

CASE REPORT

Is it toxoplasma encephalitis, HIV encephalopathy or brain tuberculoma?

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SUMMARY

A 31-year-old Malaysian man was presented with an episode of seizures by the roadside, after having been recently diagnosed as HIV positive accompanied with miliary tuberculosis. On physical examination, he was oriented to person, but not to time or place. There was no neck stiffness or papilloedema. The other systemic examination was unremarkable. Chest examination revealed crepitations at the upper zone of the right lung. After diagnosis suspicion, the case was confirmed as toxoplasma encephalitis by MRI and serological tests. Patient was treated with trimethoprim/sulfamethoxazole 480–2400 mg/day with folic acid supplement for 60 days. Two months later, a repeat brain MRI showed resolution of the cerebral lesions.

BACKGROUND

Toxoplasmosis is an opportunistic infection caused by *Toxoplasma gondii*, a ubiquitous obligate intracellular protozoan. *T gondii* causes encephalitis, pneumonitis and disseminated infection in immunocompromised hosts, and leads to life-threatening infections in some patients.¹ Toxoplasmosis in those patients is usually the result of reactivation of latent infection rather than primary infection.^{2 3} Diagnosing cerebral toxoplasmosis in immunocompromised patients is often difficult because the symptoms and signs are non-specific. Therefore, it is important to take toxoplasmosis into account as one of the differential diagnoses in febrile immunocompromised patients.

CASE PRESENTATION

A 31-year-old Malaysian man was picked up by the ambulance crew from a roadside. According to eyewitnesses, the patient stopped by a shop and suddenly fell unconscious, and had generalised jerky movements which lasted about 2 min. When the ambulance arrived, the patient was alert, but still drowsy. He was admitted to the Accident and Emergency Department, Universiti Kebangsaan Malaysia Medical Centre.

The patient is an intravenous drug abuser. He was accidentally diagnosed to be HIV positive 1 month earlier in Hospital Kuala Lumpur. At that time, he was admitted to the hospital due to prolonged fever and productive cough. Acid-fast staining of the sputum smear was positive for *Mycobacterium tuberculosis*. He is currently on antituberculosis (TB) treatment (Isoniazid 250 mg/day, Rifampicin 450 mg/day, Pyrazinamide 125 mg/day, Ethambutol 100 mg/day and Pyridoxine 10 mg/day).

On physical examination, the patient is feverish (temperature; 38.3°C), blood pressure is 110/60 and his heart rate is 110/min. The left cervical lymph nodes are palpable and lung auscultation revealed crepitation at the upper zone of the right lung. There is no neck stiffness or papilloedema. Other systemic examination is unremarkable.

INVESTIGATIONS

On admission, full blood count shows mild anaemia (haemoglobin; 10.2 g/dl); white cell count, 3000/μl; platelets, 181×10³/μl and CD4 count of 36 cells/ml. The results for serum glucose, electrolytes, urea, nitrogen and creatine are normal. The results of cerebrospinal fluid (CSF) examination are as follows: opening pressure, 9.5 cm H₂O; lymphocytes, 5/mm³; protein, 153.7 mg/dl and glucose, 79 mg/dl. Gram staining, acid-fast staining and culture of the CSF did not reveal any microorganisms. Chest x-ray shows features of miliary TB with lobar consolidation and perihilar infiltrate (figure 1). An MRI scan of the brain revealed multiple, variable-sized ring-enhancing lesions with surrounding oedema in the cerebral hemispheres and brain stem (figure 2). The features are suggestive of multiple brain abscesses. The patient was treated empirically with intravenous ceftriaxone, gentamycin and metronidazole. Intravenous dexamethasone was also given to reduce cerebral oedema. After 4 days, the patient underwent another bout of seizures which lasted for a minute it was relieved upon receiving a 10 mg



Figure 1 Chest x-ray revealed tuberculosis of miliary pattern.

