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Case Report:
Cerebral Phaeohyphomycosis: A Rare Case from South India

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ABSTRACT

Background and Importance: Cerebral phaeohyphomycosis is a rare but frequently fatal clinical entity caused by dematiaceous fungi like Cladophialophora bantiana. Fungal brain abscess often presents with subtle clinical symptoms and signs, and present diagnostic dilemma due to its imaging appearance that may be indistinguishable from other intracranial space-occupying lesions. Still, certain imaging patterns on Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) help to narrow down the differential diagnosis and initiate prompt treatment of these infections.

Case Presentation: A 48-year-old immunocompetent man presented with right-sided hemiparesis and hemisensory loss and a provisional diagnosis of stroke was made. The radiological evaluation suggested the possibility of a cerebral abscess. Accordingly, surgical excision of the lesion was performed and the histopathological examination of the specimen revealed the etiology as phaeohyphomycosis. The patient was further treated with antifungals and discharged when general conditions improved.

Conclusion: Fungal Central Nervous System (CNS) infections present diagnostic challenges and should be considered while interpreting ring-enhancing CNS lesions in immunocompetent patients. Surgical resection and antifungal treatment should be considered in all patients with cerebral phaeohyphomycosis.

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Highlights

- Cerebral phaeohyphomycosis is a rare but frequently fatal clinical entity caused by dematiaceous fungi.
- It is even rarer in the immunocompetent.
- Even though the radiological findings are often nonspecific, certain imaging patterns can help reach the diagnosis.
- Early recognition is vital to initiate prompt treatment with surgical resection and antifungal agents.

Plain Language Summary

Cerebral phaeohyphomycosis is a rare fungal infection of the brain, especially in those having a normally functioning immune system. And it can lead to high mortality if prompt treatment fails. Fungal infections of the Central Nervous System (CNS) present diagnostic challenges. Radiological findings are often nonspecific. However, recognition of characteristic imaging patterns on Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) helps to narrow down the differential diagnosis and initiate early treatment. This case report highlights the relevance of considering cerebral phaeohyphomycosis in the differentials while analyzing ring-enhancing CNS lesions in immunocompetent patients.

1. Background and Importance

Fungal infections of the central nervous system are rare and most of them are observed in immunocompromised hosts [1]. Aspergillosis, cryptococcosis, mucormycosis, and candidiasis are among the most common ones [2, 3]. Even though the severe immunocompromised status is the most important risk factor for life-threatening fungal infections, they are increasingly recognized in the immunocompetent as well [4].

Cerebral phaeohyphomycosis is rare, but many times fatal clinical entity diagnosed in patients with deep-seated cerebral infections secondary to dematiaceous fungi. These fungi are common soil inhabitant, true pathogens that are known for their neurotropism; however, central nervous system seeding may occur through hematogenous route, probably initiated by respiratory colonization consequent to inhalation or through inoculation in the skin of extremities following a slight or minor trauma. CNS phaeohyphomycosis presents with unusual features and is associated with poor prognosis without appropriate treatment [4].

Fungal brain abscess often presents with subtle clinical symptoms and signs. It is a diagnostic dilemma due to its imaging appearance that may be indistinguishable from other intracranial space-occupying lesions. Still, certain imaging patterns on Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) help to narrow down the differential diagnosis and initiate prompt treatment for these potentially fatal infections [5].

This study reports on a rare case of cerebral phaeohyphomycosis in an immunocompetent patient, from south India, diagnosed with the aid of neuroradiological imaging and managed successfully through surgical resection and anti-fungal therapy.

2. Case Presentation

A 48-year-old immunocompetent male with no comorbidities in the past presented to our hospital with a history of sudden onset weakness of right upper and lower limbs. There was no history of trauma or sinus infection. On examination, the patient was conscious, well-oriented in time, place, and person, and with stable vitals. Right-sided hemiparesis with hemisensory loss was observed. No signs of cranial nerve palsies were present. Thus, a provisional clinical diagnosis of stroke was made and the patient was sent for radiological imaging.

