The Egyptian Journal of Radiology and Nuclear Medicine (2011) **42**, 397–404

Egyptian Society of Radiology and Nuclear Medicine

The Egyptian Journal of Radiology and Nuclear Medicine

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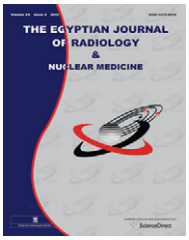

Role of magnetic resonance imaging in distinguishing fungal from nonfungal multiple brain abscesses

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Received 15 April 2011; accepted 29 June 2011
Available online 30 July 2011

KEYWORDS

Cladophialophora bantiana;
Fungal brain abscesses;
Magnetic resonance imaging

Abstract *Cladophialophora bantiana* is a neurotropic dematiaceous fungus known for affecting immunocompromised and immunocompetent hosts. We report a case of 24 year old immunocompetent male presenting with headache, fever and vomiting. MRI was suggestive of multiple fungal brain abscesses. He underwent total excision of abscesses. Pus culture was suggestive of brain abscess caused by *C. bantiana*. We report a culture proven case of *C. bantiana* emphasizing on specific MRI features which are critical in differentiating fungal from nonfungal brain abscesses.

1. Introduction

Cladophialophora bantiana is known to cause brain abscess in immunocompromised patients including solid organ transplant recipients and those with congenital or acquired immunodeficiency. Most of the past studies have reported cases having single abscess where description of MRI findings is pertinent to that abscess only, whereas in case of multiple abscesses the MRI findings are varied depending upon certain factors. We report a case of multiple cerebral abscesses in a young immunocompetent patient with no predisposing factors and discuss the variations in MRI findings on various sequences in the case of multiple cerebral fungal abscesses and discuss the cause for these variations.

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0378-603X

Peer review under responsibility of Egyptian Society of Radiology and Nuclear Medicine.
doi:10.1016/j.ejrnm.2011.06.008

2. Case report

A 25 year old Asian male presented to the neurology clinic with complaints of generalized headache, fever and vomiting since one year and subsequent development of right sided weakness of upper and lower limbs. He was initially treated by the family physician and was partially relieved of symptoms. His headache used to subside and resurface again so he consulted the neurology clinic at our hospital.

He gave no history of trauma, seizures, loss of consciousness, no history of immunosuppression, or diabetes. He was not a smoker, alcoholic or an I.V drug abuser.

On clinical examination patient had weakness of upper and lower limbs and unsteady gait. He was well oriented in time, place and person.

Patient was referred to radiology department for MRI of brain. After obtaining a written consent, scan was performed. Preoperative gadolinium enhanced MRI revealed multiple well defined ring enhancing conglomerated round to oval lesions of various sizes in left frontoparietal region. The lesions were heterointense on T2W images with hypointense walls and crenated margins (Fig. 1a, b). There were hypointense projections attached to the walls projecting to the center with hyperintense core. On T1W images the projections were isointense to hypointense with a hypointense core (Fig. 1c, d). On T1W post contrast images the lesions showed enhancement of walls with no enhancement of projections (Fig. 2a, b). There was significant vasogenic edema with compression of adjacent structures (lateral and third ventricle) with resultant dilatation of right lateral ventricle with a midline shift of 7 mm toward right side (Fig. 2a, b). On diffusion weighted images some lesions showed restricted diffusion (hyperintensity) in the periphery with non-restricted diffusion (hypointensity) at the center, while some showed restricted diffusion both at the periphery and at the center (Fig. 3a, b). Apparent diffusion coefficient (ADC) mapping showed low values in the intracavitatory projections and high values in the cavity (Fig. 3c, d). Gradient echo images revealed hypointense wall of the abscess due to susceptibility artifacts due to the presence of melanin in the fungus (Fig. 4). Multivoxel Proton magnetic resonance spectroscopy (PMRS) at TE Value 144, at cavity (a), projection (b) and wall (c) reveals elevated lipid with reduction in NAA, Choline and Creatinine (Fig. 5).

