Invasive Fungal Carotiditis: A Rare Manifestation of Cranial Invasive Fungal Disease: Case Series and Systematic Review of the Literature

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Background. Rhinosinusitis, malignant otitis externa, and skull base osteomyelitis represent a spectrum of cranial invasive fungal disease (IFD). These syndromes have distinct characteristics, yet they may progress to involve similar structures, resulting in inflammation and invasion of the adjacent internal carotid artery (ICA). Invasive fungal carotiditis can have devastating consequences, including cerebral infarction, subarachnoid hemorrhage, and death.

Methods. We retrospectively studied all patients diagnosed with cranial IFD and carotid involvement at our institution from 2003 to 2018. We also searched Medline/PubMed for reports of Aspergillus or Mucorales cranial infections with ICA involvement. All cases with mycologic evidence of cranial IFD and radiographic or pathologic evidence of ICA involvement were included.

Results. We identified 78 cases of invasive fungal carotiditis between 1958 and 2018, including 4 cases at our own institution. Forty-one were caused by Aspergillus and 37 by Mucorales species. Presenting symptoms included vision changes (73%), cranial nerve palsy (69%), and headache (42%). Carotid events included occlusion, aneurysm formation, and vessel rupture. Cerebral infarcts occurred in 50% of cases. Mortality at 6 weeks, 12 weeks, and 2 years was 27%, 41%, and 71% respectively. The median time from symptom onset to death was 150 days for cases due to Aspergillus and 51 days for cases due to Mucorales species.

Conclusions. Invasive fungal carotiditis is a rare but morbid manifestation of cranial IFD. Early suspicion of IFD and administration of antifungal treatment, vascular imaging, and endovascular interventions should be considered to reduce the high mortality of this disease.

Keywords. aspergillosis; carotid artery; invasive fungal disease; mucormycosis.

Acute and subacute invasive rhinosinusitis, sino-orbital infection, malignant otitis externa (MOE), and skull base osteomyelitis (SBO) represent a spectrum of presentations of cranial invasive fungal disease (IFD) [1–6]. Although each of these syndromes exhibits distinct clinical characteristics, they all may progress to involve similar anatomical structures including the skull base and cavernous sinus (CS) [1, 7–9]. IFD of the skull base or CS results in fatal vascular complications through inflammation or invasion of the adjacent internal carotid artery (ICA), leading to intraarterial thrombosis, aneurysm formation, or rupture [10–13]. Invasive fungal carotiditis can have devastating consequences, including cerebral infarction, subarachnoid hemorrhage (SAH), and death. Despite these associations, vascular complications are infrequently considered or screened for in patients diagnosed with cranial IFD.

The incidence of IFD, including invasive aspergillosis (IA) and invasive mucormycosis (IM), continues to rise despite the development of novel antifungal agents for treatment and prophylaxis [14–18]. Presentations of cranial IFD are usually nonspecific, making a prompt clinical and microbiological diagnosis challenging [6, 19–21]. With a growing population of immunosuppressed patients, and the high mortality rate of IFD, it is imperative to better understand the diverse clinical presentations of these invasive mycoses [14–16, 18, 22].

We present 4 cases of invasive fungal carotiditis originating from the external auditory canal or paranasal sinuses, with eventual involvement of the ICA. To further characterize this clinical syndrome, we performed a systematic review of the literature and identified an additional 74 cases, suggesting that vascular and specifically carotid complications should be considered in patients presenting with cranial IFD.

METHODS

Case Series

We conducted a retrospective study of all patients diagnosed with carotid involvement related to direct extension of IFD at
Mucorales described single case reports. Full-text articles were reviewed, and clinical information was removed if infection or unspecified treatment and outcome were excluded. Matonic inoculation were excluded. Cases with unclear origin of secondary to hematogenous dissemination or surgical or traumatic canal and temporal bone or skull base were classified as sino-orbital, and cases with involvement of the external auditory canal and temporal bone or skull base were classified as sino-nasal, radiographic evidence of contiguous infection were included. Nasal infection (sino-orbital, sino-nasal, skull base, carotid), and basosis, aneurysm formation, rupture, mycologic evidence of cranial age, 70 years). The most common comorbidities were DM (58%), HM (12%), and chronic kidney disease (CKD; 10%).

