CASE REPORT: EOSINOPHILIC MENINGITIS DUE TO *GNATHOSTOMA SPINIGERUM* IN AN INFANT IN SOUTHERN THAILAND

Tipaporn Thongmak, Palapa Banjerdlak, Sareeporn Iamprasertkul and Kanokporn Rangsitsathian

Pediatric Division, Hat Yai Hospital, Songkhla Province, Thailand

Abstract. Eosinophilic meningitis due to *Gnathostoma spinigerum* is rare in infants. We report here the case of an 11-month-old male diagnosed with eosinophilic meningitis due to *Gnathostoma spinigerum* and review the literature on this type of infection. The infant presented to Hat Yai Hospital, Songkhla, Thailand with a 5-day history of a high-grade fever, irritability and vomiting. This progressed to weakness and pain in both legs. Serum and cerebral spinal fluid immunoblot tests were positive for *Gnathostoma spinigerum*. He was treated with albendazole 400 mg daily and prednisolone 2 mg per kilogram daily for 14 days. He gradually improved over the 2 weeks and at 3 months follow up had returned to normal and exhibited normal growth and development. Gnathostomiasis can cause eosinophilic meningitis and should be considered in the differential diagnosis in a child who presents with eosinophilic meningitis.

Keywords: eosinophilic meningitis, *Gnathostoma spinigerum*

Correspondence: Tipaporn Thongmak, Pediatric Division, Hat Yai Hospital, 182 Rattakarn Road, Hat Yai District, Songkhla 90110, Thailand
Tel: +66 (08) 6958 9339; Fax: +66 (0) 7427 3161
E-mail: tipaing@gmail.com

INTRODUCTION

Eosinophilic meningitis can be caused by parasites, bacteria, viruses and non-infectious conditions such as lymphomas, leukemia and hypereosinophilic syndrome (Lo Re and Gluckman, 2003; Shah *et al*, 2015). Eosinophilic meningitis defined as having the symptoms of meningitis and finding ≥10 eosinophils/l in the cerebral spinal

fluid (CSF) or finding ≥10% eosinophils on a CSF leukocyte differential analysis (Lo Re and Gluckman, 2003). In Thailand, the most common causes of eosinophilic meningitis are the parasites *Angiostrongylus cantonensis* and *Gnathostoma spinigerum*. These parasite infections are contracted by the ingestion of undercooked fish or meat (Sawanyawisuth and Chotmongkol, 2013). Most cases of eosinophilic meningitis reported in the Thai literature are among older children and adults (Sawanyawisuth *et al*, 2013; Schmutzhard *et al*, 1998). We report here a rare case of eosinophilic meningitis in an infant caused by *Gnathostoma spinigerum*.

We received ethical clearance to report this case from the Ethics Committee of Hat Yai Hospital, Thailand (HYH EC 051-64-01).

CASE REPORT

A previously healthy 11-month-old male presented to Hat Yai Hospital, Songkhla, Thailand with a 5-day history of high fever, nausea and vomiting. The parents denied a history ingestion of raw or uncooked fish, frogs, pork, or eels. His diet consisted of infant formula and baby food appropriate for age. He had no history of any major medical problems and his growth and development were appropriate for his age. He was up to date on his childhood vaccines for his age.

On physical examination he had a temperature of 38.5°C. His height and weight were both at the 25th percentile for his age. He was alert but irritable. He had no nuchal rigidity. He had no palpable lymph nodes; his chest was clear to auscultation and his heart sounds were normal without murmurs. His abdomen was soft, nontender and there was no palpable hepato- or splenomegaly. His muscle strength was normal throughout both upper and lower extremities, proximally and distally, bilaterally. His deep tendon reflexes were 2+ (normal) throughout, both upper and lower extremities bilaterally.

On laboratory examination, his complete blood count (CBC) showed leukocytosis with a total white blood cell (WBC) count of 28,610 cells/mm^3 with 72% neutrophils and 0% eosinophils. His hemoglobin was low at 11 gm/dl and his platelet count was elevated at 524,000/mm^3.

The patient was initially diagnosed as having an occult bacterial infection with bacteremia. He was treated with ceftriaxone 75 mg/kg/day.

After 4 days of hospitalization, he continued to have high fever and irritability. On examination his temperature was 39°C and the only new finding of physical examination was the new presence of nuchal rigidity.

