

# Rhinocerebral Mucormycosis: How Proton MR Spectroscopy Assisted Diagnosis of Acute Infarction Superimposed with Cerebritis

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**A 75-year-old female patient with poorly-controlled diabetes who developed rhino-cerebral mucormycosis and acute stroke is reported. The magnetic resonance (MR) imaging revealed acute stroke in the territory of left anterior cerebral artery territory and corresponding steno-occlusive lesion on MR angiography. Proton MR spectroscopy (MRS) of her brain was obtained with chemical shift imaging, which revealed increased choline peak at 3.2 ppm and a succinate peak at 2.4 ppm. This was not usually present in patients with stroke. Cerebritis caused by mucormycosis may be diagnosed with the aid of MRS.**

**Key words:** Infarct, Brain; Magnetic resonance, spectroscopy; Mucormycosis

Mucormycosis is a phycomycosis from the genus *Mucor*. Involvement of the central nervous system by mucormycosis may occur in the uncontrolled diabetic or immunocompromised patients and still attains a high mortality rate if an early diagnosis is not achieved [1]. Therefore an early diagnosis is essential and does improve the prognosis [2, 3]. We present a case with rhinocerebral mucormycosis complicated with left anterior cerebral artery infarction. Magnetic resonance spectroscopy (MRS) assisted diagnosis of superimposed cerebritis in the infarcted brain parenchyma. We propose that magnetic resonance (MR) images combined with MRS can improve early detection of cerebral mucormycosis. In our review of literature, this is the first presentation of in vivo MRS concerning infarction superimposed with mucormycosis cerebritis.

## CASE REPORT

A 75-year-old woman with poorly controlled diabetes, hypertension and chronic renal insufficiency presented to the outpatient department of our hospital with chief complaint of headache. Analgesics were prescribed without further imaging study. One week later, she was sent to our emergency department due to conscious disturbance. Her left eye was swollen with ptosis. On neurological examination, the left 2nd, 3rd, 4th and 6th cranial nerve palsy was diagnosed by our ophthalmologist and neurologist.

Laboratory data revealed high blood glucose value (571 mg/dl), elevated WBC (18570 /ul with neutrophil count 90.3%), anemia (9.3 g/dl), hyponatremia (118 mEq/l), and hyperkalemia (5.8 mEq/l). Blood pressure dropped to 84/56 mmHg. Computed tomography (CT) showed mucosa thickening of the ethmoid sinus and left nasal cavity without evidence of intracranial lesion. Under the impression of rhinitis, paranasal sinusitis and left cavernous sinus syndrome, this patient was admitted to our infectious disease ward.

Her consciousness deteriorated further four days

after admission. Follow up CT study showed interval development of symmetric low-density lesions at the inferior aspects of bilateral frontal lobes and abnormal soft tissue at the left retrobulbar space. Functional endonasal sinus surgery (FESS) was performed and a specimen from the left middle turbinate was proven to be mucormycosis histologically (Fig. 1). Rocephin (Ceftriaxone sodium) and Amphotericin B were used for coverage of possible opportunistic bacterial and fungal infections.

Due to further deterioration of consciousness 3 days after the 2nd CT study, she underwent MRI (3.0T, GE Medical Systems, Milwaukee, WI, U.S.A.), which revealed high signal intensity lesions at the right inferior frontal region and overall territory of left anterior cerebral artery on T2-weighted (Fig. 2a) and fluid attenuated inversion-recovery (FLAIR) images (Fig. 2b). The left parietal lobe outside the territory of anterior cerebral artery (ACA) also showed high signal intensities on T2-weighted images. Diffusion-weighted images revealed bright signal intensities over the corresponding areas. Calculated apparent diffusion coefficient (ADC) value at left ACA territory was  $0.43 \times 10^{-3} \text{ mm}^2/\text{s}$ , which was 48% of that at the contralateral brain parenchyma (Fig. 2c). Mild leptomeningeal enhancement was also seen on T1-weighted images (Fig. 2d) after intravenous administration of Gd-DTPA (Magnevist, Schering, Berlin, Germany). Three-dimensional time-of-flight (TOF) MR angiogram showed complete occlusion at A2 segment of left ACA (Fig. 2e).

