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Review

Aspergillus endocarditis: a review of the literature

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SUMMARY

We present a case of cardiac device-related Aspergillus endocarditis in a patient with a pacemaker and an allogeneic bone marrow transplant to segue into a review of the Aspergillus endocarditis literature. Aspergillus endocarditis should be suspected in patients with underlying immunosuppression, negative cultures, and a vegetation on echocardiography. Diagnosis ultimately requires confirmation by tissue histology and culture. The optimal treatment approach often requires aggressive surgical debridement in conjunction with prolonged antifungal therapy.

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1. Introduction

Aspergillus species have the ability to cause severe invasive infections in almost every major organ system, including, but not limited to, the sinuses and lungs, heart, and central nervous system. Aspergillus most commonly infects immunocompromised hosts in the respiratory tract. Aspergillus endocarditis and Aspergillus implantable cardiac device-related infective endocarditis (CDRIE) are uncommon.

Here we present a case of pacemaker-associated *Aspergillus fumigatus* endocarditis in a host with an underlying hematological malignancy, and follow this with a review of the literature and discussion of the prevalence, predisposing factors, and diagnostic and treatment modalities for Aspergillus endocarditis.

2. Case presentation

An 18-year-old Caucasian male, who had received an allogeneic bone marrow transplant at age 5 years for acute myeloid leukemia, presented with cyanotic spells, night sweats, chills, and a 4.5 kg weight loss over 3 months. Over the last several months, he had experienced recurrent lower respiratory tract infections, for which his hematologist had placed him on empiric, monthly intravenous immunoglobulin infusions. He had undergone pacemaker placement for viral myocarditis at age 13 years, with pacemaker device replacements due to malfunction at ages 14 and 15 years with retention of leads. In addition to hypothyroidism and asthma, he had a past history of graft-versus-host disease; a recent bone marrow biopsy revealed 5% cellularity and cytogenetics suggesting an evolving myelodysplastic syndrome (MDS). Outpatient medications included cyproheptadine, levothyroxine, and montelukast. His only pets were cats and dogs, and he reported no recent travel.

On admission, his temperature was 35.8 °C, he had a pulse of 75 beats per min, blood pressure of 86/55 mmHg, and respiratory rate of 18 breaths per minute. Heart sounds were regular, with a loud S1 and split S2, but no murmur was audible. No evidence of peripheral or central cyanosis, clubbing, or peripheral stigmata of endocarditis was found on physical examination. The pacemaker site was without erythema, swelling, or tenderness.

Laboratory evaluation revealed normal chemistries and liver enzymes. The white blood cell count was normal (9.9×10^9 cells/l), but demonstrated a left shift (71% neutrophils and 13% bands). Low hemoglobin (8.4 g/dl) and platelets ($9 \times 10^9/\mu l$) were noted. Multiple sets of blood cultures were obtained. A chest X-ray demonstrated pacemaker leads in the right atrium and ventricle, but no other abnormalities. Right bundle branch block and right axis deviation was present on electrocardiogram (ECG). A transthoracic echocardiogram (TTE) revealed a 3.5 cm × 2 cm vegetation on the pacemaker wire (Figure 1), mild right ventricular enlargement, mild mitral and pulmonary insufficiency, and an ejection fraction of 50%. Blood cultures remained negative.

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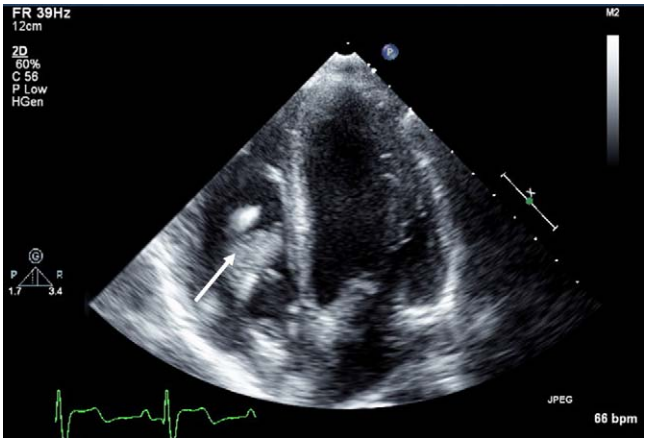

Figure 1. Transthoracic echocardiogram: 3.5 cm × 2 cm vegetation on the pacemaker lead and tricuspid valve protruding into the right ventricle (arrow).

