Mucormycosis creeping along the nerves in an immunocompetent individual

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ABSTRACT

Mucormycosis is a rare opportunistic fungal infection, often life-threatening. We report an unusual case of rhinocerebral mucormycosis in an immunocompetent patient. A 23-year-old male presented with headache, speech disturbance and hearing difficulty for 4 weeks. Magnetic resonance imaging (MRI) revealed right cerebellar abscess and enhancing soft tissue in the nasal cavity, extending to cranial and infratemporal fossae. Computed tomography (CT) revealed the widening of foramen rotundum and sclerosis involving the sphenoid and ethmoid sinuses. MR Spectroscopy revealed multiple peaks between 3.6 and 3.8 parts per million (ppm) which could represent trehalose. Nasal mucosa scrapings confirmed mucormycosis. Suspicion of a fungal infection needs to be considered even in the absence of immunocompromised status.

CASE REPORT

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A 23-year-old male presented to medicine OPD with headache, vomiting and decreased hearing in the right ear for 4 weeks. The patient also had right facial paresis, diplopia and slurred speech. The patient had no significant past medical or surgical history.

MRI Brain was done, which revealed a thick-walled peripherally enhancing lesion measuring 2.1x1.7x1.9 cm with perilesional edema in the right cerebellar hemisphere (Fig. 1A). It showed central diffusion restriction on diffusion-weighted imaging (DWI) (Fig. 1B, C). These findings were suggestive of an abscess.

An intensely enhancing soft tissue lesion was seen in the right nasal cavity and ethmoid sinus (Fig. 2A) which was extending to the right pterygopalatine fossa (PPF). It was extending laterally into the right infratemporal fossa (ITF) (Fig. 2B) through the pterygomaxillary fissure. Hyperintense signal intensity was seen involving the right pterygoid muscles (Fig. 3A, B), which had an increased post contrast enhancement.

Posteriorly, it was reaching till the right cavernous sinus (CS) through the right foramen rotundum. It was enlarging the cavernous sinus without invasion of the cavernous portion of the right internal carotid artery (Fig. 4A).

The lesion was further extending posteriorly to cause the widening of right Meckel's cave (Fig. 4B) and involving the right cerebellopontine (CP) angle (Fig. 4C). Abnormal hyperintense signal intensity was seen involving the right half of pons (Fig. 5A) at the root of the trigeminal nerve. Further extension was noted along the right middle cerebellar peduncle up to the cerebellar abscess previously described (Fig. 5B).

There was nodular mucosal thickening involving the sphenoid and ethmoid sinuses with post contrast enhancement (Fig. 6A). Lateral displacement of right medial rectus muscle was due to the expansion of right ethmoid sinus (Fig. 6B). The cerebral parenchyma was normal. MR angiography was normal.

A CT scan was also performed, which demonstrated that the lesion was widening the right foramen rotundum with sclerosis involving the right ethmoid and sphenoid sinus (Fig. 7).

MR Spectroscopy revealed multiple peaks between 3.6 and 3.8 parts per million (ppm), which could represent trehalose. It also revealed an elevated choline peak at 3.2 ppm (Fig. 8). However, Choline/Creatine (Cho/Cr) was approximately 1.5 and hence, not significantly elevated to suggest malignancy.

Scrapings taken from the nasal cavity showed non-septate hyphae with 90° branching confirming mucormycosis (Fig. 9).

The patient was referred to the ENT department and was treated after admission with 10mg/kg/day of Amphotericin B for 6 weeks. The patient showed an improvement in clinical symptoms with the antifungal treatment. However, the patient did not turn up for a follow-up MRI and did not give consent for a brain biopsy.

DISCUSSION

Etiology & Demographics:

Mucormycosis is a fungal infection caused by members of the Mucorales order [1]. Rhizopus oryzae is the most common cause of mucormycosis followed by Mucor indicus. They are responsible for ~70% of all cases of mucormycosis. It is more common in males and older age [2–4]. The exact incidence of rhinocerebral mucormycosis is not available in the literature.

It most commonly affects immunocompromised patients like Acquired immunodeficiency syndrome (AIDS), diabetes mellitus, hematopoietic disorders, and transplant recipients. Diabetic patients most commonly present with rhinocerebral or pulmonary mucormycosis [5,6]. 25% of chronic rhino-orbito-cerebral mucormycosis cases are seen in immunocompetent individuals [7]. Other forms of mucormycosis are cutaneous, gastrointestinal or disseminated [5,6].

Clinical & Imaging findings:

We describe a case of chronic rhino-orbito-cerebral mucormycosis in a young immunocompetent individual with intracranial extension through the PPF. It was a challenging case as the patient had few symptoms and no risk factors. Overall a great deal of suspicion is needed to diagnose it [7].

Enhancing soft tissue is due to the fungal elements. Central diffusion restriction can be seen in fungal abscess [8,9]. As the patient was immunocompetent, there were no vasculitic infarcts, which are characteristic of fungal infection in immunocompromised patients. Non-septate hyphae with 90° branching correspond to the fungi in the order of Mucorales [3].

Rhinocerebral infection is the most common type of mucormycosis. Depending on the time of evolution, the infection can be acute or chronic. The latter has a low frequency (5.6% of rhinocerebral mucormycosis cases) [10]. Mucormycosis is characterized by the angioinvasive nature of the fungi. However, they may have a decreased ability to grow at body temperature, hence compromising their angioinvasive nature [10,11]. A trehalose peak is characteristic of a fungal infection. It is seen as multiple peaks between 3.6 and 3.8 ppm. It is a source of energy for the fungi [9].