**Systematic Review**

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed [24]. We searched the Medline/PubMed database from January 1958 to December 2018 for reports of *Aspergillus* or *Mucorales* infection with related occlusion, rupture, or aneurysm of the ICA. Cases before 1958 were omitted given the lack of antifungal therapy available before the approval of amphotericin B [25, 26]. The search terms included text words, including *Aspergillus* OR aspergillosis, *Mucorales* OR mucor OR mucormycosis, AND stroke, carotid, aneurysm, sinus OR sinusitis, orbital apex, skull base, malignant otitis externa. The search strategy for PubMed is listed in Supplementary Figure 1. The searches were limited to human studies published in or translated to English. Additional studies were identified by reviewing references cited in relevant articles.

All cases of proven or probable IFD caused by *Aspergillus* or *Mucorales* species in patients aged ≥12 years with involvement of the sphenoid, ethmoid, or maxillary sinus, orbit, cavernous sinus, external auditory canal, clivus, temporal bone, or mastoid bone were considered [24]. Cases with ICA occlusion, thrombosis, aneurysm formation, rupture, mycologic evidence of cranial infection (sino-orbital, sino-nasal, skull base, carotid), and radiographic evidence of contiguous infection were included. Cases with localized sinus disease were classified as sino-nasal, those with involvement of the sinus and orbit were classified as sino-orbital, and cases with involvement of the external auditory canal and temporal bone or skull base were classified at ototemporal. Patients with IFD and vascular complications secondary to hematogenous dissemination or surgical or traumatic inoculation were excluded. Cases with unclear origin of infection or unspecified treatment and outcome were excluded. Full-text articles were reviewed, and clinical information was extracted. Study quality was not assessed, as most manuscripts described single case reports.

Potential reports were screened for inclusion, first by title and abstract, and then assessed for eligibility and quality by full-text review. Data extraction was performed with a standardized data extraction tool, and a standardized protocol was followed. Patient characteristics extracted included age, gender, medical comorbidities, presenting symptoms, origin of infection, areas of involvement within the skull base, carotid involvement, empiric steroid therapy, infectious complications, fungal species diagnosed, antifungal therapy, surgical interventions, and death. For patients who received >1 antifungal agent, the primary treatment regimen was determined to be the primary antifungal that was administered for >1 month after diagnosis of cranial IFD.

We compared baseline characteristics using the Fisher exact test or Wilcoxon test according to the nature of the covariate. The primary outcome was median survival time from onset of symptoms. We generated survival curves using the Kaplan-Meier method. Statistical analysis was performed using JMP 14.0 (SAS Institute Inc, Cary, NC). The secondary outcome was to describe the presentation and clinical evolution of patients with invasive fungal carotiditis.

**RESULTS**

**Case Series**

We identified 4 cases of invasive fungal carotiditis at our institution from 2003 to 2018. Characteristics of the cases are summarized in Table 1. IFD risk factors included diabetes mellitus (DM; n = 3), glucocorticoid use (n = 3), and hematologic malignancy (HM; n = 2). All cases were caused by *Aspergillus* species. Two cases were ototemporal, 1 was sino-orbital, and 1 was sino-nasal in origin. All patients were treated with antifungals with activity against *Aspergillus* species, with initial improvement in symptoms, imaging, or decrease in BG and GM serum values. All patients subsequently presented with occlusion or aneurysm of the ICA and cerebral infarcts. Relevant imaging findings for each patient are presented in Figure 1. Three patients died within 1 year of diagnosis, whereas 1 patient remained alive at last follow-up after left superficial temporal artery to middle cerebral artery bypass and long-term antifungal therapy.

**Systematic Review**

**Demographics and Comorbidities**

We identified 74 additional cases of invasive fungal carotiditis between January 1958 and December 2018. This review focused on localized cranial IFD; cases of IFD secondary to hematogenous dissemination were excluded. Forty-one cases were caused by *Aspergillus* and 37 by *Mucorales* species. Patient demographics and comorbidities are presented in Table 2. Among cases, patients with IM were younger overall compared with patients with IA (IM median age, 47 years; IA median age, 70 years). The most common comorbidities were DM (58%), HM (12%), and chronic kidney disease (CKD; 10%).
### Table 1: Cases of Invasive Fungal Carotiditis at Brigham and Women’s Hospital, 2003–2018

