Case Report: A Probable Case of Human Neurotrichinellosis in the United States

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Abstract. Human neurotrichinellosis is seldom reported. This is likely the result of the low incidence of parasites from the genus Trichinella in the United States domestic food supply, as well as difficulties in diagnosing the disease, especially when neither the organism nor the source of the infection are readily available. Although trichinellosis from domestic food supplies has been decreasing for many years, a resurgence has occurred in cases derived from the consumption of wild game. We report a rare case of neurotrichinellosis in the United States and implicate wild game as the source of the infection. These results suggest that clinicians should consider the potential for Trichinella infection in cases where wild game is common in the diets of the patients.

INTRODUCTION

Parasites of the genus Trichinella are globally-distributed, tissue-dwelling nematodes that predominantly infect mammals, although certain species are also known to infect birds and reptiles.1 In the past, most human infections caused by parasites of this genus, which is comprised of eight species and three genotypic variants,2 were the result of ingesting raw or improperly cooked Trichinella-infected pork. However, more stringent sanitary measures have made this occurrence rare in the United States, where the consumption of wild game harboring sylvatic species of Trichinella is now being implicated in a greater number of cases.3 When sufficient parasites are ingested to induce clinical signs, the initial enteral phase of the infection is accompanied by nausea, vomiting, and diarrhea. The subsequent parenteral phase, when the larvae begin penetrating striated muscle, is characterized by fever, periorbital edema, myalgias, eosinophilia, and elevation of muscle enzyme levels.4

According to criteria defined by the Centers for Disease Control and Prevention, the diagnosis of trichinellosis is made by a positive serologic test result or a Trichinella-positive muscle biopsy specimen in a patient exhibiting one or more clinical symptoms compatible with trichinellosis, such as eosinophilia, fever, myalgia, or periorbital edema.5 However, the identification of new species in conjunction with its high prevalence in wild game could complicate the clinical picture of trichinellosis given that symptomology is not necessarily congruent among Trichinella species.6 Similarly, a review by Dupouy-Camet and others7 proposed a more stringent algorithm for determining the probability of acute trichinellosis in humans ranging from “very unlikely” to “confirmed” based solely upon clinical grounds and without parasitologic data. Using that algorithm, we report a case classified as a “confirmed trichinellosis” in the absence of a positive biopsy specimen, and present further clinical evidence of neurologic involvement.

CASE REPORT

A 53-year-old woman with a previous history of diabetes mellitus was admitted to a local hospital in West Point, Nebraska, on August 7, 2005, after being found unconscious at home. The patient was admitted to the hospital with a fever (38.5°C) and was found neurologically unresponsive with weakness in the left upper extremity. A complete blood count showed leukocytosis (16.5 × 10⁶ cells/mm³, normal = 4.3–10.8 × 10⁶ cells/mm³) with left shift and no eosinophils. Levels of serum glucose (124 mg/dL; normal = 70–125 mg/dL) and electrolytes were normal. Results of a urinary drug screen and a test for serum ethanol levels were negative. A computed tomographic (CT) scan of the head was unremarkable. A lumbar puncture was traumatic and showed multiple red blood cells, 8 white cells (neutrophils), and mild elevation in the levels of protein (64 mg/dL; normal = 15–45 mg/dL) and glucose (140 mg/dL; normal = 40–70 mg/dL). Gram stain, culture results, enzyme-linked immunosorbent assay (ELISA) results for serum and cerebrospinal fluid (CSF) antibodies to West Nile virus, and polymerase chain reaction (PCR) results for herpes virus in CSF were negative. The patient was empirically started on ceftriaxone, vancomycin, and acyclovir and transferred to the Nebraska Medical Center in Omaha, Nebraska within 24 hours after her initial assessment.

Upon arrival in Omaha, the patient was still unconscious. With the initial suspicion of an early intracranial abscess or cerebritis, the patient was switched to intravenous ceftriaxone and metronidazole with no resolution of the symptoms. Magnetic resonance imaging (MRI) of the brain only showed non-specific white matter changes.

Three days after admission to the Nebraska Medical Center in Omaha, the patient was awake but remained disoriented and aphasic. She developed periorbital edema with petechiae and conjunctivitis on the left side (Figure 1). A re-evaluation of her peripheral blood count showed 16.4 × 10⁶ white blood cells/mm³ with 22% eosinophils, and elevated creatine kinase levels at 467 U/L (normal < 145 U/L). We were informed by a relative that the patient and her husband would occasionally supplement their diets with wild game obtained by hunting. An ELISA for IgG antibodies to conserved immunodominant Trichinella antigens was performed (ARUP Laboratories, Salt Lake City, UT) and a positive result was obtained (> 1.0 optical density [OD] units at a serum titer of 1:64; positive > 0.3 OD units) using rabbit and human sera as positive and negative controls, respectively.

Based upon a putative diagnosis of trichinellosis, the patient’s drug regimen was switched to albendazole, 400 mg orally twice a day, and prednisone, 60 mg orally four times a day.
Trichinella—Concomitant peripheral eosinophilia is common. Likewise, and Montana. are normally found. – Symptoms of neurologic involvement appear early after the infection, and may include headache, tinnitus, vertigo, deafness, aphasia, seizures, and apathy. Concomitant peripheral eosinophilia is common with Trichinella-associated encephalopathy; however, in some cases, it may not be prominent until one week later. Nonetheless, hyper eosinophilia as reported herein (> 3,700 cells/mm³) is significantly higher in patients with neurologic dysfunction than in those not exhibiting neurologic signs, and is directly associated with the intensity of infection. In addition to the other symptoms, the unconscious state of the patient at the time of admission and her obtunded and disoriented condition after regaining consciousness were consistent with neurologic involvement.