Treatment & Prognosis:

A combination of surgical debridement and medical therapy is used for treating fungal infections. Amphotericin B is the drug of choice for mucormycosis. Only Amphotericin B and its lipid formulations, and recently Isavuconazole have been studied as first-line therapy for mucormycosis. On the contrary, Posaconazole has been mainly studied as salvage therapy [12]. Mucormycosis is a rare opportunistic fungal infection that may prove fatal. Immune response and extension determine prognosis [5,6].

Differential Diagnoses:

We narrowed down our diagnosis to the following- infective etiology, Triton tumor, nerve sheath tumor, adenoid cystic carcinoma, and neurosarcoid. Headache, vomiting and slurred speech could be explained by the involvement of the cerebellum and the cerebellar peduncle. Decreased hearing in the right ear and right facial paresis could be explained by the pontine involvement. The mass effect on the right medial rectus muscle was responsible for the diplopia. The pathology was following the course of the trigeminal nerve and its branches. Hence, the above differential diagnoses were considered. The lesion was involving multiple compartments; hence infective etiology was our first differential diagnosis. Due to the involvement along the trigeminal nerve, we kept other differential diagnoses.

Triton tumor:

Triton is a malignant nerve sheath tumor in which malignant Schwann cells coexist with malignant rhabdomyoblasts. It is seen in young adults. But confirmation can only be made with biopsy and immunohistochemistry [13]. The large size and neural spread favoured the diagnosis. However, the patient had no stigmata for neurofibromatosis, which is a usual association with a triton tumor. Nonetheless, triton tumor is rare and only 5 cases of intracranial malignant triton tumor have been published in the literature [13].

Neurosarcoid:

It usually affects the pituitary or the meninges, which appear thickened and show post contrast enhancement [14]. Isolated neurosarcoid without systemic manifestations is seen

only in 1 % cases. Another manifestation of neurosarcoid is cranial nerve involvement. The most common nerves involved are the facial and optic nerves. The nerves appear thickened and show post contrast enhancement. Our patient was in the second decade of his life. Neurosarcoid has prevalence in the third or fourth decade of life.

Nerve sheath tumor:

It presents as a spindle-shaped mass along the course of a nerve. Contrast enhancement is variable. Widening of associated neural foramina may be seen. The lack of malignant rhabdomyoblasts differentiates it from a triton tumor.

Adenoid cystic carcinoma:

It arises from the minor salivary glands in the sinonasal region and can affect individuals who are 18 to 80 years of age. It has a propensity for perineural spread and bony invasion (latter was absent in our case), which can lead to significant skull base involvement and intracranial extension. [15]

TEACHING POINT

We have to maintain a strong suspicion of rhinocerebral mucormycosis even in immunocompetent individuals with perineural spread and no vasculitic infarct. Advanced imaging techniques like diffusion-weighted imaging and spectroscopy can be helpful in narrowing the diagnosis to a fungal abscess in view of central diffusion restriction and a trehalose peak. They can be used as problem solvers.

