A case of cryptococcal meningitis successfully treated with liposomal amphotericin-B, Fulcytosine, and Voriconazole

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Abstract

A case of cryptococcal meningitis that developed in a healthy subject is reported. The patient received a three-drug therapy using Liposomal amphotericin-B, fulcytosine, and Voriconazole, and a good effect of the treatment was observed. Cryptococcal meningitis is often aggravated, and early diagnosis and the long-term continuation of treatment are important.

Key Words: Cryptococcal meningitis, Liposomal amphotericin-B, Fulcytosine, Voriconazole

Introduction

Cryptococcal meningitis is common in patients with decreased immunocompetence. The disease is easily aggravated and has a high mortality rate. We report on a case of cryptococcal meningitis that developed in a healthy subject. The meningitis was markedly improved by a three-drug therapy using Liposomal amphotericin-B (L-AMB), fulcytosine (5-FC), and Voriconazole (VRCZ).

A case report

The patient was a 59-year-old man. His occupation was related to agriculture and forestry. The main complaints exhibited were vomiting, disturbed consciousness, and gait disturbance. There were no issues of relevance in the patient's medical history or his family's history. He consulted a local doctor in February, 2009, because of the development of a fever and a headache,. A diagnosis of common cold was made and the prescription of an orally administered medicine did not improve the symptoms. The symptom worsened, and vomiting and disturbed consciousness developed on the tenth day of the illness; walking also became difficult. He was admitted to our hospital on the 16th day of the illness. In a general physical examination conducted upon admission, no specific abnormality of note was identified. The level of consciousness was affected, and the patient could follow simple orders. In addition, a strong tendency for somnolence was exhibited. In the cranial nerve system, pupillary light reflex was dull in the right. Pupil diameter differed between the right and left eyes: that of the right eye was 4 mm and that of the left eye was 3 mm. In terms of the kinetic and sensory systems, clear muscle weakness and sensory disturbance were not observed. Cervical rigidity was pronounced. Upon admission, no abnormal laboratory findings were obtained except for a slight inflammatory response shown by a blood test. β-D-glucan was negative

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and no increase in adenosine deaminase (ADA) was observed.