The patient became febrile a few days into his hospital course. Empiric vancomycin and ceftriaxone were initiated for culture-negative endocarditis, but fevers persisted. On day 9 of his hospital stay he underwent surgical extraction of the pacemaker and leads. Although the operative mortality of this procedure is known to be high, it was decided the benefit outweighed the risk of embolization with medical management alone. Intraoperatively, invasion by the vegetation of the right atrium, tricuspid valve, interatrial septum, and superior vena cava was noted, and these areas were debulked. There was no indication at that point for a pacemaker, therefore it was not reimplanted. Operative pathology revealed tissue invasion by branching fungal hyphae (Figure 2) and several operative cultures grew pure cultures of *A. fumigatus*. Antibiotics were changed to intravenous voriconazole. On hospital day 17 he was discharged home on indefinite suppression with oral voriconazole. The galactomannan antigen assay (Bio-Rad Laboratories, Hercules, California), sent while on antifungal therapy, was positive (index = 0.94; positive reference cut-off: index ≥0.5). The 1→3-β-D-glucan assay was not performed. At 6-month follow-up he continued to do well, had gained weight, and clinically had had no apparent recurrence of Aspergillus disease or progression of MDS. It is anticipated that he will remain on voriconazole indefinitely.

3. Prevalence

Aspergillus species cause approximately 20–30% of all fungal endocarditis cases.[1,2] The proportion of fungal endocarditis caused by Aspergillus was similar in 1965–1971 (18/64 or 28%) and 1988–1995 (14/58 or 24%), suggesting that the prevalence of Aspergillus did not change significantly between 1965 and 1995.[1] The ratio of Aspergillus to Candida (1:2) has also remained constant over the last three decades.[1] A recent review of fungal endocarditis between 1995 and 2000 yielded 152 cases of fungal endocarditis, 28 (18%) of which were caused by Aspergillus.[2] The majority of cases were caused by *A. fumigatus* (54%), followed by *Aspergillus terreus* (18%), *Aspergillus niger* (7%), and *Aspergillus flavus* (7%).

Aspergillus species have also been associated with CDRIE. A retrospective review of all infected cardiac devices at the Mayo Clinic between 1991 and 2003 found 44 patients who met the definition of CDRIE; 75% of these cases of CDRIE were associated with pacemakers and 25% with automated implantable cardiac defibrillators. Fungal infections were demonstrated in only three of the 44 patients with CDRIE, two of which were Aspergillus (5% of all CDRIE cases).[3] A similar retrospective study of infections among 33 patients with pacemaker endocarditis was performed in Paris, France between 1988 and 1996.[4] In this study, two of 33 patients had fungal endocarditis, one case of which was caused by Aspergillus (3% of CDRIE cases).

