

Retrospective Analysis of Patients With Acute Invasive Fungal Rhinosinusitis in a Single Tertiary Academic Medical Center: A 10-Year Experience

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Abstract

Background: Acute invasive fungal rhinosinusitis (AIFRS) is an aggressive, potentially fatal disease that can spread rapidly to the orbit and intracranial structures causing significant mortality and morbidity.

Objective: In this study, we present a 10-year experience from a tertiary academic medical center of patients presenting with AIFRS. Data on presentation, mortality rate, comorbidities, surgical, and medical management were analyzed.

Methods: A retrospective chart review was performed in a tertiary academic medical center of patients with AIFRS from January 2009 through February 2019. Data collected included demographics, presenting symptoms, comorbidities, immunosuppression status, endoscopic and imaging findings, orbital and intracranial complications, surgical and medical management, as well as outcomes and mortality.

Results: A total of 34 patients were identified. In our series, mortality was noted to be 61.8%, excluding patients who were lost to follow-up. The most common presenting symptoms included facial pain, ophthalmologic complaints, headaches, and proptosis. Only 4 of the 34 patients did not undergo surgical intervention, as they were not deemed surgical candidates; they all succumbed to their disease. Twenty-six of the 30 surgical patients (86.7%) underwent endoscopic sinus surgery, 8 underwent an open approach (26.7%), while 7 patients underwent orbital exenteration (23.3%). All patients had surgical pathology consistent with AIFRS. Fungal species isolated from culture included *Aspergillus*, *Mucor/Rhizopus*, *Candida*, *Cunninghamella*, *Scedosporium boydii*, *Paecilomyces*, and *Scopulariopsis*. Medical therapies included intravenous amphotericin B, caspofungin, posaconazole, voriconazole, isavuconazole, and micafungin.

Conclusion: AIFRS was associated with 61.8% mortality in our series of 34 patients over the past 10 years. Early diagnosis, as well as rapid and aggressive surgical and medical management, is necessary for optimal outcomes in this devastating disease.

Keywords

rhinology, outcomes, invasive fungus, fungus, sinus, rhinosinusitis, mucor, comorbidities, mortality

Introduction

Acute invasive fungal rhinosinusitis (AIFRS) is a rare and potentially fatal disease of the paranasal sinuses and nasal cavity. It has a rapidly progressive course due to the ability of the hyphae to invade mucosa and neurovascular structures causing local as well as distant ischemia, necrosis, and hemorrhage. This life-threatening infection advances quickly and has the potential to spread to involve the orbit as well as intracranial tissues.¹ While most often found in those with diabetes and hematologic

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malignancies, including bone marrow transplant recipients, AIFRS is also found in other immunocompromised populations, including patients with acquired immunodeficiency syndrome, solid organ transplants, iron overload, protein-energy malnutrition, or those on prolonged courses of steroids.¹⁻³ Presenting symptoms are often nonspecific but may include sudden onset of facial pain, fever, epistaxis, and nasal congestion.^{3,4} Outcomes in patients with AIFRS are variable but uniformly unfavorable, with mortality noted in the literature as high as 50% to 80%.^{1,5}

Prompt diagnosis of AIFRS is critical, as it is correlated with early treatment and lower rates of morbidity and mortality.¹ However, given the heterogeneous nature of initial presenting symptoms of AIFRS, prompt diagnosis remains a challenge. In previous studies, frequent presenting symptoms included orbital pain, vision loss, headaches, and neurological deficits.^{4,6} These symptoms are typically associated with more advanced progressions of AIFRS and poor prognosis.⁷ Imaging with computed tomography (CT) and magnetic resonance is frequently used to assist with diagnosis and to further evaluate the orbital and intracranial extension. Imaging findings such as unilateral nasal cavity mucosal thickening and soft tissue infiltration, bony dehiscence, orbital invasion, and intracranial invasion are seen with advanced presentations of AIFRS and are associated with increased morbidity and mortality.⁸ Given the varying specificity of imaging findings, histopathology demonstrating angioinvasive fungi remains the gold standard in diagnosis. The use of frozen section biopsies for suspected AIFRS has been shown to reduce time to initial surgery and consequently improved outcomes.¹

Given the rarity and high mortality of AIFRS, further analysis is critical to help guide future practice patterns. We analyzed all cases of AIFRS at a single tertiary academic center over a recent 10-year period and determined factors associated with increased mortality and morbidity. To our knowledge, this study is one of the largest single institution series investigating factors associated with mortality and morbidity in AIFRS.