CT scan revealed a hypodense lesion in the left parietal lobe (Figure 1). MRI scan, done for further characterization, showed a well-defined, irregularly marginated, heterogeneous lesion in the left parietal lobe with perilesional edema causing mass effect. The lesion was heterogeneously hyperintense in T2-weighted images with the irregular hypointense wall showing crenations (Figure 2). It showed central T1-hypointensity, with isointense intracavitary projections (Figure 3). There

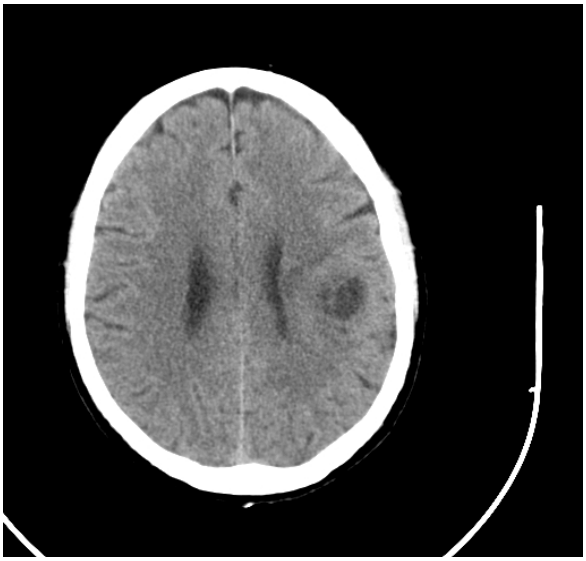

Figure 1. CT brain (axial) showing a hypodense lesion with the isodense periphery in the left parietal lobe

was diffusion restriction within the lesion, with a greater reduction in ADC (apparent diffusion coefficient) values in the wall (Figure 4). Thick peripheral post-contrast enhancement was present (Figure 5). Focal perilesional leptomeningeal enhancement was also seen. On MR spectroscopy, elevated choline to creatine and choline to NAA ratio was noted with lipid lactate peaks. A possibility of the cerebral abscess was given.

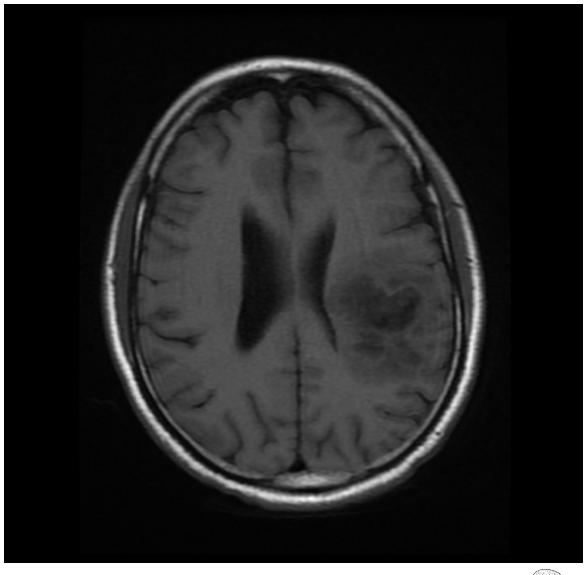

Figure 3. T1WI MRI brain (axial) showing hypointense core with isointense intracavitary projections

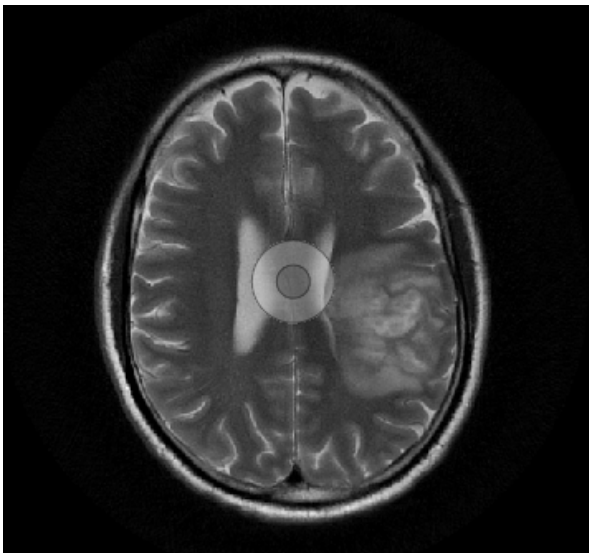

Figure 2. T2WI MRI brain (axial) showing heterogeneously hyperintense lesion with an irregular hypointense wall, crenations, and perilesional edema

Fungal infections of the central nervous system are rare and often develop when the fungal virulence factors outsmart the host's immune system. The number of susceptible hosts is increasing, likely due to the rise in patients having transplant surgeries, chemo-radiation therapies, metabolic syndromes, and HIV infections. Routes of infections include direct implantation by trauma, local extension from sinonasal, orbital, or spinal infections, or hematogenous spread from distant focus like lungs [6]. However, in our case, the patient was immunocompetent and with no previous history of trauma or infections elsewhere, unlike the reports presented by a few authors.

