Intracranial Space-Occupying Lesions

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Abbreviations

CNS	Central nervous system
CSF	Cerebrospinal fluid
CT	Computed tomography
MRI	Magnetic resonance imaging
SOLs	Space-occupying lesions

20.1 Introduction

Fungal infections of the central nervous system (CNS) represent a diagnostic and therapeutic challenge with a generally poor outcome despite surgical and medical treatment attempts. Invasive systemic fungal pathogens including *Cryptococcus neoformans*, *Candida* spp., and *Aspergillus* spp. have been commonly associated with CNS involvement. While the species of *Candida* and *Aspergillus* remain the most common causes of invasive fungal infections, other yeasts, filamentous fungi, and opportunistic yeast-like fungi and molds are increasingly being recognized (Richardson and Lass-Flörl 2008). Immunocompetent individuals usually do not get infected by the fungal pathogens due to opportunistic nature of fungi including *Cryptococcus*, *Aspergillus*, *Zygomycetes*, and *Candida* (McKeever 2012). *Aspergillus* is the most common pathogen which causes intracranial granulomas (Naik et al. 2015). Fungal space-occupying lesions (SOLs) include intracranial fungal granulomas, abscesses, and cysts, particularly in the primary parenchymal location. These nonneoplastic fungal SOLs of the CNS can grow expansively and easily mimic their neoplastic counterparts in both clinical and radiological evaluations. Fungal granulomas are the most frequently encountered form of the disease in clinical practice, but fungal abscesses or a compound of these lesions can be seen in decreasing frequency. Intraparenchymal cysts which locate in basal ganglia typically occur in cryptococcal infection. *Candida*, *Aspergillus*, *Cladosporium*, and *Mucorales* commonly produce primary parenchymal fungal abscesses. Hematogenous dissemination of fungi from an extracranial site causes multiple foci of infection within the brain. Initial meningoencephalitis leads to vasculitis thrombosis and late hemorrhagic cerebral infarction. When an abscess develops, it may rapidly expand. Aspergillosis, histoplasmosis, blastomycosis, paracoccidioidomycosis, cladosporiasis, mucormycosis, and cryptococcosis may produce CNS fungal granulomas which mimic tuberculomas but differ by the presence of more

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fibrosis. Frontal and temporal granulomas generally occur due to spread from paranasal sinuses as in aspergillosis and mucormycosis, whereas parietal granulomas occur due to hematogenous spread of other fungi (Raman Sharma 2010).

20.2 Epidemiology

The incidence of CNS fungal infections is similar to that of systemic fungal infections and has been rising due to increased life expectancy, large ageing population, malignancy, extensive use of immunosuppressive drugs, longer survival of patients, increased frequency of acquired immunodeficiency syndrome (AIDS), and poor nutritional status (Naik et al. 2015). The estimated annual incidences of invasive fungal infections caused by opportunistic pathogens per million of the population vary between 12 and 228 infections according to causative agent (Raman Sharma 2010). The Indian subcontinent has the highest reported frequency of histologically verified intracranial fungal mass lesions in geographic distribution with one to two cases per year. Hot and dry climate with high content of fungal spores in agrarian dust was blamed for endemic form of the disease in India, Africa, and California (Naik et al. 2015). Predisposing factors include diabetes, tuberculosis, HIV, steroids, immunosuppression, and chemotherapy (Naik et al. 2015). Intracranial fungal mass lesions had a 0.5–1% cumulative prevalence in transplant recipients (Rajshekhar 2007).

20.3 Pathogenesis

Infection usually spreads to the CNS via the bloodstream from a primary pulmonary infection, or it can extend directly from a close focus such as wound infection, otitis, osteomyelitis, or an infected cranial sinus (McKeever 2012). In the presence of an infected paranasal sinus, infection could spread gradually from the sinus to bone, extradural space, meninges, orbit, anterior and middle skull base, and parasellar region. Extension to the intracranial space can be via anatomical apertures such as orbital apex, and communicating perivascular spaces act as a bridge for spreading to subarachnoid space. Retrograde thrombophlebitis was also blamed for the development of cerebellopontine angle and cerebellar masses. Although fungal pathogens can cause meningitis, encephalitis, abscess formation, vasculitis, or granulomas, they tend to cause granulomatous meningitis following an acute phase of infection and can affect the meninges, calvarium, brain, and intracranial vessels in distinct forms, severity, and compositions (Naik et al. 2015).

