Intracranial fungal granuloma: a single-institute study of 90 cases over 18 years

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OBJECTIVE Intracranial fungal granuloma (IFG) remains an uncommon entity. The authors report a single-institute study of 90 cases of IFG, which is the largest study until now.

METHODS In this retrospective study, all cases of IFG surgically treated in the years 2001–2018 were included. Data were obtained from the medical records and the pathology, microbiology, and radiology departments. All relevant clinical data, imaging characteristics, surgical procedure performed, perioperative findings, and follow-up data were recorded from the case files. Telephonic follow-up was also performed for a few patients to find out their current status.

RESULTS A total of 90 cases consisting of 64 males (71.1%) and 26 (28.9%) females were evaluated. The mean patient age was 40.2 years (range 1–79 years). Headache (54 patients) was the most common presenting complaint, followed by visual symptoms (35 patients), fever (21 patients), and others such as limb weakness (13 patients) or seizure (9 patients). Cranial nerve involvement was the most common sign (47 patients), followed by motor deficit (22 patients) and papilledema (7 patients). The mean duration of symptoms before presentation was 6.4 months (range 0.06–48 months). Thirty patients (33.3%) had predisposing factors like diabetes mellitus, tuberculosis, or other immunocompromised status. A pure intracranial location of the IFG was seen in 49 cases (54.4%), whereas rhinocerebral or paranasal sinus involvement was seen in 41 cases (45.6%). Open surgery, that is, craniotomy and decompression, was performed in 55 cases, endoscopic biopsy was done in 30 cases, and stereotactic biopsy was performed in 5 cases. Aspergilloma (43 patients) was the most common fungal mass, followed by zygomycosis (13 patients), chromomycosis (9 patients), cryptococcoma (7 patients), mucormycosis (5 patients), and candida infection (1 patient). In 12 cases, the exact fungal phenotype could not be identified. Follow-up was available for 69/90 patients (76.7%). The mean duration of the follow-up was 37.97 months (range 3–144 months). The mortality rate was 52.2% (36/69 patients) among the patients with available follow-up.

CONCLUSIONS A high index of suspicion for IFG should exist for patients with an immunocompromised status and diabetic patients with rhinocerebral mass lesions. Early diagnosis, aggressive surgical decompression, and a course of promptly initiated antifungal therapy are associated with a better prognosis.

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KEYWORDS intracranial; fungal granuloma; immunocompromised; immunocompetent

FUNGAL infections of the central nervous system are rare. However, the incidence and diagnosis of these disease entities are increasing,^{9,38} mostly because of better diagnostic modalities such as imaging studies, microbiological tests, and pathology tests. Etiological factors contributing to the increasing incidence include immunocompromised states such as diabetes mellitus, renal failure, malnutrition, acquired immunodeficiency syndrome,

lymphoproliferative malignancies, and neutropenia, as well as the use of broad-spectrum antibiotics. Other possible factors are longer life expectancy, larger proportion of an aging population, widespread use of immunosuppressive drugs, longer survival of immunocompromised patients, increasing numbers of human immunodeficiency virus (HIV) infections, and poor nutritional status.^{2,18,38} These infections can involve the meninges, calvaria, brain,

ABBREVIATIONS ACF = anterior cranial fossa; AMB = amphotericin B; HIV = human immunodeficiency virus; IFG = intracranial fungal granuloma; PNS = paranasal sinus.
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and intracranial vessels in different forms, severity, and combinations.^{4,7,22,30}

Fungal infections pose a diagnostic challenge to clinicians and radiologists because of their resemblance to a pyogenic abscess, benign lesion, or even malignancy. They have high rates of death and morbidity, but early diagnosis and prompt treatment with surgery and antifungal drugs may cure a significant proportion of patients.