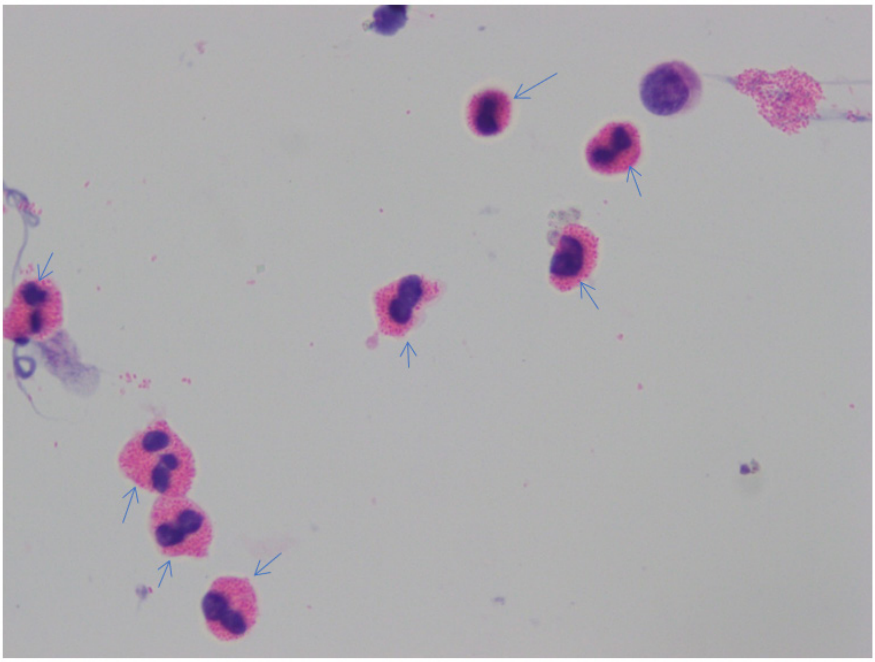

Fig 1 - Wright-Giemsa-stained smear of cerebrospinal fluid shows numerous eosinophils (blue arrows) (1000X)

A lumbar puncture was done and the CSF was clear. The CSF WBC count was 55/mm^3 with 23% neutrophils and 77% lymphocytes. The CSF glucose level was 57 mg/dl and the protein was 36.7 mg/dl. The blood sugar was 90 mg/dl. The patient was diagnosed with having bacterial meningitis and the dosage of ceftriaxone increased to 100 mg/kg/day.

A week later the patient continued to have high fever and irritability and began to get watery diarrhea. He began to have pain when his legs were touched or moved. He was unable to sit or stand by himself and he developed urinary retention.

On physical examination, he continued with high fever, irritability and nuchal rigidity. He was also noted to have hypotonia. His muscle strength had decreased to III/V in both lower extremities and his deep tendon reflexes in both legs decreased to 0. He had no clonus and he had negative Babinski signs bilaterally. He also had a loss in sphincter tone.

On laboratory examination his peripheral blood CBC showed mild leukocytosis with a WBC count of

14,860/mm^3 with 50% neutrophils and 30% eosinophils (absolute eosinophil count of 4450/mm^3). He continued having mild anemia and thrombocytosis. A repeat lumbar puncture revealed clear CSF, an opening pressure of 18 cm H_20 and a closing pressure of 11 cm H_20. The CSF total WBC count was 290/mm^3 with 77% eosinophils (Fig 1). The CSF glucose was 42 mg/dl and the protein was 122 mg/dl. The blood sugar was 122 mg/dl. Latex agglutination tests on the CSF for *Streptococcus pneumoniae* and *Haemophilius influenzae* Type b were negative and the CSF bacterial culture was negative. Serum and CSF immunoblot tests for gnathostomiasis were weakly positive and for angiostrongyliasis were negative. A stool examination showed no WBC or red blood cells or parasites. A magnetic resonance imaging (MRI) scan of the brain and spine showed smooth leptomeningeal enhancement along the temporooccipital lobe, brainstem and cauda equina.

The patient was diagnosed as having eosinophilic meningitis due to *Gnathostoma spinigerum* and was treated with albendazole 400 mg daily for 14 days and prednisolone at 2 mg per kilogram per day for 14 days.

By one week of the albendazole and prednisolone the fever had defervesced and the leg pain had resolved. He was able to sit and pull up to a standing position.

By 10 days of treatment on the CBC the percentage of eosinophils had decreased to 3%.

At a 3-month follow up visit, the patient had normal growth and development for age. He was asymptomatic and his physical and neurological exams were normal.