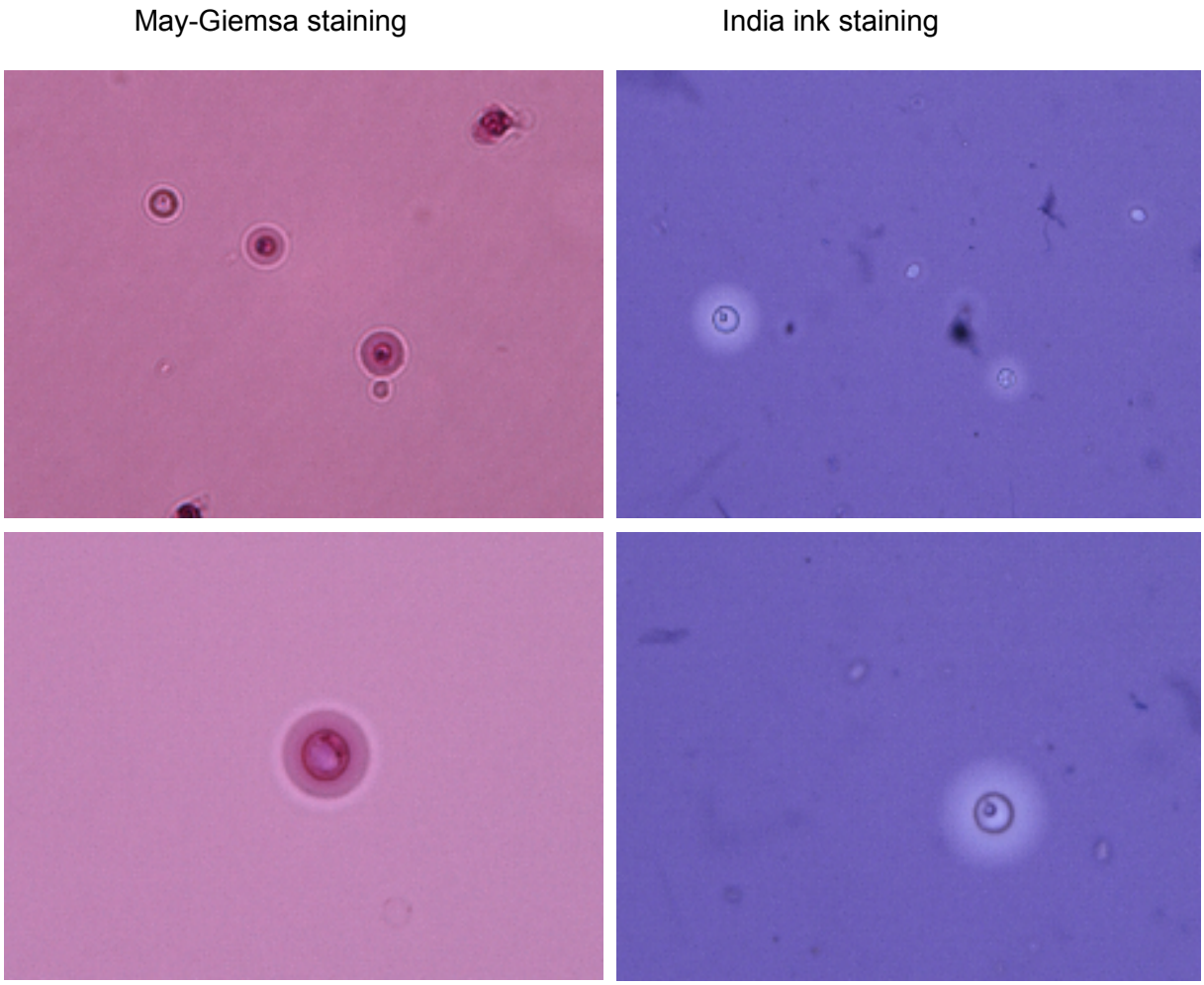

Figure 1. Cytodiagnosis of cerebrospinal fluid. May-Giemsa staining and India ink staining showed many bacterial bodies with a capsule.

Virus-associated antigen antibody was negative, including those for mumps, herpes, cytomegalovirus, varicella zoster, HIV, and HCV. The appearance of the cerebrospinal fluid included xanthochromia with a lemon yellow colour. The pressure increased markedly with first pressure 44 cm H_2O. The cell count increased to 208/mm3 (mononuclear leukocyte predominance), the protein concentration rose to 114 mg/dl, and the sugar concentration decreased to <3 mg/dl (blood sugar, 122 mg/dl). May-Giemsa staining showed many bacterial bodies with a capsule and even India ink staining produced similar results (Figure 1). The level of cryptococcus antigen increased 256-fold. There was a contrasting effect along the sulcus of the brain in gadolinium-contrasting MR imaging of the head (Figure 2). Treatment with combination therapy [1] using Liposomal amphotericin-B (L-AMB) and fulcytosine (5-FC) was started promptly upon the diagnosis of cryptococcal meningitis at our hospital. Decompression was planned in the thing except 20-30 ml of cerebral fluid in periodical (three times / week) [4]. Cerebral fluid analysis results and those obtained by clinical examination of the patients improved slowly. However, on the 45th day of hospitalisation, left facial paralysis developed. Furthermore, left trick syndrome developed. A new lesion appeared in the right thalamus as determined by head MRI (Figure 3). Expansion of the contrasting area along the sulcus of the brain was found by contrasting MRI. It was determined that the cryptococcal meningitis had become aggravated, and three-drug therapy, involving the addition of

Voriconazole (VRCZ), was provided. The cerebral fluid analysis results and the clinical manifestations subsequently improved.

