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Case report

Rare appearance of Candida tropicalis infection of the brain: Multiple micro-abscesses combined with diffuse hemorrhages

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Abstract

We report a case of cerebral Candida tropicalis infection in a middle-aged patient who suffered from multiple cerebral micro-abscesses associated with diffuse hemorrhage due to perforation of esophagus. MRI revealed multiple irregular, nodular, ring-like enhancing lesions with restricted diffusion and multiple micro-hemorrhages as well as some leptomeningeal enhancements. Blood, sputum and urine cultures showed Candida tropicalis. The lesions were resolved after the patient was given early and effective treatment of anti-fungal medicine. The imaging findings provided limited differential diagnosis, leading to early diagnosis and treatment for this patient.

Keywords: Candida tropicalis; Brain; Micro-abscesses; Micro-hemorrhages; MRI

1. Introduction

Candida species are an uncommon cause of central nervous system (CNS) infection. Most cases of cerebral Candida infection are caused by Candida albicans. Until now, few cases of Candida tropicalis infection of CNS have been reported in the medical literature [1,2]. The typical imaging appearances of Candidia infection of CNS are irregular meningeal enhancements, multiple circular lesions and subdural effusion. Cerebral micro-abscesses, meningitis, cerebral macro-abscesses, and arteritis hydrocephalus are four main pathologic changes identified in the CNS Candidiasis [3]. Given the rarity of this infection, the epidemiology, prognosis, and optimal therapy of Candida meningitis are poorly defined. We report a case of secondary cerebral Candida tropicalis infection caused by esophageal perforation in a middle-aged patient. We describe the detailed imaging characterization and follow-up imaging. We also review and discuss other reported cases of Candida tropicalis meningitis in the medical literature.

2. Case report

A 59-year-old immune-competent woman was admitted to the hospital with the chief complains of chest pain and fever for three days and loss of consciousness for one day. Eleven days before admission, the patient had chest pain after eating fish, but no treatment was given. Chest pain persisted for three days and was accompanied by fever (temperature up to 38.7 °C). One day before admission endoscopy showed a 2.0 cm fish bone embedded in the esophageal wall 30 cm from the incisor-tooth, which caused contralateral mucosal ulceration and perforation.

Physical examination revealed loss of consciousness, eyes straight, limbs stiff. Her blood pressure is 152/82 mmHg,

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pulse is 85 times/min and respiration 18 times per minute. The results of the routine blood test were as follows: white blood cell (WBC) 16.26 $\times$ 10^9/L(↑), number of neutrophils 14.77 $\times$ 10^9/L(↑) , the neutrophils ratio 92.2% (↑) and platelets 57 $\times$ 10^9/L(↓). The fibrinogen 4.23 g/L(↑), prothrombin activity 74% and D-Dimer > 10,000/L(↑). Multiple low densities in the right frontal, parietal, occipital lobe and bilateral cerebellum was seen on Computed tomography (CT) examination on the second day of admission (Fig. 1a) (64 slices; slice thickness = 5 mm; intersection gap = 5 mm). Also multiple limited diffusion lesions were found on diffusion weighted imaging (DWI) (TR/TE = 4000/105 ms; matrix = 160 $\times$ 160; NEX = 3; field of view = 23 cm; *b*-value = 1000 s/mm^2; slice thickness = 5 mm; intersection gap = 1 mm) and no abnormal findings were found on susceptibility weighted imaging (SWI) (TR/TE = 27/20 ms; 1 acquisition; receiver bandwidth = 120 Hz/pixel; FOV = 230 $\times$ 200 mm; flip angle = 15°; number of slices = 56; acquisition time = 179 s; voxel resolution = 0.5 $\times$ 0.5 $\times$ 2 mm^3) (Fig. 1b,c). The imaging findings were suspicious of an infectious lesion and further examinations were needed to find the causative pathogen. The cultures of the peripheral and central venous blood, sputum and urine showed Candida tropicalis on the 2 day of admission. Because the patient condition was not allowed, examination of cerebrospinal fluid had not been done at early stage after admission. The patient continued to remain unconscious along with fever for the next two days in spite of the antifungal medicines that were given. The results of the follow-up routine blood test on the 4th day were WBC 13.02 $\times$ 10^9/L (↑), mean corpuscular volume 82.40 fL(↓) and neutrophil ratio 96.30% (↑). Blood biochemistry showed increased Glucose (12.97 mmol/L) and decreased albumin (32.30 g/L). The prothrombin activity (61%) descended. On the 4th day, follow-up head CT showed multiple high densities within the low density of right frontal and occipital lobes and a high nodular density in the left parietal lobe which was suggestive of hemorrhage (Fig. 2). Contrast-enhanced magnetic resonance imaging (CE-MRI) showed multiple circular contrast enhancement lesions in the whole brain (Fig. 3a). The most important finding was the presence of diffuse micro-hemorrhages in the brain on the SWI (Fig. 3b). Hemorrhagic necrotizing meningo-encephalitis was confirmed based on the findings of CT and MRI.

