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Acute meningoencephalitis as initial presentation of human immunodeficiency virus infection: report of two cases

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Since the advent of pandemic of the human immunodeficiency virus infection, the possible pathogens responsible for acute meningoencephalitis have broadened. Human immunodeficiency virus itself can cause acute meningoencephalitis, and the immunocompromise associated with human immunodeficiency virus infection predisposes the infected patients to acute meningoencephalitis caused by a variety of other infectious or non-infectious etiologies. Here reported are 2 cases of acute meningoencephalitis with history of blood transfusion and travel to southeast Asia; both are positive for screening tests of human immunodeficiency virus infection. One of the pathogen causing central nervous system infection, *Mycobacterium tuberculosis*, was identified by polymerase chain reaction; the other left undiagnosed. It is known that patients of human immunodeficiency virus infection or acquired immunodeficiency syndrome can present with acute central nervous system infection. The need for routine screening of human immunodeficiency virus antibody is currently under debate; nevertheless, the possibility of human immunodeficiency virus infection has to be kept in mind in patients with acute meningoencephalitis.

Key words: Human immunodeficiency virus, meningoencephalitis

Acute meningoencephalitis (AME) is characterized by varying outcome and potential sequelae [1]. Partly due to its nonspecific clinical manifestations, AME can elude physicians' notice, leading to delay in studying cerebrospinal fluid (CSF) and instituting appropriate antimicrobial therapy. In clinical practice, even when patients present with typical features such as fever, headache, nuchal rigidity, disturbance of consciousness, and seizure, specific pathogens of AME can be identified in only some cases despite the use of conventional diagnostic methodologies.

Since the advent of human immunodeficiency virus (HIV) pandemic, the number of reported pathogens causing central nervous system (CNS) infections has continued to increase [2]. Previous studies have revealed that AME can be the only manifestation of primary HIV infection, and that itself HIV can cause CNS infection [3,4]. On the other hand, early HIV infection predisposes to contract AME of infectious, or non-infectious etiologies [5]. Nevertheless, AME is an infrequent primary presentation of HIV infection or AIDS. Here we report 2 HIV-infected Taiwanese presenting with AME. The aim of this report is to emphasize that the possibility of HIV infection has to be kept in mind in diagnosing and treating patients with AME.

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Case Report

Case 1

Case 1 was a 52-year-old married man who worked as a bus driver of a medical center and had 2 adult daughters. He was admitted following 3 days' duration of fever, sweating, and headache in late May 1998. He had no neck pain, photophobia, nausea, vomiting, or rash. In 1979, 9 years prior to this admission, he had undergone a simple closure for bleeding duodenal ulcer with transfusion of 2000 mL of whole blood and 1000 mL of packed red blood cell. He denied use of alcohol, tobacco, illegal drugs, or foreign travel.

On admission, the patient was alert; body temperature was 39.1°C, pulse rate 106 /min, respiratory rate 21/min, and blood pressure 154/80 mm Hg. The rest of the physical examination was unremarkable except for a linear operation scar was seen on his abdomen. Hematologic and biochemical tests were within normal ranges (Table 1). Chest film,

electrocardiography (EKG), and abdominal sonography were normal.

Empiric therapy with cefazolin and gentamicin was started. On the 3rd day of admission, the patient became drowsy and confused with infrequent myoclonic jerks. On physical examination he was lethargic with an elevated body temperature of 38.2°C, a Glasgow coma score of 8 to 9, no meningeal signs, and no focal neurologic findings. Magnetic resonance image of the brain showed normal leptomeninges and T2-weighted imaging showed high-intensity lesions on the left temporal region without enhancement (not shown). Lumbar puncture revealed a white cell count of 315 / mm^3 (94% lymphocytes), a CSF glucose of 57 mg/dL, and protein of 139 mg/dL (Table 1). Multiple cultures of blood, urine, and CSF were negative for fungi, *Mycobacterium tuberculosis*, or other bacteria. Serologic test for Japanese encephalitis was negative. Polymerase chain reaction (PCR) for herpes simplex virus was not performed. Screening HIV test by enzyme-linked immunosorbent assay (ELISA) was positive; followed with a confirmatory Western blot (New LAV BLOT, BLO-RAD, Paris, France) of HIV-1 infection (Fig. 1). The assays of CD4, CD8, and viral load were not performed.

His condition deteriorated rapidly with intractable vomiting and hiccups, and he died in status epilepticus 11 days after admission.

Table 1. Laboratory tests of patients with acute meningoencephalitis

Category	Case 1	Case 2
WBC (10^9/L)	4.8	8.1
Neutrophils (%)	54	65
Lymphocytes (%)	40	24
Hematocrit (%)	44	44
Platelet (10^9/L)	14	20
Creatinine (mg/dL)	1.4	1.0
AST (IU/L)	92	62
ALT (IU/L)	70	92
RPR	Negative	Negative
CSF		
RBC (/mm^3)	34	0
WBC (/mm^3)	315	44
Lymphocytes (%)	94	89
Protein (mg/dL)	139	140
Glucose (mg/dL)	57	45
Chloride (mEq/L)	121	ND
VDRL	Negative	Negative
India ink	Negative	Negative
Cryptococcal antigen	Negative	Negative

Abbreviations: WBC = white blood cell; AST= aspartate transaminase; ALT= alanine transaminase; RPR= rapid plasma reagent; CSF= cerebrospinal fluid; RBC = red blood cell; ND = no detection; VDRL= venereal disease research laboratory

Case 2

Case 2 was a 27-year-old married man who worked as an assistant at a family-run restaurant. He visited the emergency department in early September in 1997 with the complaint of fever and headache for 2 weeks. The patient had been in good health until 2 weeks prior to the visit, when he developed fever, coryza, productive coughing, sore throat, bilateral earache, and headache. Because of exacerbating headache and new onset of vomiting, eye pain, and vertigo, he was admitted on suspicion of meningitis. The patient had traveled to southeast Asia and had unprotected sex with a prostitute a few months before, but denied use of alcohol, tobacco, or illegal drugs.

