

Opportunistic central nervous system infection in human immunodeficiency virus infected patients in Thammasat Hospital, Thailand

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Abstract

Recent therapeutic advances have altered the natural history of human immunodeficiency virus infection as well as the occurrence of opportunistic infections. Small proportion of human immunodeficiency virus infected patients can afford highly active antiretroviral therapy in Thailand. The aim of this study was to investigate the prevalence, characteristics and clinical manifestations and cerebrospinal fluid findings of opportunistic central nervous system infection in human immunodeficiency virus infected patients who were treated at Thammasat Hospital, Thailand. All medical records of human immunodeficiency virus infected patients with central nervous system infection treated at inpatient or outpatient clinic at Thammasat University Hospital from January 1998 to September 2002 were reviewed. One hundred and twenty six patients were studied. The opportunistic central nervous system infections of the patients in the study were cryptococcal meningitis (94 patients, 75%), unidentified intracranial mass lesion, suspected cerebritis (11 patients, 9%), tuberculous meningitis (9 patients, 7%), cerebral toxoplasmosis (8 patients, 6%), cryptococcal meningitis and cerebral toxoplasmosis (2 patients), bacterial meningitis (1 patient) and meningitis (unidentified organism) (1 patient). Mean age of the patients was 35 years old. None of them received highly active antiretroviral therapy. Most patients (96%) had CD4 cell count less than 200 cells/ μ L. Ninety- four patients (75%) had previous opportunistic infections. Headache and fever were the most common symptoms. Clinical manifestations and cerebrospinal fluid findings were similar to previous studies but the prevalence of AIDS-defining opportunistic central nervous system illness was different from Western countries.

INTRODUCTION

Human Immunodeficiency Virus (HIV)-infected patients are prevalent in clinical practice in Thailand. By October of 1999, 128,606 cases have been reported to the Division of Epidemiology, Thai Ministry of Public Health. From Thailand's surveillance program, 13,775-25,788 new acquired immunodeficiency syndrome (AIDS) were reported each year (from 1994-1999) showing substantial increase over the years.¹ Most of the AIDS patients were admitted due to opportunistic infections. Some of these (19-46% of admission) were due to central nervous system (CNS) infection.²⁻⁴

Recent therapeutic advances have altered the natural history of HIV infection as well as the occurrence of opportunistic infections. In Western countries, the most common AIDS-defining opportunistic CNS illness is HIV encephalopathy, cerebral toxoplasmosis, cytomegalovirus retinitis and primary CNS lymphoma.⁵ Small proportion

of HIV-infected patients can afford highly active antiretroviral therapy (HAART) in Thailand. So reported prevalence, characteristics and clinical manifestations of opportunistic CNS infection in HIV-infected patients may be different from Western countries. The aim of this study was to investigate the prevalence, characteristics and clinical manifestations and cerebrospinal fluid (CSF) findings of opportunistic CNS infection in HIV-infected patients who were treated at Thammasat Hospital.

METHODS

All medical records of the HIV-infected patients with CNS infection who were treated at outpatient clinic and inpatient at Thammasat University Hospital from January 1, 1998 to September 30, 2002 were retrospectively reviewed. Baseline personal characteristics, clinical manifestations, history of seizure, previous history of opportunistic infections, HAART, prophylaxis of

Pneumocystis carinii (PCP), total lymphocyte count and/or CD4 cell count, abnormal physical examinations such as papilledema, altered mentation and focal neurological deficit were collected.

Some HIV-infected patients with CNS infection did not have CD4 cell count measured. They were assumed to have CD4 cell counts greater than or equal to 200 cells/ μ L if their total lymphocyte counts were over $2.0 \times 10^9/L$.⁶

Diagnosis of cryptococcal meningitis was based on detection of *Cryptococcus neoformans* by India ink preparation or the detection of cryptococcal antigen in CSF. Diagnosis of tuberculous meningitis was based on CSF profile, clinical course and response to antituberculosis drugs. Diagnosis of bacterial meningitis was based on clinical, CSF profile and bacterial identification from CSF culture. Diagnosis of cerebral toxoplasmosis was based on demonstration of intracranial mass lesions from computed tomography (CT) brain scan and good response to empiric treatment of cerebral toxoplasmosis.

RESULTS

One hundred and twenty six HIV-infected patients with CNS infection were identified in the study. There were 85 males and 41 females. Mean age was 35 years (range from 18-63). None of the patients received HAART. Most (96%, 121 out of 126 patients) had CD4 cell count less than 200 cells/ μ L. Ninety- four patients (75%) had previous opportunistic infections and 57 patients (45%) had trimetoprim-sulfamethoxazole for PCP prophylaxis.

Cryptococcal meningitis was the most common opportunistic CNS infection (75%, 94 out of 126 patients). Table 1 lists the etiology of the CNS

infection among these patients. Table 2 lists the clinical and investigatory features of the patients with cryptococcal meningitis, tuberculous meningitis and cerebral toxoplasmosis. Table 3 lists the CSF findings of these patients.