20.4 Diagnosis

A high index of suspicion is critical for early diagnosis and avoidance from associated significant morbidity and mortality. Past medical history of the patient or the patient's close relatives should be taken into consideration. Like other intracranial space-occupying lesions, headache, nausea, vomiting, altered vision, and mental status, focal neurological deficits are commonly encountered presentations. Invasion of the cavernous sinus and orbital apex could cause visual symptoms, proptosis, ophthalmoplegia, superior orbital fissure syndrome, and cranial nerve palsies. Other uncommon manifestations include seizures, stroke, subarachnoid hemorrhage, and mycotic aneurysm formation (Naik et al. 2015).

20.5 Imaging Findings

Computed tomography (CT) scan is a common first-line investigation tool with a few characteristic findings. Irregular iso-/hyperdense lesion with perilesional edema and thin heterogeneous contrast enhancement are well-known features. In the case of primary sinus disease (Fig. 20.1), proximity of lesions, evidence of bone destruction, and infarcts due to arteritis may promote a fungal etiology (Naik et al. 2015). Primary parenchymal lesions showed heterogeneous attenuation with predominantly low-density areas, while dural-based lesions showed isodense to hyperdense attenuation (Saini et al. 2010).

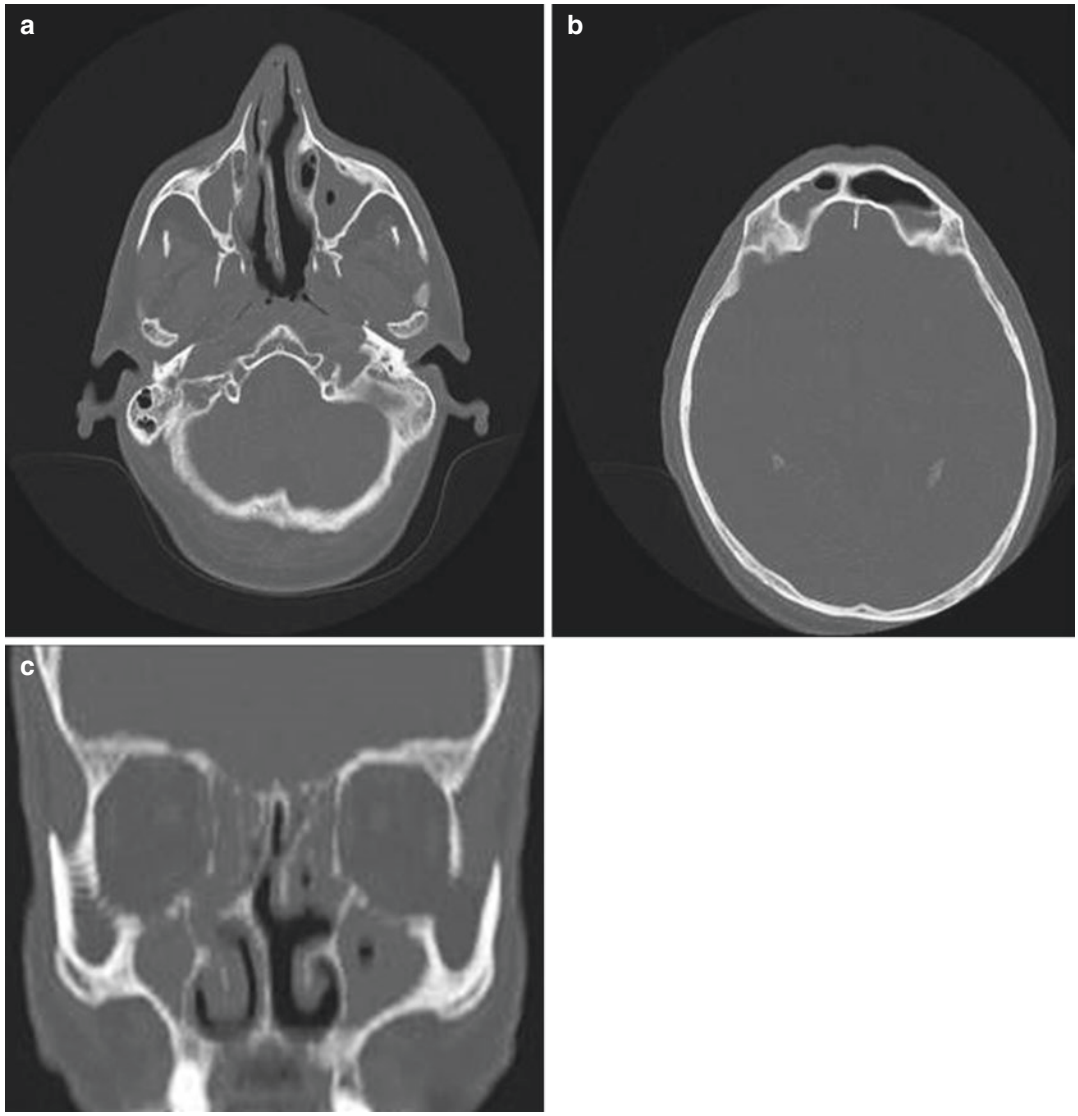

Fig. 20.1 Paranasal sinus computed tomography (CT) of a 45-year-old male patient with common variable immunodeficiency. Complete filling of maxillary (**a**) and frontal sinus with pus and pansinusitis appearance (**c**)

Multiple lesions in an immunocompromised patient should prompt further investigation with magnetic resonance imaging (MRI).

