GRANULOMATOUS AMEBIC ENCEPHALITIS : REPORT OF TWO CASES WITH NEUROIMAGING FINDING.

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ABSTRACT

Granulomatous amebic encephalitis is quite rare but highly fatal. We reported two cases of this disease included clinical presentation, investigations and neuroimaging finding. The disease should be differentiated from other space occupying lesions or unusual cerebritis. Because the examination is nonspecific, the neuroimaging will encourage brain biopsy for definite diagnosis.

INTRODUCTION

Free-living amebas rarely cause diseases in human, however, they can directly invade the central nervous system especially in immunosuppressed patients. Entamoeba histolytica is the most common amebic infection of human and also in Thailand. By contrast, primary amebic meningoencephalitis (PAM) due to Naegleria fowleri and granulomatous amebic encephalitis (GAE) due to Acanthamoeba sp and leptomyxid amebas have rarely been reported. In Thailand, the incidence of GAE is quite rare. There are only two reports of granulomatous amebic encephalitis (Jariya et al., 1992,[1] Sangruchi et al, 1994).[2] Our report is the third report of two cases of GAE caused by Acanthamoeba sp. and neuroimaging seen in GAE has been described.

CASE REPORT

CASE 1.

A 43 year-old man with underlying disease of alcoholic cirrhosis came to Siriraj Hospital with history of prolonged fever for one month, hematemesis and confusion for one day. He also had first episode of generalized clonic-tonic seizure a month before admission, nevertheless, investigations for causes of seizure were unremarkable.

Physical examination on admission revealed body temperature of 38.5°C, respiratory rate of 24/min, pulse rate of 100/min, blood pressure of 170/100 mmHg. He was confused with partially response to command. He had moderately pale, mild jaundice, signs of chronic liver disease, no skin lesion and no superficial lymphadenopathy. Cardiovascular and respiratory system were normal. Neurological examination revealed no stiff neck, no papilledema, no motor weakness and no focal neurological deficit.

Investigations showed seronegative for HIV, hematocrit 19 percent, white blood cell count 11,400 cells/mm^3 with polymorphonuclear cell predominate, platelet count 229,000 cells/mm^3. Several hemoculture were negative, however, he

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still had intermittent fever. Treatment of upper gastrointestinal (GI) hemorrhage and hepatic encephalopathy was administered with improvement of GI hemorrhage. He still confused and developed right hemiparesis grade III/IV with bilateral Babinski sign, nine days after admission. The chest film showed bilateral peribronchial infiltration with bilateral pleural effusion. The CT brain revealed multiple hypodensity in gray matter, gray-white junction and periventricular region of cerebrum and cerebellum. Some lesions showed faint incomplete ring enhancement (Figure 1). Focal or adjacent parenchymal infarction or edema were also demonstrated. Lumbar puncture revealed an open pressure of 160 mmH_2O, white blood cell of 9 cells/mm^3 with lymphocytic predominate, red blood cell of 1820 cells/mm^3 , cerebrospinal fluid (CSF) sugar of 18 mg/dl (blood sugar 98 mg/dl), CSF protein of 1,229 mg/dl. Gram stain, acid fast bacilli (AFB) stain and india ink preparation were negative. Cefotaxime and ampicillin high dose were administered for empirical treatment of brain abscess, however, CSF culture showed no growth. He developed sepsis syndrome and death on the eleventh day after admission. Granulomatous amebic encephalitis was diagnosed postmortem (Figure 2).