Besides, mucosa thickening in the left nasal cavity, ethmoid sinus, left maxillary and left frontal sinuses were also identified with contrast enhancement. The abnormal soft tissue in the ethmoid sinus destroyed the cribriform plate and extended into the bilateral inferior frontal regions and retrobulbar space of left orbit. There was also bulging of left cavernous sinus with heterogeneous enhancement, which indicated cavernous sinus thrombosis. The falx cerebri was thickened and enhanced. Partial loss of integration of falx cerebri between bilateral gyrus rectus was also appreciated.

Proton MR spectroscopy (chemical shift imaging) showed significantly decreased NAA/choline ratio on color mapping (Fig. 3a). The spectrum (Fig. 3b) obtained with voxel placed at left ACA territory showed abnormal high level of succinate with a peak at 2.4 ppm. N-acetyl aspartate (NAA) peak at 2.0 ppm was decreased. The choline at 3.2 ppm was elevated. There was also markedly high peak at 1.3 ppm, which represented the peak for lipid/lactate.

The patient was transferred to our neurological



**Figures 1.** Photomicrograph (x400; Periodic acid-Schiff stain) shows broad non-septate hyphae with pink stain (arrow), which is characteristic for mucormycosis.

intensive care unit 4 days after the MRI study. Even though Amphotericin B was given continuously, the patient died with severe brain edema on the 17th day in the intensive care unit.