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FIGURES

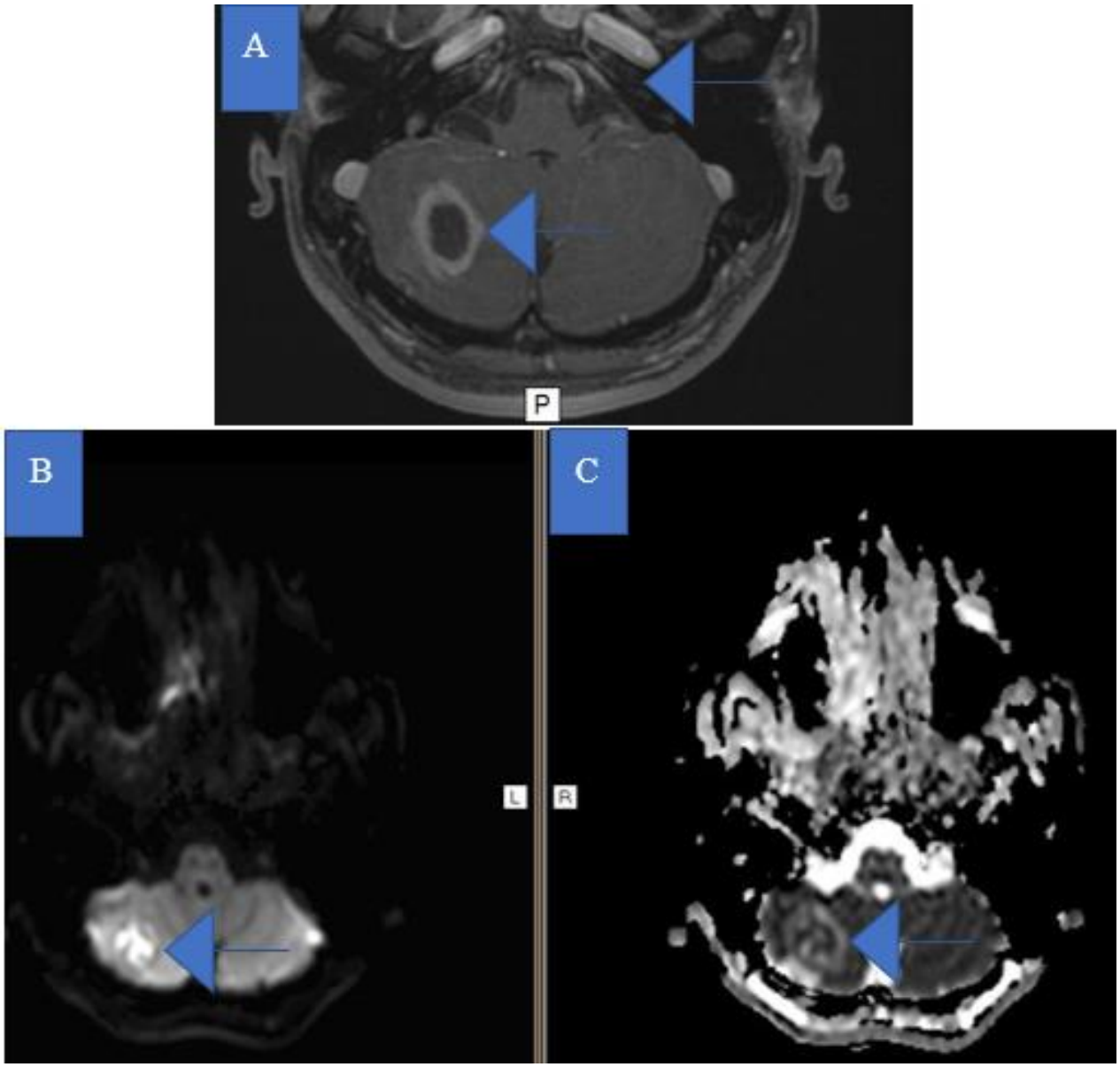

Figure 1: 23-year-old immunocompetent male with rhinocerebral mucormycosis.

FINDINGS: (A) Post contrast axial T1WI of the right cerebellar abscess with thick, shaggy and irregular walls. (B) DWI and (C) Apparent diffusion coefficient (ADC) of the right cerebellar abscess with central diffusion restriction.

TECHNIQUE: 1.5 Tesla scanner (GE Signa hdxt), 5 mm slice thickness, 1.5 mm interslice gap, b value for DWI-1000, TE for DWI-73, TR for DWI-5000, TE for Post contrast axial T1WI-12, TR for Post contrast axial T1WI-460, Magnevist 10 cc.

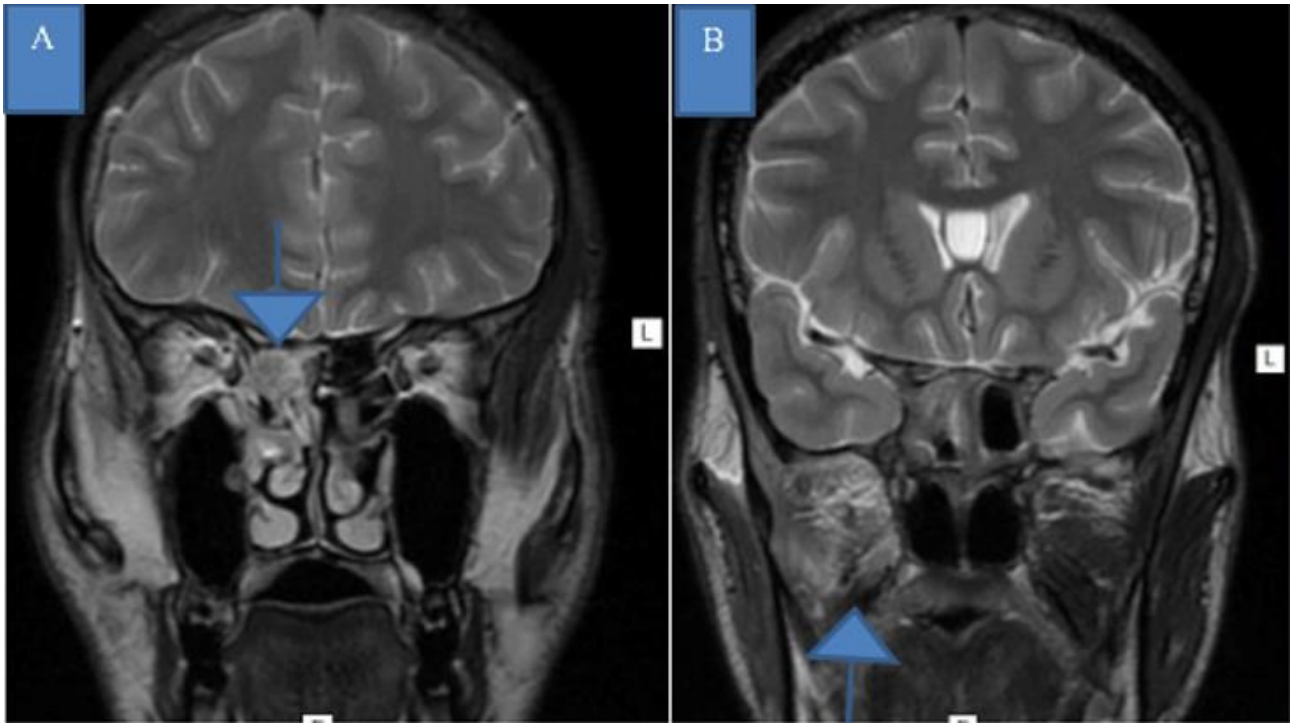

Figure 2: 23-year-old immunocompetent male with rhinocerebral mucormycosis.