MRI findings have been reported to vary depending on the immunological status of the patients and on the age of the lesions. Again primary sinus disease gains importance for establishing correct diagnosis with thickened mucosa or complete filling appearance. Isointense to hypointense signals of the lesion on both T(1)-weighted (T1W) and T(2)-weighted (T2W) images are primary findings. Primary parenchymal lesions show heterogeneous signal intensity pattern with predominantly hypointense signal on T1W and hyperintense signal intensity on T2W images. The lesions could enhance contrast in a homogenous or peripheral ring pattern. There is commonly a lack of contrast enhancement or surrounding edema in immunocompromised patients, reflecting reduced immune

response. The wall of the fungal abscess is usually regular and thin. Irregularity of the rim can vary depending on the aggressiveness of the fungus and the host's ability to exert an immune response (Hadley et al. 2017). Infiltration of the orbit, extraocular muscles, or cranial nerve compression can be detected with MRI. Restricted diffusion on diffusion-weighted imaging similar with pyogenic abscess, decreased perfusion on perfusion-weighted imaging, and presence of hemorrhage on gradient echo sequence gave worthy supporting data (Fig. 20.2) (Naik et al. 2015; Saini et al. 2010). The infarcts distribute commonly at the gray-white matter junction as well as basal ganglia, thalamus, corpus callosum, and perforating small artery territories in disseminated fungal infection (DeLone et al. 1999). The involvement of perforating arteries without involvement of the distal major arterial territories stresses the pathophysiologic difference between

