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Concise Article

Prosthetic Vascular Graft Infection Due to *Aspergillus* Species: Case Report and Literature Review

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Abstract A case of *Aspergillus* prosthetic graft infection is reported here, accompanied by a review of the literature on this topic. The literature search revealed only 13 other cases reported to date. This infection is usually acquired through contamination at the time of surgery and affects immunocompetent patients. *Aspergillus fumigatus* is the causative species in most cases. Remarkably, fever is absent in about one-half of all cases, and blood cultures are usually negative. Concomitant vertebral osteomyelitis is commonly observed when the aorta is involved. Cure of this serious infection may be achieved with antifungal therapy, excision of the infected graft and extra-anatomic bypass.

Introduction

Bacterial infection of prosthetic grafts constitutes a serious complication of vascular derivation surgery that occurs in less than 3% of implants [1, 2]. Fungal infections of vascular grafts are infrequent, with most cases caused by *Candida* organisms [3]. *Aspergillus* infection of prosthetic vascular grafts constitutes a very uncommon event. A survey of the literature using Medline files and cross-references from the selected articles yielded only 13 cases reported to date [4–15]. We report a patient with prosthetic vascular graft infection due to *Aspergillus fumigatus* and review the literature for similar cases caused by this organism.

Case Report

A 67-year-old man with chronic ischemia of the lower limbs underwent a left femoropopliteal bypass in 1985 and a right iliofemoral thromboendarterectomy and right sympathectomy in 1991. During the following years, the bypass became progressively nonfunctional, but some circulation was maintained through collateral vessels. Because of progressive intermittent claudication, a Dacron left iliofemoral graft was placed in May 1998 to bypass additional atheromatous stenoses. In February 1999, a pseudoaneurysm of the proximal anastomosis of the Dacron graft, thought to be due to mechanical breakdown, was surgically repaired, which allowed the prosthetic graft to be retained. Material sent for culture was sterile.

Seven weeks later the patient developed pain in the left inguinal area, which was due to dehiscence of the proximal suture of the prosthesis. The graft was entirely removed, and a Dacron right aortofemoral bypass and right-to-left femoro-femoral grafts were placed through a clean field and connected to the femoral anastomoses of the previous left iliofemoral graft. Culture of the removed graft yielded *Aspergillus fumigatus*. Three blood cultures were negative. One week later lymphorrhagia appeared at the level of the right inguinal wound. Culture of the percutaneous aspirate of a right inguinal collection yielded *Aspergillus fumigatus*. The patient remained afebrile. He was treated with amphotericin B lipid complex (3 mg/kg/day) for 2 weeks, which resulted in complete resolution of lymphorrhagia. Itraconazole 400 mg/day was then started. Six weeks later the patient developed an episode of toxic encephalopathy, which was thought to be related to itraconazole. Upon discontinuation of the drug, the encephalopathy resolved. Itraconazole was reinitiated a few days later at a lower dose, 200 mg/day, without further complications.

One year later, the patient developed acute ischemia of the left leg. A thrombus was removed from the left side of the femoro-femoral graft, which was heavily colonized by *Aspergillus*. Itraconazole was stopped, and treatment with amphotericin B lipid complex was reinitiated. Three days later the patient developed acute pulmonary edema and died. At necropsy, no signs of

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Table 1 Reported cases of prosthetic vascular graft infections due to *Aspergillus* species

Year [ref.]	Age/ sex	Type of graft	Time from surgery to diagnosis (months)	Species	Vertebral osteomyelitis	Fever	Results of blood cultures	Leukocytes ($\times 10^6$/l)	Hematocrit	ESR (mm/h)	Surgical treatment	Antifungal therapy (time/total dose)	Outcome (follow-up)
1980 [4]	15/M	aortic	32	*fumigatus*	no	yes	neg.	leukocytosis	NA	55	change of prosthesis	AmB (6 wks./1 g) and 5-FC (6 wks./NA); then KET (4 mos./24 g)	survived (4 mos.)
1982 [5]	71/M	aortofemoral	28	*terreus*	yes	yes[a]	neg.	11,900	23%	135	in situ replacement	AmB (2 wks./NA)	died (during admission)
1982 [6]	18/M	aortic	4	*fumigatus*	no	low-grade	pos.	NA	NA	NA	in situ replacement	AmB (NA/NA)	died (during admission)
1984 [7]	73/M	aortofemoral	32	NA	yes	no	NA	NA	NA	NA	extra-anatomic bypass	AmB (4 wks./2 g)	survived (6 mos.)
1984 [8]	21/M	aortic	6	NA	no	no	NA	NA	NA	NA	extra-anatomic bypass	AmB (6 wks./NA)	survived (11 mos.)
1985 [9]	73/M	aortofemoral	32	*fumigatus*	yes	low-grade	NA	9,600	30%	NA	extra-anatomic bypass	AmB (NA/2 g)	survived (6 mos.)
1990 [10]	64/M	aortofemoral	39	*fumigatus*	no	yes[a]	NA	NA	NA	NA	extra-anatomic bypass	5-FC (14 mos./293 g)	survived (20 mos.)
1990 [10]	53/M	aortofemoral	19	*fumigatus*	yes	no	NA	NA	NA	NA	in situ (recurrence), then extra-anatomic bypass	AmB (6 wks./0.5 g); then 5-FC (6 mos./27 g) and ITR (7.5 mos./116 g)	survived (10 mos.)
1992 [11]	65/M	aortofemoral	1	*fumigatus*	no	yes	neg.	normal	27%	96	bifemoral thrombectomy	AmB (4 wks./1.5 g)	died (during admission)
1993 [12]	11/M	aortic	6	*fumigatus*	no	yes	neg.	leukocytosis	anemia	NA	prosthetic derivation	AmB (NA/NA), RIF (NA/NA)	died (during admission)
1993 [13]	69/M	iliofemoral	5	*fumigatus*	no	no	neg.	NA	NA	75	extra-anatomic bypass	AmB (6 wks./1.5 g), later ITR (9 mos./165 g)[b]	survived (3 yrs.)
1995 [14]	57/M	aortic	4	*flavus*	no	yes[a]	pos.	15,000	NA	NA	none	antimycotic (2 days/NA)	died (during admission)
1999 [15]	54/M	aortobifemoral	3	*fumigatus*	no	no	NA	mild leukocytosis	NA	NA	extra-anatomic bypass	AmB (4 wks./1 g) and 5-FC (4 wks./140 g); then ITR (8 mos./195 g)	survived (>10 mos.)
2001 [present report]	66/M	iliofemoral	10	*fumigatus*	no	no	neg.	10,200	39%	41	extra-anatomic bypass	AmB-LC (2 wks./3.2 g); then ITR (14 mos./95 g)	died (15 mos.)