| Characteristic | Patient 1 | Patient 2 | Patient 3 | Patient 4 |
|----------------|-----------|-----------|-----------|-----------|
| **Age, sex**   | 66 y, male | 79 y, male | 66 y, male | 77 y, female |
| **Comorbidities** | Follicular NHL treated with fludarabine; paraneoplastic pemphigus requiring alemtuzumab and IVIG | CLL treated with rituximab and alemtuzumab in remission; type II DM | Renal transplantation on tacrolimus, azathioprine; type II DM | End-stage renal disease; type II DM |
| **Presenting symptoms** | Headache, CN III/VI palsy | Headache, left vision loss, periorbital pain, CN III palsy | Headache, facial pain, otalgia, left ear drainage | Headache, facial pain, otalgia, left ear drainage |
| **Diagnostic imaging** | MRI/MRA with right parietal stroke, sphenoid and maxillary sinus disease, occlusion of right ICA | CT face with mass extending from left sphenoid sinus to orbit with dehiscence between the orbital apex and left sphenoid sinus | CT face with soft tissue density extending from left EAC to mastoid with narrowing of left ICA | CT face with opacification of left EAC and mastoid air cells with bony erosion of sphenoid sinus and narrowing of left ICA |
| **Peak serum BG and GM index** | BG >500 pg/mL<sup>a</sup> GM 0.26 index | BG 337 pg/mL GM 0.31 index | BG >500 pg/mL GM 1.23 index | BG 329 pg/mL GM 1.51 index |
| **Origin** | Sino-nasal | Sino-orbital | Ototemporal | Ototemporal |
| **Diagnostic criteria** | Proven: biopsy with positive pathology and culture | Proven: biopsy with positive pathology and IHC | Probable: positive BG and GM, positive clinical criteria | Proven: biopsy with positive pathology and culture |
| **Histopathology** | Right sphenoid sinus biopsy with hyphal forms | Left orbital biopsy with hyphal forms and positive Aspergillus immunostain | Left nasopharyngeal, skull base, sphenoid biopsies negative | Left mastoid and posterior ear canal with hyphal forms |
| **Microbiology** | Right sphenoid sinus culture with *Aspergillus fumigatus* | Left orbital cultures negative | Otic, skull base, chial, sinus cultures negative | Left posterior mastoid culture with *Aspergillus flavus* |
| **Antifungal treatment, d** | Isavuconazole, 104; Voriconazole, 19 | Amphotericin, 16 Isavuconazole, 43 | Voriconazole, 294 Recrudescence → Voriconazole, 998 | Isavuconazole, 37 |
| **Surgical intervention** | Sinus debridement | Orbitotomy | STA-MCA bypass | Tymano-mastooidectomy, left ICA embolization |
| **ICA involvement** | Right ICA occlusion | Left ICA occlusion | Left ICA occlusion | Left ICA ruptured aneurysm |
| **Complications** | Cerebral infarct, SAH, basilar myotic aneurysm | Cerebral infarct, intracranial empyema | Cerebral infarct | Cerebral infarct, ruptured myotic aneurysm |
| **Death** | Y | Y | N | Y |
| **Time to death, d** | 210 | 120 | 1823, alive as of 1/1/2019 | 150 |

**Abbreviations:** BG, (1→3)-β-D-glucan; CLL, chronic lymphocytic leukemia; CN, cranial nerve; CT, computed tomography; DM, diabetes mellitus; EAC, external auditory canal; GM, galactomannan; ICA, internal carotid artery; IHC, immunohistochemistry; IVIG, intravenous immunoglobulin; MCA, middle cerebral artery; MRI/MRA, magnetic resonance imaging/angiography; NHL, non-Hodgkin’s lymphoma; SAH, subarachnoid hemorrhage; STA, superficial temporal artery.

<sup>a</sup>Attributed to intravenous immunoglobulin at the time.

<sup>b</sup>From symptom onset.
Few patients (4%) had undergone allogeneic hematopoietic cell transplantation (HCT). Sixteen patients (21%) had no apparent risk factors for cranial IFD that were identified. Fifty-one patients (65%) had 1 risk factor for IFD, and 11 (14%) had multiple risk factors. Diabetes was the most frequent individual risk factor for IFD (44%). Patients with cases due to IM were more likely to have DM as a primary risk factor (62% vs 27%; \( P = .003 \)), and patients with cases due to IA were more likely to have no identifiable risk factors (32% vs 8%; \( P = .02 \)).

