STUDY OF EOSINOPHILIC MENINGITIS IN HO CHI MINH CITY, VIETNAM

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Abstract. This hospital-based study aimed to describe the predominant clinical manifestations and epidemiologic details of cases with eosinophilic meningitis at the Hospital for Tropical Diseases in HCMC during January 2002 to January 2006. Of the 56 cases collected during this time, 49 (87.5%) were positive for IgG of *Angiostrongylus cantonensis*. The majority of cases occurred in the 15-50 age group, which accounting for 73% of the total cases. Males were affected three times more frequently than females. The occupation distribution showed that 34% were farmers and 36% were laborers. Patients came from different provinces in the south of Vietnam, including 54% from Mekong Delta. Those who had previously eaten raw snails accounted for 46% of cases. The incidence was notably high (75%) from September to March. The incubation period ranged from 1-43 days, with an average of 17 days. The predominant clinical manifestations were headache (91%) and fever (89%). Meningeal signs were detected in only 44% of cases. Cranial nerve palsies were detected in 45% of cases. Neurological disorders were found more often in cases of late admission. Eosinophilia was observed in 92% of cases. Parasitic meningitis, especially *Angiostrongylus* meningitis, is emerging in Vietnam. Early diagnosis was difficult due to the lack of meningeal signs. Immunoblot and IgG subclass antibodies should be used for screening that is more sensitive and more specific to confirm human cases.

INTRODUCTION

Since *Angiostrongylus cantonensis* was initially discovered by Chen from the pulmonary artery of the brown rats in Guangzhou in 1935, many cases of *Angiostrongylus* meningitis have been reported in the world (Liang, 1986). Other pathogens, such as *Strongyloides*, *Cysticercosis*, and *Toxocara*, sometimes caused meningitis. *Gnathostoma spinegerum* has also been reported, mainly in Southeast Asia, related to raw food. In Vietnam, eosinophilic meningitis was first reported in humans before the 1970s.

During the recent years, the number of cases of eosinophilic meningitis has increased in the Hospital for Tropical Diseases, Ho Chi Minh City. They often had been transferred from a community or local medical center. In the cases of late diagnosis, serious complications and some neurological sequella were experienced for several years afterwards. The difficulty in diagnosing these cases was due to the unremarkable clinical symptoms, the lack of epidemiological awareness, and the unavailability of serological tests. This study aimed to define the epidemiological factors and risk habits related to exposure, the main clinical signs, and the serological patterns of cases with eosinophilic meningitis in the south of Vietnam.

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MATERIALS AND METHODS

Fifty-six in-patient cases were admitted from January 2002 to January 2006 with fever, headache, eosinophils in CSF >10% white cell count (or CSF eosinophils >10 cell/mm3), and a positive ELISA test for one of the following pathogen: *A. cantonensis, G. spinigerum, T. canis* or *C. cellulosae*. Among them, 42 were men, age range from 2-71 years (average age was 29.4 ± 16.2). For every case, information about exposure or risk behavior, the incubation time, epidemiologic details, and clinical symptoms and signs were recorded. Serologic test were done to detect antibody to 4 parasites as above at the Hospital for Tropical Diseases (*G. spinigerum, T. canis*, or *C. cellulosae*) and at the School of Medicine, Ho Chi Minh City (*A. cantonensis*). An MRI was performed in cases with local neurological signs.

RESULTS

Epidemiological factors

Among the 56 cases, 74% were farmers or laborers. The ratio between male and female gender was 3/1. Seventy-three percent of the cases ranged in age from 15-50 years; especially among this age group, the male/female ratio was about 5/1 (34/7). Forty-six percent of cases (26 cases) had previously eaten raw snails, and 17% cases (9 cases) had used raw fish. However, among the cases from An Giang, 84% (16/19) had histories of eating raw snails. The incubation period ranged from 1-43 days (17 ± 12.5 days).

The number of cases increased sharply after September, reaching a peak in November, and decreasing dramatically thereafter until January, right before the end of annual rainy seasons and flooding time in the Mekong Delta river region. Seventy-five percent of the cases were detected during September to March.

Clinical presentations

Mild to severe headache and mild fever were the most commonly symptoms (91% and 89%). Nausea or vomiting was founded in 54% of cases. Meningeal (Kernig's or Brudzinski's) signs were seen only in 46%. In cases with late admission, there were focal neurologic signs (45%): with Bells' palsy (16%), and with diplopia or eyeball abduction disorder (29%). Paraplegia or quadriplegia was seen in 7% of cases and hemiplegia in 5%. Local or general paresthesia (scorching or burning sensation) and/or local muscle pain was reported in 13% and 14% of cases, respectively. Macular or papular rashes made fugitive appearances in 9% of cases. Abnormal neurological presentations, with focal lesion seen in cerebral or spinal cord (13/34 cases, 38%), were seen in cases of late admission.

Fig 1- Locations of study sites.

Laboratory test

Ninety-three percent of cases had eosinophilia and 64% of cases had moderate to high eosinophil counts (> 1,500 cell/mm3) in their blood. The CSF showed mild increases of protein and eosinophilia, and mildly increased CSF pressure. The IgG antibody to *A. cantonensis* was detected in 49/56 cases (87.5%). The IgG antibody to *G. spinigerum* was detected in 14 cases (25%). Of these latter cases, 11/14 tested positive for the IgG antibody for both *Angiostrongylus* and *Gnathostoma*. The test for the IgG antibody to *A. cantonensis* and *G. spinigerum* in the cerebrospinal fluid were done in 27 cases; of which, 16/27 cases (60%) tested positive for *A. cantonensis* and 5/27 cases (18%) for *G. spinigerum*.