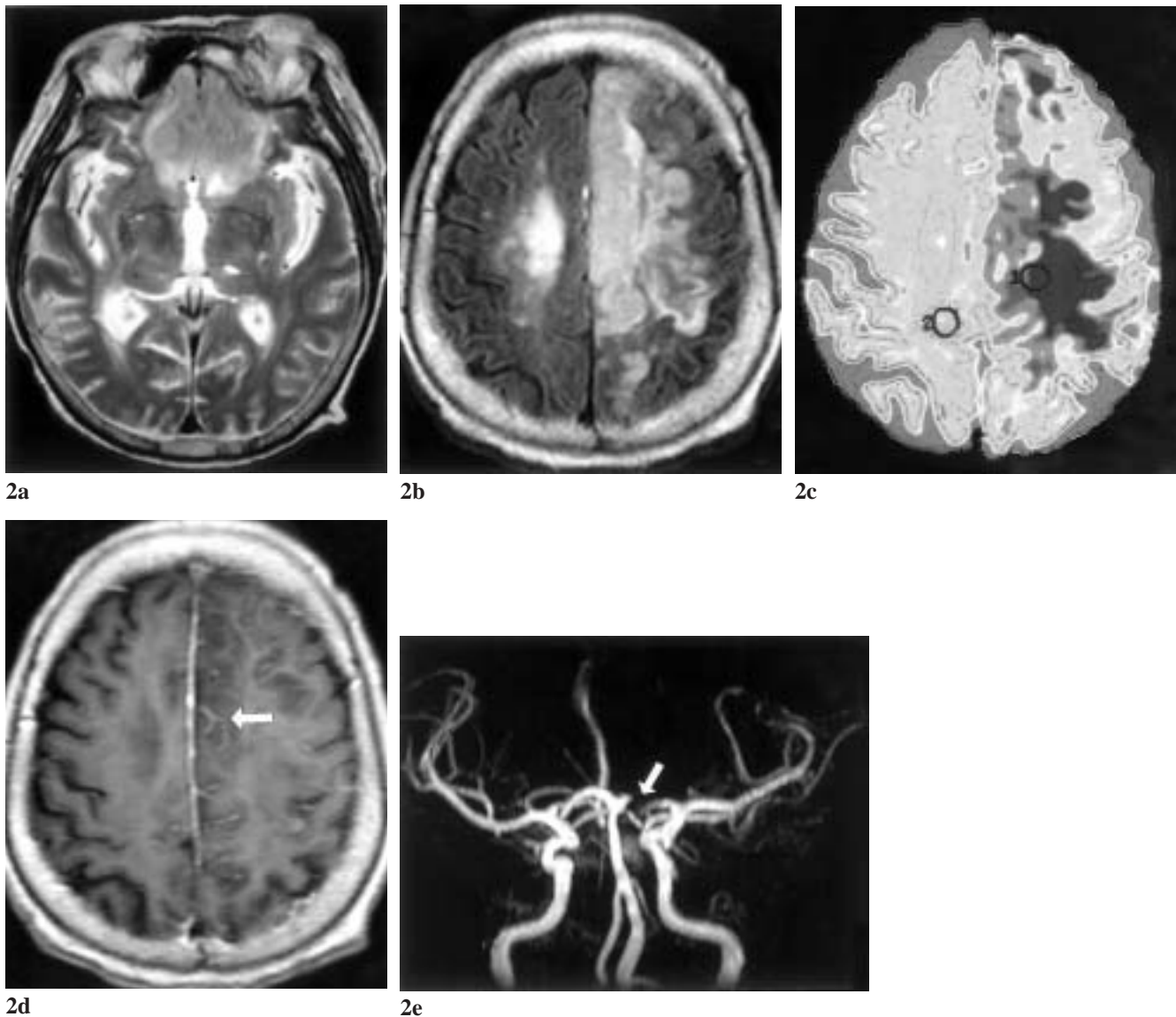
## DISCUSSION

Rhino-cerebral mucormycosis is a life threatening disease in the immunocompromised patient if early diagnosis is not achieved. Therefore, a high index of clinical suspicion is required in patients with predisposing factors such as uncontrolled diabetes and an immune compromised status [4]. This patient presented with headache as the primary symptom. Rhinitis and paranasal sinusitis were first impressed. However, the fungus infection progressed with direct invasion through the cribriform plate resulting in infection/infarction at the bilateral gyrus rectus and meningitis of falx cerebri.

For an infarct 1 to 8 days old, the calculated ADC value has been estimated at  $0.51 \pm 0.18 \times 10^{-3} \text{ mm}^2/\text{s}$  [5]. Therefore, the diffusion change at the left ACA territory and segmental occlusion on MR angiography of our patient is compatible with image findings of an acute cerebral infarction.

Leptomeningeal enhancement of the left ACA territory could be image finding of the early infarct and meningitis. It offers no help in differentiation between acute infarct and infection.

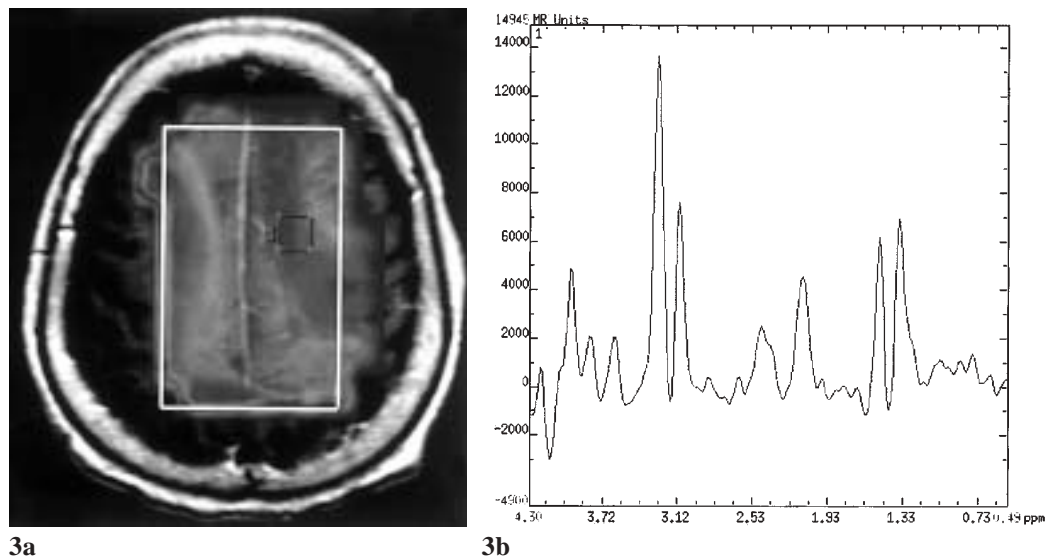
The MRS of an acute infarction supposedly shows a decreased NAA resonance due to loss of neuron or neuronal function. Lactate is immediately detected after the onset of ischemia and may remain