Although fungal infections themselves are relatively frequent, actual granulomatous masses due to fungal infections are rare. The rarity of the disease even in a high-volume center can be seen from the sparsity of the literature on this topic. In the last 2 decades, only six large series from India have described fungal granulomas.^{9,23,24,31,32,36} Here, we report our experience with fungal granulomas surgically managed over the last 18 years at our institute. Detailed clinical, radiological, surgical, pathological, and microbiological characteristics are described.

Methods

This retrospective study from a single institute (National Institute of Mental Health and Neurosciences, Bangalore, India) was focused on all cases of intracranial fungal granuloma (IFG) surgically treated in an 18-year period (2001–2018). Case files were taken from the medical record section. Relevant imaging details from CT or MRI of the brain, chest radiography, or paranasal sinus (PNS) CT were obtained from the radiology department. In a few cases, imaging details were not available in the radiology department; in such cases imaging findings mentioned in case sheets were used for our analysis. Additional data regarding fungal morphology and phenotype were also obtained from our neuropathology department. Culture reports from the Department of Neuromicrobiology at our institute were available in 60% of the cases. In some cases, even during the surgery, fungal granuloma was not kept in the differential diagnosis; hence, biopsy material could not be sent for culture. Other tests such as blood test and urine culture in almost all cases, sputum culture in those having tuberculosis, and CD4 counts in HIV-infected cases were performed. After surgical treatment, all patients were started on antifungal drugs based on the fungal morphology. Amphotericin B (AMB) was used most frequently. Based on final histopathology, different antifungal drugs such as fluconazole, flucytosine, or voriconazole were used in different combinations. Intravenous route delivery was used for a minimum of 6 weeks, and then depending on the culture report, it was converted to oral medications. All the relevant clinical data such as age, sex, signs and symptoms, symptom duration, predisposing factors, location of the disease with special attention to the PNS, surgical procedure performed, intraoperative findings, and follow-up data were recorded from the case files. For a few patients, no follow-up information was available in the case file, so in those cases, patients were contacted via telephone to find out about their current status.

Results

Clinical Presentation

A total of 90 cases of IFGs were studied. The mean pa-

TABLE 1. General demographic details and outcomes of 90 patients with IFGs

Variable	Value
Mean age in yrs	40.2 ± 15.97 (1–79)
Sex	
Male	64 (71.1%)
Female	26 (28.9%)
Mean symptom duration in mos	6.36 ± 9.22 (0.06–48)*
Patients w/ FU	69/90 (76.7%)
FU period in mos in 69/90 patients	37.97 ± 43.18 (3–144)
Deaths among those w/ FU	36/69 (52.2%)

FU = follow-up.

Values are expressed as the mean ± standard deviation (range) or as frequency (%).

* Two days to 48 months.

tient age was 40.2 years (range 1–79 years), and there were 64 (71.1%) males and 26 (28.9%) females (Table 1). The mean duration of symptoms before presentation to the hospital was 6.36 months (range 0.06–48 months). Headache (54 patients) was the most common presenting complaint, followed by visual symptoms (35 patients), fever (21 patients), limb weakness (13 patients), and seizure (9 patients; Table 2). Cranial nerve involvement was the most common sign (47 patients), followed by motor deficit (22 patients) and papilledema (7 patients). Ocular motor nerves (cranial nerves III, IV, and VI) and optic nerves were most frequently involved most likely because of the close relation of the orbital apex/cavernous sinus to the PNSs. Hemiparesis was seen in 22 patients because of either direct mass effect from the lesion or its associated perilesional edema over the motor cortex, basal ganglia, or internal capsule.

Predisposing Factors

Of the 90 patients, 30 (33.3%) had predisposing factors like diabetes mellitus, tuberculosis, trauma/direct inoculation, contiguous (mastoid) or remote (infective endocarditis) infection, or other immunocompromised status like HIV infection, neutropenia, Guillain-Barré syndrome, or a post-chemoradiation therapy status (Table 3). Direct inoculation in our series implies the development of IFG after a traumatic compound skull fracture.