Materials and Methods

Records were queried for all patients hospitalized at Ronald Reagan UCLA Medical Center with confirmed cases of AIFRS from 2009 to 2019. This was conducted through the pathology department by searching their internal database for all tissue positive cases of invasive fungal rhinosinusitis. Patients were included if the Head and Neck Surgery consult service had a high suspicion for AIFRS, and the diagnosis was confirmed by mucosal and neurovascular invasion on pathology. Patients without a positive tissue biopsy were excluded from this review. Institutional review board approval was

obtained through the University of California, Los Angeles (UCLA). Patient demographics were collected, including age, sex, comorbidities/risk factors, length of stay, hemoglobin A1c (HbA1c), and absolute neutrophil counts. Additional information extracted from patients' charts included presenting symptoms, findings on initial physical examination, organisms isolated from surgical specimens, disease characteristics, imaging findings on CT and magnetic resonance imaging (MRI), treatment modalities, and outcomes. Statistical analyses were carried out using Stata 16.0 (Stata Corp LLC, College Station, TX).

Results

Between 2009 and 2019, a total of 34 cases were identified as having invasive fungal rhinosinusitis on tissue histopathology by the UCLA Pathology department. Demographic data are shown in Table 1. The average patient age was 57.3 years (range: 2–81 years). The male-to-female ratio was 1.62:1. The most common comorbidity present on admission was diabetes mellitus (17 patients, 50%), followed by patients on immunosuppressant medications (16 patients, 47.1%). Thirteen patients presented with a comorbidity burden of 2 comorbidities (38.2%). A total of 21.4% were transferred from an outside hospital for a higher level of care at UCLA.

Presenting symptoms and physical examination findings are shown in Table 2. Facial pain was the most

Table 1. Summary of Individual Cases.

Characteristic	Totals
Number of patients	34
Demographics	
Age in years, mean (range)	57.3 (2–81)
Sex, male/female ratio	1.62:1
Comorbidities, no (%)	
Diabetes mellitus	17 (50.0)
Immunosuppressant medications	16 (47.1)
Leukemia/lymphoma	12 (35.3)
Transplant, solid/bone marrow	8 (23.5)
Liver disease	6 (17.6)
CKD/ESRD	4 (11.7)
Solid tumor	3 (8.8)
Comorbidity burden, no (%)	
No comorbidities	2 (5.9)
One comorbidity	10 (29.4)
Two comorbidities	13 (38.2)
Three comorbidities	6 (17.6)
Four comorbidities	3 (8.8)
Length of stay, mean days	35.1
Absolute neutrophil count, no (mean)	10 (4.2)
HbA1c, no (mean)	11 (8.9)

Abbreviations: CKD, chronic kidney disease; ESRD, end stage renal disease; HbA1c, hemoglobin A1c.

Table 2. Presenting Symptoms.

Number of patients	34
Presenting symptoms, no (%)	
Facial pain	17 (50.0)
Headache	12 (35.3)
Sinus congestion/nasal drainage	9 (26.5)
Eye pain	7 (20.6)
Physical examination findings, no (%)	
Vision changes	17 (50.0)
Proptosis	11 (32.4)
Neurologic changes	6 (17.6)
Facial numbness	6 (17.6)
Visible eschar on examination	3 (8.8)
EOM weakness	3 (8.8)
Fever	1 (2.9)

Abbreviation: EOM, extraocular muscle.

Table 3. Isolated Organisms.

Number of patients	34
Organism, no (%)	
<i>Mucor/Rhizopus</i>	15 (44.1)
<i>Aspergillus</i> sp.	13 (38.2)
<i>Candida</i> sp.	3 (8.8)
Multiple organisms	5 (14.7)
Atypical organisms	4 (11.8)
None isolated	3 (8.8)

common presenting symptom (17 patients, 50%), followed by headache (12 patients, 35.3%). The most common findings on physical examination were vision changes (17 patients, 50%), followed by proptosis (11 patients, 32.4%).

Of 34 cases, causative organisms were isolated in 31 cases (Table 3). The majority of cases were caused by *Mucor/Rhizopus* (15 patients, 44.1%), followed closely by *Aspergillus* (13 cases, 38.2%). Atypical organisms were isolated in 11.8% of cases and included *Cunninghamella*, *Scedosporium boydii*, *Paecilomyces*, and *Scopulariopsis*. Three cases had no species isolated from surgical pathology, but tissue histopathology was confirmatory for invasive fungus with hyphae identified.