**Clinical Features**

The most common presenting symptoms were changes in vision including diplopia or vision loss (IA 73%, IM 73%), cranial nerve palsy (IA 66%, IM 73%), headache (IA 51%, IM 32%), and facial or periorbital pain (IA 37%, IM 35%) (Table 2). Patients with mucormycosis frequently had periorbital edema or proptosis (59% vs 22%; \( P = .001 \)). Other presenting symptoms included retro-orbital pain, otalgia or otorrhea, epistaxis, and rhinorrhea or sino-nasal symptoms.

**Disease Manifestations**

The close proximity of anatomical structures in the sinuses and skull base as well as limitations to radiologic diagnosis make the categorization of subtypes of cranial IFD challenging. In this review, cases were divided into sino-nasal, sino-orbital, and ototemporal modes of extension to the ICA. Cases of sino-nasal origin or sino-orbital origin most commonly progress from the paranasal sinuses to involve the cavernous sinus or via the sphenoid to invade the skull base. Cases of ototemporal origin typically progress via the external auditory canal to involve the skull base via the temporal bone. Sino-nasal and sino-orbital modes of extension comprised 41% and 54% of cases, respectively. Only 4 patients developed invasive fungal carotiditis of ototemporal origin. Though almost all cases displayed involvement of the sinuses, only 14% of patients noted sino-nasal symptoms or rhinorrhea on presentation.

**Diagnosis and Microbiology**

Seventy-four cases were diagnosed as proven IFD by histopathology [23]. Four cases caused by *Aspergillus* species were diagnosed as probable IFD by host factors, clinical features, and mycological evidence (positive GM \( n = 2 \), nonsterile sinus culture \( n = 2 \)). Seventeen patients (41%) with invasive fungal carotiditis secondary to IA were empirically treated with systemic glucocorticoids before obtaining diagnosis, and 13 (32%) were diagnosed postmortem. Six patients (16%) with IM were treated with empiric glucocorticoids, and 8 (22%) were diagnosed postmortem. Patients were misdiagnosed with giant cell arteritis, optic neuritis, inflammatory pseudotumor (IgG4 disease), and other inflammatory syndromes.

Microbiologic data are presented in Table 3. The species isolated by culture included *Aspergillus fumigatus*, *Aspergillus flavus*, *Aspergillus niger*, *Rhizopus microsporus*, and *Rhizopus arrhizus*. In 8 cases, *Rhizopus* was identified by
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In 1 case, *Rhizomucor* was identified by culture, and in 1 case *Rhizomucor* was identified by histopathology. In 23 and 24 cases, respectively, *Aspergillus* and *Mucorales* were identified by histopathology alone.

**Table 3. Microbiology of Invasive Fungal Carotiditis**

| Fungal Species | Frequency, No. (%) |
|----------------|--------------------|
| Aspergillus (n = 41) | |
| *Aspergillus fumigatus* | 14 (34) |
| *Aspergillus flavus* | 1 (2.5) |
| *Aspergillus niger* (histopathology) | 1 (2.5) |
| *Aspergillus* (histopathology)\(^b\) | 23 (56) |
| Probable case (galactomannan positive) | 2 (5) |
| Mucorales (n = 37) | |
| *Rhizomucor* (culture or histopathology)\(^a\) | 2 (5) |
| *Rhizopus* (culture)\(^b\) | 8 (21) |
| *Rhizopus microsporus* | 1 (3) |
| *Rhizopus arrhizus* | 2 (5) |
| *Mucorales* (histopathology)\(^b\) | 24 (63) |

\(^a\)Special immunostaining for *Rhizomucor*.

\(^b\)Identification to the species level was not performed or reported.

**Treatment**

Treatment of invasive fungal carotiditis is reviewed in Table 4. Patients with IA received predominantly amphotericin-based (34%) or voriconazole-based (17%) regimens, though several (7%) received isavuconazole. Patients with IM primarily received amphotericin-based regimens (73%). Twenty-two patients overall (28%) did not receive antifungal therapy due to delayed diagnosis or poor prognosis. A majority of patients (65%) underwent surgical debridement. Other interventions included aneurysm coil embolization (n = 9), aneurysmal clipping (n = 2), carotid stenting (n = 2), and carotid bypass surgery (n = 2).