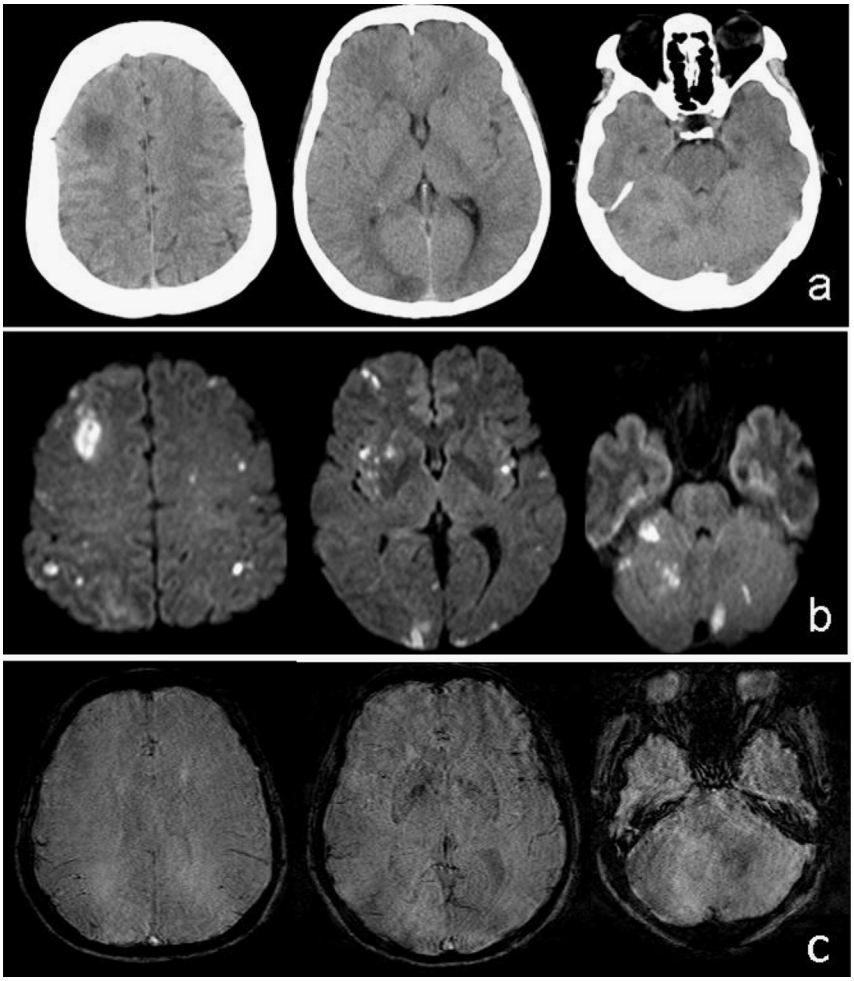

Fig. 1. CT on 2nd day of admission showed multiple patchy low-density areas on right frontal, parietal, occipital lobes and bilateral cerebella (1a). MRI on the same day showed multiple patchy limited diffusion lesions on bilateral frontal, parietal, and occipital lobes and bilateral cerebella on DWI (1b). No abnormality was found on SWI (1c). Findings on both CT and MRI support that the lesion was infectious but the etiology needs to be further confirmed.