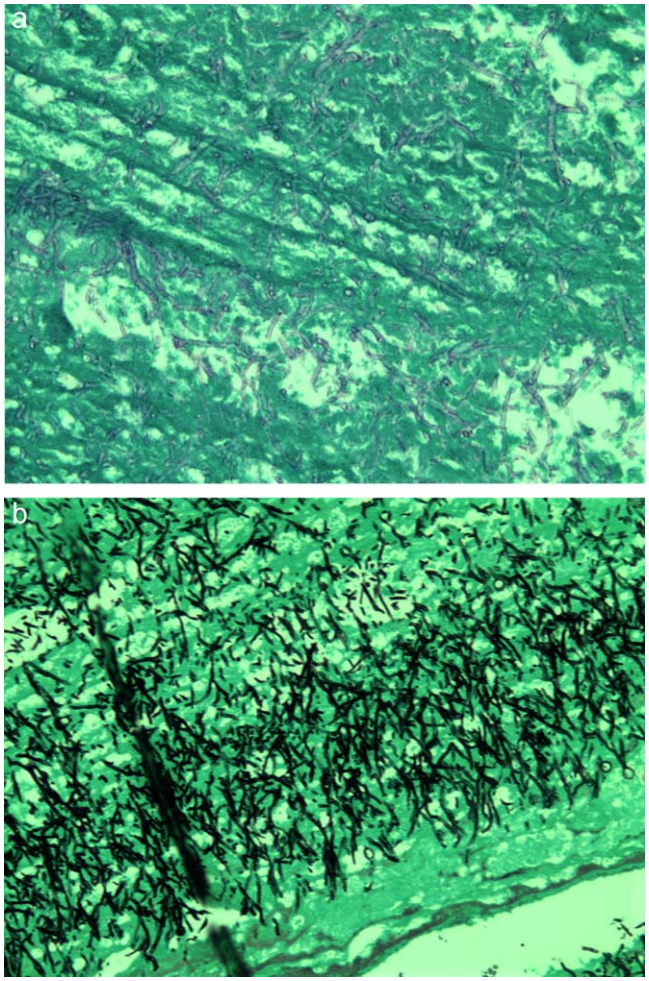

Figure 2. Operative pathology at 400×: (a) PAS stain and (b) GMS stain for fungus demonstrating tissue invasion by fungal hyphae and acute-angle branching.

4. Risk factors

A review of the literature indicates that most patients with Aspergillus endocarditis are male and possess a predisposing condition.[2,5,6] Pierrotti and Baddour assessed risk factors for mold-related endocarditis among 39 patients, the majority of which was caused by Aspergillus, and found an association with underlying cardiac abnormalities (41%), prosthetic valves (39%), malignancy (18%), solid-organ transplants (18%), and bone marrow transplants (18%).[2] Woods et al. reported steroid treatment (55%), prolonged antibiotic exposure (31%), hematological malignancy (28%), and chemotherapy and cytotoxic therapy (28%) as the most common predisposing factors for Aspergillus endocarditis in 29 patients.[5] Among children, congenital heart disease appears to be the most common risk factor, accounting for 67% of cases in one pediatric series of 15 patients.[6]

In our patient, the major predisposing conditions were the evolving MDS and previous pacemaker. He had not received recent immunosuppressive therapy and was not known to have congenital heart disease.

5. Literature review of Aspergillus endocarditis

We conducted a Medline search for cases of Aspergillus endocarditis using search terms ‘Aspergillus’ and ‘endocarditis’

Table 1
Aspergillus endocarditis cases reported in the medical literature between 1950 and 2009

Ref.	Age/ sex	Co- morbidities	Initial presentation	Valve involved	Complications	Diagnostic modality	Species	Surgical treat- ment	Antifungal treatment	Duration of treatment	Outcome
17	34/M	AVR	Dyspnea, chest pain, STEMI, RCA thrombosis	Aortic	Emboli to the brain and spleen; endophthalmitis	Aortic root culture	*fumigatus*	Yes	Voriconazole, liposomal amphotericin	Not documented	Survived
18	19/F	CF, ABPA lung transplant	New murmur, ankle edema, decline in FEV_1	Aortic	Aortic root abscess	Mitral valve culture	*fumigatus*	Yes	Voriconazole	6 weeks	Died 14 months later with valve abscess
18	24/F	CF, ABPA lung transplant	Right eye pain and vision loss	Mitral	Endophthalmitis and mesenteric emboli	Valve culture	*fumigatus*	Yes	Voriconazole	5 days (continued until death)	Died 5 days after surgery
19	58/M	COPD, steroids	Abdominal pain, amaurosis fugax	Mitral	Mesenteric and renal artery emboli	Valve pathology and culture, blood culture	*fumigatus*	Yes	Voriconazole	45 days (continued until death)	Died 45 days after surgery
20	57/M	COPD, IPF, lung transplant, Aspergillus in explanted lung	Chest pain, STEMI, LAD thrombosis	Mitral	Emboli to LAD	Valve pathology and culture	*fumigatus*	Yes	Caspofungin, amphotericin	6 weeks	Survived
21	17/M	Aplastic anemia, steroids	Fever, lobar pneumonia with nodules, pleural effusion	Mitral	Emboli to the brain	Lung nodule pathology	Not specified	No	Amphotericin, liposomal amphotericin	5 weeks (continued until death)	Died after 5 weeks
21	31/F	Aplastic anemia, steroids	Abdominal pain and right arm weakness	Mitral, aortic	Emboli to the brain, lung, kidney, and spleen	Skin nodule pathology and culture	*fumigatus*	No	Amphotericin, liposomal amphotericin	69 days	Died after 69 days
22	29/M	IVDU, *S. mitis* endocarditis	Focal seizure involving left arm	Aortic	Emboli to the brain, eye, and femoral artery	Vitreous culture	*fumigatus*	Yes	Amphotericin, anidulafungin, voriconazole	2 years+	Survived
23	34/M	IVDU, AIDS	Fever	Mitral	Emboli to the brain and LAD	Post-mortem skin, lymph node, pericardial effusion pathology/ culture	*fumigatus*	N/A	Died before initiation of treatment	Died prior to antifungal treatment	Died within a few days
24	34/M	Subaortic membrane excision	Acute onset bilateral lower extremity pain	Aortic	Emboli to femoral artery	Culture of femoral artery thrombus	*terreus*	Yes	Amphotericin	1 month+ (continued until death)	Died within 1 month
24	45/M	MVR	Fever, TIA, left hemiparesis	Mitral, aortic	Emboli to the brain and femoral artery	Culture of femoral artery thrombus	*flavus*	Yes	Amphotericin	17 days (continued until death)	Died after 17 days
25	28/M	AVR	Fever, diplopia, back pain	Aortic	Periaortic abscess, emboli to the iliac, hepatic, and renal arteries	Aortic pathology and culture	*fumigatus*	Yes	Amphotericin	15 days (continued until death)	Died after 15 days
25	56/M	AVR	Fever, new murmur	Aortic	Emboli to the brain, perivalvular abscess	Post-mortem coronary cusp pathology	Not specified	Yes	Died prior to initiation of treatment	Died prior to antifungal treatment	Died after 7 days
25	50/M	AVR	Fever, weight loss	Aortic	Emboli to the brain; aortic abscess and pseudo-aneurysm	Aortic valve pathology and culture	*niger*	Yes	Amphotericin, itraconazole	2 months (continued until death)	Died after 2 months
26	35/M	IVDU, AIDS	Fever, new murmur	Tricuspid	Pulmonary emboli; RBBB	Post-mortem valve pathology and culture	*fumigatus*	No	No antifungal	Died prior to antifungal treatment	Died after 5 days
26	31/M	IVDU	Fever	Aortic	Emboli to the iliac arteries and brain	Iliac thrombus culture	*niger*	No	Amphotericin	5 days (continued until death)	Died after 5 days
26	39/M	IVDU, AIDS	Fever, dyspnea	Aortic	Cardiogenic shock	Post-mortem heart valve pathology	Not specified	No	Fluconazole	4 days (continued until death)	Died after 4 days