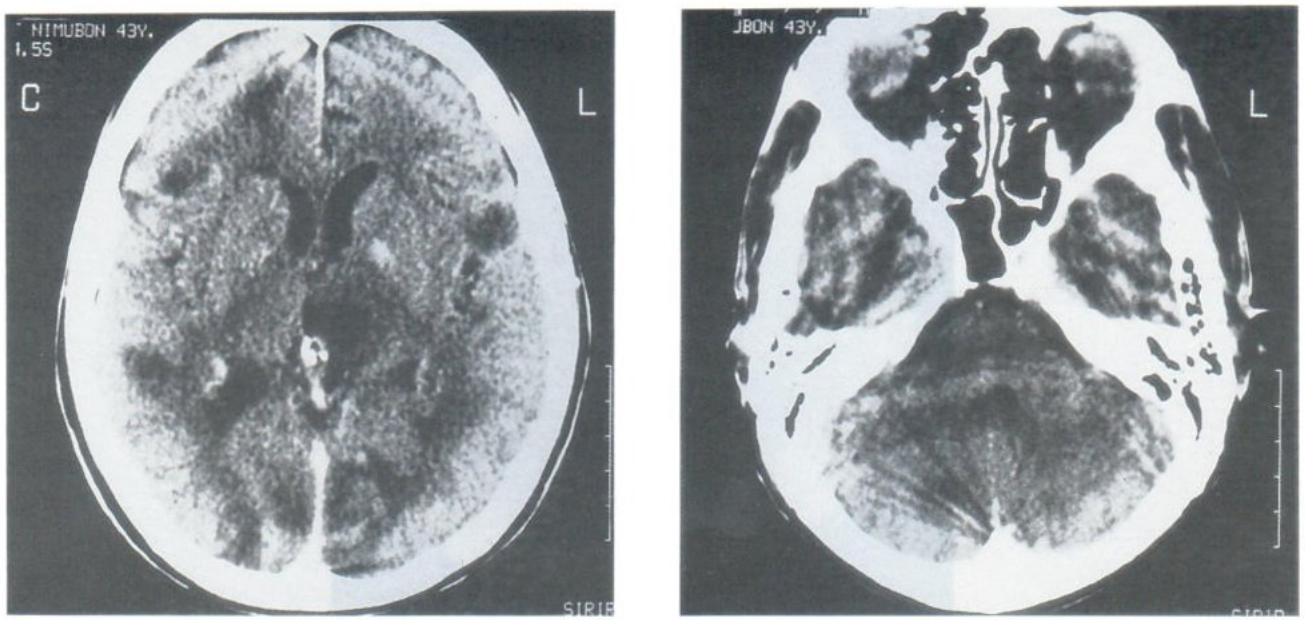
CASE 2

A 17 year-old woman with underlying disease of systemic lupus erythrematosus (SLE) presented with symptoms of fever and productive cough for six days, severe generalized dull aching headache with vomiting for two days, and generalized tonic-clonic seizure one day before admission. She had no previous history of seizure. She had regularly followed up at Siriraj Hospital since her diagnosis of SLE and her last medication was oral prednisolone 15 mg per day.

Physical examination on admission revealed body temperature of 39°C, respiratory rate of 28/min, pulse rate of 104/min, blood pressure of 120/80 mmHg, no skin lesion and no superficial lymphadenopathy. Chest examination revealed hyperpnea and medium crepitation of left lower lung field. The cardiovascular system and the abdomen were normal. Neurological examination showed neck stiffness and Kernig's sign was positive while other examinations were unremarkable.

Complete blood count showed hematocrit 28 percent, white blood cell count 6,030 cells/mm^3 with polymorphonuclear cell 63 percent, platelet count 164,000 cells/mm^3. Sputum examination for gram stain, AFB stain, and culture were all negative finding. Chest radiogram showed perihilar infiltration. Lumbar puncture revealed an open pressure of 380 mmH_2O, white blood cell of 56 cells/mm^3 with lymphocytic predominate, red blood cell of 13 cells/mm^3 , CSF sugar of 30 mg/dl, CSF protein of 125 mg/dl and negative finding of gram stain, AFB stain and india ink preparation. Hemoculture and CSF culture showed no growth. Treatment of tuberculous meningitis was given. CT brain was done three days later and showed multiple hypodensity areas with no enhancement in gray matter, gray-white junction, periventricular region in cerebrum and cerebellum (Figure 3). The MRI of brain revealed multiple enhancing nodules in the corresponding regions with some focal meningeal involvement (Figure 4A,B). There was some area of nonenhanced lesion compatible with infarction (Figure 5B).

The brain biopsy was done at left frontal lobe lesion for definite diagnosis. Pathological section demonstrated acute vasculitis with cerebritis without any organisms. Intravenous co-trimoxazole was administrated as empirical treatment of Nocardial brain abscess. She developed sepsis and expired sixteen days after admission. The autopsy was done and granulomatous amebic encephalitis was diagnosed later (Figure 5A, 6).



1A 1B

Fig. 1. Contrast enhanced CT of Case 1 (A,B) demonstrate multiple low density areas in supratentorial and infratentorial location with some faint enhancement.