Cerebral phaeohyphomycosis is a blanket term used for brain infections caused by a dematiaceous fungus [7]. Most cases of cerebral phaeohyphomycosis occur as secondary infections following the development of infection in other sites, mainly paranasal sinuses. The species known to have a high neurotropic potential include Cladophialophora bantiana, Ramichloridium mackenziei, Ochroconis gallopavum, and Exophiala dermatitidis, out of which, Cladophialophora bantiana accounts for the majority of cases [4, 8].

Clinical symptoms of a brain abscess include focal neurologic deficits based on the site of involvement with signs of raised intracranial pressure. It is potentially fatal, if not promptly diagnosed and treated. The disease

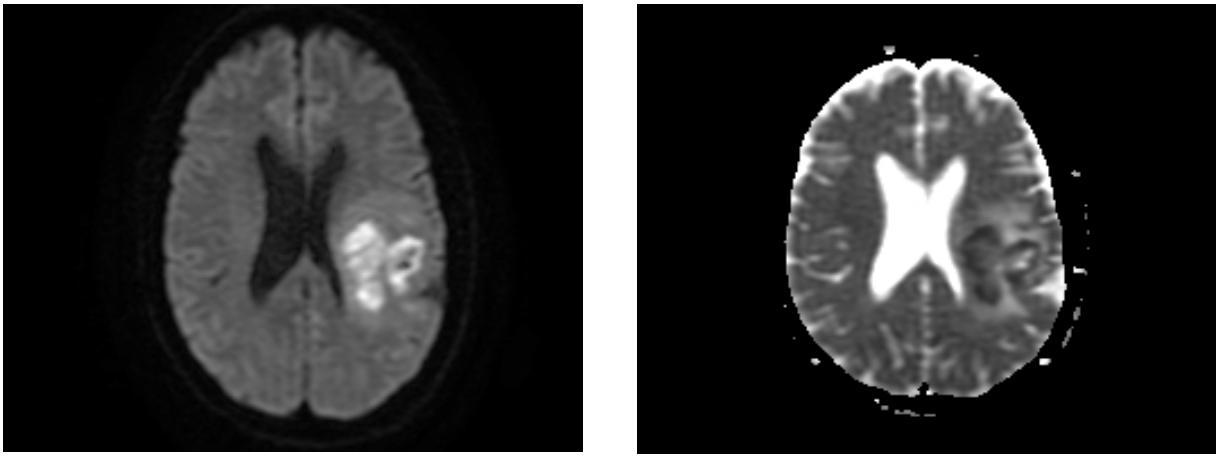

Figure 4. DWI and corresponding ADC showing, DWI hyperintensity with low ADC signals, and lower ADC values in the wall compared to the rest of the lesion

is most common in men similar to our case who was an immunocompetent man [4, 8].

Although radiological appearance may be often indistinguishable from other intracranial space-occupying lesions, certain imaging patterns can be useful in refining the differentials and reach the diagnosis. Computed tomography is the initial imaging technique for assessment of CNS infections due to its availability, even though MRI provides more characteristic information. CT also allows rapid evaluation of potential complications including mass effects, herniation syndromes, hydrocephalus, and intracranial hemorrhage [9].

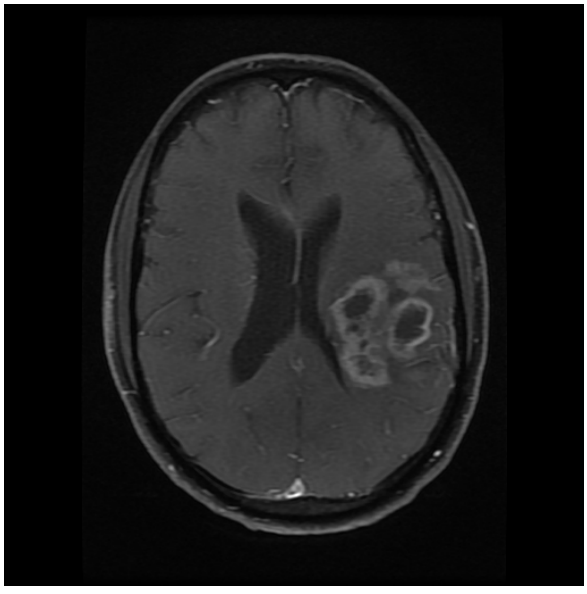

Figure 5. Post-contrast image showing thick irregular peripheral enhancement

The most sensitive imaging technique for specifying the characteristics of the intracranial abscess, cerebritis, ventriculitis, leptomeningitis, and empyema is contrast-enhanced magnetic resonance imaging. The common sequences used for assessing the infectious processes include T1-Weighted Imaging (T1WI), T2-Weighted Imaging (T2WI), T2-FLAIR, Diffusion-Weighted Imaging (DWI), contrast-enhanced T1WI, and spectroscopy [9].