FINDINGS: (A) Coronal T2WI showing hyperintense soft tissue in the right ethmoid sinus. (B) Coronal T2WI showing hyperintense signal involving the right infratemporal fossa.

TECHNIQUE: 1.5 Tesla scanner (GE Signa hdxt), 5 mm slice thickness, 1.5 mm interslice gap, TE-108, TR-5980.

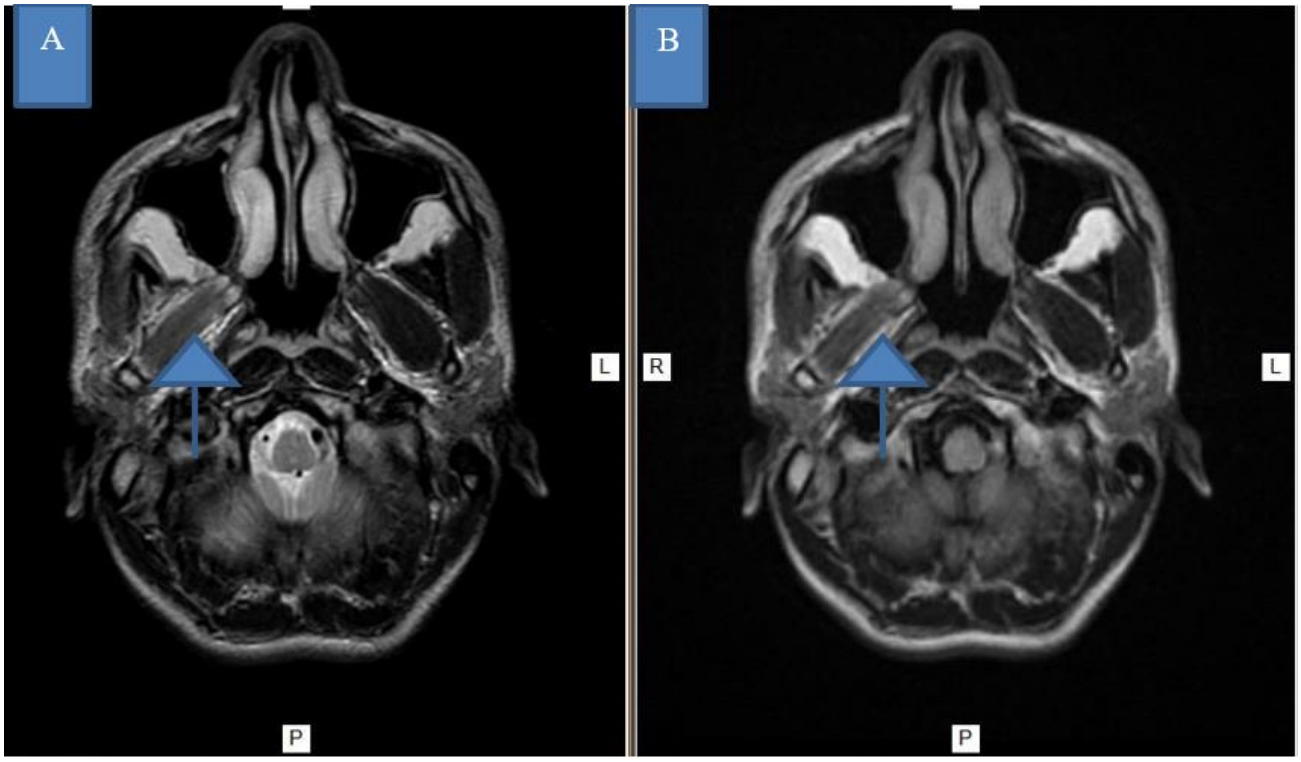

Figure 3: 23-year-old immunocompetent male with rhinocerebral mucormycosis.

FINDINGS: (A) Axial T2WI and (B) FLAIR image showing hyperintense signal involving the right pterygoid muscles.

TECHNIQUE: 1.5 Tesla scanner (GE Signa hdxt), 5 mm slice thickness, 1.5 mm interslice gap, TE for T2WI-99, TR for T2WI-5000, TE for FLAIR-100, TR for FLAIR-9000.