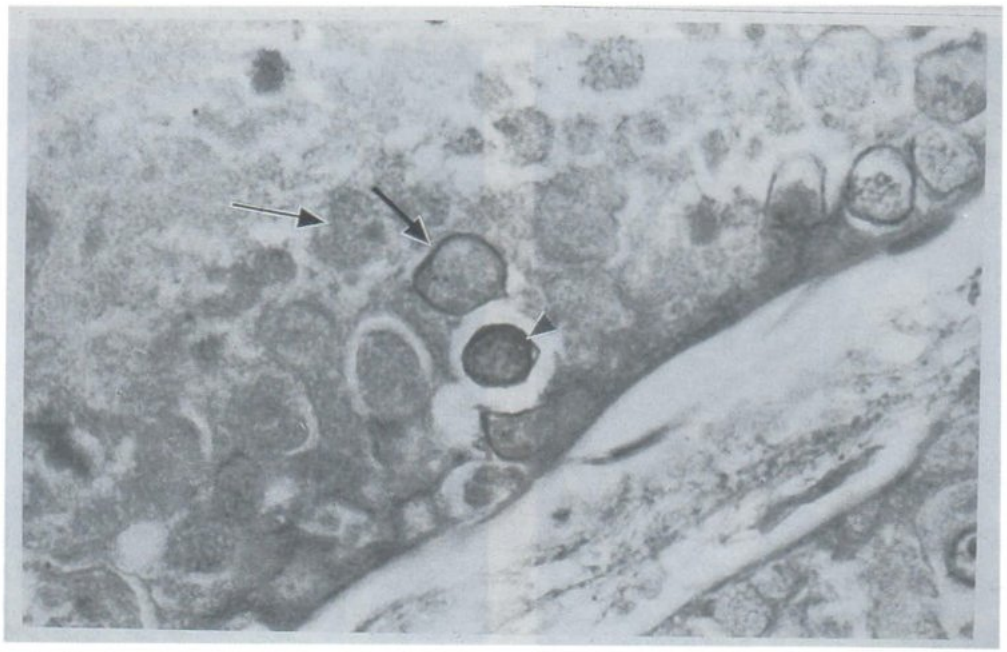


Fig. 2. Numerous trophozoites (→) and cysts (▶) were found around thrombosed vessel in brain autopsy tissue. (H&E 400X)