Diagnostic testing for patients included CT and often MRI. Findings on imaging are shown in Table 4. Extent of disease was classified by findings on imaging depending on the extent of invasion. As expected, 100% of patients were found to have invasive sinus mucosal disease, with bone erosion found in 25 patients (73.5%). Other patients had more extensive disease, with orbital extension identified in 22 patients (64.7%), pterygopalatine fossa and infratemporal fossa extension in 12 patients (35.3%), cavernous sinus invasion in 7 patients (20.6%), and intracranial extension in 14 patients (41.2%).

Table 4. Disease Characteristics on Imaging.

Number of patients	34
Extent of disease, no (%)	
Sinus mucosal disease	34 (100.0)
Bone erosion	25 (73.5)
Orbital extension	22 (64.7)
PPF/infratemporal fossa involvement	12 (35.3)
Cavernous sinus invasion	7 (20.6)
Intracranial extension	14 (41.2)

Abbreviation: PPF, pterygopalatine fossa.

Table 5. Surgical and Medical Management.

Surgical approach, no (%)	30
ESS	26 (86.7)
Open approach	8 (26.7)
Orbital exenteration	7 (23.3)
Medical management, no (%)	33
Amphotericin B	26 (78.8)
Caspofungin	16 (48.5)
Posaconazole	14 (42.4)
Voriconazole	7 (21.2)
Isavuconazole	6 (18.2)
Micafungin	1 (3.0)
Type of medical therapy, no (%)	
Single drug therapy	8 (24.2)
Double drug therapy	14 (42.4)
Triple drug therapy	10 (30.3)
Quadruple drug therapy	1 (3.0)
Treatment, no (%)	
Surgical	30 (88.2)
Declined surgery	4 (11.8)
Surgical interventions, mean	1.6

Abbreviation: ESS, endoscopic sinus surgery.

Information on treatment modality was available for all patients and included various combinations of medical management and surgery (Table 5). The majority of patients were treated with a combination of medical management and surgery (87.9%). Of patients who were managed surgically (30/34), the majority underwent endoscopic sinus surgery (86.7%). Patients with more extensive disease were treated with more invasive approaches, with 26.7% of patients undergoing an open approach and 23.3% of patients undergoing orbital exenteration. The remaining 4 patients who did not undergo surgical treatment were not treated due to the extent of disease and/or to the patient declining surgery. Three patients received medical therapy only. One patient did not receive any medical treatment at all. This patient arrived to UCLA with a Glasgow Coma Score of 3, and the family declined any further therapy.

due to intracranial involvement and overall poor prognosis.

Nearly all patients (33/34) underwent medical management, with the majority of patients receiving amphotericin B as either a single agent or part of multimodal drug cocktail (78.8%). Patients in our series most often received double drug therapy (42.4%), followed by triple drug therapy (30.3%). We did not identify any trends in our series with regard to number (single, double, and triple) or type of agent (no trends with the use of amphotericin or posaconazole). However, there was a slight decrease in the use of amphotericin and a slight increase in the use of posaconazole when looking at combination therapies. These combination therapies also included other antifungal agents. From 2009 to 2014, 80.0% of patients received a cocktail with amphotericin, and 40% of patients received a cocktail with posaconazole. From 2015 to 2019, 74.0% of patients received a cocktail with amphotericin, and 47.3% of patients received a cocktail with posaconazole.

Patient outcomes are shown in Table 6. Mortality rate in our series was 61.8%. Of those patients who survived (24.4%), 1 survived with neurological deficits from orbital exenteration (2.9%), while the remaining patients were alive at follow-up without any neurological deficits (23.5%). Unfortunately, data on 4 patients (11.8%) were unavailable, as they were lost to follow-up. When stratified by comorbidity count, a correlation was seen with increasing number of comorbidities and mortality, with 100% of patients with 0 comorbidities alive at follow-up, and 60%, 61.5%, and 77.8% of patients dead at follow-up with 1, 2, 3, or more comorbidities, respectively (Table 7). When further stratified by the extent of disease on imaging and outcome, orbital involvement, pterygopalatine fossa/infratemporal fossa extension, and intracranial involvement all had higher proportions of mortality than local sinus disease alone (Table 8). Outcomes were further investigated by transfer status, as a high percentage of patients (20.6%) were transferred to UCLA for a higher level of care. Of these patients, 85.7% did not survive compared with 55.6% of patients not surviving a primary admission for AIFRS (Table 9). We investigated the differences between patients transferred from outside hospitals with those diagnosed and treated at UCLA and found that the transfer patients

had more extensive disease. A total of 85.7% of transfer patients had intracranial spread of disease on imaging compared with 29.6% of primary UCLA admission patients. No transfer patients had disease limited to

Table 7. Patient Outcomes by Comorbidity Count.

