Intracranial Fungal Granulomas: A Single Institutional Clinicopathologic Study of 66 Patients and Review of the Literature

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Key words
- Intracranial fungal granuloma
- Outcome
- Recurrence
- Surgery

Abbreviations and Acronyms
CSF: Cerebrospinal spinal fluid
CT: Computed tomography
ICFG: Intracranial fungal granuloma
ICP: Intracranial pressure
MRI: Magnetic resonance imaging
PNS: Paranasal sinuses

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INTRODUCTION: **Fungal granulomas of the central nervous system are rare and have a high rate of mortality and morbidity, irrespective of treatment. The authors report their experience of managing 66 patients during 15 years and discuss the clinical, radiological, surgical, and pathologic findings. This series is among the largest reported.**

MATERIAL AND METHODS: **A retrospective analysis was performed on patients with intracranial fungal granulomas (ICFGs), treated in the authors' institution, between January 1997 and May 2011. Only mass-forming histopathologically proven ICFGs were included in this study.**

RESULTS: **The age of the patients ranged from 7 years to 67 years (mean = 32.3 years), and most patients were in the third and fourth decades of life. The study population comprised 47 male and 19 female patients. The most common symptom was headache (41 patients), followed by vomiting (16 patients) and blurring of vision (16 patients). Only 3 patients presented with fever. The duration of symptoms was less than 6 months in all cases and less than 3 months in 39 cases. Anterior cranial fossa and frontal lobe was involved in 35 cases (54.5%), followed by middle cranial fossa in 20 cases (30.3%). Three cases had granulomas in the cerebellopontine angle. Three cases had multicompartmental involvement, and 4 had multilobar involvement. Nine patients had predisposing factors for fungal infection Based on clinical and imaging data, preoperative diagnosis of a possible fungal lesion was made in 44 (some had only computed tomography imaging) patients. All the patients were treated surgically, followed by antifungal treatment with amphotericin-B and/fluconazole/itraconazole for a period of 6 weeks. Eight patients had symptomatic recurrence of lesions 3–12 weeks after treatment and underwent reoperation. Six patients were lost to follow-up. Nine patients died in the postoperative period (within 30 days postoperatively). Fifteen patients died during follow-up because of recurrent lesions, repeat surgery, renal failure, and unrelated causes. Overall mortality was 24 (36.3%). Poor neurologic status before surgery, emergency craniotomy, severe brain edema with mass effect, and opening of ventricles during surgery were associated with poor outcome. *Aspergillus* species were the causative organism in an overwhelming majority of patients (n = 52) followed by *Mucor* in 7 cases, *Cladosporium* in 3 cases, eumycetoma in 2 cases, and maduramycosis and blastomycosis in 1 case each.**

CONCLUSION: **ICFGs have high rates of morbidity and mortality. Early diagnosis, radical surgery, and antifungal treatment for 6 weeks may improve outcome. Poor neurologic status of patients at the time of presentation, immunocompromised state, contamination of ventricular cerebrospinal during surgery, and renal failure (attributable to amphotericin-B) are associated with poor outcome.**

INTRODUCTION

The realm of fungi is vital for human life, because these organisms produce much of the soil necessary for agriculture. Many, however, act as pathogens in diseases ranging from skin infections to septicemia, including fatal brain lesions. Fungi are generally robust, ubiquitous, and current fungicidal drugs have substantial toxicity. Fungal infections of the central nervous system are relatively rare. These can involve the meninges, calvarium, brain, and intracranial vessels in different forms, severity, and combinations (3, 10, 29, 42). The incidence of such infections seems to be increasing because of longer life expectancy, larger proportion of aging population, widespread use of immunosuppressive drugs, longer survival of immunocompromised patients, increasing numbers of HIV infections, and poor nutritional status (1, 25, 48).

Fungal granulomas in the central nervous system are great mimics, posing a diagnostic challenge to clinicians and radiologists alike. These have high rates of mortality and morbidity, but early diagnosis and prompt treatment with surgery and fungicidal drugs may potentially cure a significant proportion of patients. Extensive review of existing literature reveals apart from 3 large series published in last 10 years (15, 32, 43), most of the data on

intracranial fungal granulomas (ICFGs) are in the form of individual case reports and small series of patients (2, 9, 28, 30, 35, 49). The authors report their experience of managing 66 patients during the last 15 years and discuss the clinical, radiological, surgical, and pathologic findings.