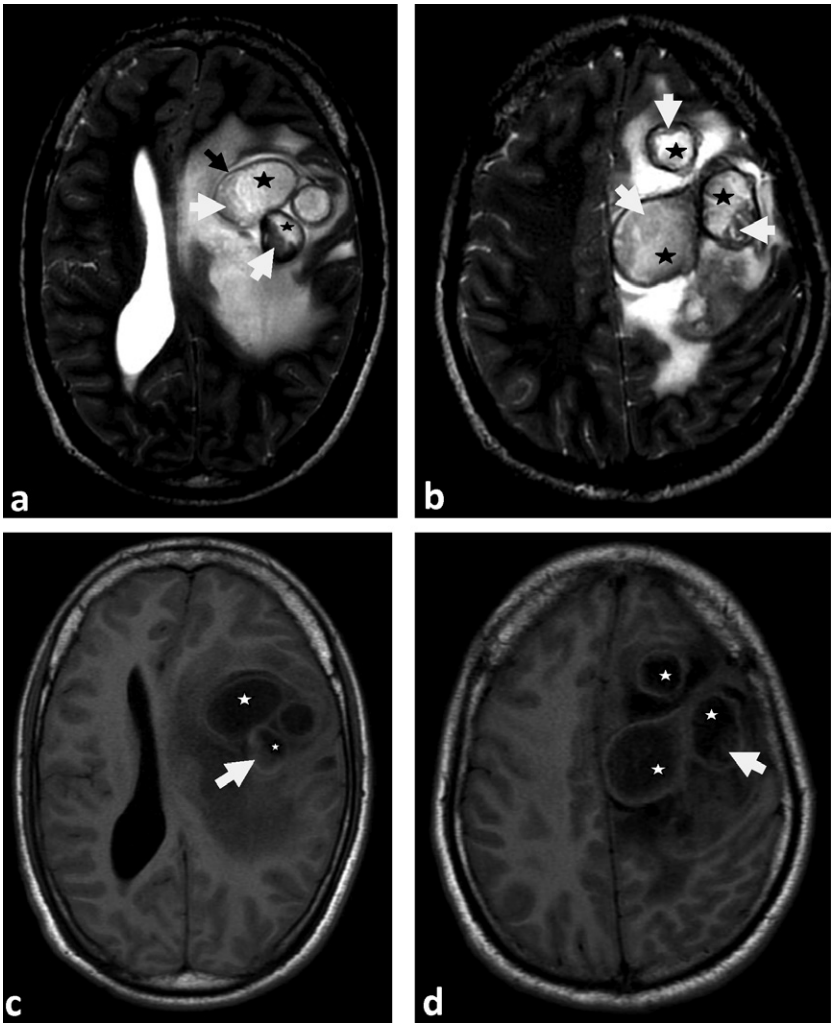

Figure 1 (a–d), (a and b) T2W axial sections show well defined multiple round to oval heterointense lesions with hypointense wall (black arrow) and hypointense projections (white arrow) extending from wall to the center is characteristic of fungal abscess with a hyperintense core (star).