[a] Concomitant infection
[b] Itraconazole was started because of *Aspergillus* knee arthritis 3 months after amphotericin B was stopped
ESR, erythrocyte sedimentation rate; NA, not available; neg., negative; pos., positive; AmB, amphotericin B; 5-FC, 5-flucytosine; KET, ketoconazole; ITR, itraconazole; RIF, rifampin; AmB-LC, amphotericin B lipid complex

Aspergillus infection outside the vascular graft were found.

Discussion

Aspergillus infection of prosthetic vascular grafts usually seems to be acquired through contamination of the graft in the operating room with airborne fungal spores [5, 6, 9, 11–13, 15, present report]. Table 1 summarizes the clinical features of patients with prosthetic vascular grafts infected with *Aspergillus* spp., including the present observation. Interestingly, all patients were male and none was immunosuppressed. This finding indicates that the grafts were contaminated at the time of surgery, since invasive and generalized *Aspergillus* spp. infections are uncommon in immunocompetent patients, and previous foci of infection were not identified in the cases reported. The median age was 60.5 years, and the median time from the placement of the graft to diagnosis was 8 months, a period appreciably longer than that observed in *Candida* spp. graft infections, which is usually less than 6 weeks [3]. *Aspergillus fumigatus* was responsible for all but two of the infections in which the species was reported, and in four cases the infection was accompanied by vertebral osteomyelitis [5, 7, 9, 10]. Fever was absent in about one-half of the cases, and blood cultures were positive in only two of the eight patients for whom this information was reported. It is not known why sterile blood cultures are commonly observed in *Aspergillus* endocarditis and other invasive infections, despite the easy access of *Aspergillus* to the bloodstream [16]. Most patients had mild leukocytosis, anemia, and increased erythrocyte sedimentation rates. *Aspergillus* was identified in the graft in all cases. In addition, it was found in osseous or articular samples [5, 7, 9, 10, 13], peripheral thrombotic material [4, 6, 8, 11, 14], and groin collections [15, present report].

As in *Candida* infections [3], the aortic location at either the thoracic or the abdominal level was the most common site of involvement, a finding somewhat surprising considering that the location of graft implants should have resulted in a higher incidence of groin infections. In addition to our patient, only two others had primary infra-aortic involvement [13, 15], and only one of them [15] developed, like our patient, an inguinal collection, a very uncommon manifestation. On the other hand, Motte et al. [13] reported a case that was similar to ours in the graft location and in the surgical and medical treatments used, except that a saphenous vein was implanted for the femoro-femoral bypass, and the patient survived the infection.

Optimal treatment for this condition consists of a combination of surgery and antifungal agents. The outcome seems to be strongly related to the type of surgical procedure. Excluding one case in which such a procedure was not detailed enough [4], in situ replacement or no excision of the infected graft was associated with recurrence of the infection and death in all cases, whereas all patients who survived underwent extra-anatomic bypass through a clean field. Of note, one patient had a recurrence of the infection after in situ replacement, but he was considered cured after an extra-anatomic bypass was placed during a second intervention [10]. Another surgical procedure that has yielded promising results in bacterial prosthetic infections consists of removal of the grafts and in situ replacement by deep veins from the leg [17]. However, the usefulness of this technique in *Aspergillus* graft infections cannot be evaluated as it has not been used in these patients. Unfortunately, our patient had a late recurrence despite extra-anatomic bypass and long-term antifungal therapy. However, it should be noted that the median follow-up period of the eight survivors was 10 months, and only two patients [10, 13] had a follow-up period longer than our patient. Consequently, late recurrences of the infection cannot be dismissed in patients that have been considered cured after shorter follow-up periods.

In addition to our patient, three other patients received itraconazole [10, 13, 15], and another received ketoconazole [4]; all of them were considered cured. The median time of treatment with AmB in this series was 4 weeks. Although long-term therapy seems advisable considering the severity and the insidious course of the infection, three patients were considered cured after relatively short follow-up periods of 6 weeks or less, during which time only AmB treatment was given [7–9].

In summary, prosthetic graft infections due to *Aspergillus* spp. constitute an uncommon but serious complication of vascular surgery. The organism seems to be acquired through contamination with fungal spores at the time of surgery. This infection is usually located in the aortic anastomosis of the graft, and it is frequently accompanied by vertebral osteomyelitis. Fever is absent in many patients, and blood cultures are usually negative despite the intravascular nature of the infection. The experience accumulated with the published cases suggests that optimal treatment consists of antifungal therapy, resection of the infected graft, and placement of an extra-anatomic bypass through a clean field.

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