CLINICAL MANIFESTATIONS AND OUTCOME OF PATIENTS WITH SEVERE EOSINOPHILIC MENINGOENCEPHALITIS PRESUMABLY CAUSED BY *ANGIOSTRONGYLUS CANTONENSIS*

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Abstract. The clinical manifestations and outcome of patients with severe eosinophilic meningoencephalitis has never been reported. We reported 11 comatose patients with eosinophilic meningoencephalitis. Most of them presented with subacute to chronic headache and fever, followed by acute coma. Cerebrospinal fluid abnormalities were similar to alert patients with eosinophilic meningitis. None of them had received antihelmintic drug and seven patients were treated with corticosteroids. Ten patients died and one patient is still in a coma. Corticosteroids seem to be ineffective in severe eosinophilic meningitis.

INTRODUCTION

Angiostrongylus cantonensis is the most common cause of eosinophilic meningitis. Acute severe headache with nonfocal neurological findings, with the exception of occasional involvement of the cranial nerve, are the most common presenting symptoms (Punyagupta *et al*, 1975; Yii, 1976). There is no specific treatment. Thiabendazole and mebendazole had some effects in infected rat. However, there have been only a few reports of antihelmintic therapy in humans and those with thiabendazole which was ineffective (Kliks *et al*, 1982). A 2-week course of prednisolone is beneficial in relieving headache (Chotmongkol *et al*, 2000).

Patients with severe eosinophilic meningoencephalitis which presented with coma rarely occurred (< 1 %) (Punyagupta *et al*, 1975; Yii, 1976). To our knowledge, the detail of clinical manifestations and outcome has never been reported. We herein reported 11 comatose patients with eosinophilic meningoencephalitis.

PATIENTS AND METHODS

Study population

Retrospective study from chart-record forms was performed. Adult comatose patients (aged ≥15 years) who had eosinophilic meningitis and who were admitted to the Department of Medicine, Srinagarind Hospital (Khon Kaen, Thailand) were studied. The diagnosis of eosinophilic meningitis was based on findings of ≥10% eosinophils in the CSF, with negative results of Gram, acid-fast, and India ink staining, cryptococcal antigen testing, and culture. Data were analyzed by descriptive statistics.

RESULTS

From 1986 through 2000, there were 11 comatose patients with eosinophilic meningitis. The clinical and laboratory features of the patients are shown in Table 1. All of them were healthy before this illness and presented in the coma on admission. Ten patients had eaten raw pila snails and 1 patient had eaten raw yellow tree monitor (*Varanus bengalensis*) before the illness developed. Prior to admission, most of them had subacute to chronic headache, followed by acute severe encephalitis. Of the 2 patients who had hemiparesis, the symptom developed about 1 week after admission. CT scan of the brain was performed in 8 patients which demonstrated normal findings in 7 patients, including 2 patients with hemiparesis,

Table 1
Clinical and laboratory features of the study patients.

Feature	
No. of patients	11
Age (year)	45.3 (30-61)
Sex, male	8
Incubation (day)	13.2 (1-30)
Signs or symptoms	
Headache	9
Duration (day)	18.2 (5-30)
Coma	
Duration (day)	2.3 (1-4)
Fever (T $\geq$ 38.0ºC)	7
Duration (day)	8.3 (1-21)
Stiff neck	10
Hemiparesis	2
6^{th} unilateral CNP	1
7^{th} unilateral CNP	1
Seizure (focal)	1
Blood eosinophilia ($\geq$ 700 cell/mm^3)	7
CSF abnormalities	
High opening pressure ($\geq$ 300 mm H_2O)	3
WBC/mm^3	626.3 (50-1,500)
Eosinophilia (%)	44.5 (16-68)
Protein content, mg/dl	134.1 (61-224)
Glucose ratio, CSF/blood (%)	36.9 (18-43)

Note: Data are no. of subjects or mean (range). T = temperature; CNP = cranial nerve palsy.

