EOSINOPHILIC MENINGOENCEPHALITIS DUE TO TOXOCARA CANIS:
CASE REPORT AND REVIEW OF THE LITERATURE

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Abstract. Toxocariasis is usually manifested as visceral larva migrans. Nervous system involvement is a rare complication. In this report, we describe one case of meningoencephalitis due to Toxocara canis and review the literature. We report a previously healthy two-year-old boy who was admitted after 24 hours of severe neurologic symptoms with marked eosinophilic pleocytosis in the cerebrospinal fluid and a single subcortical lesion detected by cerebral magnetic resonance imaging. Both serum and spinal fluid tested positive for T. canis. Initial treatment with thiabendazole was ineffective. After marked improvement in clinical and laboratory results were achieved using albendazole and corticosteroids, the child was discharged.

INTRODUCTION

Neurohelminthiases are more prevalent in developing countries. However, these diseases often go undiagnosed because they are not recognized by physicians or because appropriate testing is unavailable.1 Eosinophilic pleocytosis is rarely found in human cerebrospinal fluid (CSF), and most of the infectious agents are parasitic.2 Globally, Angiostrongylus cantonensis is the main cause.3 However, the differential diagnosis is broad and includes nematodes, cestodes, and trematodes. In young children with geophagia and previous exposure to puppies, toxocariasis is usually manifested as visceral larva migrans. In its most florid state, this syndrome is characterized by eosinophilia, fever, and hepatomegaly. Accompanying lesions in the eye are more common in older children and adults. The central nervous system (CNS), although seldom involved, represents ectopic sites of infection. We present a rare case of eosinophilic meningoencephalitis due to Toxocara canis and discuss clinical, laboratory and therapeutic issues.

CASE REPORT

A previously healthy two-year-old boy was referred to our hospital after 24 hours of fever, headache, mental confusion, and progressive weakness. On examination, the child was tachycardic, dyspneic, and pale, but had no fever. He was lethargic, irritable, and presented nuchal rigidity, motor weakness, and accentuated deep tendon reflexes in both legs. His sounds were normal, and his abdomen showed no hepatomegaly. The results of a funduscopic examination were normal. His white blood cell count (WBC) was 17,100/mm³ with 2% eosinophils. Results of serum electrolyte, blood urea nitrogen, glucose, and liver function tests were normal. An urgent computed tomography scan of the brain showed no abnormalities. An electroencephalogram (EEG) disclosed mild diffuse cerebral involvement.

A lumbar puncture on the day of admission showed 3 cells/mm³ with normal protein and glucose concentrations. Results of gram stain, culture, and latex agglutination for bacteria were negative. Blood and CSF cultures for mycobacteria and fungi showed no growth. The patient was transferred to the Intensive Care Unit and treatment with acyclovir and ceftriaxone was started. On the second day of hospitalization, another lumbar puncture showed 161 cells/mm³ (27% neutrophils, 50% lymphocytes, 23% eosinophils), a CSF glucose level of 45 mg/dL, and a CSF protein level of 42 mg/dL. Treatment with thiabendazole (75 mg/kg/day, 1,200 mg in three doses) was started. Results of serum and CSF immunologic tests for toxoplasmosis, cytomegalovirus, and cisticercosis were negative. The findings of an evaluation for cryptococci, herpes simplex virus, and varicella-zoster virus were normal, and the results of cytologic testing were not helpful.