The patient did not recall ingestion of fresh game or pork prior to the incidence. However, evidence is clear that some forms of Trichinella found in sylvatic hosts can withstand freezing for long periods of time and remain infectious for up to a year or longer after freezing. Thus, the consumption of fresh infected meat is no longer requisite for acquiring an infection. In the United States, freeze-resistant genotypes of Trichinella have been identified in game meat from New Hampshire, and Montana. One report indicated Trichinella infection from ingesting improperly processed cougar meat that had been frozen. A higher incidence of trichinellosis has been reported in Alaska, where the inhabitants consume a greater proportion of wild animal meat (particularly bear meat) in their diets, and where freeze-resistant species of Trichinella are normally found.

Other parasitic infections that may cause abnormal mental status and eosinophilia include toxocariasis, angiostrongyloidiasis, and baylisascariasis. Although we did not specifically test for these conditions, the absence of pets at home or contact with raccoons, the lack of eosinophils in the CSF, and the lack of ocular larva migrans on examination argue against these possibilities. Moderate eosinophilic pleocytosis is quite common in toxocariasis patients with CNS involvement, where 80% of patients exhibit eosinophilia ≥10% in CSF. Likewise, Angiostrongylus cantonensis can cause eosinophilic meningitis and peripheral eosinophilia, although this infection is predominantly found in southeast Asia and the

**DISCUSSION**

It is estimated that the central nervous system (CNS) is involved in 10–24% of symptomatic cases of trichinellosis. Small lesions in the cerebral cortex and white matter can be identified using CT or MRI scans in severe cases. However, most reports of neurotrichinellosis describe cytobiochemically normal CSF, as did the case in our report. As such, neurologic manifestations are protean, making the diagnosis enigmatic. This is likely the reason that no cases of neurotrichinellosis have been reported in the United States since 1987.

Central nervous system inflammatory infiltration and damage may result from the secretion of toxic parasite antigens, larval migration and vascular obstruction, or eosinophil infiltration, although to date none of these hypotheses have ever been validated. It has been reported that myocardial injury and/or infarction often accompanies neurotrichinellosis, as assessed by electrocardiographic data. However, this is likely related to the severity of infection and resulting ischemia rather than any causal relationship between the foci.

After ingestion of contaminated meat and maturation of adult worms in the small bowel (enteral phase), larvae are released into the blood stream (parenteral phase) and travel to muscles and potentially other organs such as the brain. These phases are clinically associated with nausea and transient diarrhea during the first week of infection, and with myalgia, periorbital edema, conjunctivitis and neurologic symptoms during weeks 2–8 after infection, by which time the patient usually seroconverts. Symptoms of neurologic involvement appear early after the infection, and may include headache, tinnitus, vertigo, deafness, aphasia, seizures, and apathy. Concomitant peripheral eosinophilia is common with Trichinella-associated encephalopathy; however, in some cases, it may not be prominent until one week later. Nevertheless, hyper eosinophilia as reported herein (> 3,700 cells/mm³) is significantly higher in patients with neurologic dysfunction than in those not exhibiting neurologic signs, and is directly associated with the intensity of infection. In addition to the other symptoms, the unconscious state of the patient at the time of admission and her obtunded and disoriented condition after regaining consciousness were consistent with neurologic involvement.

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**Figure 1.** Periorbital petechia and conjunctivitis in a patient with neurotrichinellosis. This figure appears in color at www.ajtmh.org.
Pacific Islands. Nonetheless, no eosinophils were seen in the CSF of our patient. In contrast, CNS involvement by Baylisascaris is most often fatal. Those who survive are generally left in a persistent vegetative state, or with severe residual side effects.

Although the United States does not require inspection of pork products for Trichinella, the number of cases of trichinellosis has been progressively decreasing from approximately 400 cases and 15 deaths per year in the 1940s to approximately 12 cases per year (range = 11–23) and no deaths during the last survey spanning 1997–2001. During this period, 76% of the patients had at least one common sign or symptom of trichinellosis: 54% eosinophilia, 46% fever, 64% myalgia, and 31% periorbital edema. Globally, outbreaks of the disease still occur in regions where the guidelines for meat inspection are lacking or poorly regulated. However, cases of neurotrichinellosis have been poorly documented because of a combination of low incidence and misdiagnosis, given the polymorphic manifestations of the disease. Nonetheless, diagnosis of neurotrichinellosis should be considered in patients with hyper eosinophilia, elevation of muscle enzyme levels, and neurologic abnormalities in the setting of wild game consumption. Given the rapid onslaught of physical symptoms, unused portions of meat should be sought to confirm the source and species of the causative agent of the disease. However, as was the case herein, biopsy specimens may not always be positive, possibly because of a shortened time interval between the appearance of symptoms and the biopsy, and infected meat may not be available for parasite identification. In these cases, it is important to rely upon a paradigm such as that defined by Dubouy-Camet and others for final diagnosis. In this case, the rapid resolution of the symptoms after treatment with an antiparasitic drug is further evidence of a correct diagnosis.

Received March 13, 2007. Accepted for publication April 18, 2007.

REFERENCES