Table 2
Treatment with corticosteroid and outcome of seven patients with severe eosinophilic meningoencephalitis.

Case no.	Treatment modality	Outcome
1	iv dexamethasone 5 mg every 6 hours for 7 days, then iv dexamethasone 5 mg every 8 hours for 3 days, then iv dexamethasone 5 mg every 12 hours for 5 days	Death
2	iv dexamethasone 5 mg every 6 hours for 5 days, then oral prednisolone 60 mg/d for 9 days	Death
3	oral prednisolone 60 mg/d for 14 days	Death
4	iv dexamethasone 5 mg every 6 hours for 2 days	Death
5	iv dexamethasone 5 mg every 12 hours for 3 days, then iv dexamethasone 5 mg every 6 hours for 5 days	Death
6	oral prednisolone 60 mg/d for 7 days	Death
7	iv dexamethasone 5 mg every 6 hours for 7 days	Still coma

and diffuse brain edema in one patient. None of them had received antihelmintic drug. Seven patients were treated with corticosteroids after admission, as shown in Table 2.

During treatment, the coma state did not improve in all patients. Hospital-acquired pneumonia developed in 4 patients, 2 of them received corticosteroids. Finally, ten patients died. Autopsy was performed in only 1 case; parasite was found in blocks of brain tissue. For the patient who survived, he was still in a coma.

DISCUSSION

Infection of human by third-stage larvae of *A. cantonensis* commonly occurs by ingestion of raw, infected snails. The yellow tree monitor can be infected with this larvae by the snail eating habit and there was a high percentage of positive findings of infected yellow tree monitors as a natural paratenic host (Radomyos *et al*, 1994). Thus, ingestion of raw yellow tree monitors especially its liver can cause eosinophilic meningitis, as in our patient. When third-stage larvae are ingested, they penetrate the blood vessels in the intestinal tract and are carried to the meninges, where they soon die. Little is known about the effects of this parasite on the central nervous system, since most patients recover uneventfully. The reason for differences in disease presentation that most patients had good clinical outcome while certain patients developed coma state are not exactly known. Pathological changes that found in autopsy reports demonstrated that there was infiltration of the meninges and around intracerebral vessels by varying proportions of lymphocytes, plasma cells and eosinophils. Numerous tracks and microcavities were found in the brain and perhaps in the spinal cord, and in age, with older tracks containing debris and gitter cells, newer tracks showing disruption of brain tissue, with or without hemorrhage. Numerous 4^{th} and 5^{th} stage *Angiostrongylus* larvae, alive and dead, were found in the meninges, brain tissue and spinal cord, sometimes in blood vessels or perivascular spaces, with a granulomatous response to dead larvae. There was also vascular reaction of nonspecific character leading to thrombosis and rupture of vessels and arteritis leading to aneurysmal formation. A small abscess containing parasitic remnants, foreign-body giant cells, eosinophils and neutrophils was noted. The rest of the brain showed diffuse degeneration, predominantly in white matter (Tangchai *et al*, 1967; Sonakul, 1978; Koo *et al*, 1988). From these findings, the pathologic mechanisms should be from ingestion of large numbers of larvae, directed invasion of motile worms, inflammatory responses to foreign bodies and possible toxicity of worm excretory products.

In our patients, although serological testing was not available in our hospital, *A. cantonensis* was most likely the causative agent of eosinophilic meningitis, because all of them had a history of ingestion of snails or yellow tree monitor before their illness. The CSF abnormalities in comatose patients were similar to patients with eosinophilic meningitis who presented with headache and normal consciousness (Chotmongkol *et al*, 2000). Our data demonstrated that coma could occurr in severe eosinophilic meningoencephalitis, resembling viral encephalitis or other infective organisms that produced encephalitis. The important point for differentiation from each other depends on epidemiology, eating habits and accuracy of the differentiation of leukocytes in CSF. Our data also demonstrated that the prognosis of this setting was usually fatal and corticosteroids seem to be ineffective for treatment of comatose patients with eosinophilic meningoencephalitis.

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