Given the persistence of an eosinophilic pleocytosis in his spinal fluid, CNS toxocariasis was suspected, and the diagnosis was confirmed using enzyme-linked immunosorbent assays (ELISAs). Both serum and CSF showed reactivity for T. canis. After 10 days of treatment with thiabendazole, no improvement in clinical or mental status was observed. A third lumbar puncture showed 29 cells/mm³ (58% eosinophils) and a normal WBC count with 1% eosinophils. Magnetic resonance imaging (MRI) of the brain identified a single lesion with high signal intensity (Figure 1), and an EEG showed severe diffuse cerebral involvement. Albendazole (50 mg/kg/day, 800 mg in two doses) plus corticosteroids (dexamethasone, 0.15 mg/kg/day, 10 mg in four doses) was substituted for thiabendazole. After seven days, the child was alert, speaking simple words, and eating normally, although exhibiting moderate generalized hypotonia, right-arm monoparesis, and a continued inability to walk. An additional lumbar puncture showed 2 cells/mm³, a CSF glucose level of 56 mg/dL, and a CSF protein level of 31 mg/dL. Results of ELISAs for T. canis in serum and CSF remained positive. Audiometric assessment showed moderate to severe deficit of auditory capacity and the EEG was normal. After four weeks of receiving albendazole, the patient was discharged to a rehabilitation center.

At a three-month follow-up, the general state of the patient was good. He was able to walk. However, he exhibited slight motor-strength deficiency and lower-limb hypotonia, as well as moderately spastic right-arm monoparesis.

DISCUSSION

In 1951, Beautyman and Woolf4 published a report of a child with clinical and pathologic evidence of neurologic involvement due to an encapsulated larva, identified as probably Ascaris lumbricus. Nichols5 in 1956 provided more precise data on the morphology of Toxocara, which induced other investigators to reconsider the structure of the larva seen in 1951. In 1966, 15 years after the previous report, Beau-
tyman and others\textsuperscript{6} suggested that the parasite identified was not \textit{A. lumbricus}, but \textit{T. canis}. This study is the first report of a case of CNS toxocariasis.

Using the electronic databases of the MEDLINE system (National Library of Medicine Bethesda, MD) and manually searching journals published between 1982 and 2002, we found 12 cases\textsuperscript{7–18} of CNS involvement due to \textit{T. canis}. Cerebral infection was considered to be defined by neurologic symptoms in conjunction with 1) histopathologic or parasitologic diagnosis,\textsuperscript{9,13,17} 2) a positive immunodiagnostic test result for serum and CSF,\textsuperscript{11,12} or 3) peripheral eosinophilia (with or without eosinophilic pleocytosis in CSF) and an immunodiagnostic serum test.\textsuperscript{7,8,10,14–16,18} Cases with incomplete clinical or parasitologic information were excluded.

Although visceral larva migrans is a characteristic disease in children, CNS toxocariasis was seen more frequently in adults.\textsuperscript{2,9,16} The clinical spectrum of CNS toxocariasis is broad, causing various syndromes: eosinophilic meningoencephalitis and meningitis,\textsuperscript{7,8,10} meningoencephalitis or meningoencephalomyelitis,\textsuperscript{11,12,17} encephalitis\textsuperscript{15,18} extramedullary space-occupying lesion,\textsuperscript{13,16} brain vasculitis,\textsuperscript{15} seizures,\textsuperscript{14} and probably behavior disorder.\textsuperscript{9} Some reports have emphasized the severity of neurologic disorders and serious sequelae, namely mental and psychomotor retardation, paresis, amaurosis, and conduct disorders.\textsuperscript{8,10,15,16} Less commonly, a benign, self-limiting form of the disease has been described.\textsuperscript{9,18}

Toxicariasis has been suggested as a co-factor for epilepsy, but a case-control study in children found rates of \textit{Toxocara} seropositivity in epileptic patients with a known etiology (other than toxocariasis) to be similar to those in patients with idiopathic epilepsy.\textsuperscript{19}

The diagnosis of meningitis or meningoencephalitis due to \textit{T. canis} is suggested by the presence of clinical features, peripheral eosinophilia, and CSF eosinophilic pleocytosis. Interestingly, our case did not present peripheral eosinophilia, despite the elevated eosinophils count in spinal fluid. This aberration had been previously described\textsuperscript{19} and may reflect the small size of the CNS larvae population, which is likely sufficient to cause local lesions, but is insufficient to provoke blood eosinophilia. In contrast, there were related brain focal lesions, which presented peripheral eosinophilia, but no eosinophils in the spinal fluid.\textsuperscript{14,17,18} Although rare, diagnosis may be made during the later stages of the disease through discovery of a \textit{Toxocara} larva, either in the CSF,\textsuperscript{17} after surgery,\textsuperscript{16} or at autopsy.\textsuperscript{9}