**Figures 2.** B. Magnetic resonance images. **a.** Axial T2-weighted image (TR/TE/excitations=4000ms/101ms/2 NEX) shows high-signal intensity lesions at bilateral rectus gyri with mild mass effect. **b.** Axial FLAIR image (8627/172/0.5) shows extensive high signal intensity lesion involving left ACA territory. Less degree of high signal change outside the left ACA territory is also identified. **c.** ADC map of diffusion-weighted image shows significant decrease in ADC. **d.** Axial T1-weighted image (1800/9.89/0.5) with contrast enhancement shows some leptomeningeal enhancement (arrow) and mild enhancement of falx cerebri. **e.** 3D time-of-flight (TOF) MR angiogram shows non-visualization of the A2 segment of the left ACA and steno-occlusive lesion (arrow) at A1 segment.

elevated for days to weeks [6,7]. Lactate is an end product of anaerobic glycolysis and is considered a marker of hypoxia [6, 7, 8]. In this case, MRS with voxel of interest at the “infarcted” left ACA territory showed abnormally high peak of succinate at 2.4 ppm, which is not usually present for acute stroke. Succinate is considered to be the end product of homolactic and heterolactic fermentation arising from microorganisms [8, 9, 10]. High choline levels along

with the presence of lipid/lactate resonance can be found in patients with malignant neoplasm and infective or inflammatory lesions [11]. These changes on MRS were also appreciated in our patient. Malignant neoplasm was less likely in this case according to clinical course and image studies. We consider the elevation of choline and lipid/lactate levels part of the spectroscopic evidence for cerebral mucormycosis.



**Figures 3.** Proton magnetic resonance spectroscopy. A. Color map ( NAA/choline ratio ) of MRS ( 2DCSI PRESS sequence at 3.0T, Slice thickness 20mm,TR 1500 ms; TE 144 ms, Phase encoding number 16 ) shows significantly decreased in NAA/choline ratio. B. The spectra obtained with voxel of interest placed at the left ACA territory shows decreased NAA resonance at 2.0 ppm, an abnormal peak at 2.4 ppm representing succinate, elevation of lipid/lactate resonance at 1.3 ppm and increased choline resonance at 3.2 ppm.

Besides, high T2-weighted signal change extending to the area outside the left ACA territory also are not typical MR image features for acute ACA infarction.

In our literature review, there was only one report demonstrating MRS characteristic of cerebral mucormycosis [8]. In that report, the lesion was a cavitation lesion, which may be due to “cystic/ necrotic/ hemorrhagic” change of cerebral fungal abscess. Both cases have obvious succinate, choline and elevated lipid/lactate peak levels on MRS. However, it will be very difficult to detect coexistence of cerebritis with acute infarction in our patient without information provided by MRS. The peak of NAA was detected but was significantly decreased in our study, but in the study by Siegal et al, it was depleted due to placement of voxel of interest within the center of “cystic” lesion. The hypothesis of discriminating pyogenic abscess from mucormycosis by lack of a 0.9-ppm peak from amino acids (-CH<sub>3</sub> moieties from valine, leucine, and isoleucine) also stands in this study [8,10]. However, the validity of this hypothesis needs to be confirmed by further study.

In conclusion, early diagnosis of rhino-cerebral mucormycosis is essential for preventing life-threatening outcome in the immune-compromised or diabetic patient. MRS is helpful in detecting cerebritis caused by mucormycosis, which is significant clinically when conventional MRI display features mimicking pure acute ischemic stroke. ◆

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## 鼻腦白黴菌病：如何用質子核磁共振頻譜幫助診斷急性中風合併腦炎

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我們報告一位76歲的女性病患，有慢性糖尿病且控制不好的病史，病人感染了鼻腦白黴菌病且併發急性腦中風。病人腦部的磁振影像可看到左前大腦動脈供血區域的缺氧及磁振血管攝影上相對應的血管堵塞。質子磁振頻譜則顯示出一個上升的的choline peak在3.2 ppm和一個不正常succinate peak在2.4 ppm。這在急性中風區域的質子磁振頻譜是不常見的。因此，質子磁振頻譜也許可以幫助診斷由鼻腦白黴菌引起的腦炎。

關鍵詞：腦梗塞，核磁共振頻譜，白黴菌病