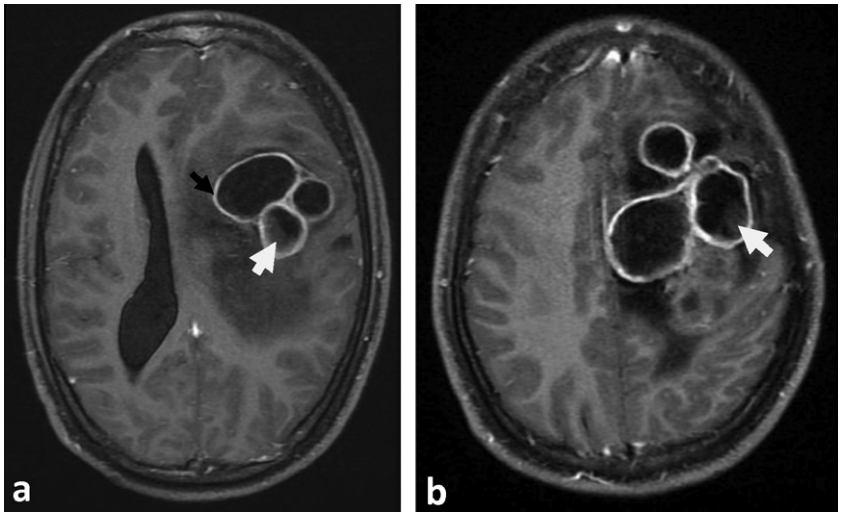

Figure 2 (a and b) post contrast T1W images show peripheral enhancement of the walls (black arrow) with no enhancement of the projections (white arrow).

Looking into the intracavitatory projections in the lesions and their appearance on various pulse sequences, Diagnosis of multiple fungal brain abscesses was made.

Patient was posted for surgical evacuation of abscesses. His pre operative work up was as follows:

Total leukocyte count was 10,480, neutrophils 74%, lymphocytes 18%, and monocytes 07%. Erythrocyte sedimentation rate was 42 mm/1st hour by Westergren's method. HIV and HBsAg were negative and chest X-ray was normal.

Patient underwent surgery for evacuation of abscess by left fronto parietal parasagittal craniotomy route. Post operative period was uneventful. Pus from the abscesses was sent to the microbiology lab for evaluation; on examination pus was negative for Acid fast bacilli (AFB), however, both the Ziel Neelsen and Gram stained (Fig. 6a) smears showed plenty of septate hyphae and inflammatory cells. The potassium hydroxide (KOH) (Fig. 6b) mount showed light brown septate hyphae with long chains of conidia. Looking at the dematiaceous nature, septation, long chains of spores and immunocompetence of the patient, the presence of *C. bantiana* was suspected as it is the commonest neurotropic phaeoid fungus. The tuberculous polymerized chain reaction (TB PCR) (MTB Real-TM kit, Sacace Biotechnologies, Italy) on the pus sample was negative. The routine and AFB cultures did not show any growth. The Sabouraud's Dextrose Agar (Fig. 6c) gave deep green to black colonies with velvety growth.

Slide culture performed using biosafety cabinet (level II A-2, Kartos International, Noida, India); growth at 42° C and positive urease test confirmed the identification. The isolate was also confirmed as *C. bantiana* by division of mycology PGI Chandigarh. Patient was put on antifungal therapy and discharged three weeks later.

Patient came for follow up at two months after surgery and he was advised MRI scan, Post Operative Images Fig. 7 T2 W (a and b) Gradient echo (c) and post contrast (d) images show complete resolution of the previously seen abscesses with a solitary fluid intensity cystic lesion in the left high parietal region having hypointense wall on gradient images and show mild enhancement on post contrast study due to post-operative changes. There is no mass effect and near complete resolution of edema.

3. Discussion

Phaeohyphomycosis is a term used to describe infections caused by fungi which contain melanin in their cell walls. *C. bantiana* is a soil based neurotropic fungus known to cause cerebral phaeohyphomycosis because of its affinity to glial tissue [1].

Most infections are seen in the second and third decades of life, with the youngest reported case of a six day old neonate. Young males are the frequently involved group. Involvement of immunocompetent hosts is the usual feature of *C. bantiana* infection [2]. In the review conducted by Filizzola et al. there were varied presentations with single or multiple, uniloculated or multiloculated brain abscesses and diffuse granulomatous encephalitis [3]. Common presentation was a single brain abscess seen in 71% of cases with overall mortality of 73% [4].

Clinical manifestations are headache, low grade fever, focal neurological signs. Patients do not give history of exposure to molds [5].

Present case was a 25 yr male, who was immunologically competent presenting with headache, fever and vomiting with no history of exposure to molds. On radiological investigation multiloculated fungal cerebral abscesses was detected.