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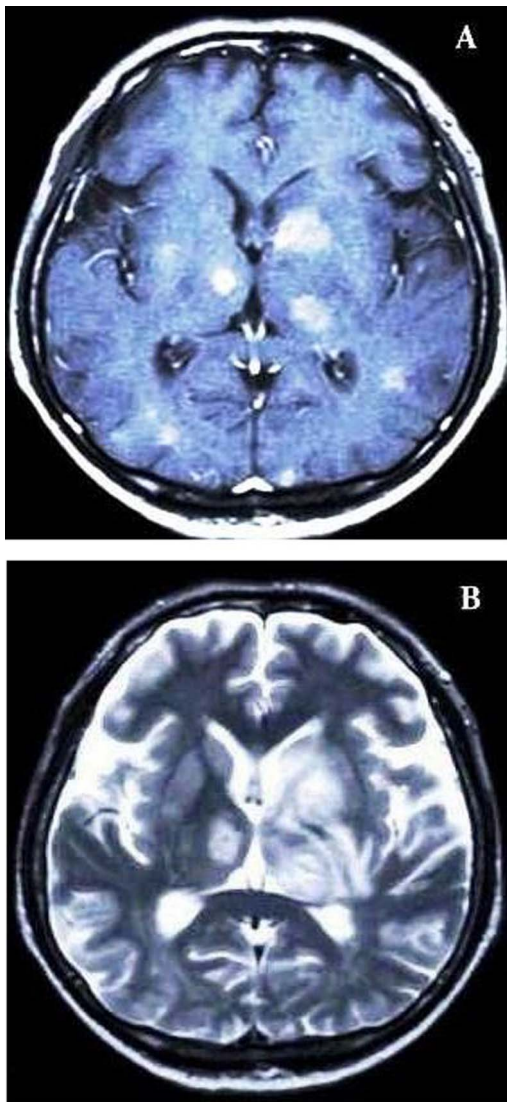


Figure 2 MRI scans of the brain show multiple variable-sized ring-enhancing lesions with oedema (A, B) suggest focal haemorrhage.

intravenous injection of diazepam. An infectious diseases physician was consulted, and he suggested serological study for toxoplasma antibodies. ELISA test shows positive antitoxoplasma IgG with a titre exceeding 300 IU/ml.

TREATMENT

The patient received trimethoprim/sulfamethoxazole 480–2400 mg/day with folinic acid supplement for 2 months. Another MRI scan of the brain performed after treatment was completed, which showed improvement of the multifocal granulomatous lesions, with decreased size and number of enhancing lesions and a reduction in the amount of surrounding oedema compared with the previous scan result (figure 3).

OUTCOME AND FOLLOW-UP

Two months later, a repeat brain MRI showed resolution of the cerebral lesions.

DISCUSSION

The incidence of toxoplasmosis in HIV patients in Malaysia is relatively high⁴ as toxoplasmosis is quite prevalent in this

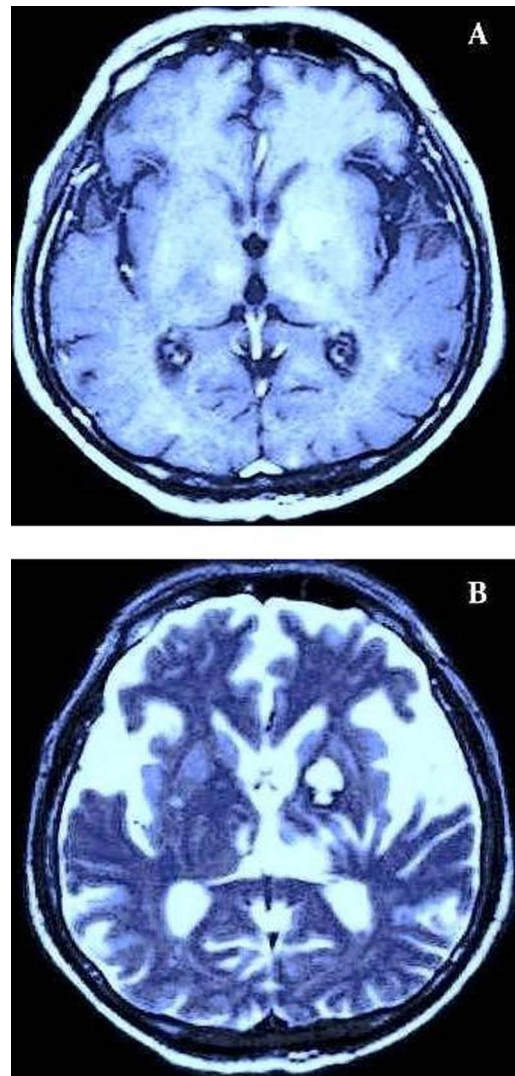


Figure 3 MRI scans of the brain show improvement of the brain after treatment for 2 months.