Differentiation of a fungal from a bacterial etiology may be aided by certain characteristic imaging features. Fungal abscesses are usually multiple and can involve the basal ganglia, whereas bacterial abscesses are often solitary lesions and spare the basal ganglia. Intracavitary projections are seen within the fungal abscesses that

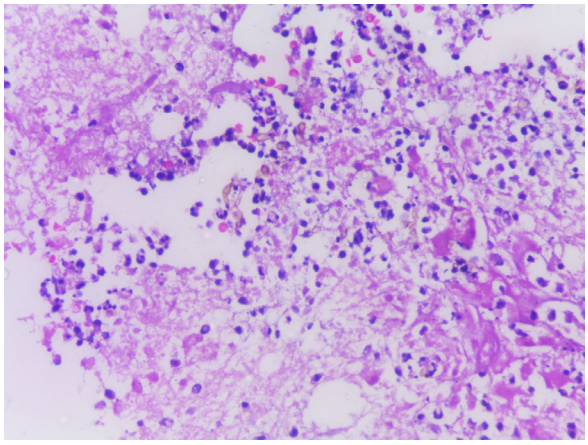

Figure 6. Histopathology section of the lesion – H and E staining: granuloma formation and suppuration in the brain tissue with pigmented fungal hyphae and spores (brownish foci) consistent with phaeohyphomycosis

show reduced diffusivity along with the abscess wall while sparing the central portions of the lesion [10, 11].

On T1-weighted MR imaging, fungal abscesses show a central hypointense area with an iso to the mildly hyperintense peripheral rim. Corresponding T2-weighted imaging demonstrates increased signal intensity in the center with the hypointense rim. Intracavitary projections protruding from the fungal abscess wall into the abscess cavity core were noted in many cases [12] which demonstrated the presence of fungal elements [11] along with iron and other paramagnetic substances on the inner surface of the abscess wall [13]. The post-contrast study showed peripheral enhancement. A distinctive imaging feature of the pyogenic abscess is the "dual rim sign" on diffusion-weighted imaging [12]. Most of our findings were in favor of a fungal etiology, except that there was only a single abscess sparing the basal ganglia.

On MR spectroscopy, fungal abscesses may contain lipids, lactate, alanine, acetate, succinate, and choline [14]. However, a distinctive feature is the disaccharide trehalose peak (3.6 ppm) in the abscess wall [10]. In our case, the spectroscopic findings were inverted Choline/NAA ratio with lipids and lactate.

We confirmed the etiological agent through histology. Treatment of most of the cases of cerebral phaeohyphomycosis has been unsatisfactory. It must be individualized with surgical resection and optimized antifungal therapy. Since azoles are very effective against dematiaceous fungi and can be prescribed safely for a longer period, they are the commonly used antifungal agent. Amphotericin B is also used in the treatment by many, but itraconazole is even known to cure the relapses after amphotericin B therapy [8].

4. Conclusion

Fungal CNS infections present diagnostic challenges. Neuroimaging of fungal CNS infections are often non-specific. However, recognition of certain imaging patterns on CT and MRI are of vital importance to help narrow down the differential diagnosis and initiate prompt treatment. Cerebral phaeohyphomycosis should be considered while analyzing the specimens from ring-enhancing CNS lesions in immunocompetent patients. Specimens should be dealt with biosafety level 2 because of the known pathogenesis of these organisms for immunocompetent individuals. Surgical resection and antifungal treatment with azoles should be considered in all patients with cerebral phaeohyphomycosis.

Ethical Considerations

Compliance with ethical guidelines

All ethical principles are considered in this article. The participants were informed of the purpose of the research and its implementation stages. They were also assured about the confidentiality of their information and were free to leave the study whenever they wished, and if desired, the research results would be available to them. A written consent has been obtained from the subjects. principles of the Helsinki Convention was also observed.

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Authors' contributions

Conception and design: M. G Sabarinadh; Data collection: M. G Sabarinadh; Drafting the article: M. G Sabarinadh; Critically revising the article: Josey T Verghese, Suma Job; Reviewing submitted version of manuscript: M. G Sabarinadh, Josey T Verghese, Suma Job; Approving the final version of the manuscript: M. G Sabarinadh, Josey T Verghese, Suma Job.

Conflict of interest

The authors declared no conflict of interest.

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