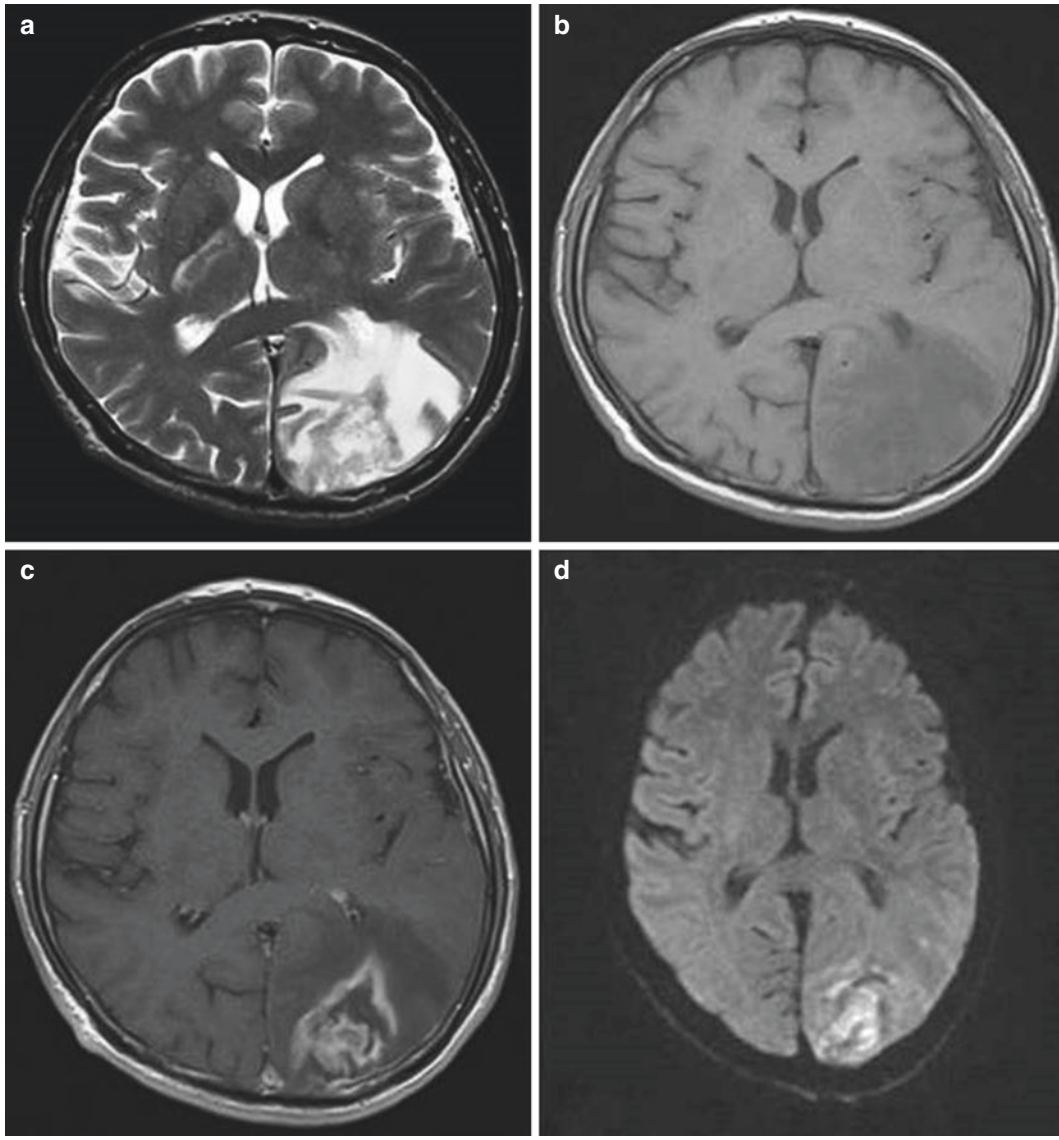

Fig. 20.2 T2-weighted pre-gadolinium (**a**), T1-weighted pre-gadolinium (**b**), and post-gadolinium (**c**) axial magnetic resonance imaging (MRI) sections showed a fungal space-occupying lesion (SOL) at the left occipital lobe of the same patient. Note the irregular rim pattern (**c**) and restricted diffusion on diffusion MRI (**d**)

septic fungal and thromboembolic infarction (Yamada et al. 2002). Corpus callosum involvement can be used for distinguishing fungal infection from pyogenic infection and thromboembolic infarction as the latter do not commonly involve the corpus callosum. But other processes such as glioblastoma, lymphoma, and multiple sclerosis should keep in mind for differential diagnosis (DeLone et al. 1999).

20.6 Management

Antifungal medications and surgery are the mainstay treatment options. Treatment modality preference depends on the primary location, size, and number of the lesions. General medical status of the patient carries high importance. Small fungal SOLs can be managed with aggressive antifungal medications and supportive care, whereas significantly large lesions that compress adjacent brain structures need radical surgical excision. Urgent decompression can be lifesaving in emergency situations. Surgical options include stereotactic procedures, craniotomy, shunt surgery, and mycotic aneurysm surgery. Indications of the stereotactic procedures include deep-seated lesions and lesions in the eloquent brain regions for the establishment of tissue diagnosis (Murthy and Sundaram 2014). Surgical excision reduces infection load, reduces mass effect, and improves efficacy of following medical treatment. Radical excision of lesions without excessive contamination of cerebrospinal fluid (CSF) spaces was advocated (Naik et al. 2015). Survival rates are much better in patients treated with combined medical and surgical treatment in patients treated with medical treatment only (Gonzalez et al. 2002). Adherence/invasion of the lesion to basal vessels and cranial nerves leads to specific challenges and complicates the postoperative course by leading to arteritis and infarcts, cavernous sinus thrombosis, meningoencephalitis, ventriculitis, etc. Shunt surgery could be imperative due to hydrocephalus with elevated intracranial pressure (Gonzalez et al. 2002). Ommaya reservoir insertion for intralesional administration of amphotericin B was reported in patients with sinocranial aspergillus granulomas with dense fibrous tissue (Murthy and Sundaram 2014). Surgical clipping or endovascular treatments with aggressive antifungal treatment are indicated for the patients with mycotic aneurysms (Rajshekhar 2007). Prognosis after treatment depends on the prompt recognition and management of the disease as well as preoperative neurologic status of patient, immunocompromised state, contamination of ventricular CSF during surgery, and renal failure (due to amphotericin B) (Naik et al. 2015). Previously reported gloomy surgical results (Dubey et al. 2005; Sharma et al. 1997; Yanai et al. 1985) were improving slowly (Naik et al. 2015). Naik et al. recommended preoperative antifungal treatment for 1–2 weeks, followed by radical surgery and antifungal treatment for the following 6 weeks (Naik et al. 2015).