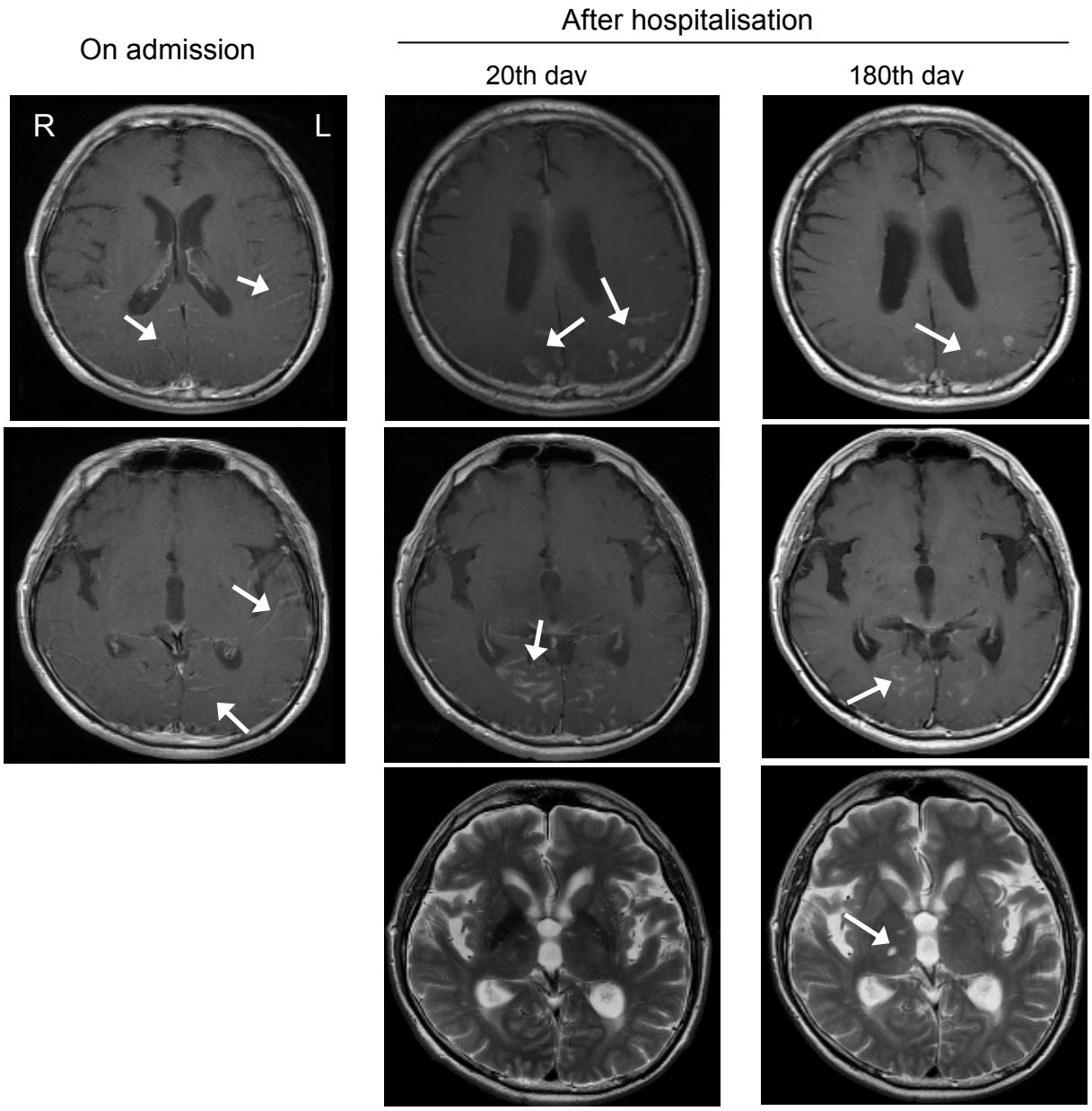

Figure 2. Gadolinium-enhanced brain MRI showing contrasting effect along the sulcus of the brain during the clinical course.