**Outcomes**

Carotid complications identified in this review included occlusion, thrombosis, aneurysm formation, and rupture. Outcomes are represented in Table 4. In cases involving *Mucorales*, occlusion or thrombosis of the ICA was more frequent (84% vs 46%; \(P = .001\)) compared with IA. Patients with IA were more likely to develop SAH (41% vs 5%; \(P < .001\)). Half of all patients experienced cerebral infarcts. All-cause mortality at 6 weeks, 12 weeks,
and 2 years was 27%, 41%, and 71%, respectively. Mortality at 6 weeks was significantly higher for patients with invasive fungal carotiditis due to IM (46% vs 10%; \( P = .001 \)), whereas mortality was similar for patients with IM and IA at 2 years (65% vs 76%; \( P = .429 \)). Survival curves are presented in Figure 2.

Five patients who died quickly (4 with mucormycosis, 1 with aspergillosis) with no follow-up time specified were assigned a follow-up time of 7 days. The median time from symptom onset to death was 150 days for cases due to *Aspergillus* and 51 days for cases due to *Mucorales* species.

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**Table 4. Treatment and Outcomes of Invasive Fungal Carotiditis**

| Treatment and Outcomes | Aspergillus sp. (n = 41) | Mucorales (n = 37) | Total (n = 78) | \( P \) |
|------------------------|--------------------------|-------------------|---------------|------|
| **Antifungal treatment, No. (%)** |                          |                   |               |      |
| Amphotericin B          | 14 (34)                  | 27 (73)           | 41 (53)       |      |
| Voriconazole            | 7 (17)                   | 0                 | 7 (9)         |      |
| Isavuconazole           | 3 (7)                    | 0                 | 3 (4)         |      |
| Echinocandin            | 2 (5)                    | 0                 | 2 (3)         |      |
| Other antifungal        | 2 (5)                    | 1 (3)             | 3 (4)         |      |
| No treatment            | 13 (32)                  | 9 (24)            | 22 (28)       |      |
| **Adjunctive therapies, No. (%)** |                        |                   |               |      |
| Hyperbaric oxygen       | 0                        | 6 (16)            | 6 (8)         | .885 |
| **Surgical intervention, No. (%)** |                      |                   |               |      |
| Surgical debridement    | 26 (63)                  | 25 (68)           | 51 (65)       | .885 |
| Coil embolization        | 6 (15)                   | 3 (8)             | 9 (12)        | .590 |
| Aneurysm clipping        | 2 (5)                    | 0                 | 2 (3)         | .546 |
| Carotid stent           | 1 (2)                    | 1 (3)             | 2 (3)         | .942 |
| Carotid bypass          | 2 (5)                    | 0                 | 2 (3)         | .546 |
| **Outcomes, No. (%)**   |                          |                   |               |      |
| Carotid involvement     |                          |                   |               | .001 |
| Occlusion or thrombus   | 19 (46)                  | 31 (84)           | 50 (64)       | .012 |
| Aneurysm or rupture     | 22 (54)                  | 6 (16)            | 28 (36)       | .001 |
| **Complications**       |                          |                   |               |      |
| Cerebral infarct        | 20 (49)                  | 19 (51)           | 39 (50)       | .999 |
| Subarachnoid hemorrhage | 17 (41)                  | 2 (5)             | 19 (24)       | .001 |
| Cavernous sinus thrombosis | 3 (7)               | 12 (32)           | 15 (19)       | .012 |
| Mortality at 6 wk (42 d) | 4 (10)                  | 17 (46)           | 21 (27)       | .001 |
| Mortality at 12 wk (84 d) | 10 (24)                | 22 (59)           | 32 (41)       | .003 |
| Mortality at 2 y (720 d) | 31 (76)                 | 24 (65)           | 55 (71)       | .429 |

**Figure 2.** Survival time from symptom onset of invasive fungal carotiditis due to *Aspergillus* and *Mucorales*.
IFD is an increasingly important cause of mortality among immunosuppressed patients [15–17]. Invasive fungal carotiditis is a unique presentation of IFD that typically progresses by contiguous extension from sinusoidal, sino-orbital, or oto-temporal locations to involve the carotid artery, with devastating consequences.