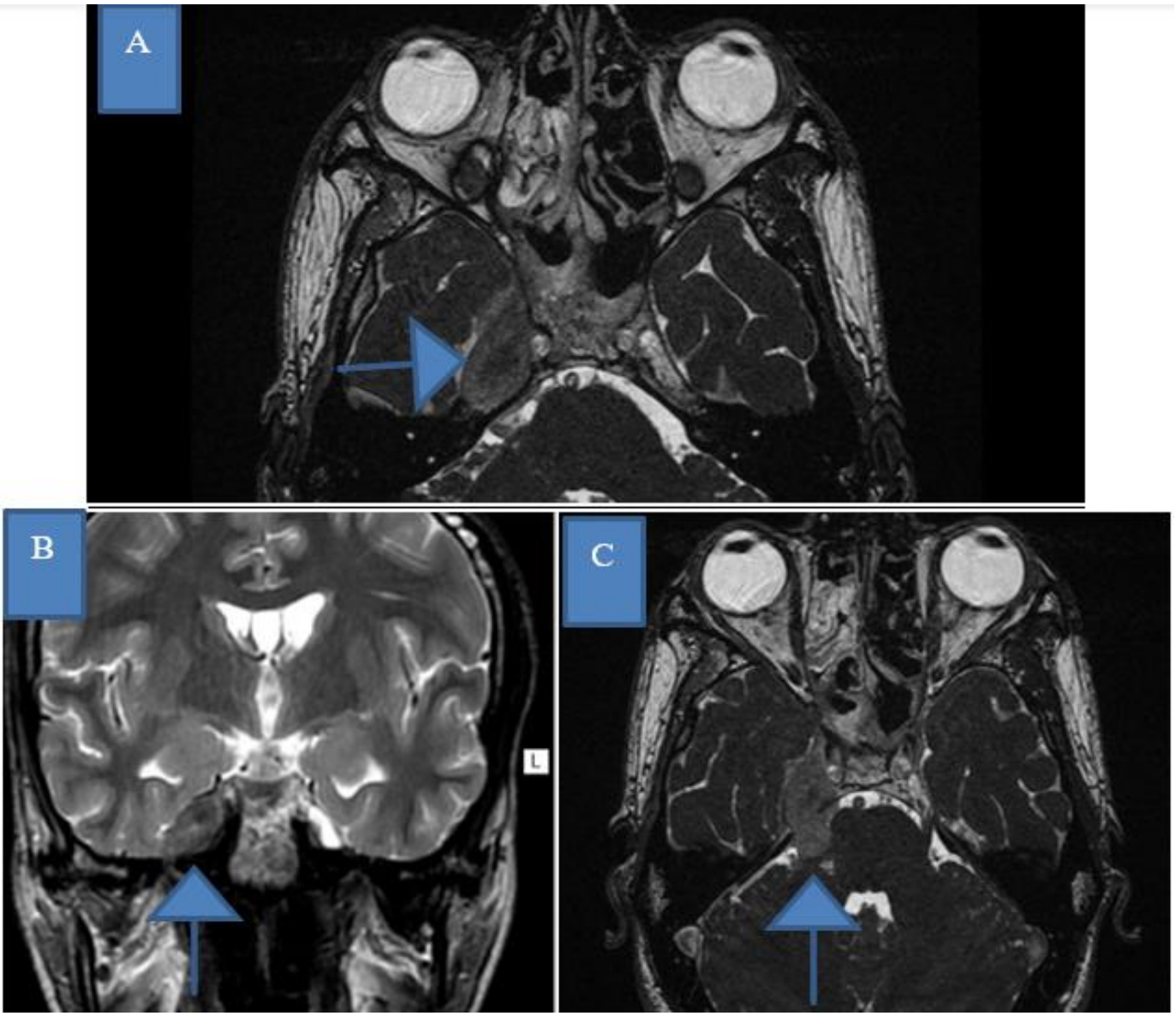

Figure 4: 23-year-old immunocompetent male with rhinocerebral mucormycosis.

FINDINGS: (A) Axial FIESTA image showing abnormal soft tissue obliterating the right cavernous sinus without thrombosis of the internal carotid artery. (B) Coronal T2WI showing abnormal soft tissue widening the right Meckel's cave. (C) FIESTA image showing extension in the right CP angle.

TECHNIQUE: 1.5 Tesla scanner (GE Signa hdxt), 5 mm slice thickness, 1.5 mm interslice gap, TE for T2WI-99, TR for T2WI-5000, TE for FIESTA-2.9, TR for FIESTA-6.

