

Clinical features of space occupying lesion due to fungal infections mimicking brain tumor: Case report

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ABSTRACT

Diagnosis and treatment of masses due to fungal infection of the central nervous system is often difficult. Radiologic features are often non-specific and are often confused with malignant lesions so that a new diagnosis can be made by histological examination after resection. The combination of medical and surgical treatment of fungal infections of the central nervous system is optimal in shortening the duration of antifungal therapy, providing a definitive diagnosis and improving patient outcome.

A 57-year-old male patient was conscious with complaints of weakness in the left half of the body, progressive chronic headache for 6 months and seizures, with physical examination results in the form of papilledema dextra, paresis N VI dextra et sinistra, paresis N VII S supranuclear, hemiparesis flaccid of left with grade 2/3, chronic progressive cephalgia and with a history of partial seizures become secondary common. Non-reactive HIV, CT scan of the head supporting a primary brain tumor with suspicion of intratumoral bleeding and cerebral edema. After surgery, histopathological examination results suitable for cerebral abscess, leading to fungal infection that is *Cryptococcus neoformans*. The patient was treated with 600 milligrams of Fluconazole every 12 hours intraoral for 6 months, the complaints improved and the head MRI was evaluated as normal.

Conclusions. Diagnosis of fungal infection is still a challenge. The combination of surgical medical therapy in a mass fungal infection of the central nervous system is optimal in shortening the duration of antifungal treatment, providing a definitive diagnosis, and improving patient outcomes.

Keywords: : *Cryptococcus neoformans*, fungal infection, non HIV, space occupying lesion

INTRODUCTION

Diagnosis and treatment of masses due to fungal infections of the central nervous system are often difficult. Radiologic features are often non-specific and are often confused with malignant lesions so that a new diagnosis can be made by histological examination after resection. It is important to consider a fungal lesion in the differential diagnosis of a malignancy or a mass in the central nervous system. Under normal circumstances relatively few fungal species are pathogenic, however, several species that can cause infection are important to note [1].

In general, fungi are free-living organisms everywhere and if there is an infection by fungi in a

healthy person, it usually comes from the environment and enters the body by inhalation, ingestion, or directly. Of the approximately 50,000-200,000 known species of fungi, only less than 200 species have been recorded to cause disease in humans. However, in certain circumstances, more types of fungi can cause disease; For example, in immunocompromised, infection can be caused by fungi that are in good health living in the mouth or gastrointestinal tract without causing disease. In addition, it can also be caused by fungi that are in the vicinity [2].

Clinically, fungal infections are divided according to the site of infection and the type of pathogenicity. Several conditions that can cause an immunocompromised state include neutropenia,

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damage to cellular and humoral immunity, changes in physical barriers, poor nutrition, obstruction and changes in bacterial flora. The diagnosis of fungal infections of the central nervous system is often difficult and highly dependent on the alertness of the clinician. In addition to clinical symptoms, it is very important to carry out radiological examination of the lungs and other organs, serum antibodies and examination of cerebrospinal fluid. Isolation of germs from lesions and cerebrospinal fluid is an important diagnostic complement [3].

This study has obtained ethical clearance issued by the Research Ethic Commission of Faculty of Medicine, Udayana University, Sanglah General Hospital, Denpasar.

CASE PRESENTATION

A 57-year-old male patient came with his family in a conscious state, experiencing weakness in the left half of the body that has been occurring slowly since 4 months, which is getting worse over time. Initially the patient felt weakness was still able to walk, but now it is said that the left hand can only move and the left leg can be lifted lightly but cannot be maintained for a long time. The complaints persisted until the patient was brought to the hospital. History of seizures (+) since 1 month ago with a pattern of eyes turning to the left accompanied by stomping movements of the left hand followed by swaying of the whole body. Seizures last for approximately 5 minutes. Seizures stop on their own without medication. Before and after the seizure the patient is unconscious. The history of headache was felt since 6 months but it came and went. Headache feels throbbing, especially on the right side of the head. The patient has routinely visited the neurosurgery poly at Sanglah Hospital Denpasar with a brain tumor. The patient routinely takes seizure medication and so far the seizures have been controlled. The last seizure was because the patient was said to be late in taking the medicine. Patients often complain of headaches that occur intermittently since the last 1 year. History of other systemic diseases. There is no family member who suffers from the same complaints as the patient. The patient is a farmer, smoking and alcohol habits are denied. Patients often consume herbal medicine if they feel unwell, have headaches or joint pain. Vital signs were within normal limits with a pain scale of 2. From the neurological examination, the patient had GCS E4V5M6, papilledema at right, paresis N VI right and left, paresis N VII S supranuclear, hemiparesis flaccid of left grade 2/3, chronic progressive cephalgia and with a history of partial seizures became secondary generalized. From supporting ex-