There are reports of several MRI alterations in CNS toxocariasis: vascular areas identified by angiogram,\textsuperscript{15} focal lesions,\textsuperscript{14} and non-specific T2-weighted areas of increased signal.\textsuperscript{11,18} A T2-weighted MRI of our patient revealed a non-specific single image.

Serologic and CSF tests based on ELISAs or enzyme immunoassays have been used,\textsuperscript{7,8,10–14} and appear to specifically confirm a presumptive diagnosis. However, a negative spinal fluid test result does not rule out CNS involvement\textsuperscript{13,18} or even meningitis.\textsuperscript{14}

The differential diagnosis of eosinophilic meningitis consists primarily of parasitic etiologies. In Southeast Asia, China, and Japan, \textit{A. cantonensis} and \textit{Gnathostoma spinigerum} are the principal causes. Other parasitic etiologies, including cystercerosis, ascaridiasis, trichinosis, strongyloidiasis, echinococcosis, schistosomiasis, paragonimiasis, and fascioliasis, exist worldwide.\textsuperscript{1} Tuberculosis, syphilis, coccidiodomycosis, and lymphoma involving the meninges can all occasionally cause CSF eosinophilia.\textsuperscript{2,3}

No anthelminthic agent has been formally evaluated for efficacy in treating CNS toxocariasis, and there are only anecdotal reports of successful treatment in humans with diethylcarbamazine, thiabendazole, and albendazole.\textsuperscript{7,14,17}

Albendazole has proven effective in the treatment of intestinal nematode infection and some neurohelminthiases such as cystercerosis and hydatidosis. Studies suggest that albendazole is better than other anthelminthic drugs because of its pharmacologic profile: high serum concentrations of albendazole sulfoxide (responsible for the systemic anthelmintic effects), good penetration into the CNS (a drug concentration in serum of approximately 40%), and less toxicity.\textsuperscript{20,21}

In addition to clinical rationales for the specific treatment of visceral larva migrans, Pawlowski has suggested that a preventive treatment with albendazole should also be considered, bearing in mind the increasing risk of dormant and migrating \textit{Toxocara} larvae localizing in the brain during the course of the infection.\textsuperscript{22}

There is no consensus concerning the utility of corticosteroids in the treatment of CNS toxocariasis. However, when there is ocular involvement, they are the therapy of choice. A well-designed study\textsuperscript{23} demonstrated the beneficial effect of prednisolone on the course and outcome of eosinophilic meningitis caused by \textit{A. cantonensis}, suggesting that corticosteroids play a role in controlling meningitis caused by \textit{T. canis}. In addition, Jung and others\textsuperscript{24} demonstrated that concurrent administration of dexamethasone increases albendazole levels by approximately 50%. Some case reports of toxocariasis symptoms, such as meningitis (absent encephalitis) or granulomatous lesions, noted spontaneous improvement with anthelminthic alone.\textsuperscript{9} Conversely, patients with serious neuro-
logic symptoms brought on by intense inflammatory response appear to benefit from corticosteroid therapy. However, in some cases, corticosteroid use does not prevent neurologic sequelae. Additionally, immune vasculitis, a well-known complication of other parasitic diseases, has been described in toxocariasis and has responded well to corticosteroids.

We conclude that infection with *T. canis* should always be considered in the differential diagnosis of eosinophilic meningoencephalitis or meningitis. Clinical findings associated with eosinophilic pleocytosis and CSF reactivity on an ELISA confirm the diagnosis. Although there is no proven therapy, once meningoencephalitis due to *T. canis* is suspected, therapy with anthelmintic and corticosteroids should be promptly started. If this is not done, there is a possibility of neurologic sequelae.

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