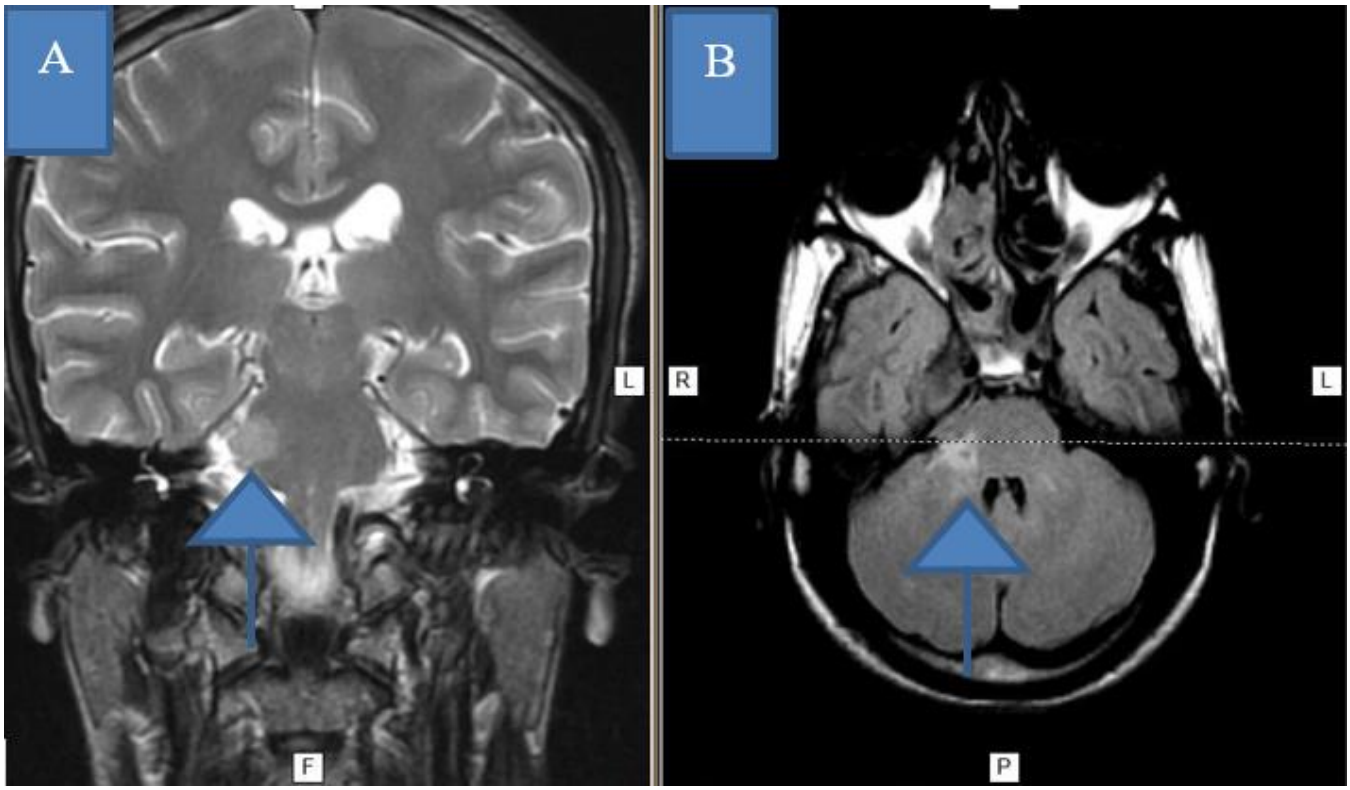

Figure 5: 23-year-old immunocompetent male with rhinocerebral mucormycosis.

FINDINGS: (A) Coronal T2WI and (B) Axial FLAIR showing extension into the right middle cerebellar peduncle and pons.

TECHNIQUE: 1.5 Tesla scanner (GE Signa hdxt), 5 mm slice thickness, 1.5 mm interslice gap, TE for T2WI-99, TR for T2WI-5000, TE for FLAIR-100, TR for FLAIR-9000.

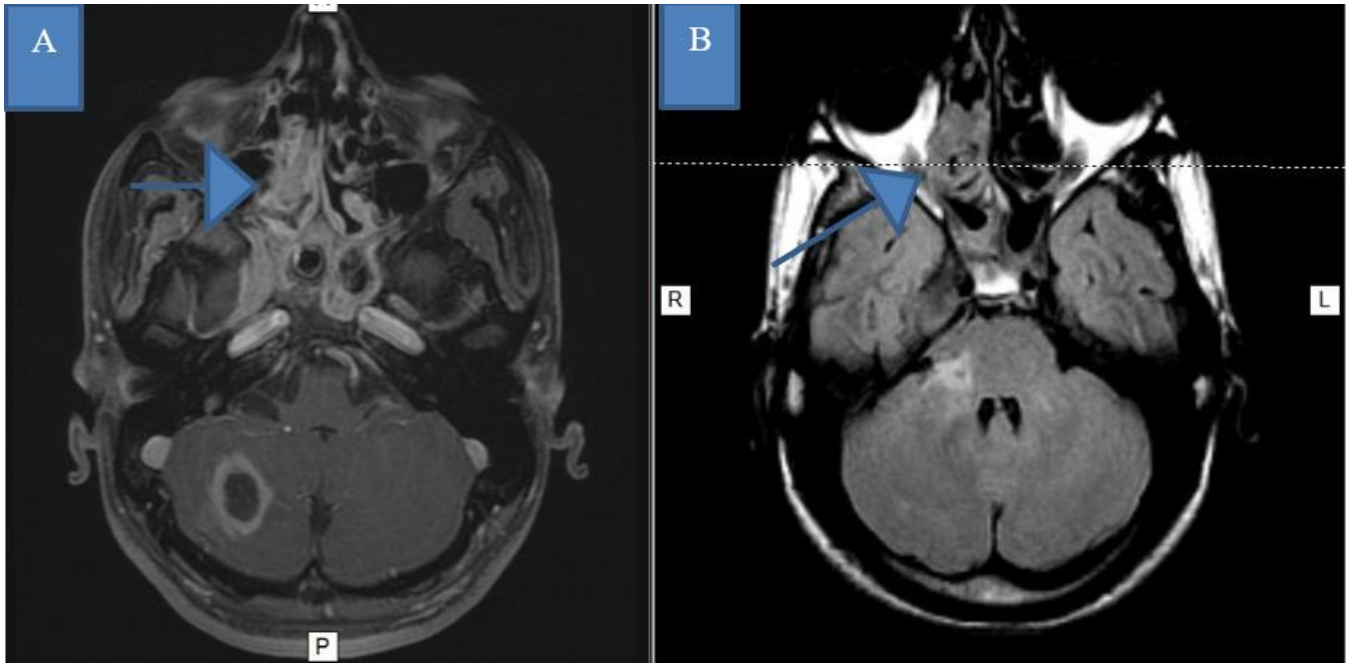

Figure 6: 23-year-old immunocompetent male with rhinocerebral mucormycosis.

FINDINGS: (A) Axial Post-contrast T1WI showing nodular mucosal thickening involving the sphenoid and ethmoid sinuses with post-contrast enhancement. (B) Axial FLAIR showing lateral displacement of right medial rectus muscle due to the expansion of right ethmoid sinus.