Exact mechanism of how this fungi cause disease in immunocompetent individuals is not understood. One of the possibilities is due to melanin present in the cell wall. It scavenges the free radicals and hypochlorite that are produced by phagocytic cells in their oxidative burst, which would normally kill most organisms. It also binds to hydrolytic enzymes, preventing their action on the plasma membrane [6].

Brain abscesses occur due to contiguous spread of infection from oropharynx, middle ear and paranasal sinuses. Hematogenous spread from distant focus of infection is another cause of brain abscess. The exact mechanism by which microorganisms enter the brain is not clearly understood, valveless emissary veins may allow micro organisms to flow into the venous system of the brain from various sites [7].

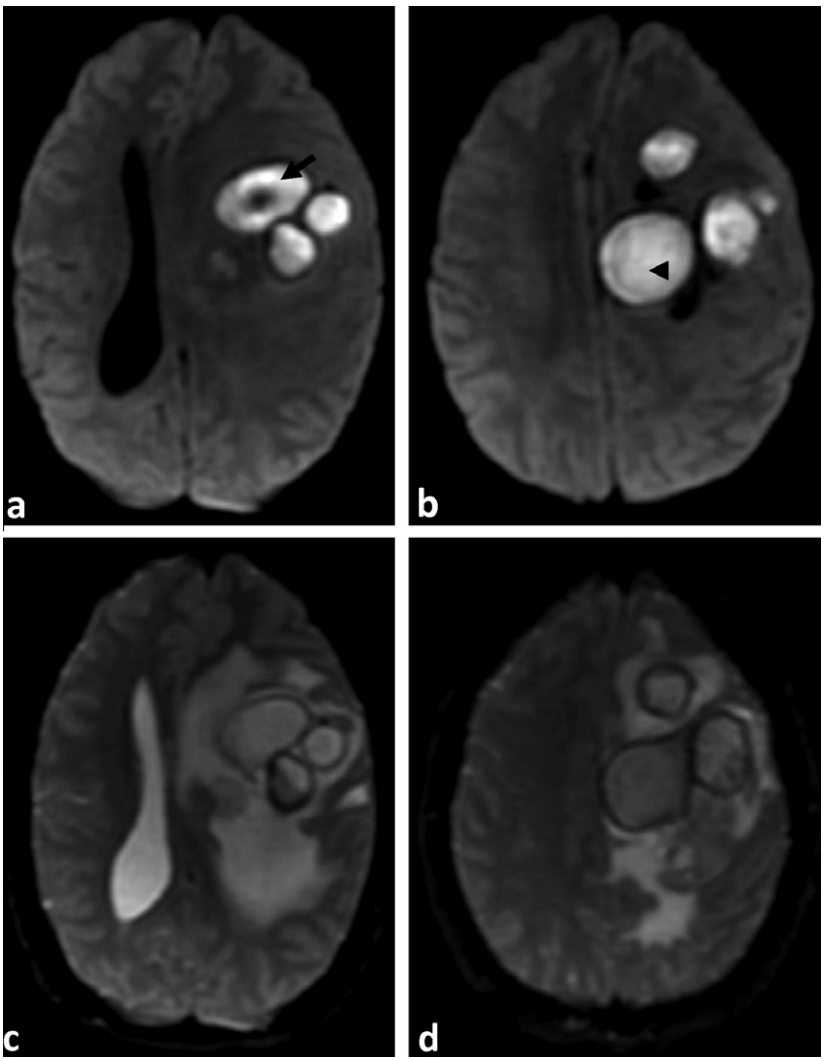

Figure 3 (a–d), (a and b) Diffusion weighted images show restricted diffusion in the periphery (black arrow) and nonrestricted diffusion at the center in some lesions with other lesions showing restricted diffusion both at the periphery and the center (black arrow head). (c and d), ADC images showed low values in the projections 0.43×10^{-3} mm/s and high values 2.30×10^{-3} mm/s in the cavity.