27	52/F	Diabetes, renal transplant, pacemaker	Left eye visual loss, uveitis, arthralgias	Mitral, aortic	Emboli to the eye, brain, pulmonary artery, colon	Post-mortem heart valve pathology/ culture	*fumigatus*	No	Amphotericin	12 days (continued until death)	Died after 12 days
28	35/F	SLE, enterococcal MV endocarditis	Fever, mitral regurgitation, respiratory failure	Mitral	Mitral regurgitation	Post-mortem valve pathology and culture	*fumigatus*	N/A	None	Died prior to antifungal treatment	Died after 2 weeks
29	64/M	Heart transplant	Diplopia, palmar nodule	Aortic	Emboli to the eye; valvular abscess	Vitreous culture	*fumigatus*	Yes	Amphotericin, voriconazole	Not documented	Survived
5	19/M	Liver transplant	Hypotension, DIC, RBBB	Tricuspid	Myocardial abscess; pulmonary emboli	Post-mortem lung and valve pathology/ culture	*flavus*	No	Amphotericin	10 days	Died prior to diagnosis
30	54/F	MVR	Fever, back pain, lower extremity paresthesias	Mitral	Emboli to the iliac and hypogastric arteries	Pathology from iliac artery thrombus	*flavus*	Yes	Amphotericin, flucytosine	Not documented	Survived
31	41/M	MVR, bacterial endocarditis	Fever, weakness	Mitral	Congestive heart failure	Post-mortem valve culture/ pathology	*fumigatus*	N/A	Died prior to initiation of treatment	Died prior to antifungal treatment	Died
32	8 mo/F	Liver transplant	Dyspnea	Mitral	None	Blood Aspergillus PCR and Ag, tracheal culture	*fumigatus*	No	Fluconazole prophylaxis, voriconazole, caspofungin, amphotericin	Chronic voriconazole suppression	Survived
33	74/F	HTN, NIDCM	ICD site infection	ICD lead	None	ICD site drainage, generator, and lead culture	*flavus*	Yes	Voriconazole	6 months	Survived
34	52/M	DM, kidney–pancreas transplant	Fever, hypoxia, hypotension	Tricuspid	Congestive heart failure, pulmonary emboli	Blood GM, valve culture	*fumigatus*	Yes	Caspofungin, voriconazole, inhaled amphotericin	63 days (continued until death)	Died 61 days after surgery
35	53/M	Heart transplant	Altered mental status	Mitral	Endophthalmitis, cerebral emboli, cardiac tamponade	Blood GM, respiratory culture	*fumigatus*	Yes	Voriconazole, caspofungin, liposomal amphotericin	174 days (continued until death)	Died 169 days after surgery
36	71/M	PM, CASHD, SVC syndrome	Fever, chest pain, hypoxia	PM lead, tricuspid and aortic valves	Cerebral, renal, and pulmonary emboli	Post-mortem lead vegetation culture and pathology	*fumigatus*	No	amphotericin	7 days (continued until death)	Died after 7 days
37	66/F	HTN, PM, SSS	Chest pain, dyspnea	PM lead	Pulmonary emboli	Lead vegetation culture	Not specified	Yes	Liposomal amphotericin, itraconazole	43 weeks	Survived
38	39/M	Alcoholic cirrhosis	Fever, syncope, lower extremity pain	Mitral, aortic	Liver, kidney, cerebral, spleen, myocardial, and aortic saddle emboli, arrhythmia	Aortic embolus pathology and culture	*fumigatus*	Yes	Amphotericin	12 days (continued until death)	Died after 12 days
39	41/M	AVR	Acute ischemia lower extremity	Mitral, aortic	Lower extremity emboli	Lower extremity embolus pathology and culture	*ustus*	Yes	Amphotericin	2 months	Survived
39	48/M	AVR	Acute ischemia lower extremity	Aortic	Lower extremity emboli; aortic outflow tract obstruction	Lower extremity embolus and valve culture	Not specified	No	No antifungal	Died prior to antifungal treatment	Died prior to diagnosis
40	13/F	MVR	Fever, lower extremity ischemia	Mitral	Cerebral, lower extremity emboli, arrhythmia	Mitral valve pathology and culture	*flavus*	Yes	Amphotericin	10 days (continued until death)	Died after 10 days