The patient with bacterial meningitis (Table 1) presented with fever and headache for 3-6 days. He had neck stiffness on physical examination. He had CD4 count of <200 cells/ μ L and abnormal CSF findings which were high opening CSF pressure (58 cm H₂O), predominant polymorphonuclear pleocytosis (70%), low CSF/blood sugar ratio (0.25) and high CSF protein (140 mg/dl).

DISCUSSION

Our study showed that cryptococcal meningitis was the most common opportunistic CNS infection in HIV-infected patients, accounting for 75% of the patients. Tuberculous meningitis and cerebral toxoplasmosis were diagnosed in 7% and 6% of these patient, respectively. Two patients had co-existing cryptococcal meningitis and toxoplasmosis.

None of our patients were treated with HAART and most of them had CD4 cell count less than 200 cells/ μ L. This might explain the difference in prevalence of AIDS-defining CNS opportunistic illness from Western countries. On the other hand, it probably also reflected the microorganism ecology of this country, as cryptococcal meningitis was an important cause of meningitis even before HIV became a common illness in Thailand.

Chhin S *et al* studied etiology of meningitis in HIV-infected patients in Phnom Penh, Cambodia. Cryptococcus was the most commonly identified pathogen (83%), followed by mycobacteria (8%).⁷ Very advanced HIV disease, with CD4 cell counts below 10 cells/mm³ was common in HIV-infected

Table 1: Etiology of the CNS infection in the HIV patients (N=126)

	No. of patients (percent)
Cryptococcal meningitis	94 (75)
Tuberculous meningitis	9 (7)
Unidentified intracranial mass lesion suspected cerebritis	11 (9)
Cerebral toxoplasmosis	8 (6)
Cryptococcal meningitis and cerebral toxoplasmosis	2 (2)
Bacterial meningitis	1 (1)
Unidentified organism (meningitis)	1 (1)
Total	126

Table 2: The clinical and investigatory findings of HIV patients with cryptococcal meningitis, tuberculous meningitis, and cerebral toxoplasmosis

	Cryptococcal meningitis No. of patients (%)	Tuberculous meningitis No. of patients (%)	Cerebral toxoplasmosis No. of patients (%)
Total number of patients	94	9	10
Sex			
Female	27 (29)	4 (45)	6 (60)
Male	67 (71)	5 (55)	4 (40)
CD4 count			
< 200 cells/ μ L	91 (97)	9 (100)	10 (100)
\geq 200 cells/ μ L	3 (3)		
History PCP* prophylaxis	47 (50)	3 (33)	4 (40)
Duration of illness			
<3 days	17 (18)	1 (11)	1 (10)
3-6 days	42 (45)	5 (56)	4 (40)
\geq 7 days	35 (37)	3 (33)	5 (50)
Symptoms			
Headache	86 (91)	7 (78)	6 (60)
Fever	51 (54)	3 (33)	1 (10)
Altered mentation	16 (17)	3 (33)	6 (60)
Seizure	9 (3)	0	1 (10)
Behavioral change	4 (4)	1 (11)	1 (10)
Limb weakness	0	0	3 (30)
Neurological signs			
Neck stiffness	56 (60)	0	6 (60)
Limitation of ocular movement	8 (9)	0	0
Papilledema	7 (7)	7 (77)	1 (10)
Abnormal pupils	3 (3)	1 (11)	0
Facial palsy	3 (3)	0	2 (20)
Babinski's sign	1 (1)	0	1 (10)
Limb weakness	0	0	3 (30)

*PCP: *Pneumocystis carinii*

patients who admitted to a public hospital in Phnom Penh, Cambodia (43.2%).⁸

Headache and fever were the most common symptoms. Altered mentation and limb weakness were found more common in cerebral toxoplasmosis than meningitis. Clinical manifestations and CSF findings of opportunistic CNS infections were quite similar to previous studies.⁹⁻¹²

In conclusion, in our study, cryptococcal meningitis was the most common CNS infection

in HIV-infected patients and other common causes were tuberculous meningitis and cerebral toxoplasmosis. Clinical features and CSF findings showed no difference from previous studies.

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Table 3 Cerebrospinal fluid findings of HIV patients with cryptococcal meningitis, tuberculous meningitis, and cerebral toxoplasmosis

	Cryptococcal meningitis	Tuberculous meningitis	Cerebral toxoplasmosis
Open pressure (cm H ₂ O)	34 (8-66)	28(13-45)	22 (15-25)
WBC count (/mm ³)	82 (1-540)	682 (3-3000)	49 (3-110)
Polymorph (%)	7.9 (0-58%)	35 (2-88%)	10 (0-18%)
Mononuclear (%)	92 (53-100%)	68 (12-100%)	90 (87-100%)
CSF/blood sugar ratio	0.36 (0.08-0.67)	0.31(0.11-0.52)	0.34 (0.3-0.4)
CSF protein (mg/dl)	88 (18-693)	102 (93-470)	77 (46-101)
Positive India ink	80 (85%)		

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