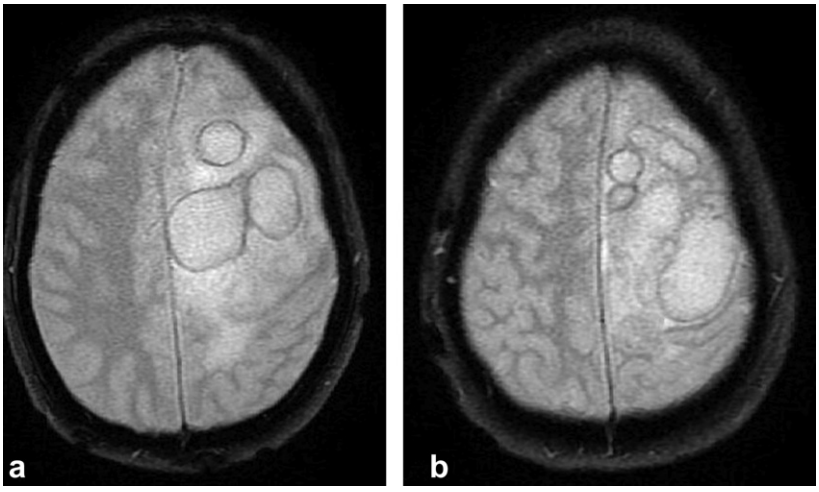

Figure 4 Gradient echo images reveal hypointense wall of the abscess due to susceptibility artifacts due to the presence of melanin in the fungus.