Number of patients	34
Zero comorbidities, no (%)	2
Alive without neurological deficits	2 (100.0)
One comorbidity, no (%)	10 (29.4)
Alive without neurological deficits	21 (61.8)
Alive with neurological deficits	4 (11.8)
Dead	6 (60.0)
Lost to follow-up	2 (20.0)
Two comorbidities, no (%)	13 (38.2)
Alive without neurological deficits	3 (23.1)
Dead	8 (61.5)
Lost to follow-up	2 (15.4)
≥3 comorbidities, no (%)	9 (26.5)
Alive without neurological deficits	2 (22.2)
Dead	7 (77.8)

Table 8. Patient Outcomes by Extent of Disease on Imaging.

Number of patients	34
Local sinus disease, no (%)	6 (17.6)
Alive without neurological deficits	4 (66.7)
Dead	2 (33.3)
Orbital involvement, no (%)	8 (23.5)
Alive without neurological deficits	1 (12.5)
Alive with neurological deficits	1 (12.5)
Dead	5 (62.5)
Lost to follow-up	1 (12.5)
PPF/ITF extension, no (%)	5 (14.7)
Dead	4 (80.0)
Lost to follow-up	1 (20.0)
Intracranial extension, no (%)	14 (41.2)
Alive without neurological deficits	3 (21.4)
Dead	9 (64.3)
Lost to follow-up	1 (14.3)

Abbreviations: ITF, infratemporal fossa; PPF, pterygopalatine fossa.

Table 6. Patient Outcomes.

Number of patients	34
Outcome, no (%)	
Alive without neurological deficits	8 (23.5)
Alive with neurological deficits	1 (2.9)
Dead	21 (61.8)
Lost to follow-up	4 (11.8)

Table 9. Patient Outcomes by Transfer Status.

Number of patients	34
Initial admission, no (%)	27 (79.4)
Alive without neurological deficits	7 (25.9)
Alive with neurological deficits	1 (2.9)
Dead	15 (55.6)
Lost to follow-up	4 (14.8)
Transfer from OSH, no (%)	7 (20.6)
Alive without neurological deficits	1 (14.3)
Dead	6 (85.7)

Abbreviation: OSH, outside hospital.

the sinuses or sinuses + orbit. Transfer patients did not have more comorbidities, but rather they presented with more advanced disease, likely leading to their poorer outcomes.

When stratifying patients into 2 groups, 2009 to 2014 and 2015 to 2019, we found that mortality rates were nearly identical. For patients from 2009 to 2014, 26.7% were alive and 60.0% were dead. For patients from 2015 to 2019, 26.3% were alive and 63.2% were dead.

When comparing patients who underwent orbital exenteration versus those who did not, 71.4% of patients who underwent orbital exenteration were dead at follow-up compared with 59.2% of patients who did not undergo orbital exenteration.

To determine whether or not predictor variables significantly impacted mortality outcomes, a series of simple logistic regression models (ie, 1 predictor per model) was conducted for the variables: age, number of comorbidities, gender, transfer status, presence of intracranial extension, and orbital exenteration. None of these variables were significantly associated with the outcome variable. Both a Fisher's exact χ^2 and an exact logistic regression were run with the variable medical therapy (single, double, or triple antifungal agent) and neither were statistically significant. These analyses were used instead of a simple logistic regression because of sparse and empty cells in the cross tabulation of medical therapy and the outcome. As this analysis was a simple logistic regression, there was no *P* value obtained (Table 10).