On examination, his consciousness was clear, body temperature was 38.1°C, pulse rate 86 /min, respiratory rate 20 /min, and blood pressure 110/62 mm Hg. Examinations of skin, oral cavity, neck, and neurologic function were unremarkable. Laboratory tests showed a white cell counts of 8.1 x 10^9/L with 65% neutrophils and 24% lymphocytes (Table 1). Chest film and EKG were normal.

Nine hours after admission, the patient became irritable and developed a generalized seizure. Computed tomography (CT) of brain did not reveal any abnormality. Cerebrospinal fluid study revealed a white cell count of 44 /mm^3 with 89% lymphocytes, a glucose level of 45 mg/dL, and protein of 140 mg/dL (Table 1). Cultures of blood and CSF were negative for fungi and bacteria; and serologic test for Japanese encephalitis was negative. Polymerase chain reaction for *M. tuberculosis* was positive (not shown). Screening test for HIV and subsequent Western blot was positive (Fig. 1). Assays of CD4, CD8, and viral load were not performed. Rapid reversal of symptoms occurred following administration of antituberculous treatment without anti-HIV agents.

Discussion

Only a few cases of primary HIV infection presenting with AME have been reported [6-11], since Ho *et al* [3] and Carne *et al* [4] reported that AME is the only manifestation of primary HIV infection. The postulate of HIV causing AME is supported by the subsequent seroconversion and isolation of HIV from the CSF of patients. In this report, 2 patients with AME are positive for screening test of HIV, whether the HIV infection was primary or not remained unclear.

Immunocompromise caused by HIV infection makes the patient vulnerable to a wide variety of infectious diseases, including CNS infections [5]. Furthermore, the initial presentation in 10% to 20% of

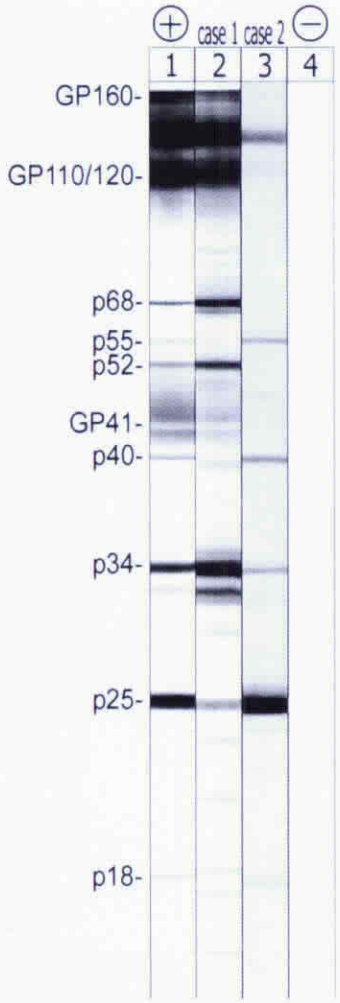

Fig. 1. Western blotting of patients with HIV-I infection. Both patients are positive for p18, p25, p40, and p55 of Gag, p34 and p68 of Pol, and gp110/120 and gp160 of Env, except the bandings of p52 of Pol and gp41 of Env present in case 1.

AIDS patients includes neurologic manifestations [6]. Accordingly, a substantial proportion of patients with AME need to be tested for HIV infection although selective criteria have not yet been established. As a consequence, underdiagnosis seems to be unavoidable if screening for HIV infection in patients with AME is not performed. In the first case of this report, the screening test for HIV infection was carried out since testing ruled out the presence of common pathogens causing AME, although none of the risk factors for HIV infection were noted except for a remote operation with blood transfusion 9 years prior to admission. In the second reported case, the screening test was partially attributed to the history of travel and prostitution in southeast Asia. When confronting with AME and searching for the definite causative agent, physicians should maintain a high index of suspicion for HIV infection in patients with AME; otherwise, the underlying HIV infection, which may be the real culprit, will go unnoticed if screening test is not performed.

There is a wide range of microorganisms causing AME as the initial presentation of HIV infection or AIDS, with the most common being cytomegalovirus [10], *Treponema* [11], *Cryptococcus* [12], and *Toxoplasma* [6]. However, *M. tuberculosis* as a cause of AME is rare. The second case of AME of this report is also the first reported case of tuberculous meningitis as the initial presentation of HIV infection. Polymerase chain reaction was used to identify the mycobacteria in CSF in this patient.

In summary, the possibility of HIV infection has to be kept in mind in patients with AME. Whether or not a screening test for HIV antibody in patients with AME should be routine is debatable.

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