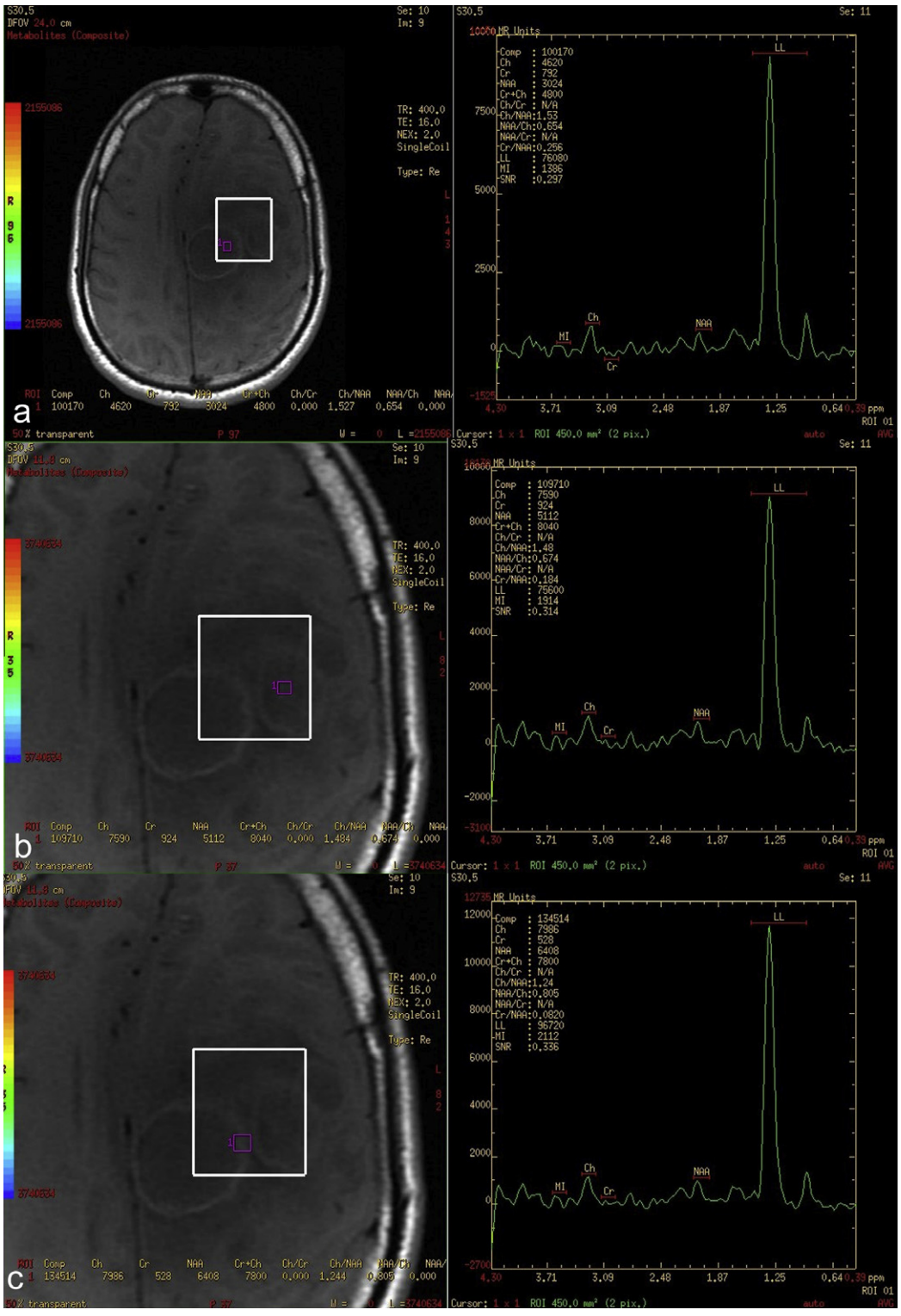

Figure 5 Multivoxel Proton magnetic resonance spectroscopy at TE Value 144 at cavity (a), projection (b) and wall (c) reveals elevated lipid with reduction in NAA, Choline and Creatinine.

4. Diagnosis – role of imaging

Advent of newer technologies like MRI with its new extended applications has greatly improved the diagnostic efficacy in arriving at a diagnosis.

In a study conducted by Luthra et al. fungal abscesses had crenated walls in 50% of the cases, appeared heterointense on T2 weighted images and had intracavitatory projections extending from wall to center with low ADC values in these projections. On diffusion weighted images the projections

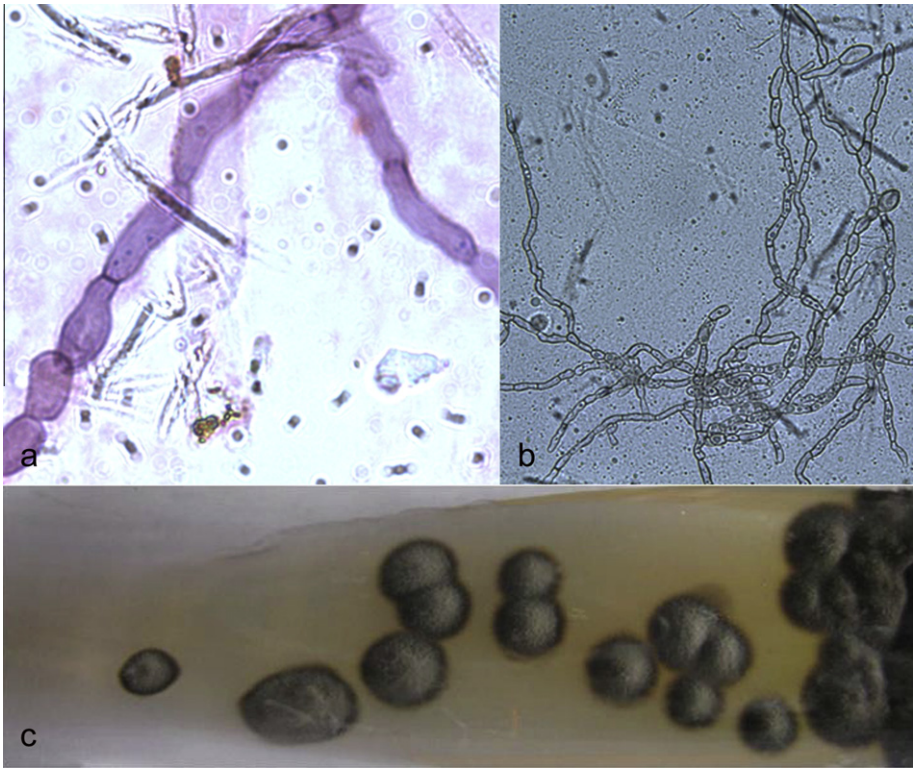

Figure 6 Grams stain (a) and KOH mount (b) show light brown broad septate hyphae and spores Culture on Sabouraud's Dextrose Agar (c) shows deep green to black colonies with velvety texture.