DISCUSSION

Parasitic meningitis is more common in tropical areas, such as the Pacific and Southeast Asia regions. Some pathogens cause meningitis during their migration inside their accidental hosts, such as *Gnathostoma* and *Toxocara*. Cysticercosis more often causes intracerebral-specific lesions with special changes in magnetic resonance. *A. cantonensis* was the leading causes of meningitis worldwide and in Southeast Asia. It is necessary for *Angiostrongylus* to stay in the brain before subsequently migrating to the lung and completing their next cycle in other hosts. Eggs from infected rats infected snails

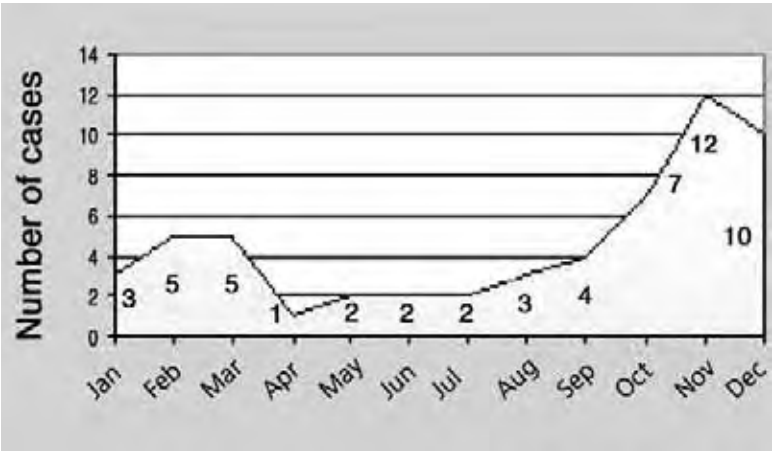

Fig 2- Annual trend of cases.

and other mollusk intermediate hosts. Their larvae are transmitted to humans as accidental hosts to continue their life cycle. *A. cantonensis* causes meningitis with a predominance of eosinophils, tortuous tracts of various sizes in the brain and spinal cord surrounded by an inflammatory reaction and degenerating neuron, and granulomatous response to the dead parasite and the non-specific vascular reactions including, thrombosis, rupture of vessel, arteritis, and aneurysm formation (Nye *et al*, 1970). In our hospital, the disease was sporadic during the time of study, but increased precipitously in 2005.

In this study, most of the cases were among the 15-50 age group (73%), male (70%), and did manual work (74%). Half of them had eaten raw snails, and 21% had drunk water from rivers. This subpopulation was likely to have leisure time sharing suppers with raw or improperly cooked snails and drink (Châu *et al*, 2003). The cultural background and eating habits have been known as causative for the disease among different populations and geographic areas (Sato and Otsuru, 1983).

The number of case was especially high in An Giang and Dong Thap, along the Mekong Delta River and on the Cambodia border, but not in other provinces downstream of the Mekong River. We did not have any investigation to determine whether or not there was an existing endemic of disease in rats or other animals in these two provinces.

An outbreak, reported in Wenchou City, China, also appeared during October to November in 1997 that was related to *Angiostrongylus* and *Ampullaris gigas* snails (Xue *et al*, 2000). Another study on *Gnathostoma* in Ho Chi Minh City reported an increased rate and level of infection in eels during the rainy season (Xuan and Rojkittigul, 2000). In this study, the number of cases increased from September, one month after the rains. It is likely that rain and flood changed the environment suitably for snails and fish. These environmental factors enabled the opportunity for humans to be exposure and infected, thus explaining the increased cases in man in rainy season.

Meningeal signs were only found in half of the cases, so that eosinophilia and headache were the only modest clues for investigating the cerebrospinal fluid. The IgG antibody to *A. cantonensis* was founded in 87.5% of cases, compared with *G. spinigerum* (25% of cases). The IgG antibody to *A. cantonensis* in the CSF was also predominant, as well as predominant in the blood, suggesting that *Angiostrongylus* was the main pathogen in this study.

in conclusion, parasitic meningitis, especially *Angiostrongylus* meningitis, is emerging in Vietnam. Early diagnosis should be undertaken, based on the presence of headache, epidemiological details (raw snail consuming, local cases), and eosinophilia. The infection statuses in animals need to be investigated further

in the future. Immunoblot and IgG subclass antibodies to parasite in blood and cerebrospinal fluid should be used for more sensitive screening and more specific confirmation in human cases.

REFERENCES

Châu TT, Thwaites GE, Chuong LV, *et al*. Headache and confusion: the dangers of a raw snail supper. *Lancet* 2003;361:1866.

Liang H. A summary of the epidemiology of *Angiostrongylus cantonensis*. *Chin J Epidemiol* 1986;7:61-3.

Nye S, Hill C Tangchai P, *et al*. Lesions of the brain in eosinophilic meningitis. *Arch Pathol* 1970;89: 9-19.

Sato Y, Otsuru M. Studies on eosinophilic meningitis and meningoencephalitis caused by *Angiostrongylus cantonensis* in Japan. *Southeast Asian J Trop Med Public Health* 1983;14:515-24.

Xuan LT, Rojkittigul. A survey of infective larvae of *Gnathosthoma* in eels sold in HCM. *Southeast Asian J Trop Med Public Health* 2000;31:133-7.

Xue DY, Ruan YZ, Lin BC *et al*. Epidemiological investigation on an outbreak of *angiostrongyliasis cantonensis* in Wenzhou. *Zhongguo Ji Sheng Chong Xue Yu Ji Sheng Chong Bing Za Zhi* 2000;18:176-8. (in Chinese)