement of the legs is a relatively uncommon occurrence as a presenting sign; it has, however, been previously reported by other authors.[2,6]
A yet rarer presentation of candidal endocarditis is a cardiac mass resembling a tumor.
In infants and neonates, prenatal and postnatal factors are as important in terms of pathogenesis as the immune deficiency states such as cancer chemotherapy.[3]
The mortality rate is 75-90%. The principal reason is that it is difficult to make the diagnosis, with the other reasons being the lack of effective antifungal drugs or the need for surgical intervention, not to mention the presence of underlying or predisposing conditions.[4]
Over a 4-year period, we studied six cases of fungal endocarditis, four of which were caused by *Aspergillus sp* and the remaining two were candidal. In our patients, both sides of the heart showed involvement by these infections. Our youngest patient was four months old and the oldest one was 62 years old.
A high index of clinical suspicion together with histopathological and microbiological studies can be used as tools to diagnose and treat the patients in due course. What is important is to send fresh specimens for tissue culture studies in sterile normal saline and

not in fixatives such as formaldehyde. Pathologically, not only are the special staining methods such as Periodic acid-Schiff (PAS) useful in the demonstration of fungal elements in tissue or vegetation sections, but the routine hematoxylin and eosin stain is also capable of showing their structures.

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