showed restricted diffusion with the core showing no restriction. These projections seem to be characteristic of fungal abscesses as were present in all the cases of fungal abscess and absent in nonfungal abscesses. These projections were later confirmed to be fungal hyphae on histopathological examination [8].

Present case showed multiple abscesses in the left fronto parietal region. These lesions were heterointense on T2W images with hypointense walls and crenated margins. There were hypointense projections attached to the walls projecting to the center with hyperintense core. The features of which were specific of fungal abscesses.

In a study conducted by Jain et al. the projections were isointense to hypointense on T1W images and hypointense on T2W images. On post contrast T1W images the lesions showed rim enhancement with no contrast enhancement in the projections. PMRS reveal elevated lipid, with reduction in other metabolites [9].

The projections in this case were isointense to hypointense on T1 W images and hypointense on T2 W images. On T1W post contrast images the lesions showed enhancement of walls with no enhancement of projections. PMRS revealed elevated lipid, with reduction in other metabolites.

In a study conducted by Paola gaviani et al., multiple abscesses showed different diffusion patterns depending upon development of capsule; some abscesses showed prominent central hyperintensity and ADC maps showed hypointensity (restricted diffusion). In some patients abscess showed restricted diffusion along the periphery of the abscesses but nonrestricted diffusion in the central portion, which on histopathology revealed that the lesion had not yet developed a well defined capsule [10].

This case showed restricted diffusion (hyperintensity) in the periphery with nonrestricted diffusion (hypointensity) at the center in some while others showed restricted diffusion both at the periphery and at the center. ADC mapping showed low values in the intracavitatory projections and high values in the cavity.

5. Differential diagnosis

Fungal abscess needs to be differentiated from pyogenic and tubercular abscess. Role of conventional MRI in demonstrating intracavitatory projections is of utmost importance as these projections are specific only for fungal abscesses and not seen in others.

Pyogenic abscess can be differentiated from fungal and tubercular abscesses on PMRS by the presence of acetate and succinate as it is seen only in pyogenic abscess. PMRS cannot reliably differentiate fungal from tubercular abscess as both show lipid peak with the absence of other metabolites. The presence of multiple signals between 3.6 and 3.8 ppm is assigned to disaccharide trehalose which was noted in some fungal abscesses but not all of them. The absence of these resonances in some cases of fungal abscesses was due to lower concentrations of these metabolites below the sensitivity of proton magnetic resonance spectroscopy on a 1.5 T MRI [8].

Diffusion alone cannot differentiate fungal abscess from nonfungal ones as diffusion pattern in fungal abscess is varied and resembles either pyogenic or tubercular abscess depending