TECHNIQUE: 1.5 Tesla scanner (GE Signa hdxt), 5 mm slice thickness, 1.5 mm interslice gap, TE for FLAIR-100, TR for FLAIR-9000, TE for Post contrast T1WI-12, TR for Post contrast T1WI-480, Magnevist 10 cc.

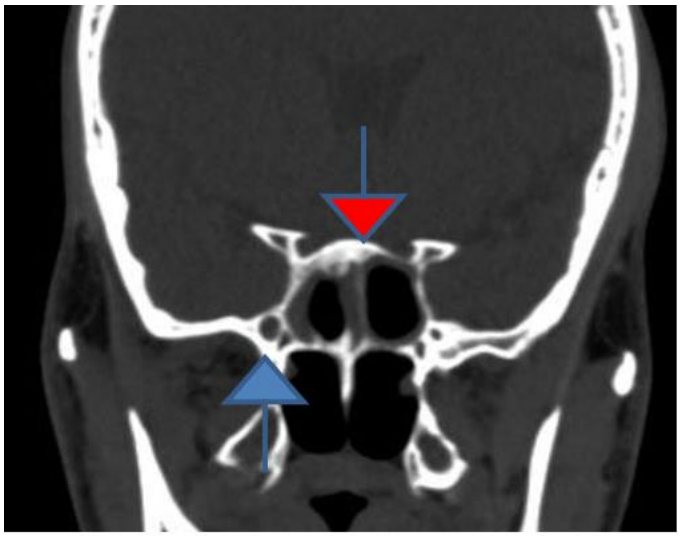

Figure 7 (right): 23-year-old immunocompetent male with rhinocerebral mucormycosis.

FINDINGS: Coronal image reveals the widening of right foramen rotundum (blue arrow) and sclerosis involving sphenoid sinus (red arrow).

TECHNIQUE: 128 slice scanner (Somatom Definition, Siemens, Germany), 120kV, 35 mAs, 0.6 mm slice thickness.

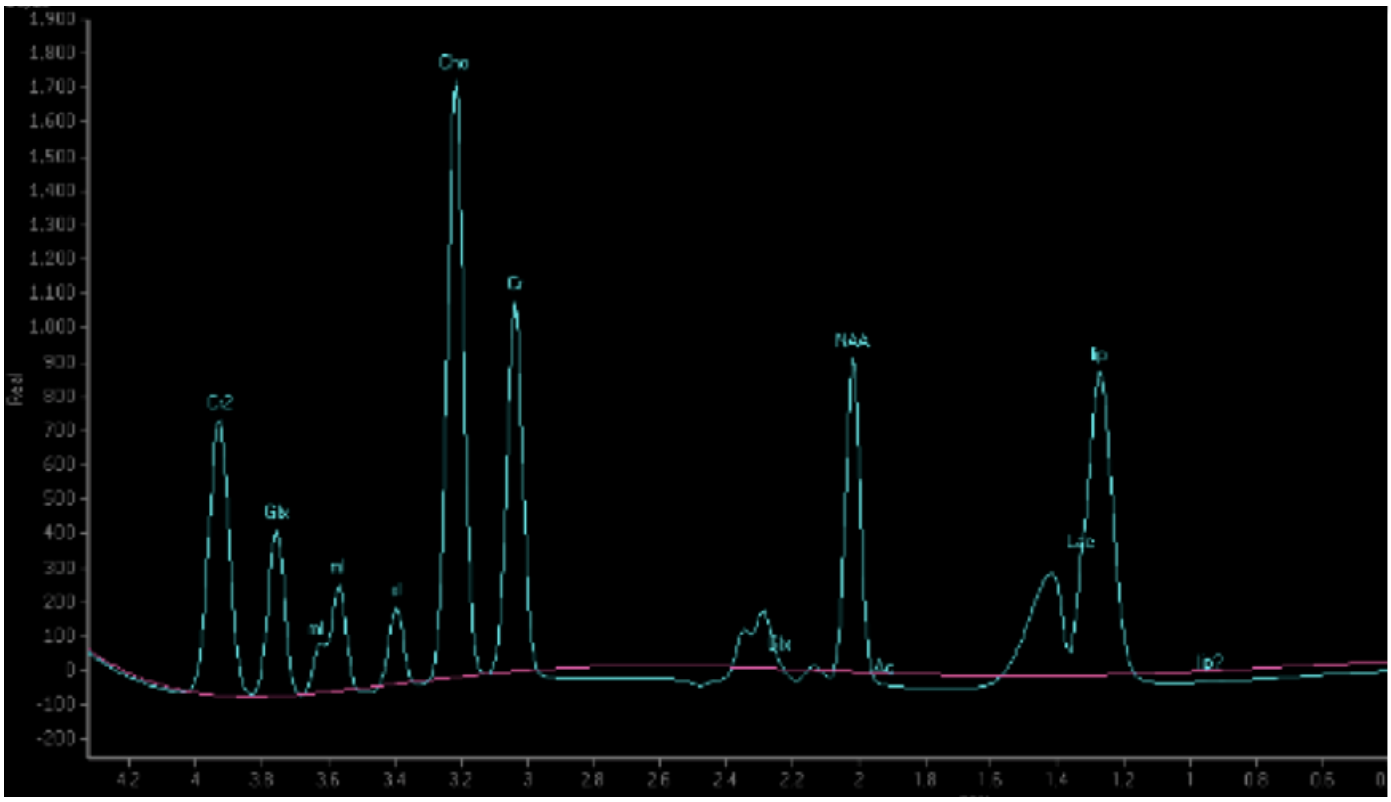

Figure 8: 23-year-old immunocompetent male with rhinocerebral mucormycosis.