Table 1 (*Continued*)

Ref.	Age/ sex	Co- morbidities	Initial presentation	Valve involved	Complications	Diagnostic modality	Species	Surgical treat- ment	Antifungal treatment	Duration of treatment	Outcome
41	12/F	TOF, PVR, VSD repair, tricuspid valve annuloplasty	Fever	Tricuspid, pulmonic	Tricuspid valve obstruction	Tricuspid valve pathology and culture	*flavus*	Yes	None	Died prior to antifungal treatment	Died prior to diagnosis
42	63/M	AVR	Orthopnea, night sweats, superficial thrombo-phlebitis	Aortic	Cerebral emboli	Post-mortem aortic valve culture and pathology	*niger*	No	None	Died prior to antifungal treatment	Died prior to diagnosis
43	60/M	CABG	Chest and abdominal pain, fever	Aortic	Congestive heart failure, annular abscess, aortitis	Aortic valve pathology and culture	*clavatus*	Yes	Amphotericin	16 days (continued until death)	Died 16 days after surgery
44	66/M	AVR	Acute visual loss, fever, anorexia	Aortic, mitral	Aortic root abscess and pseudo-aneurysm, renal, IMA, and cerebral emboli	Aortic valve pathology and culture	*fumigatus*	Yes	Amphotericin	4 weeks (continued until death)	Died 4 weeks after surgery
45	60/F	ALL	Fever, anorexia	Mitral	Mitral regurgitation, iliac, splenic, renal, and aortic emboli	Blood culture, mitral valve culture and pathology	*terreus*	Yes	Amphotericin	7 days (continued until death)	Died 6 days after surgery
46	44/M	MVR	Fever, arthralgias	Aortic	IVS abscess, cerebral emboli, arrhythmia, and aortic fistula	Mitral valve culture and pathology	*niger*	Yes	Amphotericin, itraconazole	6 months	Survived
47	57/M	MVR	Fever	Mitral	None	Mitral valve culture and pathology	*niger*	Yes	Amphotericin, itraconazole	1 year	Survived
48	32/M	Renal transplant	Lumbago	Mitral	Renal, iliac, and common femoral artery emboli	Embolus culture and pathology	*fumigatus*	No	Amphotericin	2 days (continued until death)	Died 2 days into treatment
49	11/M	AML	Necrotic lesion on nose	Mitral, tricuspid	Possible pulmonary invasive aspergillosis	Nose biopsy culture and pathology	*flavus*	No	Liposomal amphotericin (high dose)	Not specified	Survived
50	31/M	Lung transplant, CF	Skin nodules, hip pain, upper extremity ischemia	Mitral	Recurrent upper and lower extremity emboli, mitral regurgitation	Skin nodule and brachial artery embolus pathology, culture of hip arthrocentesis	*fumigatus*	No	Liposomal amphotericin, itraconazole	17 weeks (continued until death)	Died after 17 weeks
51	53/F	AVR	Fever, upper extremity monoparesis	Aortic	Aortic aneurysm, cerebral emboli	Aortic valve pathology and culture	*niger*	Yes	Amphotericin, itraconazole, liposomal amphotericin	70 days	Died 3 months after diagnosis
52	55/M	ICD, CASHD	Fever, weight loss	ICD lead and tricuspid valve	Tricuspid regurgitation, pulmonary emboli	ICD and tricuspid valve pathology and culture	*fumigatus*	Yes	Liposomal amphotericin, itraconazole, voriconazole	Not specified	Survived
53	61/F	TTP	Fever, acute dyspnea	Mitral	Mitral regurgitation and papillary muscle rupture, cerebral, splenic, and renal emboli, IVS abscess	Mitral valve pathology and culture	*fumigatus*	Yes	Liposomal amphotericin, itraconazole	2 months (continued until death)	Died 2 months after initial surgery
54	62/M	AIDS, DM, HTN	Fever, dyspnea, cough	Mitral	Ventricular arrhythmia, mitral regurgitation, cerebral, renal, and adrenal emboli	Post-mortem mitral valve pathology	Not specified	No	None	Died prior to antifungal treatment	Died prior to diagnosis