Discussion

AIFRS is a rare, devastating disease that most often afflicts patients who are immunocompromised due to systemic medications or from systemic diseases that impair the body's own immune defenses. The rarity of this disease limits investigation of treatment strategies and to date, no standardized treatment algorithm exists. Most often, AIFRS progresses rapidly, leaving no time for misdiagnosis or delay in the initiation of appropriate antifungal treatment and concomitant surgical debridement. The majority of the literature consists

of retrospective chart reviews and case reports that report an overall survival rate of 50% or less.^{7,9,10}

The average age at presentation in our series was 57.3 years, ranging from 2 to 81 years. Three patients in this series were under the age of 18 years, with the youngest (2 years) admitted with liver failure/awaiting liver transplant and an absolute neutrophil count of 0.11. Of the remaining pediatric cases, one was caused by non-Hodgkin lymphoma, while the other did not have any comorbidities on presentation. This contrasts with another series in which the majority of pediatric cases with AIFRS were due to relapsing leukemia/lymphoma.²

The literature reports a preponderance for this disease in immunocompromised hosts, namely, those with diabetes mellitus and leukemia. A systematic review by Turner et al.⁷ found most patients to present with diabetes mellitus and hematologic malignancy. Similarly, most published case series also identified diabetes and blood malignancy as the most common presenting comorbidities.^{4,8,10,11} The literature is confounded among publications, reporting diabetes as both a negative¹⁰ and positive prognostic factor.^{5,7} Our study found diabetic patients to have a mortality of 76% compared with 47% in nondiabetic patients, therefore supporting its association with poor outcome. We went on to further investigate whether or not the presence of multiple immunosuppressant comorbidities was associated with worsened outcomes and found that mortality rates increased with an increasing number of comorbidities.

Definitive diagnosis of AIFRS requires the presence of tissue invasive fungus.¹ A large multi-institutional study by Wandell et al.¹² identified *Aspergillus* as the most common causative agent, followed by *Mucor* and *Rhizopus*, and atypical organisms in 12%. Furthermore, this study found atypical organisms to be associated with a 2- to 3-fold higher risk of death on multivariate analysis. Similarly, multiple other studies have identified *Aspergillus* as the most commonly isolated fungal species in AIFRS.^{5,8} In contrast, a recent review identified *Mucor* and *Rhizopus* as the most commonly isolated organisms.¹⁰ Our series identified *Mucor* and *Rhizopus* as the most commonly isolated organisms, followed by *Aspergillus*. The presence of atypical organisms was not associated with worse outcomes in our patient population. A recent large database study by Burton et al.⁵ found that the presence of *Mucor* was associated with a higher inpatient mortality, similar to our findings that patients with *Mucor/Rhizopus* had a higher mortality (76.4%) compared with patients with *Aspergillus* alone (66.7%).

Patients presenting with AIFRS often present with nonspecific sinonasal symptoms that have been present for 1 month or less, including facial pain, nasal obstruction, and fever. Facial numbness, vision changes/ptosis, headache, or palatal necrosis may indicate

Table 10. Predictors of Mortality.

Predictors	OR (95% CI)	<i>P</i>
Age	1.02 (0.98–1.06)	.32
Number of comorbidities	2.0 (0.91–4.42)	.09
Gender	0.98 (0.24–4.08)	.98
Transfer versus admission	1.72 (0.28–10.51)	.56
Intracranial extension	0.88 (0.22–3.52)	.85
Orbital exenteration	1.72 (0.28–10.51)	.56
Medical therapy ^a	1.13 (0.47–2.74)	

Abbreviations: CI, confidence interval; OR, odds ratio.

^aMedical therapy refers to no therapy or single, double, or triple therapy.

neurovascular, orbital, or intracranial invasion and a more advanced disease process.¹⁰ In this series, vision changes, proptosis, and neurologic changes were the most common findings on initial physical examination, indicating more advanced disease on presentation compared with symptoms and physical examination findings reported in another study³ and suggesting that our cohort of patients overall presented with more advanced disease.

Most commonly reported CT findings in AIFRS are unilateral nasal cavity mucosal thickening and soft tissue infiltration of the maxillary periantral fat planes. More specific features of AIFRS include orbital invasion, bone dehiscence, and intracranial extension that are often seen in advanced disease. A recent retrospective review by Middlebrooks et al.⁸ found that fungal invasion beyond the sinuses often does so without invading bone and rather by neurovascular spread. In our series, the most commonly identified radiographic findings were sinus mucosal disease, followed by bone erosion and orbital extension. Intracranial extension was seen in more than one-third of our cases, further supporting more advanced disease on presentation in our cohort. The literature is in disagreement when it comes to the impact of disease extent on imaging on prognosis, with a study by Monroe et al.¹³ finding invasion of orbit or brain associated with worse survival while a recent multi-institutional study by Wandell et al.¹² finding disease extent to not be a negative prognostic factor. In our series, the extent of disease was found to correlate with mortality rates; patients with orbital involvement, pterygopalatine fossa/infratemporal fossa invasion, and intracranial extension were all found to have increasing rates of mortality.