Location of the IFG

A pure intracranial location of the IFG was seen in 49/90 cases (54.4%), whereas rhinocerebral or PNS involvement was seen in 41/90 cases (45.6%; Table 4). IFG was seen as a single lesion in 75 cases (83.3%) and in multiples in 15 cases (16.7%). The frontal lobe was most frequently involved either in isolation or in most cases as an extension from the sphenoid sinus, orbital region, or anterior cranial fossa (ACF) base. Cavernous sinus and parasellar region involvement were frequently seen. Pure cerebellar involvement was seen in 5 cases and the thalamus in 3 cases.

Imaging

CT was used as the sole modality for diagnosis in 55

TABLE 2. Presenting clinical symptoms and signs of 90 patients with IFGs

	No. (%)
Symptom	
Headache	54 (60%)
Visual disturbance	35 (38.9%)
Fever	21 (23.3%)
Limb weakness	13 (14.4%)
Seizure	9 (10%)
Altered sensorium	6 (6.7%)
Nasal discharge	2 (2.2%)
Loss of smell	1 (1.1%)
Wound discharge	1 (1.1%)
Hearing loss	1 (1.1%)
Sign	
Cranial nerve involvement	47 (52.2%)
Motor deficit	22 (24.4%)
Papilledema	7 (7.8%)
Cerebellar signs	6 (6.7%)
Meningismus	3 (3.3%)
Anosmia	2 (2.2%)
Aphasia	2 (2.2%)
Behavioral changes	1 (1.1%)
Periorbital edema	1 (1.1%)

cases, whereas MRI was available in 35 cases. We had seen two different patterns of IFG on CT. The first pattern was a predominantly hyperdense lesion on plain CT (36 patients) with surrounding edema (hypodense), and the second pattern was a hyperdense periphery with a hypodense central part of the lesion along with perilesional edema (19 patients). Bony destruction was seen if the lesion involved the skull base. The enhancement pattern was either uniform or a peripheral ring pattern. On MRI, the most common finding of IFG was T1 hypointense/isointense and T2 hypointense with heterogeneous contrast enhancement (22 patients; Fig. 1). Less commonly (13 patients), the lesion was hypointense/isointense on T1-weighted images and hyperintense on T2-weighted images with an occasional peripheral rim of hypointensity. Magnetic resonance spectroscopy was done in 10 cases, and all scans showed an increased lipid-lactate peak with a reduction in other metabolites. Diffusion-weighted imaging was available in 8 cases, all of which showed diffusion restriction. In 33 patients (36.7%), IFG was not the working diagnosis. In the remaining 57 patients (63.3%), even though IFG was not diagnosed based on clinical or imaging features, it was kept as one of the main differential diagnoses.

Treatment

Most of the patients underwent open surgery, i.e., craniotomy and excision (55 cases). Endoscopic biopsy (transnasal with or without transsphenoidal approach) was performed in 30 cases, and 5 patients underwent stereotactic biopsy. Three patients required a ventriculoperitoneal

TABLE 3. Predisposing factors of patients with IFGs

Factor	No.
DM	16
TB	4
Trauma/direct inoculation	2
HIV	2
Infection (contiguous/remote)	
CSOM	1
Infective endocarditis	1
Immunocompromised	
CD4 count <200 cells/mm ³	1
Neutropenia	1
GBS	1
Post-chemoradiation	1

CSOM = chronic suppurative otitis media; DM = diabetes mellitus; GBS = Guillain-Barré syndrome; TB = tuberculosis.

shunt for obstructive hydrocephalus. A solid/firm lesion was seen during surgery in 71 cases (78.9%), whereas 19 cases (21.1%) had an abscess.