20.7 Conclusion

It is concluded that:

- CNS fungal infections have been diagnosed increasingly over the last few decades, due to the increase of immunocompromised patients under risk.
- Although some improvements have been achieved, CNS fungal infections constitute a diagnostic and therapeutic challenge.
- Antifungal medications and surgery are the mainstay treatment options.
- Radical excision of SOLs without excessive contamination of CSF spaces improves outcome.

References

DeLone DR, Goldstein RA, Petermann G, et al. Disseminated aspergillosis involving the brain: distribution and imaging characteristics. AJNR Am J Neuroradiol. 1999;20:1597–604.

Dubey A, Patwardhan RV, Sampth S, et al. Intracranial fungal granuloma: analysis of 40 patients and review of the literature. Surg Neurol. 2005;63:254–60. https://doi.org/10.1016/J.SURNEU.2004.04.020.

Gonzalez CE, Rinaldi MG, Sugar AM. Zygomycosis. Infect Dis Clin North Am. 2002;16:895–914. https://doi.org/10.1016/S0891-5520(02)00037-5.

Hadley C, Haneef Mohamed AW, Singhal A. Central nervous system fungal infection in a young male with a history of intravenous drug abuse and hepatitis C. Radiol Case Rep. 2017;12:590–6. https://doi.org/10.1016/j.radcr.2017.03.016.

McKeever PE. Pathologic basis of central nervous system infections. Neuroimaging Clin N Am. 2012;22:773–90. https://doi.org/10.1016/j.nic.2012.06.001.

Murthy JMK, Sundaram C. Fungal infections of the central nervous system. Handb Clin Neurol. 2014;121:1383–401. https://doi.org/10.1016/B978-0-7020-4088-7.00095-X.

Naik V, Ahmed FU, Gupta A, et al. Intracranial fungal granulomas: a single institutional clinicopathologic study of 66 patients and review of the literature. World Neurosurg. 2015;83:1166–72. https://doi.org/10.1016/j.wneu.2015.01.053.

Rajshekhar V. Surgical management of intracranial fungal masses. Neurol India. 2007;55:267–73. https://doi.org/10.4103/0028-3886.35688.

Raman Sharma R. Fungal infections of the nervous system: current perspective and controversies in management. Int J Surg. 2010;8:591–601. https://doi.org/10.1016/j.ijsu.2010.07.293.

Richardson M, Lass-Flörl C. Changing epidemiology of systemic fungal infections. Clin Microbiol Infect. 2008;14(Suppl 4):5–24. https://doi.org/10.1111/j.1469-0691.2008.01978.x.

Saini J, Gupta AK, Jolapara MB, et al. Imaging findings in intracranial aspergillus infection in immunocompetent patients. World Neurosurg. 2010;74:661–70. https://doi.org/10.1016/j.wneu.2010.06.017.

Sharma BS, Khosla VK, Kak VK, et al. Intracranial fungal granuloma. Surg Neurol. 1997;47:489–97. https://doi.org/10.1016/S0090-3019(96)00209-1.

Yamada K, Shrier DA, Rubio A, et al. Imaging findings in intracranial aspergillosis. Acad Radiol. 2002;9:163–71.

Yanai Y, Wakao T, Fukamachi A, Kunimine H. Intracranial granuloma caused by Aspergillus fumigatus. Surg Neurol. 1985;23:597–604.