The gold standard for diagnosis and treatment remains classic histopathological confirmation followed by aggressive surgical and medical management. Recent advances in histopathological diagnosis with the use of novel stains such as periodic acid-Schiff stain for fungus for frozen biopsy have decreased false-negative rates and led to more prompt diagnosis.¹ Following diagnosis, early surgery with debridement and medical management with antifungals remain critical factors for reducing morbidity and mortality. Interestingly, Wandell et al.¹² found that longer intervals between symptom onset to surgery and antifungal use to be associated with higher survival are likely explained by a more indolent disease process in this group.

The literature remains currently unclear on when and which patients should have orbital exenteration. The pathophysiological mechanism of ophthalmoplegia in AIFRS remains uncertain but can be a result of a multitude of factors including involvement in the orbital tissues, intracavernous invasion, and retrograde spread, or involvement of vasculature supplying the orbital apex.¹⁴ The decision-making process for choosing

orbital exenteration is rather complex, taking into consideration several factors, including involvement of the orbit, extent of intracranial disease, and overall prognosis. In our series, if the surgeon believed that all the involved diseased tissue could be removed by performing an orbital exenteration, leaving healthy vascularized tissue behind, then it was done. However, if the disease was so extensive, with intracranial or bilateral orbital involvement, and prognosis for survival was very poor, then serious discussion with the patient's family was undertaken regarding the futility of the surgery, and it was not done. Similar to other series, patients who underwent more aggressive surgeries presented with more advanced disease and therefore had poorer outcomes than those who underwent less aggressive surgeries.^{7,9-13} The decision on type and extent of surgery needs to be balanced against other patient factors, including comorbidities and overall prognosis, and detailed discussion needs to take place between family members and treating physicians.

In addition to surgical debridement, the mainstay of medical management includes antifungal therapy. However, there is a lack of consensus guidelines in precise medical management.¹⁵ Amphotericin remains the mainstay of treatment for most cases of AIFRS, with the exception of voriconazole for *Aspergillus* and other rare fungal species.¹⁰ Posaconazole is often used as a second-line agent instead of amphotericin, since posaconazole is not mainly secreted by the kidneys and avoids nephrotoxicity.¹⁶ Isavuconazole, a new broad spectrum triazole, is another alternative used in the treatment of *Mucor* and *Aspergillus*, with lower nephrotoxicity than amphotericin and improved safety side effect profile over voriconazole.¹⁵ In our series, amphotericin remained the most commonly used antifungal medication. Most of the patients in our cohort were treated with double or triple drug therapy. Many of our patients were also placed on posaconazole, and some had to be switched to posaconazole due to the high toxicity of amphotericin.

While this study is one of the largest single institutional studies to date and presents data to help with the identification and management of AIFRS, it is not without limitations. The major limitations of the study relate to those inherently derived from performing a chart review over a significant time period. Due to the high mortality of AIFRS, a fair number of our patients were sent to hospice, and therefore, survival time for these patients is unknown. Furthermore, due to the nature of patients being transferred to our hospital for a higher level of care, some of these patients who were not from the immediate area were lost to follow-up. This significantly limited our ability to extrapolate on survival data and times to follow-up.

Conclusion

AIFRS was associated with high mortality in our series of 34 patients. Ophthalmologic complaints, facial pain, headache, and proptosis were the most common complaints and physical examination findings on admission. Increased comorbidity burden was found to correlate with increasing mortality. Patients with imaging findings of orbital involvement, pterygopalatine fossa/infratemporal fossa extension, and intracranial involvement were all found to have worse outcomes than those with sinus disease alone. Patients who were transferred from an outside institution for further management and therefore presented with more advanced disease and delay in initiation of treatment had poorer outcomes than patients presenting initially to our medical center. Early diagnosis, as well as immediate initiation of surgical and medical management, remains critical for management and improved survival in patients with this devastating disease.

Authors' Note

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Declaration of Conflicting Interests

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