As determined by MR imaging, the contrast along the sulcus of the brain was reduced, but the small lesion of the right thalamus remained. The patient left the hospital after 180 days of hospitalisation. The left facial paralysis of the patient improved slowly. Hypokalemia developed as a side effect of L-AMB during hospitalisation, but it could be controlled by potassium replacement therapy in K 2.5-3.0 mEq/dl.

Discussion

We treated a previously healthy patient who exhibited good recovery after the administration of a three-drug therapy consisting of L-AMB, 5-FC, and VRCZ for a long period to treat cryptococcal meningitis. Cryptococcal meningitis often develops in patients with suppressed immunity, such as those with AIDS. It is known that the disease is sometimes aggravated. The disease rarely develops in

healthy subjects [3]. In this case, diagnosis and

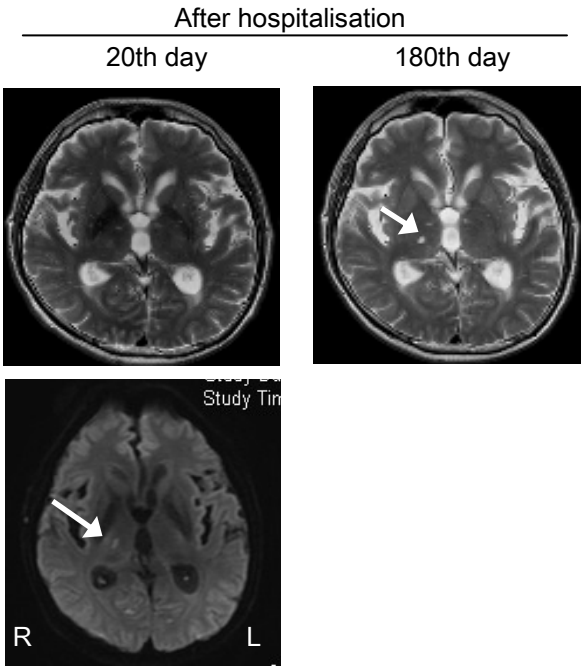

Figure 2. Brain MRI showed a new lesion in the right thalamus in T2-weighted and proton images on the 20th day after hospitalisation

than 70% [4]. However, the case which cannot be started by India ink staining quickly. The sensitivity of India ink staining for diagnosis is said to be appropriate in cases where 20% or more is present. In such cases, a general evaluation using an examination of cryptococcus antigen or of contrasting MR imaging of the head is important. Dual therapy of L-AMB and 5-FC was initially used as treatment in this case [1,2], but because its effect was insufficient, VRCZ was added, and a three-drug therapy was performed. VRCZ has been reported as effective in multiple cases of cryptococcal meningitis and central cryptococcal infection [5,6]. Our patient was able to recover after long-term administration of the combination of these three drugs. The thalamic small lesion found by head MRI was considered to be related to cerebral infarction due to cryptococcal meningitis [7]. Recovery from cryptococcal meningitis is affected by the following factors: the presence or absence of underlying disease, pressure by the examination of cerebrospinal fluid, the level of sugar in the cerebral fluid, the level of cryptococcus antigen, and the presence of the infection of many organs [8]. In this example, there was no underlying disease, and cryptococcal infection of many organs was not treatment could be carried out.
exhibited. However, there were a rise in cerebrospinal fluid pressure, a fall in sugar level in cerebral fluid, and a rise in the level of cryptococcus antigen, and it was thought that the convalescence was bad. The patient recovered well by long-term administration of the three-drug therapy. Cryptococcal meningitis is often an intractable disease, but it is thought that an early diagnosis and continuation of long-term treatment are important to improve patient prognosis.

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