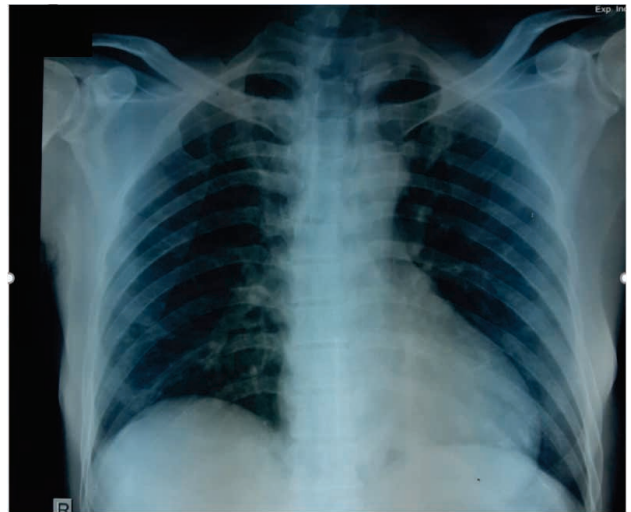


FIGURE 1. Thorax X-ray normal

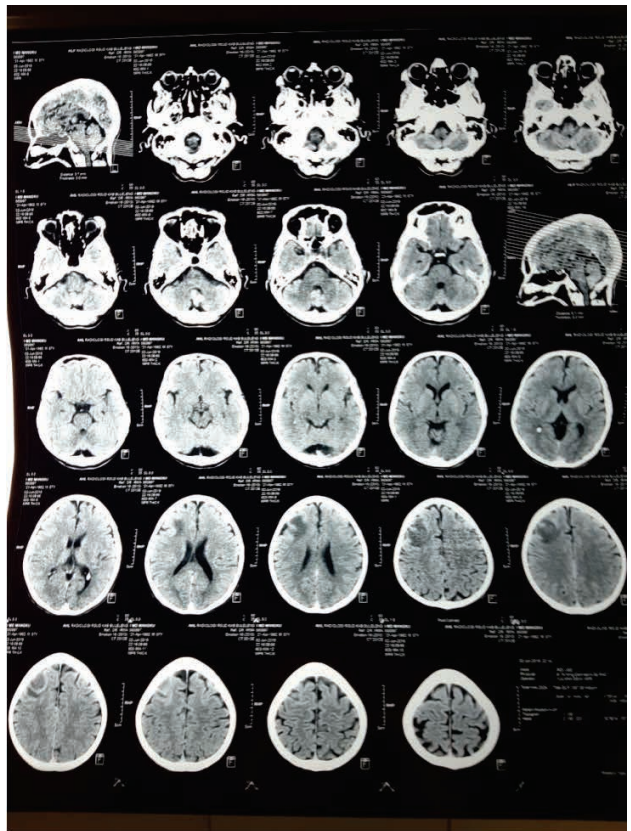


FIGURE 2. A CT scan of the head shows a solitary lesion with clear boundaries on the right frontal lobe with finger-like edema around it that urges and constricts the right lateral ventricle, supporting the picture of a primary brain tumor with suspicion of intratumoral bleeding, cerebral edema

aminations to laboratory examinations, it was within normal limits and a non-reactive HIV rapid test was obtained. Microbiological examination of Gram stain and antibiotic sensitivity test with pus specimens showed no signs of bacterial infection. The chest X-ray was within normal limits (Fig. 1). CT scan of the head with contrast shows a solitary le-