Pathogen

Aspergilloma (43 patients) was the most common fungal lesion based on histopathological diagnosis, followed by zygomycosis (13 patients), chromomycosis (9 patients), cryptococcoma (7 patients), mucormycosis (5 patients), and candida infection (1 patient). Figure 2 shows the various histopathological appearances along with special stains of the fungal pathogens seen in the current study. In 12 of our cases, the exact fungal phenotype could not be identified based on histopathology (Table 5). Fungal cul-

TABLE 4. Location of the fungal lesion among 90 patients with IFGs

Location	No.
Pure intracranial	49 (54.4%)
Intraaxial	39
Frontal	17
Parietooccipital	7
Temporal	7
Cerebellar	5
Thalamus	3
Extraaxial	10
ACF	6
MCF	3
ACF & MCF	1
Sinonasal or rhinocerebral	41 (45.6%)
ACF w/ orbit	10
Cavernous sinus & parasellar region	11
ACF	9
MCF	5
ACF & MCF	2
MCF & PCF	2
ACF w/ parenchyma	2

MCF = middle cranial fossa; PCF = posterior cranial fossa.

FIG. 1. Neuroimaging of the various fungal lesions. **A:** Axial T1-weighted contrast MRI shows a heterogeneously enhancing lesion with areas of central necrosis in the right temporal base extending to the posterior fossa and also involving the ethmoid sinus (aspergilloma). **B:** Axial T2-weighted MRI shows a hypointense lesion in the left medial temporal region with involvement of the cavernous sinus and the ethmoid sinus (aspergilloma). **C:** Axial T1-weighted contrast MRI shows a peripheral enhancing lesion with a central necrotic part in the right cerebellar hemisphere (cryptococcoma). **D:** Coronal T1-weighted contrast MRI shows a heterogeneously enhancing lesion in the ACF base with involvement of the PNS (aspergilloma). **E:** Axial CT shows a well-defined hyperdense lesion in the right parietal region with a few specks of calcification at the rim (chromoblastomycosis). **F:** Axial CT shows a well-defined hypodense lesion in the right frontal region with a hyperdense rim and perilesional edema (chromoblastomycosis).

ture reports were available in only 60% of the cases ($n = 54$). In some cases, even during surgery, fungal granuloma was not kept in the differential diagnosis; in those cases, the biopsy material could not be sent for culture. Thirty-seven of the 54 cultures were positive for the fungal pathogen, and 17 cultures had no growth (Table 6).

Antifungal Agents and Outcome

Antifungal medication, mainly AMB, voriconazole, fluconazole, or flucytosine as monotherapy or in combination, was started immediately once the diagnosis of fungal infection was considered or sometimes after the biopsy report. It was given for a minimum of 6 weeks via an intravenous route and was then converted to oral form. Many patients required medications up to 18 months depending on the response to treatment based on clinical or radiological improvement.

We had a few in-hospital deaths (12 patients) because of disease progression or drug toxicity, mainly due to renal failure. Follow-up was available for 69/90 patients (76.7%). The mean duration of the follow-up was 37.97 months (range 3–144 months). The mortality rate was 52.2% (36/69 patients) among the patients with available follow-up. Of the 36 deaths, 12 occurred within a week of surgery, 6 within 1 month, 10 within 3 months, 5 within 6 months, and 3 within 2 years. Cumulative mortality at different points after surgery was as follows: 17.4% at 1

week, 26.1% at 1 month, 40.6% at 3 months, 47.8% at 6 months, and 52.2% at 2 years. Eighteen of 36 deaths had predisposing factors that led to a fatal outcome.

Discussion

Fungal infections of the central nervous system may take the form of an acute, rapidly fatal illness with meningitis, encephalitis, vasculitis, and abscess formation or a chronic form with granuloma formation.³² Our study was limited to patients with histopathologically proven fungal granulomas.