55	28/F	CF, lung transplant	Hemiparesis, lip infection, congestive heart failure	Mitral	Mitral regurgitation, cerebral emboli, endophthalmitis, heart failure	Mitral valve pathology and culture	*fumigatus*	Yes	Caspofungin	3 days (continued until death)	Died 4 days after surgery
56	25/M	Asthma on chronic steroids	Fever, dyspnea, chest pain, hemoptysis	Tricuspid	Pulmonary emboli	Tricuspid valve pathology and culture	*fumigatus*	Yes	Liposomal amphotericin, voriconazole	6 months	Survived
57	49/M	CABG	Fever, leg pain, anorexia	Aortic	Heart block, aortic root abscess, AI	Aortic valve histology	Not specified	Yes	Amphotericin, voriconazole	7 weeks (continued until death)	Died 7 weeks after surgery
58	52/M	DM, AVR	Fever, dyspnea	Aortic	Aortic root abscess	Aortic valve culture and histology	*flavus*	Yes	Liposomal amphotericin	Not specified	Survived
59	35/M	Non-diagnostic pericardio-centesis	Right leg pain	Mitral	Mitral regurgitation, iliac, superior mesenteric, splenic, hepatic, and popliteal artery emboli	Mitral valve pathology	Not specified	Yes	Amphotericin, itraconazole	148 days	Survived
60	65/M	CABG, DM, HTN, PM	Fever	Tricuspid valve, PM lead	None	Tricuspid valve pathology and culture	*fumigatus*	Yes	Amphotericin	8 weeks	Survived

ABPA, allergic bronchopulmonary aspergillosis; Ag, antigen; AI, aortic insufficiency; AIDS, acquired immune deficiency syndrome; ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; AVR, aortic valve replacement; CABG, coronary artery bypass graft; CASHD, coronary atherosclerotic heart disease; CF, cystic fibrosis; COPD, chronic obstructive pulmonary disease; DIC, disseminated intravascular coagulation; DM, diabetes mellitus; F, female; FEV_1, forced expiratory volume in 1 second; GM, galactomannan; HTN, hypertension; ICD, implantable cardioverter–defibrillator; IMA, inferior mesenteric artery; IPF, idiopathic pulmonary fibrosis; IVDU, intravenous drug use; IVS, interventricular septum; LAD, left anterior descending artery; M, male; mo, months; MV, mitral valve; MVR, mitral valve replacement; N/A, not applicable; NIDCM, non-ischemic dilated cardiomyopathy; PCR, polymerase chain reaction; PM, pacemaker; PVR, pulmonary valve replacement; RBBB, right bundle branch block; RCA, right coronary artery; SLE, systemic lupus erythematosus; *S. mitis*, *Streptococcus mitis*; STEMI, ST segment elevation myocardial infarction; SVC, superior vena cava; SSS, sick sinus syndrome; TIA, transient ischemic attack; TOF, tetralogy of Fallot; TTP, thrombotic thrombocytopenic purpura; VSD, ventricular septal defect.

for January 1950 through July 2010, yielding 53 case reports, which are summarized in Table 1. Table 1 describes the clinical presentations, associated co-morbidities, diagnostics, treatments, complications, and outcomes of these cases.