MATERIAL AND METHODS

A retrospective analysis was performed on patients with ICFGs treated in the Department of Neurosurgery, All India of Institute of Medical Sciences, New Delhi, India, between January 1997 and May 2011. Only mass-forming and histopathologically proven ICFG were included in the study. Fungal abscesses and infections without any mass effect (such as meningitis, thin extradural extensions of sinonasal disease, or postoperative fungal infections) were excluded from the study. We analyzed 66 patients with ICFG during a 15–year time span (1997–2011), and their medical records were reviewed. Relevant clinical history such as presenting signs and symptoms, clinical examination findings, location of lesions, radiologic impression, causative organism and involvement of sinuses, predisposing factors, pertinent laboratory data, and final outcomes were reviewed. All patients were treated with amphotericin-B and flucanozole/flucytosine/itraconazole, except 3 patients, who were intolerant to amphotericin-B. The follow-up period ranged from 3 months to 3 years.

OBSERVATIONS AND RESULTS

The age of the patients ranged from 7 years to 67 years (mean 32.3 years) in our study. Most of the patients were in third and fourth decade of life, and only 8 patients were in the pediatric age group (younger than 18 years). There were 47 male and 19 female patients. Their clinical features are depicted in Table 1. A large majority of patients presented with increased intracranial pressure (ICP). The most common symptom was headache (41 patients), followed by vomiting (16 patients) and blurring of vision (16 patients). Only 3 patients had fever as a presentation. The duration of symptoms was less than 6 months in all cases and less than 3 months in 39 cases.

The location of lesions is depicted in Table 2. Anterior cranial fossa and frontal lobe was the most commonly location in 35 cases (53.03%), followed by middle cranial fossa and temporal lobe in 20 cases (30.3%). Three cases had posterior fossa granulomas. Three cases had multicompartmental involvement; 4 had multilobar involvement and 1 had involvement of the cerebellum. Twenty-five patients (37.8%) had extension of disease into paranasal sinuses (PNS). We noticed that these cases presented with a longer history and had symptoms pertaining to nose/ear/sinus/orbits along with neurologic symptoms. Those without PNS extension of lesions presented more commonly with focal deficits, seizures, and increased ICP.

Nine patients had some predisposing factors for fungal infection. Four patients had diabetes, 3 were on steroid treatments, and 1 each had HIV infection and aplastic anemia. Most of our patients, however, had no known predisposing factor. Forty-nine patients underwent computed tomography (CT), and 44 underwent magnetic resonance imaging (MRI) before surgery. None of the patients had preoperative angiography performed. Additional CT scan sections (PNS and orbit) were obtained along with 3-dimensional reconstruction for coronal and sagittal images when required. There was no pathognomonic CT or MRI finding. CT scan usually showed a hyperdense or mixed-attenuation lesion with variable contrast enhancement and perilesional edema (Figure 1A). Extension of lesion in to PNS was demonstrated in 25 cases and into orbit in 9 cases (Figure 1C and D). The lesions was hypo-to-isointense on T1-weighted imaging of MRI (Figure 2A), hypointense on T2-weighted imaging (Figure 1C and Figure 2B), and of variable contrast enhancement (Figure 1D and Figure 2C). Marked hypointensity on T2-weighted imaging was the most consistent and helpful feature in making the diagnosis. Angiography was not done in any of the patients. None of the patients had imaging evidence of subarachnoid hemorrhage.

On the basis of clinical and imaging data, preoperative diagnosis of fungal lesion was made in 44 (66.6%) patients. The patients were sometimes misdiagnosed with glioma, tuberculomas, lymphomam, or neurofibroma (Table 3). Four patients were given antitubercular treatment for 2–3 months but increase in size of lesion prompted surgical decompression and revealed a fungal etiology.

The surgical procedures conducted are depicted in Table 4. Indications of surgery included features of increased ICP, neurologic deterioration, declining vision, progressive proptosis, presence of a large mass lesion on imaging, and unsure diagnosis. Four cases were operated in an emergent situation because of altered

Table 1. Clinical Features

Characteristics	No. Patients
Headache	41
Vomiting	16
Blurring of vision	16
Proptosis	13
Seizures	9
Ptosis	5
Hemiparesis	8
Altered sensorium	4
Hearing impairment	3
Anosmia	3
Fever	3
5th nerve palsy	2
7th nerve palsy	2
Nasal mass	6
Epistaxis	3
Diplopia	6
Memory loss	1
Sinus discharge	1
Cerebrospinal fluid rhinorrhea	1

Table 2. Lesion Location

Location	No. Patients
Anterior cranial fossa and frontal lobe	35
Middle cranial fossa, parasellar, cavernous region and temporal lobe	20
Posterior cranial fossa involving cerebellopontine angle, cerebellum	4
Multi compartmental	3
Mutlilobar	4