Predisposing Factors

IFGs in immunocompetent patients have been predominantly reported from India, Pakistan, Saudi Arabia, Africa, and California in the United States.^{15,35} It is postulated that a hot, dry climate with a high content of *Aspergillus* spores in the atmosphere due to agricultural dust is a probable cause of IFGs in persons residing in these regions. Nearly 50% of patients with IFGs have no overt predisposing illness or evidence of immunosuppression.^{9,14,20,32,35} It is possible that in some of these patients, there may be sub-clinical impairment of cell-mediated immunity.²⁸ Rarely, fungal infection may follow direct inoculation of the brain during intracranial or transsphenoidal surgery or following trauma.^{1,33} We had 2 such cases in which the patient

FIG. 2. Histological and immunohistochemistry images of various fungal lesions. **A:** Photomicrograph showing necrotizing granulomatous inflammation with pigmented fungal hyphae (phaeohyphomycosis, chromoblastomycosis). H & E. **B:** Photomicrograph showing necrotizing inflammation with yeast structures of *Cryptococcus*. H & E. **C:** Mucormycosis: broad aseptate hyphae branching at right angles. Periodic acid–Schiff. **D:** *Aspergillus*: granuloma with fungal hyphae within the giant cell. H & E. **E:** *Aspergillus*: slender septate hyphae branching at acute angles. Gomori methenamine silver. **F:** Granulomatous inflammation with pigmented fungal hyphae (phaeohyphomycosis, chromoblastomycosis). Gomori methenamine silver. Original magnification $\times 200$ (A–E) and $\times 100$ (F).

presented to us with IFG after a definitive history of compound fracture of the skull vault.

IFGs usually develop by the spread of fungal infection to the intracranial compartment from a systemic source of infection. The disease usually spreads through the hematogenous route, but invasion of contiguous tissues and spread into the intracranial compartment is also common in the case of PNS and mastoid infections. However, in a proportion of patients with IFG, no obvious systemic source for the fungal infection is discernible despite an extensive search.²⁸ We had only 2 cases in which there was evidence of systemic infection. One case had mastoid infection and the other had infective endocarditis.

A previous study from our institute showed that 68% of patients had some kind of predisposing factor.⁹ In the current study, however, only 33.3% had such factors, which again indicates that the incidence of IFG is on the rise even in immunocompetent patients. In a large study from India by Naik et al., most of the 66 patients did not have any predisposing factors.²⁴

Clinical Presentation

The mean age of our patients was 40.2 years, which is similar to the mean age in a previous study from our institute⁹ and comparable to 32.3 years and 28 years in the studies by Naik et al.²⁴ and Sharma et al.,³² respectively. The greater IFG incidence in males in our study

is probably the result of their increased exposure to the outside environment. This finding has also been suggested by other authors.^{21,23,27,32}

Most of our patients presented with headache (54 patients) and cranial nerve symptoms (47 patients), mainly the optic nerve and ocular motor nerves. Seizure was a rare presenting symptom and was observed in only 9 of our cases. These findings are consistent with data in other studies.^{9,24,32} Fever was seen in 21 of our patients. In the literature, there are also reports of patients who present with an increased incidence of stroke.^{12,14} Subarachnoid hem-

TABLE 5. Fungal phenotype based on histopathology*

Type	No.	%
Aspergilloma	43	47.8
Cryptococcoma	7	7.8
Chromomycosis	9	10
Zygomycosis	13	14.4
Mucormycosis	5	5.6
Candida	1	1.1
Fungal	12	13.3
Total	90	100

* Not culture proven.

TABLE 6. Culture-proven fungal pathogen

Pathogen	No.
<i>Aspergillus fumigatus</i>	7
<i>Aspergillus flavus</i>	4
<i>Aspergillus</i> spp.	4
<i>Cryptococcus neoformans</i>	5
<i>Scytalidium dimidiatum</i>	1
Septate fungi	1
<i>Cladosporium</i> spp.	1
Fungus	4
<i>Cladophialophora bantiana</i>	6
<i>Mucor</i> spp.	1
<i>Candida albicans</i>	1
<i>Fonsecaea pedrosoi</i>	1
<i>Cryptococcus gattii</i>	1
No growth	17
Total positive cultures	37 (68.5%)
Total cultures available	54/90 (60%)

orrhage (SAH) and mycotic aneurysm formation are rare presentations of IFG.^{3,23,24,32} However, none of our patients presented with stroke or SAH.