country.⁵ The patient has a complicated medical history, with the positive HIV status and TB infection. Many differential diagnoses were expected and had to be narrowed down to the most probable cause of his presentation. Most febrile conditions are readily diagnosed on the basis of presenting symptoms and a problem-focused physical examination. Occasionally, simple testing such as a complete blood count or urine culture is required to make a definitive diagnosis. The initial approach to the patient presentation should include a comprehensive history, physical examination and appropriate laboratory testing.

Diagnostic clues often are not readily apparent on physical examination in some cases; repeated examination may be essential. Careful attention to the skin, mucous membranes and lymphatic system, as well as abdominal palpation for masses or organomegaly, is important. The physician's choice of imaging should be guided by findings from a thorough history and physical examination.⁶ A suspect of primary central nervous system (CNS) lymphoma, progressive multifocal leukoencephalopathy, HIV encephalopathy and cytomegalovirus encephalitis were all in the list of probable causes in our patients.

The preliminary evaluation helps in the formulation of a differential diagnosis and guides further studies that are more invasive or expensive. The decision to obtain further diagnostic

studies should be based on abnormalities found in the initial laboratory work-up and not represent a haphazard use of costly or invasive modalities.

In this patient, brain MRI with contrast showed mass effect and ring enhancement. Mass effect is characterised by the presence of swelling, oedema and mass effect on the surrounding structures, whereas enhancement usually signifies the presence of inflammation. Toxoplasma encephalitis, primary CNS lymphoma and tuberculoma are the leading diagnosis in developing countries.⁷

In CNS lymphoma, MRI of the brain usually reveals multiple nodular masses with no central liquefaction or differential signal intensity. Although such lesions are usually associated with mild-to-moderate perilesional oedema, it demonstrates a characteristic depression along the outer margins, which is consistent with the 'notch sign'.⁸ Toxoplasmosis typically occurs as a brain lesion most commonly in AIDS, whereas malignant lymphoma commonly manifests as a brain neoplastic lesion. However, it is difficult to distinguish between the two, based on the brain image results alone.⁹ Diagnosis confirmation by early biopsy is recommended, yet in our case biopsy was considered to be a final option, reserved until other suspected causes are excluded.

Definitive diagnosis of tuberculous meningitis (TBM) depends upon the detection of the tubercle bacilli in the CSF. Every patient with TBM should preferably be evaluated by imaging with contrast enhanced CT either before or within the first 48 h of treatment. TBM would have been a rare outcome in this case, since it is usually more common in younger population.¹⁰ TBM is characterised by diffuse brain oedema and demyelination, which are usually extensive,¹¹ unlike the findings of the patient's brain MRI. Microscopically, TBM is characterised by microvascular necrosis with perivascular macrophage reaction and demyelination along with focal glial nodules in the white matter and occasional haemorrhagic lesions. Impaired consciousness, seizures, disseminated intravascular coagulation, and signs and symptoms of meningitis with or without spinal fluid changes characterise this syndrome.

Diagnosis of toxoplasmosis following HIV seroconversion is often difficult because symptoms and signs are usually non-specific. High fever is often the earliest sign; therefore, in a febrile HIV patient with neurological signs, prompt diagnostic workup is important. In this case, confirmation was obtained by the high titre IgG antitoxoplasma antibodies. Timely initiation of prophylaxis for opportunistic infections and their prompt recognition and treatment are the only economically viable options in Malaysia and other developing countries.⁷ The serological and immunological studies and the required imaging

(radiograph of the chest, ultrasonography and CT scan) if indicated can be performed in 1 day or after one outpatient visit. A cost-effective individualised approach is essential to the evaluation of these patients, and without a thoughtful and focused investigation, inappropriate tests might be performed.

Learning points

A high suspicion is important to diagnose cerebral toxoplasmosis when an HIV patient presents with fever and neurological signs, consequently toxoplasmosis should be treated accordingly as symptoms quickly seize after appropriate therapy was initiated.

Competing interests None.

Patient consent Obtained.

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