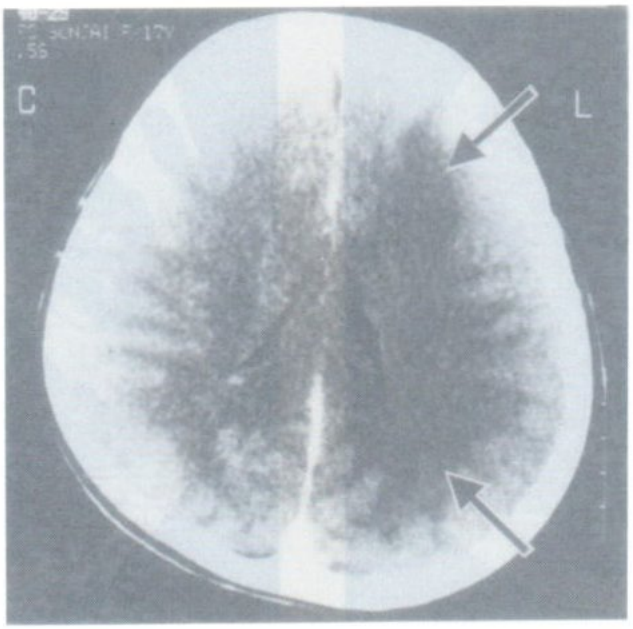
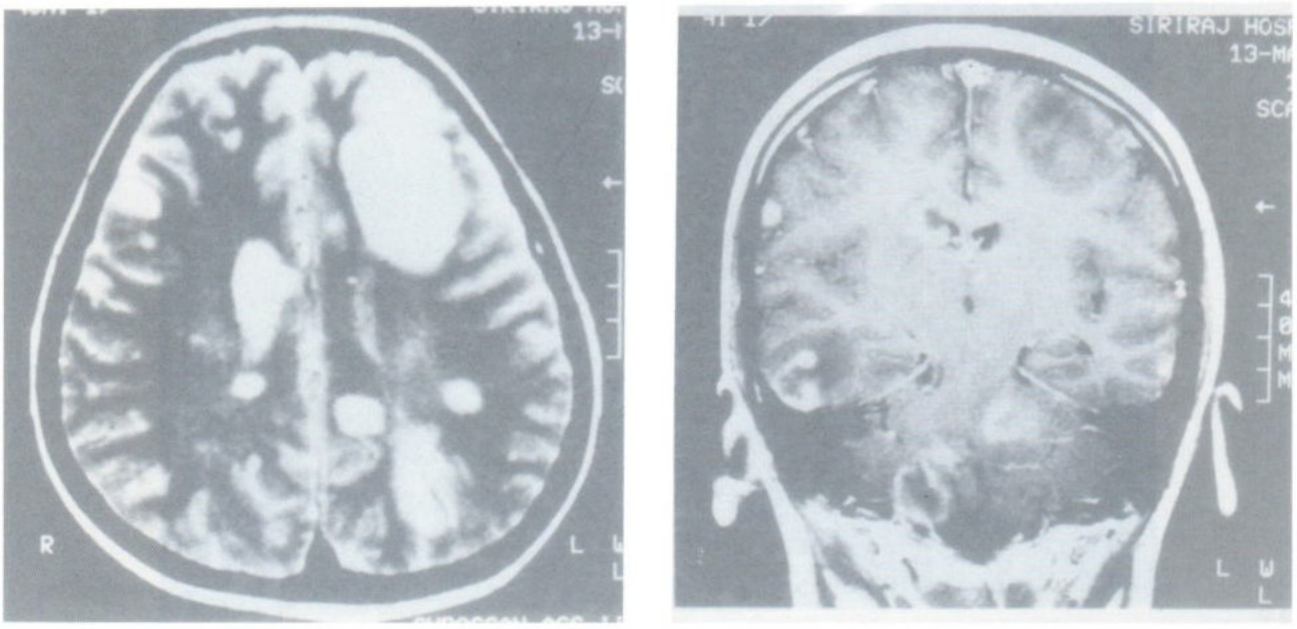
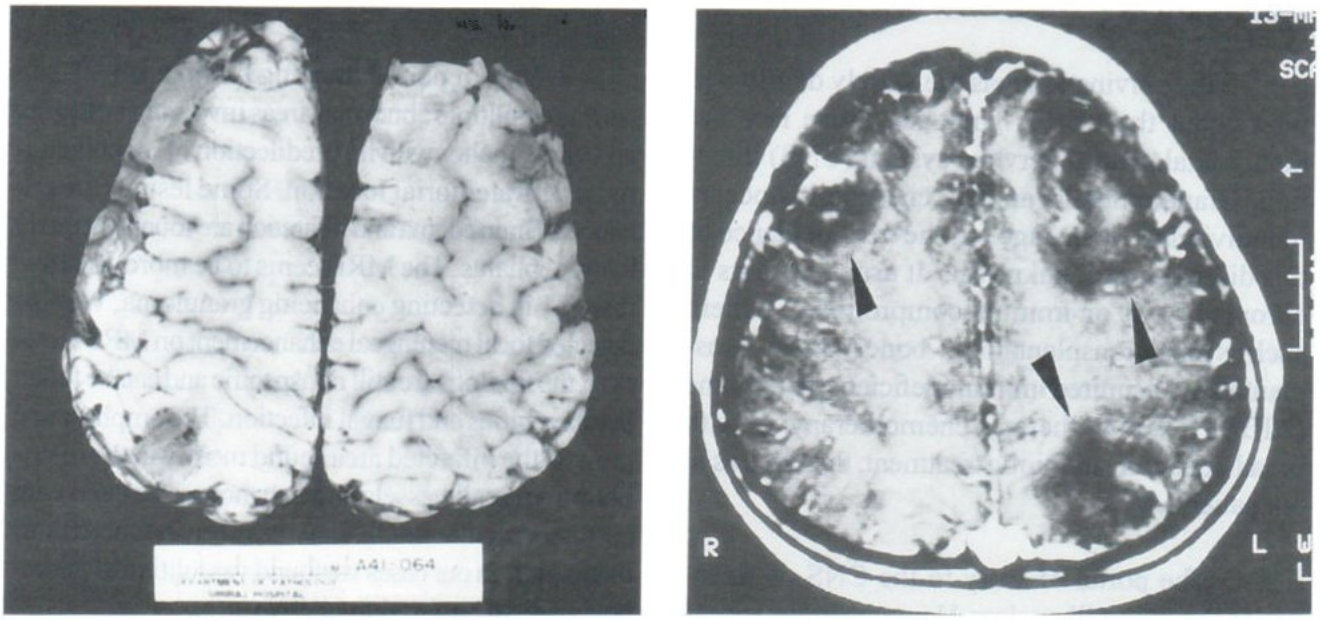


Fig. 3. Contrast enhanced CT of Case 2 reveals multiple areas of nonenhancing low density in cerebrum.



4A **4B**

Fig. 4. T_2wi (A) and Gd-T_1wi (B) of Case 2 show multiple high signal intensity with enhancing nodules.



5A 5B

Fig. 5. Multiple necrotic nodules focally involved meningeal covering (A). The areas corresponsed with infarction on MRI (B).