Location of the Granuloma

As seen in other studies, the frontal lobe, followed by the temporal lobe, was the most common site for IFG.^{9,24,32} A possible explanation would be the close relation to the PNS and ACF base. Isolated frontal IFGs have also been seen without contiguous sinus involvement. The sella, parasellar region, and cavernous sinus with the middle cranial fossa base were other common locations seen in our study (Table 4). Posterior cranial fossa involvement was rare, and we had only 5 isolated cerebellar lesions. The route of spread for the pure intraparenchymal variant has been proposed to be hematogenous or even retrograde thrombophlebitis, especially in the case of cerebellar IFGs. Selvam et al. have a detailed staging system for invasive rhinocerebral fungal granuloma according to the extent of involvement and the final outcome.³¹

Imaging Features and Differentials

In his review article on IFG, Rajshekhar has explained how it can be missed from the list of differential diagnoses.²⁸ According to him, the caseload of IFGs would not exceed two per year even in large neurosurgical centers in India. Surgery for IFGs would constitute about one per 1000 neurosurgical procedures performed at these centers. With these prevalence rates, it is not surprising that IFGs are rarely suspected in patients with isolated intracranial masses and are misdiagnosed as glioma, tuberculoma, lymphoma, meningioma, or cholesteatoma.

Several reports deal with imaging finding of IFGs.^{8–10,16,17,25,32,34} Irregular isodense/hyperdense lesions with faint heterogeneous contrast enhancement on CT scan and perilesional edema are features of fungal lesions.^{10,13,25,26,34} Evidence of PNS involvement, lesions close to the PNS,

small areas of bone destruction, and infarcts caused by arteritis favor a fungal etiology.^{5,6,10,11,17,24,25,33} Neuroimaging patterns that have been reported vary depending on the immunological status of the patient and the age of the lesions.^{10,17,33} Saini et al. have described the characteristic imaging features of aspergilloma in immunocompetent patients.²⁹ These authors concluded that hyperdense sino-nasal disease with bone destruction and intracranial extension on CT, hypointense signal intensity of the lesions on T2-weighted MRI, areas of restricted diffusion, decreased perfusion on perfusion-weighted imaging, and hemorrhages are key to the imaging diagnosis of fungal infection. Dubey et al. have shown the distinguishing feature between cryptococcoma and aspergilloma based on MRI.⁹

The classic CT finding for IFG in our study was a predominantly hyperdense lesion on plain CT with peripheral edema or hyperdense periphery with a hypodense central portion of the lesion. Bone destruction was common in skull base lesions. The typical pattern on MRI was isointense/hypointense on T1-weighted imaging and hypointense on T2-weighted images. T2 hyperintense lesions have also been seen with a peripheral rim of hypointensity and heterogeneous contrast enhancement. Magnetic resonance spectroscopy and diffusion-weighted imaging definitely help the physician in the diagnosis of IFG. Besides imaging the brain with CT and MRI, a few patients may have abnormality diagnosed on chest radiograph or thorax CT, especially in cases of aspergilloma. However, we did not find any such abnormal chest findings in our patients.