DISCUSSION

The majority of eosinophilic meningitis cases reported in the literature were due to *Angiostrongylus cantonensis* (Pham Thu *et al*, 2020; Sawanyawisuth *et al*, 2013; Evan-Gilbert *et al*, 2014; Raveendrakumar *et al*, 2021). There are two reported cases of central nervous system infection among children in Thailand due to *Gnathostoma spinigerum*, one in an older child and another in a 4-year old but none among infants (Punyagupta *et al*, 1990; Schmutzhard *et al*, 1998; Bunyaratavej *et al*, 2008).

The reported prodrome of gnathostomiasis includes abdominal pain, nausea, vomiting, diarrhea and fever due to parasite penetration of the gut wall (Graeff-Teixeira *et al*, 2009). These initial symptoms usually last less than 5 days and are followed by 1 of 3 clinical courses: cutaneous, visceral or central nervous system infection (Shah *et al*, 2015; Graeff-Teixeira *et al*, 2009; Nawa *et al*, 2004). Central nervous system infection due to *Gnathostoma spinigerum* may result in radicular pain, myelitis, intracranial hemorrhage

or subarachnoid hemorrhage (Pham Thu *et al*, 2020). The radicular pain may be due to the parasite migrating through or invading the nerve root (Punyagupta *et al*, 1990; Boongird *et al*, 1997). In the case reported here the child complained of bilateral lower extremity pain but the cause is unclear due to the young age of the patient.

In our case reported here, both serum and CSF immunoblot tests for *Gnathostoma spinigerum* were positive. Examinations helpful in leading to a diagnosis include a CBC, CSF examination, radiological studies and serology tests (Graeff-Teixeira *et al*, 2009). An absolute eosinophil count in the peripheral blood >1500 cells/mm^3 suggests parasite infection (Shah *et al*, 2015). A lumbar puncture may reveal a normal or high opening pressure (Ramirez-Avila *et al*, 2009). A bloody or xanthochromic appearance of the CSF is typical for gnathostomiasis with a subarachnoid hemorrhage (Graeff-Teixeira *et al*, 2009; Punyagupta *et al*, 1990); however, clear CSF may still be found as in the case of our patient. CSF findings in eosinophilic meningitis due to *Gnathostoma spinigerum* includes eosinophilia, mild elevation of CSF proteins, low or normal CSF sugar and negative CSF stains and cultures for other organisms (Lo Re and Gluckman, 2003). A previous paper reported finding >30% eosinophils in 6% of adult patients with eosinophilic meningitis due to *Gnathostoma spinigerum* (Boongird *et al*, 1997). An MRI of the spine in those with eosinophilic meningitis due to *Gnathostoma spinigerum* may show diffuse or segmental enlargement of spine, with or without post-gadolinium linear enhancement. (Graeff-Teixeira *et al*, 2009).

The treatment of CNS gnathostomiasis has not yet been well-defined. Albendazole and Ivermectin have been reported to be used effectively (Lo Re and Gluckman, 2003; Baskar *et al*, 2002). Steroids may be useful to reduce some symptoms but its use has not been examined in randomized control trials (Sawanyawisuth *et al*, 2013; Graeff-Teixeira *et al*, 2009). Our subject had improvement after treatment with albendazole and prednisolone but it is unclear what benefit the prednisolone had.

Mortality rates reported among those with eosinophilic meningitis has been reported to vary from 7.7 to 12% (Punyagupta *et al*, 1990; Schmutzhard *et al*, 1998). However, the rate of permanent neurological sequelae, such as paraplegia, radiculopathy, cranial nerve lesion, or hemiparesis has been reported to be as high as 38.5% (Schmutzhard *et al*, 1998). Fortunately, in our case the patient had no evident neurological sequelae by 3 months post-treatment.

In summary, we reported here a case of eosinophilic meningitis due to

Gnathostoma spinigerum in an infant. The patient had bilateral leg pain, paraplegia, high eosinophil counts in both the peripheral blood and the CSF. The child responded well to treatment with albendazole and prednisolone. We conclude that although rare, *Gnathostoma spinigerum* can cause eosinophilic meningitis in infants and young children and should be in the differential diagnosis of infants with eosinophilic meningitis. Diagnostic lumbar punctures should be repeated in a child with meningitis if they do not improve.

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CONFLICTS OF INTEREST DISCLOSURE

There are no conflicts of interest to declare.

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