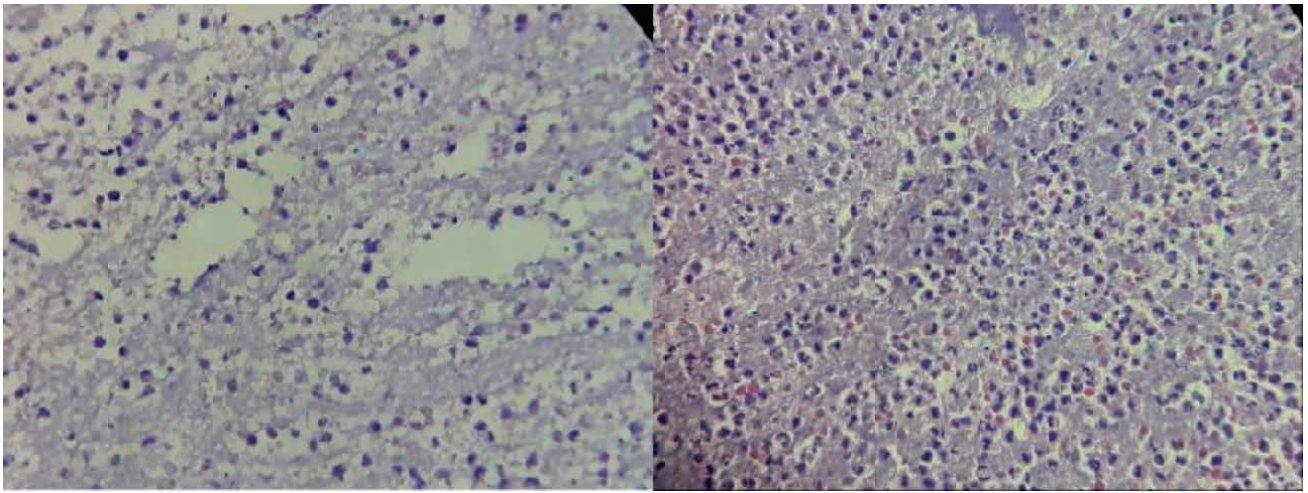


FIGURE 3. Histomorphological results suitable for cerebral abscess, suggesting a fungal infection (*Cryptococcus neoformans*)

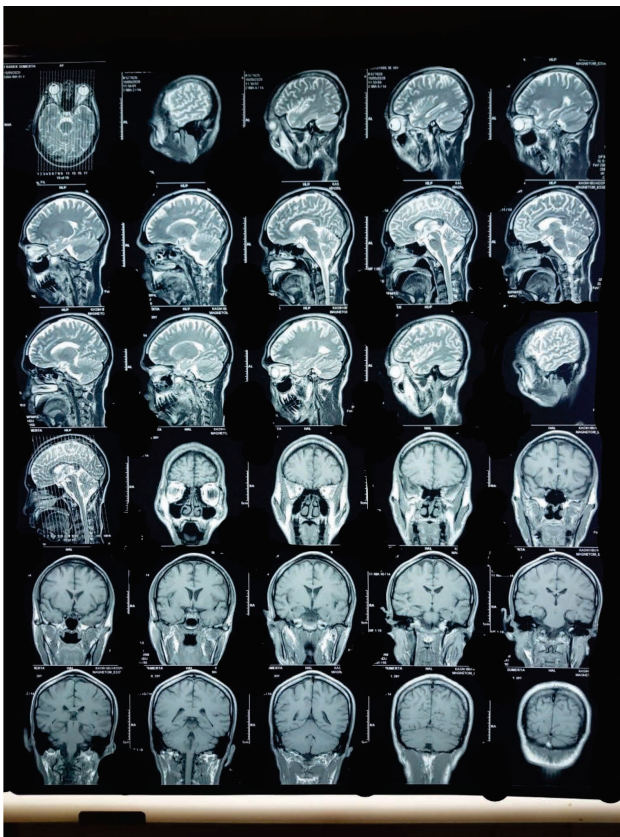


FIGURE 4. MRI of head evaluation 6 months after treatment shows normal

sion with clear borders on the right frontal lobe with finger-like edema around it that urges and constricts the right lateral ventricle, supporting the picture of a primary brain tumor with suspicion of intratumoral bleeding, cerebral edema (Fig. 2). After surgery, histopathological examination was performed with histomorphological results suitable for cerebral abscess, suggesting a fungal infection *Cryptococcus neoformans* (Fig. 3). The patient was treated with 600 milligrams of Fluconazole every 12

hours intraorally for 6 months with an MRI evaluation of the head appearing normal (Fig. 4).