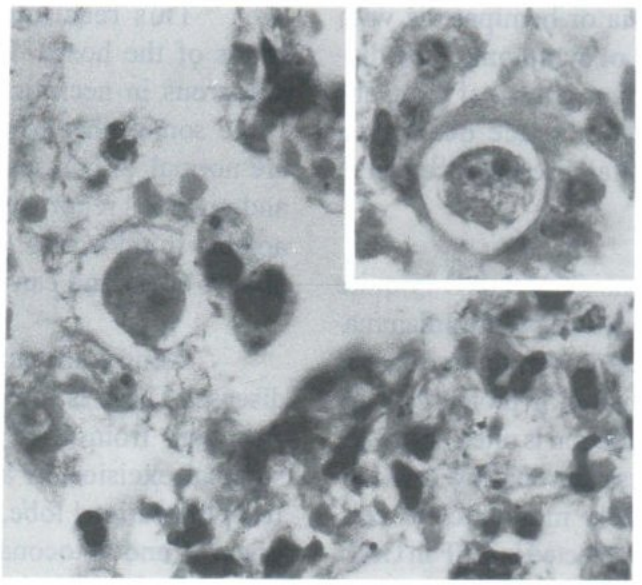


Fig. 6. A trophozoite in the lung and in a small granuloma in the brain parenchyma. (inset) (H&E 400X)

DISCUSSION

Free-living amebas are widely distributed throughout the world. They can cause rare but highly fatal central nervous system (CNS) infection. Granulomatous amebic encephalitis occurs in individuals of any age but the true incidence of this disease is still unknown.[3] It usually occurs in chronically ill or immunocompromised patient such as renal transplantation,[4] bone marrow transplantation,[5] acquired immunodeficiency syndrome (AIDS),[6,7] steroid therapy, chemotherapy, or with broad-spectrum antibiotic treatment, the same as in our patients.[8,9]

The portal of entry to the CNS of Acanthamoeba sp is still unclear. Hematogenous spread from the skin or lungs has been demonstrated,[10] therefore, it can directly invade the brain parenchyma. Both of our cases had foci in the lungs which seemed to be source of spreading. Clinical manifestations consist of altered mental status, fever, headache, convulsion, and focal neurological deficits such as aphasia or hemiparesis with subacute or gradual onset of symptoms. The disease may simulate the clinical course of brain abscess, brain tumor, or other space occupying lesions. Raised intracranial pressure can also occur.[11,12,13]

Antemortem diagnosis of GAE is quite difficult. Most patients show a nonspecific inflammatory response in the CSF. An opening pressure is usually elevated, as well as high CSF protein concentration. The glucose concentration is often normal or reduced. Leukocytes are present in only low or moderate numbers predominately mononuclear cell. Because amebas are rarely detected in CSF in GAE, specific diagnosis usually requires biopsy or autopsy specimens. Even then, the diagnosis is likely to be missed unless the pathologist is alerted in advance to consider this rare disease. However, serologic tests of Acanthamoeba may help to determine the diagnosis.[14]

Most reported imaging findings on CT and MRI are multiple abnormal areas involving both gray and white matter with no predilection of supratentorial or infratentorial location. Some lesions are enhanced. Brain edema and infarction are found but rarely hydrocephalus. The MRI seems to be more sensitive than CT in detecting enhancing granuloma. We also detected focal meningeal enhancement on MRI. However, the findings are still nonspecific and can be found in tuberculous and fungal infection. The emphasizing point is the infarcted area found mostly in the distribution of small vessels and may not asso-ciated with cortical vascular involvement as seen in tuberculous meningitis. In our cases we found vasculitis and thrombosis causing infarction.[5,15,16,17]

The pathological findings of GAE has been described.[2,12,13,18] Focal or extensive cerebral necrosis with wide range of granulomatous reaction were seen.

This reaction might indicate immune status of the hosts. Trophozoites and cysts are numerous in necrotic or granulomatous lesions while some other parts of the uninvolved brain are normal. A constant finding seen in our cases and previous reports is vasculitis with or without amebic trophozoites. Thrombosis and infarction always occur and can be detected by CT or MRI.

Almost all patients with GAE died of the disease. There is only one nonfatal case report. Recovery from GAE has been described using surgical excision of a large inflammatory mass from the parietal lobe, and following by amphotericin B and ketoconazole.[19] Amphotericin B or ketoconazole may be benefit in acanthameoba infection.

In summary, we reported two rare cases of GAE with clinical and neuroimaging findings. The disease should be differentiated from other space

occupying lesions or unusual cerebritis. Because the examination is nonspecific, the neuroimaging will encourage brain biopsy for definite diagnosis.

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