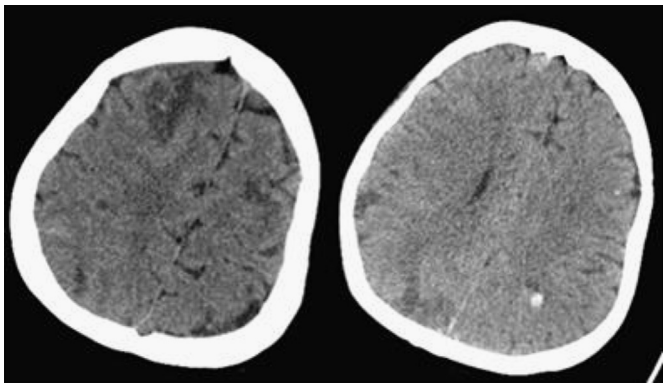

Fig. 2. Follow-up CT on the 4th day of admission showed irregular hyperdense lesions within the low density of right frontal and bilateral occipital lobes, indicating hemorrhage.

Due to persistent fever and unconsciousness of the patient, Voriconazole was used to enhance the anti-fungal treatment. After a week on the enhanced treatment, on the 17th day of admission the patient's consciousness recovered but she had aphasia. Re-examination of the blood culture was negative. The lumbar puncture yielded cerebrospinal fluid (CSF) showed a protein level of 26 mg/dL, glucose concentration of 4.22 mg/dL and chloride of 121.50 mmol/L. CSF parameters are normal. Cerebrospinal fluid microbial examination is negative. On the 26th day, follow-up contrast-enhanced MRI showed all of the circular contrast enhanced lesions were resolved except for micro-hemorrhages (Fig. 4).

Following the improvement in clinical symptoms, Fluconazole, an oral anti-fungal medicine was given. The general condition of the patient remained good with return of normal speech.

3. Discussion

The most important finding of our case was that the whole brain was affected by diffuse micro-hemorrhages and multiple micro-abscesses. On the follow-up imaging, all of the lesions were resolved except for micro-hemorrhages. There are only a few reported cases of CNS infection with Candida tropicalis.

Fungal organisms have a predilection for angioinvasion by releasing enzyme elastase, which compromises the elastin in the walls of blood vessels. An inflammatory reaction caused by digestion of elastin resulted in vasculitis. Because of its tendency to involve large- and medium-sized vessels at the base of the brain, vascular invasion can produce cerebral aneurysms and their rupture can lead to a hemorrhage in both the brain and subarachnoid space. Necropsy studies on the patients with CNS Candidiasis have shown evidence that vascular invasion, either in the vascular wall or in the arterial lumen, is present in up to 23% of the patients [4]. Severe fungal vasculitis can aggravate hemorrhagic necrosis in wide cerebral areas. In our cases, multiple micro-hemorrhages had been detected on both CT and MRI. SWI is much more sensitive to detect the micro-hemorrhages than CT scan. The developments of MRI techniques, including T2*-weighted gradient-recalled echo (T2*-GRE) and susceptibility-weighted imaging (SWI), are exquisitely sensitive to the products of bleeding. Contrast to conventional GRE sequences, SWI is a high-resolution, three-dimensional technique. SWI is currently the most sensitive sequences to visualize cerebral micro-hemorrhages in vivo [5] due to its high sensitivity to haemosiderin. SWI can detect much smaller cerebral micro-hemorrhages. In our case, multiple low intensity signal lesions of various sizes can be seen on SWI, but could not be visualized on the CT.