Over half of the 53 cases reviewed had fever (57%) or evidence of embolic disease (53%) at initial presentation (Table 1). Vegetations were often large and involved the mitral (26/53 or 49%) or aortic valves (24/53 or 45%), and less frequently, the tricuspid valve (9/53 or 17%), cardiac device leads (5/53 or 9%), or pulmonic valve (1/53 or 2%). Multi-valve involvement was seen in 21% (11/53) of cases. Complications were common and frequently involved embolization (40/53 or 75%) to the pulmonary, ophthalmic, cerebral, iliac, coronary, hepatic, splenic, renal, brachial, and/or mesenteric arteries.

Cyanotic spells are an uncommon initial manifestation of Aspergillus endocarditis, and may represent ventilation–perfusion mismatch or shunting due to recurrent septic pulmonary emboli.

6. Diagnosis

The diagnosis of Aspergillus endocarditis requires a high index of suspicion. Diagnosis was established postmortem in 11/53 (21%) cases by our review. Blood cultures are almost always negative (51/53 or 96%). Fungal vegetations are frequently large. The vegetation in our patient was large (3.5 cm $\times$ 2 cm) and demonstrated by TTE without difficulty.

The galactomannan antigen assay can be a useful adjunctive test to establish the diagnosis of invasive aspergillosis, but has not been studied in the setting of endocarditis. It is more sensitive for detecting invasive disease due to non-fumigatus Aspergillus than. *A. fumigatus* (49% vs. 13%).[7] False-positive results can occur with fungal infections (i.e., histoplasmosis, blastomycosis, cryptococcosis, and penicilliosis), as well as concomitant antibiotic therapy with piperacillin–tazobactam and amoxicillin–clavulanate.[8–13]

Ultimately, the diagnosis requires histological and tissue culture confirmation to differentiate Aspergillus from other molds and to determine the species. Pathology typically demonstrates acute angle branching and septate hyphae on Gomori methenamine silver (GMS) or periodic acid-Schiff (PAS) stains.

7. Treatment

The treatment of Aspergillus endocarditis is largely guided by evidence from the treatment of other forms of invasive Aspergillus infection. Successful treatment of endocarditis requires the combination of antifungal therapy and surgical debridement. The recommended antifungal therapy for most invasive Aspergillus infections, including Aspergillus endocarditis, is voriconazole.[14] The superiority of voriconazole to amphotericin B deoxycholate was demonstrated in a large, randomized controlled trial of invasive Aspergillus infections, the majority of which involved the lungs and sinuses (92%). Compared to amphotericin B, voriconazole was associated with improved survival, and less nephrotoxicity, electrolyte abnormalities, and infusion-related events.[15] Intravenous liposomal amphotericin formulations provide a second treatment option, with equal efficacy and less nephrotoxicity than amphotericin B in the treatment of invasive Aspergillus infections.[16]

Finally, surgical debridement is imperative for the survival of almost all cases of Aspergillus endocarditis. Our search of the literature found that only 4% (2/53) of cases were treated successfully with antifungal therapy alone. No studies have evaluated the appropriate duration of antifungal therapy, however most authors recommend lifelong suppressive therapy.

8. Prognosis

The prognosis is poor, with only 17 of 53 reported cases (32%) surviving the acute episode of Aspergillus endocarditis. This may be in part because of the immunocompromised status of the hosts, delay in diagnosis, and rapidity of embolization. Mortality approaches 100% among those who receive medical therapy alone.

9. Summary

Aspergillus endocarditis, specifically cardiac device-related infection, is very rare. It should be suspected in persons with underlying hematological malignancies, recent cardiothoracic surgery, intravenous drug use, and immunosuppression with culture-negative endocarditis and/or systemic or pulmonary emboli. Diagnosis ultimately requires confirmation by tissue histology and culture. The optimal treatment approach requires aggressive surgical debridement combined with antifungal treatment, usually requiring indefinite therapy with voriconazole.

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