DISCUSSION

In this case, the patient presented with progressive chronic complaints, in the form of headache, weakness in half of the body and seizures. These clinical characteristics are strongly suspected of being a brain tumor. However, this patient turned out to be a fungal infection, where the symptoms are usually non-specific and sub-acute lasting 2-4 weeks. Fungal infections have varied symptoms depending on the host factor, inoculum, and virulence of the organism so that the disease can spread systemically with the main predilection site being the brain [4]. The results of the history obtained can be in the form of headache, fever, nausea, vomiting, malaise, cognitive dysfunction, loss of consciousness, personality changes, memory impairment, visual impairment, hearing loss, history of weight loss. Physical examination may occur changes in consciousness, signs of meningeal stimulation in the form of neck stiffness, Kernig, Brudzinsky (I-IV), focal neurological symptoms, signs of increased intracranial pressure: headache, decreased consciousness, vomiting spray, papilledema, seizures [5].

Cryptococcus neoformans enters by inhalation, spreads via the hematogenous route and has a predilection for the central nervous system. The results of the examination of the patient's lungs on arrival were still within normal limits with normal X-Ray images. The lungs are said to be the main portal of entry for *Cryptococcus neoformans*. In patients with progressive intracranial will be followed by cranial nerve damage and other focal neurologic deficits[4] the patient experienced in the form of papilledema in right, paresis N VI in right et left, paresis N VII S supranuclear, hemiparesis flaccid of left grade 2/3.

The patients were immunocompetent patients without symptoms of meningitis but had focal deficits. Imaging of patients with cryptococcal is still a challenge so that further investigations need to be done. The diagnosis and treatment of central nervous system (CNS) cryptococcal is more complicated than meningitis. Cryptococcal are radiologically nonspecific, have a similar appearance to malignant lesions, and the diagnosis can only be made by histologic examination after resection. It is important to consider cryptococcal in the differential for malignant lesions and central nervous system masses, especially in areas where *Cryptococcus gatii* is endemic [6-8].

The diagnosis and treatment of central nervous system (CNS) cryptococcal is more complicated than meningitis. Although there are no clinical trials on which to time cryptococcal surgical resection, long-term administration of antifungal drugs is usually recommended. Corticosteroids for reducing edema and the mass effect of cryptococcal have not been systematically evaluated. The literature suggests that early surgery in cryptococcal can significantly shorten the duration of required antifungal therapy and should be considered as part of first-line therapy in all cases subject to surgical resection. In general, examination of CSF, routine blood tests, biochemical indicators, examination of Indian ink in CSF are important for diagnosis, but the definitive diagnosis of cryptococcal must be confirmed by histopathological examination. Location, In the pathological type, the degree of CNS cryptococcal can be seen on CT or MRI of the head. In the early stages, there may not be abnormalities on CT scans, but sometimes non-specific manifestations such as cerebral atrophy, hydrocephalus, brain edema may also be found [9].

Cryptococcal can look like a mass resembling a neoplasm when the fungal infection has involved the brain parenchyma. Diagnosis and early initiation of treatment are very important and related to the patient's prognosis. CNS cryptococcal is fatal if left untreated. The goals of therapy are to control early infection and lifelong antifungals for HIV-coinfected patients and to treat cryptococcal infection completely in patients without HIV-coinfection [10]. CSF should be examined to evaluate the therapeutic effect of initial therapy after 2 weeks of treatment. *Cryptococcal meningitis*, the most common feature of cryptococcal disease, is diagnosed by CSF culture, which develops into mucoid colonies in 3 to 7 days. However, this delay from suspicion to diagnosis often leads to serious infections, for which alternative screening tests are needed. A method still frequently used in clinical practice involves staining CSF with Indian ink, which allows visualization of cryptococcal cells under a microscope, such as yeast, an

encapsulated yeast organism found in more than 75% of patients. The most accurate screening method is the cryptococcal antigen test, which has high sensitivity and specificity in CSF (97% and 93 to 100%), respectively [8].