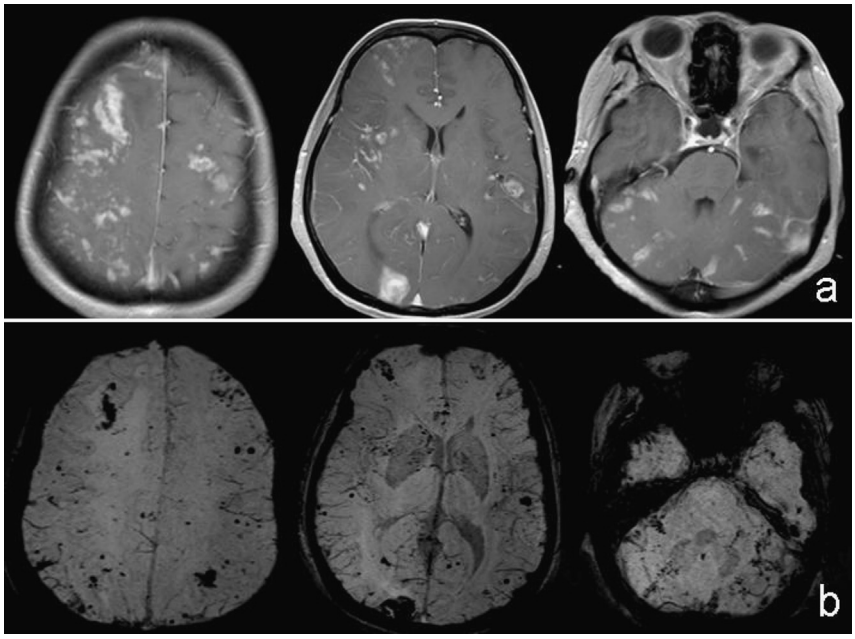

Fig. 3. Follow-up MRI on 4th day of admission showed diffuse nodular and circular contrast enhancements involving the whole brain (3a) and diffuse dotted and patchy low signal intensity on SWI which indicated the diffuse micro-abscesses and micro-hemorrhages (3b).

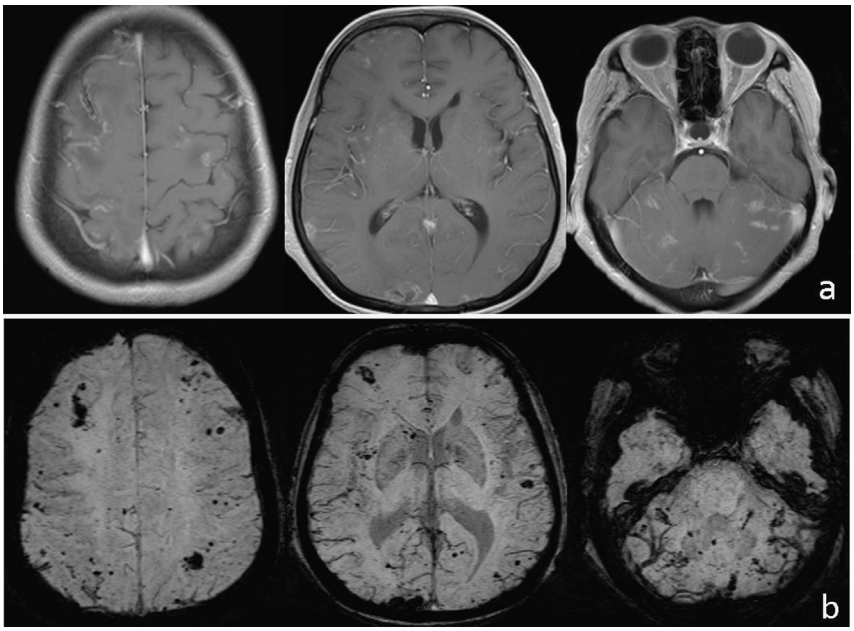

Fig. 4. Follow-up contrast enhancement MRI (26th day) showed majorities of the lesions have been resolved, except for micro-hemorrhages.