Fungal Pathogens

Aspergillus was the most common phenotype (47.8%) causing IFG in the current study as well as in previous studies.^{9,24,32,36} Other phenotypes were cryptococcoma, mucormycosis, zygomycosis, and chromomycosis (Table 5). However, when we looked at the fungal culture, only 60% of the reports were available (Table 6). *Aspergillus* with different subspecies remains the most common pathogen. *Cladophialophora bantiana* was seen in 6 patients, *Cryptococcus neoformans* in 5 patients, *Cryptococcus gattii* in 1 patient, and *Fonsecaea pedrosoi* in 1 case. All of the above pathogens have been reported from our institute as part of a case series or case report by Garg et al.,¹¹ Uppar et al.,³⁷ and Madhugiri et al.¹⁹

Treatment

Aggressive surgical excision followed by the timely administration of antifungal drugs is the cornerstone of the management of IFGs. Of the 90 patients in our study, 55 required open surgery in the form of craniotomy and excision of the granuloma. We tried to excise the granuloma completely; however, in a few places, especially in the skull base region, because of a lesion's proximity or adherence to a vital neurovascular structure, we were restricted in performing an aggressive resection. In 30 patients in whom the lesion was accessible via an endoscopic transnasal approach, endoscopic biopsy was performed, followed by the administration of antifungal drugs. In 5 cases in which the lesion was small, involving an eloquent region of the brain, and without any significant mass effect or perilesional edema, we performed stereotactic biopsy.

Three patients required CSF diversion in the form of a ventriculoperitoneal shunt for obstructive hydrocephalus.

Outcome

The final outcome of IFG remains poor; however, results are getting better with early diagnosis because of neuroimaging, increased awareness of the patient as well as the treating physician, aggressive resection, and better antifungal drugs.

If we look at mortality data from the year 1985, we note a gradual decline to the present. The initial study by Yanai et al.³⁹ in 1985 had a mortality rate of more than 95%. In 1996, Sharma et al.³² showed a mortality rate of around 50%. Similar rates of mortality have been documented: 63% by Dubey et al.⁹ in 2005, 62.8% by Young et al.⁴⁰ in 1985, and 36.4% by Naik et al.²⁴ in 2015. One study by Siddiqui et al.³⁴ has shown quite a low rate of mortality at 15%. Our study had a mortality rate of 52.2%, which is similar to rates in other major series.

We started the antifungal agents as soon as the working diagnosis of IFG was made based on clinical and imaging features. Very occasionally, we had the experience of overtreatment in some cases. In one case, a young boy had the classic presentation of the disease in the right basifrontal region extending into the frontal air sinus. The patient's history and imaging features all favored a diagnosis of fungal granuloma. The patient was started on empirical AMB and taken for surgery. Antifungal medication was continued for a week postoperatively until the definitive biopsy report came, and to the surprise of everyone, it turned out to be lymphoma. It is better to keep the diagnosis of fungal granuloma in mind and start the treatment early rather than waiting for the definitive biopsy or culture report, which takes a minimum of 5–7 days and deprives the patient of the beneficial or potentially curative effect of antifungal medications.

Study Limitations

This was a retrospective study from a single institute. In terms of follow-up, telephonic conversations were used for a few patients, and the exact cause of death could not be established for those deaths occurring outside the hospital. So, it was difficult to predict whether death was attributable to fungal disease per se, antifungal toxicity, or comorbidity.

Conclusions

A high index of suspicion for IFG should exist for patients with an immunocompromised status or diabetic patients with rhinocerebral mass lesions. Early diagnosis, aggressive surgical excision, and a course of promptly initiated antifungal therapy are associated with a better prognosis. Mortality is high for immunocompromised patients even after extensive surgery and antifungal treatment.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: all authors. Acquisition of data: Prabhuraj, Mishra, Nandeesh, Chandrashekar. Analysis and interpretation of data: Prabhuraj, Mishra, Shukla, Ramalingaiah, Arivazhagan, Bhat, Somanna, Devi. Drafting the article: Prabhuraj, Mishra, Nandeesh, Chandrashekar, Arivazhagan, Devi. Critically revising the article: Prabhuraj, Mishra, Shukla, Chandrashekar, Ramalingaiah, Arivazhagan, Bhat, Somanna, Devi. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Prabhuraj. Statistical analysis: Prabhuraj, Mishra, Shukla.

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