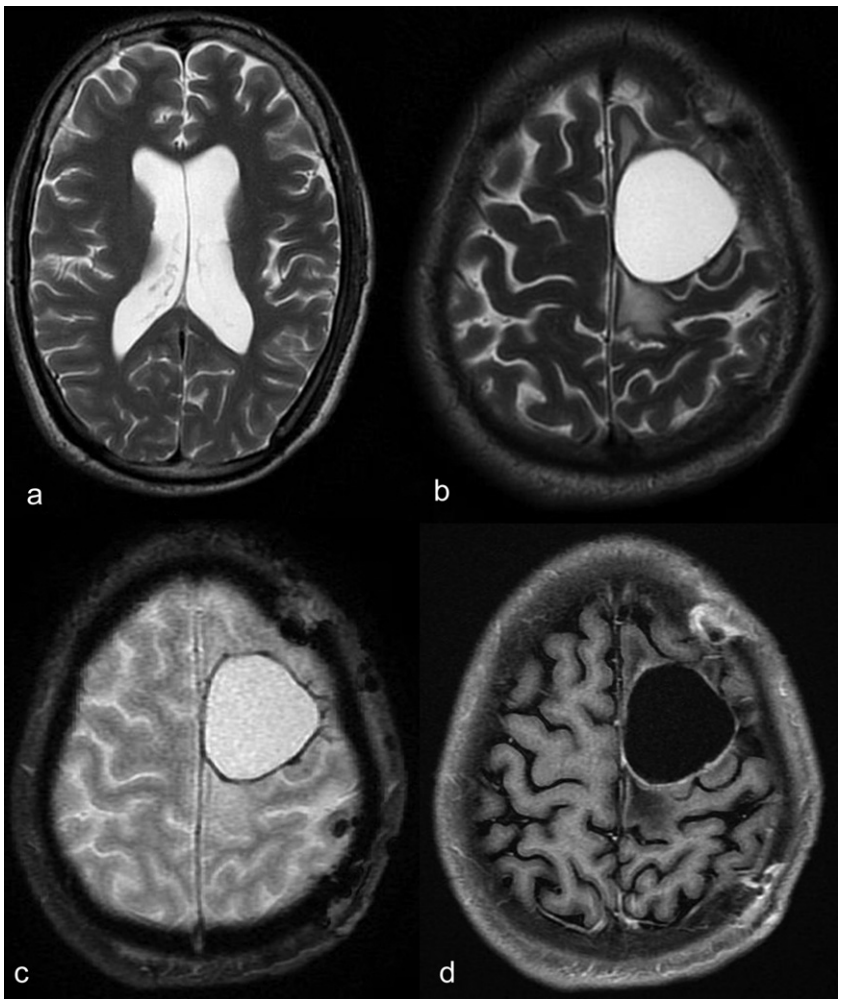

Figure 7 Post operative Images T2 W (a and b) Gradient echo (c) and post contrast (d) images show complete resolution of the previously seen abscesses with a solitary fluid intensity cystic lesion in left high parietal region having hypointense wall on gradient images and show mild enhancement on post contrast study due to post-operative changes. There is no mass effect and near complete resolution of edema.

Table 1 Comparison of fungal, bacterial and tubercular abscess on magnetic resonance imaging.

	Intracavitatory projections	T1	T2	Post Contrast	Diffusion	Spectroscopy
Fungal	Present	Hypointense	Hyperintense	Enhancing wall without enhancement of projections	Varied depending upon development of capsule	Elevated lipid lactate and resonance to disaccharide trehalose
Pyogenic	Absent	Hypointense	Hyperintense	Well defined wall enhancement	Restricted diffusion	Elevated acetate and succinate
Tubercular	Absent	Hypointense	Hyperintense	Well defined wall enhancement	Restricted diffusion	Elevated lipid lactate with absence of other metabolites

on development of capsule. However, if multiple abscesses are present showing varied diffusion pattern should make one suspect a fungal etiology which has to be further correlated with conventional MRI findings for intracavitatory projections and their appearance on various sequences for conformation.

6. Conclusion

It is possible to diagnose fungal etiology of cerebral abscesses with greater confidence level on MRI by combining conventional, diffusion and, spectroscopy features. A heterointense T2 lesion with irregular margins and intracavitatory projections (which seemed to be characteristic of fungal abscess as they represent the fungal hyphae) which appear isointense to hypointense on T1 and T2 sequences showing no enhancement on post contrast study is characteristic of fungal abscess. Diffusion and spectroscopy may help in the diagnosis only when combined with conventional MRI findings. Differentiation solely on the basis of diffusion and spectroscopy findings is not reliable. (Table 1)

Specimens from the entire suspected fungal brain abscess should be sent for microbiological evaluation as antifungal agents used in the treatment differ from species to species. The culture and speciation of the causative agent are important for successful treatment and outcome.

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