The effectiveness of empirical antifungal therapy is limited in view of its toxic effects and the narrow therapeutic range. Patients at high risk of CNS fungal infections are usually also accompanied by other medications such as antiretrovirals or immunosuppressant drugs which will lead to drug interactions. Treatment of CNS fungal infections requires agents that can cross the blood-brain barrier, usually given over a long period of time, over months to years. There are various kinds of antifungal preparations such as polyene antibiotics (amphotericin B and nystatin topical), Azoles and Flucytosine groups [2]. CSF levels of amphotericin B are generally difficult to predict, although they have shown efficacy in the treatment of CNS fungal infections. Kidney failure was the most commonly reported side effect. Fluconazole is a novel triazole antifungal agent which has unique pharmacokinetics. Bioavailability after oral administration is 80%. Fluconazole is effective in the treatment of cryptococcosis in the CNS because it can cross the blood brain barrier, has a long half-life of up to 24 hours and so can be given only once per day. Guidelines for treatment in patients with cryptococcal antifungal induction for at least 6 weeks with amphotericin B and for maintenance with oral fluconazole 400-800 mg daily for 6-18 months [11]. This patient was given fluconazole 600 milligrams every 12 hours intraorally for 6 months. The results of the MRI evaluation were normal.

Indications for surgery on cerebral abscesses, namely pressure on the brain and symptoms worsen and the size of the cerebral abscess does not decrease with conservative therapy. Treatment with operative therapy in the form of: stereotactic-guided aspiration and excision. Aspiration causes less damage to brain tissue than excision, CT (or MRI)-guided stereotaxic aspiration through a burr hole is considered an option. Some of the advantages of stereotactic aspiration are: can be performed quickly and safely through a single burr hole with the patient under local anesthesia, aspiration of an abscess allows pathological confirmation of the diagnosis, which is helpful in differentiating it from a tumor, the basic procedure of steroids with minimally invasive measures, bacterial culture of samples taken directly from the aspirated abscess, additional aspiration can be advantageous and can easily be performed with repeated stereotaxic procedures under local anesthesia.

Abscess excision is carried out in a number of circumstances such as multiloculated abscess, ab-

cess that expands with antibiotics, herniation, unencapsulated lesions due to fungal and helminthic infections, infections caused by head trauma (to remove foreign bodies), decreased consciousness, no improvement in 7 days, and/or progress of abscess development.

The patient was evaluated every month for fluconazole treatment and it was known that the condition was getting better day by day, the patient was able to walk again, seizures (-), and headaches (-). After 6 months, an MRI was re-evaluated and the results were normal. The survival rate for fungal infections in the CNS is good with regard to: young age, no neurological deficit at the onset of disease, no clinical worsening, no comorbid disease found. Poor prognosis related to: a herniation at the beginning of the disease, delayed or misdiagnosed diagnosis, expansion of the lesion on radiology (increase in size, dangerous location, multiple lesions, expansion of edema/midline shift), ventricular rupture, a fungal infection, age > 60 years. One study reported that of 47 patients who underwent brain abscess surgery, 61.7% of patients had clinical improvement, 29.8% had persistent neurologic deficits, and 8.5% of patients had new or worsening neurologic

deficits. 23.4% of patients died during follow-up [3].

Complications that can be experienced by patients with fungal infections in the CNS are persistent seizures (epilepsy), persistent mental status disturbances, focal neurologic deficits, ventriculitis, hydrocephalus, complications of ventriculitis. In this patient, due to aggressive treatment, complications did not occur [2].

CONCLUSIONS

Fungal infection should be considered in the differential diagnosis in patients with suspected central nervous system neoplasms in immunocompromised or immunocompetent patients. This patient was reported to have progressive chronic complaints, immunocompetent with radiological features of a brain tumor, but after surgery, a fungal infection was discovered and antifungal therapy was immediately administered which results for 6 months. Good patient outcomes are based on a combination of early diagnosis, prompt surgery, initiation of aggressive antifungal administration and a normal immune response to the patient (immunocompetent).

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