Major risk factors for IFD include HM, HCT, SOT, and DM. In this series, DM was a key risk factor for patients, serving as the most frequent individual primary risk factor for IFD. This was especially prevalent in cases of IM. Notably, among the cases of invasive fungal carotiditis identified, 19% of patients had no apparent risk factors for IFD. The reasons for this observation include prior bacterial or viral infections leading to disruption of the sino-nasal mucosa or ear canal epithelium, making those tissues susceptible to hyphal invasion [27], or undiagnosed immunodeficiencies in otherwise healthy hosts [28, 29]. Nonetheless, these findings indicate that early recognition of at-risk patients may be problematic.

Cranial IFD is challenging to diagnose given the nonspecific nature of the symptoms and the overlap with many autoimmune and malignant diseases involving the paranasal sinuses, orbital apex, or skull base. Patients with invasive fungal carotiditis were frequently treated with systemic glucocorticoids for misdiagnosed inflammatory syndromes. For this reason, cranial IFD should be suspected in patients with worsening symptoms or imaging findings despite antibacterial or anti-inflammatory therapy. Determining a diagnosis through biopsy ought to be considered before administration of glucocorticoids in at-risk patients.

Yet even when suspicion is high and biopsy is pursued, barriers to diagnosis remain. Involved areas of the skull base may be technically difficult to access [30, 31]. In the reviewed cases, when surgical biopsy was obtained, negative results or inadequate sampling resulted in delayed diagnosis [32]. Reinforcing these challenges, a significant group of patients (27%) were diagnosed only postmortem, suggesting that a diagnosis of invasive fungal carotiditis may be missed despite recent advances in imaging, surgery, and microbiologic testing. Novel diagnostic strategies such as polymerase chain reaction (PCR) assays should be considered to enhance diagnostic yield when suspicion for cranial IFD is high, especially with *Mucorales* species [33].

Treatment of IFD involves both medical and surgical strategies [34]. Voriconazole remains the frontline antifungal agent for the treatment of IA, though use of newer triazoles such as isavuconazole has begun to increase [35, 36], including among patients who are unable to receive voriconazole due to drug–drug interactions [37]. A majority of patients with invasive fungal carotiditis received optimal antifungal therapy and surgical intervention, yet mortality remained high. Further investigation is essential to determine the optimal therapeutic strategies of cranial IFD with carotid involvement.

Vascular complications involving the intracranial blood vessels have not commonly been associated with IFD [1, 16, 38]. Yet, 74 cases of invasive fungal carotiditis were identified in the literature, as well as 4 cases at our own institution since 2003. Half of those patients experienced associated strokes, and many others experienced SAH or CS thrombosis. Notably, even patients who appeared to improve clinically on antifungal therapy went on to develop vascular complications, raising the question of whether more aggressive vascular screening and intervention should be undertaken in patients with cranial IFD. We would recommend in patients with disease adjacent to the ICA, with or without visible narrowing of the ICA, or involving the cavernous sinus or petrous bone, that a magnetic resonance image/magnetic resonance angiogram (MRI/MRA) be performed [39]. If the MRI/MRA reveals any vascular abnormalities, the risks and benefits of endovascular intervention should be discussed. In several cases reviewed, aggressive vascular interventions including coil embolization of aneurysms or carotid bypass have led to successful outcomes [10, 12, 40].

Although IFD with carotid involvement has previously been described [11, 12, 40], this study includes the largest number of patients to date and demonstrates the diverse spectrum of clinical syndromes that may lead to carotid involvement, as well as the varying manifestations of carotid complications, including occlusion, thrombosis, aneurysm formation, or rupture. Limitations of this study include the use of retrospective data, varying follow-up times, missing data, challenges in identifying anatomic sites of infection, and lack of clear definition between distinct manifestations of cranial IFD.

Invasive fungal carotiditis is a rare but distinct manifestation of cranial IFD. Given the nonspecific presentation, technically difficult microbiologic identification, and provider inexperience involving this syndrome, diagnosis is often delayed. Little is known about the optimal therapeutic approach to this disease, but multidisciplinary collaboration between otolaryngology, vascular, medicine, and infectious disease teams is critical. Early consideration of cranial IFD, an aggressive approach to biopsy and surgical debridement, determination of appropriate antifungal therapy, and routine vascular imaging and endovascular intervention should be considered to reduce the high mortality of this unique disease.

**Supplementary Data**

Supplementary materials are available at Open Forum Infectious Diseases online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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