Candida species can cause focal necrosis in the area around the microcirculation, producing micro-abscesses mainly at the gray–white matter junction, basal ganglia, and cerebella, and they can be widely spread in the CNS [6–8]. A micro-abscess is defined as a lesion less than 3 mm in diameter and consisting of a localized collection of polymorphonuclear leukocytes associated with tissue necrosis [9]. These lesions usually show foci of necrosis surrounded by polymorphonuclear leukocytes or noncaseating granuloma with giant cells that may contain yeasts or hyphae [10]. The incidence of cerebral micro-abscesses varies between 0.2% and 0.5%. Micro-abscesses appear isodense to hypodense on non-contrast CT. MRI is more sensitive to the micro-abscesses, especially on DWI and contrast enhanced sequences. The lesions will have small rings enhanced and restricted diffusion as well as hemorrhagic components widely spread in the brain [11,12]. In our case, multiple circular and nodular enhancements were seen in both the cerebra and the cerebella. Diffuse meningeal enhancements were also seen. But the lesions were resolved after administration of anti-fungal medicine. Common differential diagnoses of multiple small, ring-enhancing lesions include infection with Candida, tuberculosis, metastasis, and multiple sclerosis. Together with the patient's history and laboratory data, MR imaging can help establish a diagnosis of Candidiasis.

Delay in treatment can lead to death. Despite the severe symptoms on admission, prognosis of our patient was good. The typical imaging findings, including multiple micro-hemorrhages and micro-abscesses, suggested that the lesions were fungal. The imaging findings can help the doctors to give prompt treatment.

In conclusion, multiple limited diffusion lesions, multiple micro-hemorrhages, and multiple circular or nodular contrast enhancing lesions were the typical MRI findings of CNS infections caused by Candida organisms. Prompt diagnosis and treatment can improve the prognosis of the patients.

References

[1] Dawson NL, Robles HA, Alvarez S. Recurrent Candida tropicalis meningitis. Clin Neurol Neurosurg 2005;107:243–5.
[2] Goldani LZ, Santos RP. Candida tropicalis as an emerging pathogen in Candida meningitis: case report and review. Braz J Infect Dis 2010;14:631–3.
[3] Jain KK, Mittal SK, Kumar S, Gupta RK. Imaging features of central nervous system fungal infections. Neurol India 2007;55:241–50.
[4] Lipton SA, Hickey WF, Morris JH, Loscalzo J. Candidal infection in the central nervous system. Am J Med 1984;76:101–8.
[5] Ayaz M, Boikov AS, Haacke EM, Kido DK, Kirsch WM. Imaging cerebral microbleeds using susceptibility weighted imaging: one step toward detecting vascular dementia. J Magn Reson Imaging 2010;31:142–8.
[6] Sánchez-Portocarrero J, Pérez-Cecilia E, Corral O, Romero-Vivas J, Picazo JJ. The central nervous system and infection by Candida species. Diagn Microbiol Infect Dis 2000;37(3):169–79.
[7] Garg RK, Sinha MK. Multiple ring-enhancing lesions of the brain. J Postgrad Med 2010;56:307–16.
[8] Kamitsuka MD, Nugent NA, Conrad PD, Swanson TN. Candida albicans brain abscesses in a premature infant treated with amphoterin B, flucytosine and fluconazole. Pediatr Infect Dis J 1995;14:329–31.
[9] Lai Ping-Hong, Lin Shu-Ming, Pan Huay-Ben, Yang Chien-Fang. Disseminated miliary cerebral candidiasis. AJNR 1997;18:1303–6.
[10] Huang CC, Chen CY, Yang HB, Wang SM, Chang YC, Liu CC. Central nervous system candidiasis in very low-birth-weight premature neonates and infants: US characteristics and histopathologic and MR imaging correlates in five patients. Radiology 1998;209:49–56.
[11] Mathur M, Johnson CE, Sze G. Fungal infections of the central nervous system. Neuroimaging Clin N Am 2012;22:609–32.
[12] Gaviani P, Schwartz RB, Hedley-Whyte ET, Ligon KL, Robicsek A, Schaefer P, et al. Diffusion-weighted imaging of fungal cerebral infection. AJNR Am J Neuroradiol 2005;26:1115–21.