FINDINGS: MR spectroscopy revealed choline peak at 3.2 ppm and multiple peaks between 3.6 and 3.8 ppm which could represent trehalose.

TECHNIQUE: 1.5 Tesla scanner (GE Signa hdxt), Multivoxel Spectroscopy, TE 35 ms.

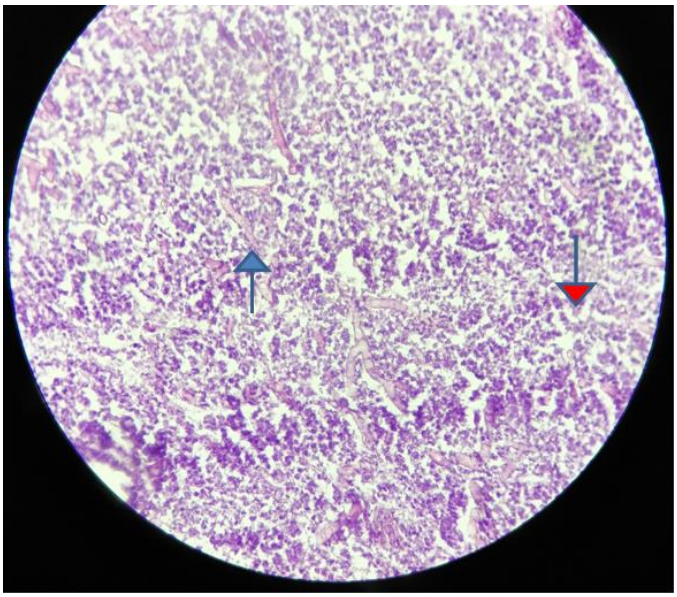

Figure 9 (left): 23-year-old immunocompetent male with rhinocerebral mucormycosis.

FINDINGS: Scrapings from the nasal cavity showed non-septate hyphae with 90° branching (blue arrow) over a background of necrotic tissue (red arrow).

TECHNIQUE: Hematoxylin and Eosinophil Staining of nasal scrapings.

Etiology	*Rhizopus oryzae* (most common), *Mucor indicus* (2nd most common)
Incidence	The exact incidence of rhinocerebral mucormycosis is not available in literature.
Gender ratio	More common in males
Age predilection	Older age at higher risk
Risk factors	An immunocompromised state like AIDS, diabetes mellitus, hematopoietic disorders and transplant recipients
Treatment	Amphotericin B (drug of choice)
Prognosis	A rare opportunistic fungal infection which may prove fatal. Immune response and extension determine prognosis
Findings on imaging	Enhancing soft tissue, may show vasculitic infarct or perineural spread, abscess formation with central diffusion restriction, a trehalose peak on MR Spectroscopy

Table 1: Summary table for Rhinocerebral Mucormycosis

Entity	CT	MRI
Rhinocerebral mucormycosis	• Enhancing soft tissue density lesion • Hypodense vasculitic infarcts • Peripherally enhancing abscesses • Widening of neural foramina due to perineural spread	• Iso to hyperintense lesion on T2WI • Enhancing soft tissue on post contrast T1WI • Vasculitic infarcts due to angioinvasive nature may show restricted diffusion • Abscesses with peripheral enhancement and central diffusion restriction • Trehalose peak on MR Spectroscopy
Neurosarcoidosis	• Nodular thickening of meninges and cranial nerves. • Post-contrast enhancement	• Nodular thickening of meninges and cranial nerves • Post-contrast enhancement
Nerve Sheath Tumour	• Spindle shaped mass along the course of nerve • Variable post contrast enhancement • Widening of neural foramina	• Spindle shaped iso to hyperintense mass along a nerve on T2WI • Variable post-contrast enhancement • Widening of neural foramina
Triton	Similar to nerve sheath tumour, differentiation on histopathology and immunohistochemistry	Similar to nerve sheath tumour, differentiation on histopathology and immunohistochemistry
Adenoid cystic carcinoma	• Heterogeneously enhancing soft tissue with bony invasion • It can lead to significant skull base involvement and intracranial extension.	• Heterogeneously enhancing soft tissue with perineural spread • Abnormal marrow signal due to bone invasion. • It can lead to significant skull base involvement and intracranial extension.

Table 2: Differential diagnosis table for Rhinocerebral Mucormycosis

ABBREVIATIONS

ADC = Apparent diffusion coefficient
AIDS = Acquired immunodeficiency syndrome
Cho/Cr = Choline/Creatine
CP angle = Cerebellopontine angle
CS = Cavernous sinus
CT = Computed Tomography
DWI = Diffusion-weighted imaging
FLAIR = Fluid attenuation inversion recovery
ITF = Infratemporal fossa
MRI = Magnetic resonance imaging
OPD = Outpatient department
PPF = Pterygopalatine fossa
ppm = parts per million
WI = Weighted images

KEYWORDS

Mucormycosis; rhinocerebral; cerebellar abscess; fungal abscess; immunocompetent

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