EOSINOPHILIC MENINGITIS

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Eosinophilic meningitis is defined by the presence of 10 or more eosinophils/ μL in the CSF or eosinophilia of at least 10% of the total CSF leukocyte count. Invasion of the central nervous system by helminthic parasites is the most common cause, but other infections as well as several noninfectious etiologies have also been associated.

Noninfectious Agents

Malignancies, Hodgkin's disease, non-Hodgkin's lymphoma, and eosinophilic leukemia have been associated with eosinophilic meningitis when there is widespread meningeal involvement. Medications, ciprofloxacin, ibuprofen, intraventricular vancomycin, gentamicin, iophendylate dye used in myelography, have also been associated with eosinophilic meningitis. Patients with ventriculo-peritoneal shunts can develop CSF eosinophilia due to an allergic reaction to the shunt material. Sarcoidosis neurologic pathology may include sarcoidosis. Idiopathic hypereosinophilic syndrome has no know etiology.

Fungi

Half of patients with *Coccidioides immitis* disseminated disease present with eosinophilic meningitis. Association with cryptococcosis is much less common.

Bacteria, Rickettsieae, And Viruses

Eosinophilic meningitis has been reported in patients with neurosyphilis and tuberculous meningitis, Rocky Mountain spotted fever, viral meningitis due to acute coxsackie B4 virus or chronic lymphocytic choriomeningitis virus.

Parasites

The nematode infections angiostrongyliasis, gnathostomiasis, and baylisascariasis are the predominant parasitic infections associated with eosinophilic meningitis. In endemic areas, eosinophilic meningitis is also associated with, *Paragonimus westermani, P. heterotrema, Schistosoma japonicum,* and *Taenia solium* cysticerci.

Epidemiology

Angiostrongylus cantonensis, a lung worm of rats, was first reported in the United States in 1985, with a probable introduction by infected rats from ships docking in New Orleans, Louisiana, during the mid-1980s. Since then, it has been reported in nonhuman primates and a boy from New Orleans, and in a horse from Picayune, Mississippi, a distance of 87 km from New Orleans. Parastrongylus cantonensis infection is herein reported in a lemur (Varencia variegata rubra) from New Iberia, Louisiana, a distance of 222 km from New Orleans, and in a wood rat (Neotomafloridanus) and in 4 opossums (Didelphis virginiana) from

Baton Rouge, Louisiana, a distance of 124 km from New Orleans (Kim DY et al 2002, J.Parasitol 88(5):1024)

The principal etiologic agent of human eosinophilic meningitis, Angiostrongylus cantonensis, was first detected in rats in Canton, China in 1933. The first human case was detected on Taiwan in 1944. Starting from the last years of world war II the parasite spread to Southeast Asia, the Western Pacific islands, (Micronesia, Melanesia, Polynesia and Australia). Cases were identified in the 1950s in Sumatra, the Philippines, Taiwan, Saipan, New Caledonia, Rarotonga, Tahiti. During the 1960s, cases were detected in Vietnam, Thailand, Cambodia, Java, Sarawak, the New Hebrides (nowadays Vanuatu), Guam and Hawaii Subsequently in the Pacific Basin the disease has appeared on Okinawa, other Ryukyu islands, Honshu, Kyushu, New Britain, American Samoa and Western Samoa, Australia, Hong Kong, Bombay, India, Fiji and mainland China. Beyond the Indopacific region, the worm has been found in rodents in Madagascar (1963), Cuba (1973), Egypt (1977), Puerto Rico (1984), New Orleans, Louisiana (1987) and Port Harcourt, Nigeria (1989). Caged primates became infected in zoos in Hong Kong (1978) and New Orleans and Nassau, Bahamas (1987).

Adult worms reside and lay eggs in the pulmonary arteries of rats. First-stage larvae hatch and migrate via the trachea and gastrointestinal tract into the feces. Snails and slugs that feed on rodent excrement serve as intermediate hosts and allow the larvae to molt into infective third-stage forms. Rats and humans become infected by consuming third stage infective larvae.

Humans accidentally acquire infection by consuming

- raw tissues of infected mollusks: either by ingesting improperly cooked intermediate hosts (snails and slugs)
- food (salad greens) contaminated by slug or snail slime or containing minute slugs
- raw paratenic hosts (freshwater shrimp, land crabs, frogs) that have eaten infected mollusks.

In humans, the third-stage larvae (approximately 500 μm in length) are transported via the bloodstream to the central nervous system where they burrow into the neural tissue, inciting an inflammatory response that eventually kills the parasites.

The probability of human infection in the USA is very small since the parasite is transmitted primarily by ingestion of raw intermediate and paratenic hosts, rarely consumed in the USA.

The incubation period is one to three weeks but ranges from 3 to 36 days.

Clinical Description

Severe headache is the main complaint. The headache is intermittent, intractable, bitemporal, or occipital and continues throughout the clinical illness. Nausea, vomiting, and moderate stiffness of the neck and/or back are frequent during the early stage of disease. Paresthesias of the trunk and extremities commonly manifest as exaggerated sensitivity to touch and may persist for several weeks or months.

Altered consciousness, generalized weakness and flaccid paralysis are rare. Low-grade or no fever is usual.

Cranial nerves are rarely affected, particularly the optic and facial nerves.

Laboratory Tests

Elevation of the initial CSF pressure above 200 mm of water with grossly opalescent or turbid (rice water), but not purulent, fluid. The CSF contains between 500 and 2000 leucocytes/mm^3 with a relatively high percentage of eosinophils, typically 25 to 75%. The eosinophilic pleocytosis reaches a peak around

one or two week of illness and gradually resolves over several months. CSF protein is elevated and CSF glucose is usually normal. Peripheral eosinophilia ranging from 15 to 50% persists for about 3 months. There is no correlation between the degree of eosinophilia in the peripheral blood and the percentage of eosinophils in the CSF. Serum biochemistry, electroencephalography, and cerebral angiography results are usually normal.

The disease is usually self-limiting. Clinical symptoms persist for 2 to 4 weeks and generally are much reduced within a few days of initial treatment. Headache may persist longer than 1 month; the neurologic deficit may last longer.

Treatment

Analgesics and sedatives give only minimal relief. Headache usually subsides dramatically, but temporarily, following lumbar puncture. Careful removal of CSF at intervals of 3 to 7 days is therefore recommended until there is definite clinical and laboratory improvement. In more critical cases, corticosteroids may be employed to reduce cerebral pressure or to treat those with cranial nerve involvement. Corticosteroids do not appear to benefit mild cases.

A. cantonensis is susceptible to broad-spectrum anthelminthics, e.g., thiabendazole, mebendazole, albendazole, and ivermectin. However, these drugs should not be used—clinical deterioration or death can result from a reaction to dead or dying worms in the brain.

Surveillance

Eosinophilic meningitis is not a reportable condition. However, since the condition is rare The Infectious Disease Section is interested in compiling reports of infection by Angiostrongylus cantonensis.

Case Definition

Clinical definition: Eosinophilic meningitis is defined by the presence of 10 or more eosinophils/ μL in the CSF or eosinophilia of at least 10% of the total CSF leukocyte count.

Epidemiologic criterion: Consumption of a raw intermediate or paratenic hosts in a known endemic area and absence of other disease associated with eosinophilic meningitis syndrome.

Investigation

Collect clinical and epidemiologic information

Prevention of transmission

Proper cooking of mollusks or paratenic hosts, and proper washing of vegetables.

Freezing of mollusks and crustaceans at −15°C for 12 hours will destroy infective larvae of A. cantonensis