Case Report: *Halicephalobus gingivalis*: A Rare Cause of Fatal Meningoencephalomyelitis in Humans

Bhavesh Papadi,* Carole Boudreaux, J. Allan Tucker, Blaine Mathison, Henry Bishop, and Mark E. Eberhard

University of South Alabama Medical Center, Mobile, Alabama; Center for Global Health, Division of Parasitic Diseases and Malaria, Centers for Disease Control and Prevention, Atlanta, Georgia

Abstract. The genus *Halicephalobus* consists of eight species of free-living nematodes. Only one species (*H. gingivalis*) has been reported to infect vertebrates. Human infection is extremely rare, and only four cases have been reported in the literature. These nematodes seem to exhibit neurotropism, but their life cycle, mode of infection, and risk factors are poorly understood. Neurohelminthiasis are not commonly recognized in the United States and when they do occur, pose great diagnostic challenges because of lack of appropriate non-invasive screening and/or confirmatory tests. We report a challenging case of meningoencephalomyelitis caused by a *Halicephalobus* sp., in which the patient had a rapidly deteriorating clinical course. The case did not raise any clinical suspicion of neurohelminthiasis, although increased eosinophils were present in the cerebrospinal fluid. This case presents an opportunity to highlight the importance of considering parasitic infection in meningoencephalitis or meningoencephalomyelitis presenting atypically.

INTRODUCTION

*Halicephalobus gingivalis,* also referred to as *Micronema deletrix* or *H. deletrix,* is a free-living saprophytic nematode belonging to the order Tylenchida and class Chromadorea. It is capable of infecting and reproducing in vertebrates, including horses, zebras, and humans. The genus *Halicephalobus* consists of eight species, of which only *H. gingivalis* has been reported to infect vertebrates and is morphologically distinct from the other seven species. The other seven species are identified only as free-living forms in soil, rotting plant matter, and fresh and salt water. Unless a well-preserved specimen of adult *H. gingivalis* worms is available, it is not possible to delineate the species on morphology from histologic sections. The other alternative is to use molecular methods. We report the fifth case of human infection caused by *H. gingivalis*. The clinicopathologic features and differential diagnosis are discussed.

CASE REPORT

A 65-year-old Caucasian woman from Pensacola, Florida, was given a diagnosis of a urinary tract infection caused by a *Klebsiella* sp. She was treated with ciprofloxacin and discharged. Soon after being discharged, nausea and vomiting developed in the patient. A week later, she had a fever and was admitted to a hospital. She also had mild congestion of sinusoidal air spaces, which was relieved by treatment with an antihistamine loratidine. She had no other symptoms and was discharged. Soon after being discharged, nausea and vomiting reappeared, and she was admitted to a hospital again. She had a rapidly deteriorating clinical course. The case did not raise any clinical suspicion of neurohelminthiasis, although increased eosinophils were present in the cerebrospinal fluid. This case presents an opportunity to highlight the importance of considering parasitic infection in meningoencephalitis or meningoencephalomyelitis presenting atypically.

*Address correspondence to Bhavesh Papadi, National Cancer Institute, National Institutes of Health, 10 Center Drive, Room 2A19, Bethesda, MD 20892. E-mail: bhavesh2papadi@yahoo.com*
observed in the sections included the presence of only adult female worms with a maximum diameter of approximately 25 μm; a smooth cuticle; a rhabditiform esophagus with corpus, isthmus, and posterior bulb; a female genital tract with single dorsiflexed ovary; a single uterus with eggs; protuberant vulval lips, and a tail that was long and tapered to a point (Figure 1). Also noted were numerous larval forms that were somewhat smaller but with the same features as the adult females, but lacking a developed reproductive system.

The worms seem to be more abundant in the perivascular region of the brain parenchyma. The inflammatory cells were predominantly neutrophils, but also included lymphocytes, macrophages and rare eosinophils. Rare worms were seen in myocardium and lung parenchyma.

**DISCUSSION**

*Halicephalobus gingivalis* is an uncommon cause of meningoencephalitis in humans. All previous cases were reported from North America and meningoencephalitis with myelitis was reported in half the cases. The mode of infection appears to be by penetration of existing lesions in the skin, although in half of the cases, including the present case, no apparent entry lesion was noted. Based on the diffuse perivascular distribution of these organisms in the meninges and the brain parenchyma, it is likely that these nematodes reach the central nervous system by hematogenous spread and penetrate the blood–brain barrier. Clinical changes common to the reported cases include fever, mental changes, and lethargy with cerebrospinal studies showing elevated leukocyte counts. Grossly, there were diffuse changes such as edema or hyperemia of brain parenchyma and dullness of meninges. Microscopically, all cases had a mixed inflammatory infiltrate containing neutrophils, eosinophils, lymphocytes, and multinucleate histiocytes. It should be noted that the age range in the previous case-patients was 5–54 years, and that the present case-patient is the oldest to date.

All reported cases of human *Halicephalobus* infections were fatal and because all of them were diagnosed postmortem, none of them were treated with anthelmintic drugs. Treatment of *H. gingivalis* infections in other animals is mostly unsuccessful and may be caused by the inability of anthelmintic drugs to cross the blood–brain barrier and penetrate the granulomatous lesions in the brain or a lack of sensitivity of *H. gingivalis* to anthelmintic drugs such as ivermectin and benzimidazole. There have been only two reports of successful treatment of extra-central nervous system–localized halicephalobiasis in horses with ivermectin alone or with diethylcarbamazine. An approach similar to treatment of disseminated strongyloidiasis may be prudent, specifically use of ivermectin alone or in combination with albendazole, but this approach would require antemortem clinical suspicion of halicephalobiasis.

Nematode infections of the brain are not common. The differential diagnosis of tissue nematodes in the brain includes *Toxocara canis*, *Angiostrongylus cantonensis*, *Strongyloides stercoralis*, *Gnathostoma spinigerum*, *Baylisascaris procyonis*, and *Lagochilascaris minor*. Size and morphologic features enable ready distinction from most of these other nematodes. Ascarid larvae (*Toxocara, Baylisascaris, Lagochilascaris*) are characterized by lateral alae, prominent excretory ducts, and thick, columnar intestinal cells. There is no development of reproductive structures in these larvae. *Toxocara* larvae are typically smaller (20 μm wide), whereas *Baylisascaris* larvae are larger (on average 50 μm in diameter) than *Halicephalobus* larvae. Immature *Angiostrongylus* spp. have two reproductive tubes, dome-shaped lateral chords, and the intestine has few, yet multinucleate, cells. When seen in the brain, *Angiostrongylus* are also larger (150–250 μm in diameter). *Gnathostoma* larvae are generally greater than 200 μm in diameter, making them much larger than either the adults or larvae of *Halicephalobus*. In addition, the presence of body spines, robust musculature, distinct intestine with prominent nuclei in each cell, and absence of developed reproductive structures allows easy differentiation from *Halicephalobus*. *Strongyloides stercoralis* is the helminth most-similar morphologically to *Halicephalobus*. In extraintestinal infection, filiform larvae may be seen but are of smaller diameter than *Halicephalobus* larvae and have small double lateral alae. Gravid female *Strongyloides* are usually not seen in the brain in cases of disseminated strongyloidiasis, and adult females have two reproductive tubes whereas in *Halicephalobus* the females have a single reproductive tube.

Neurohelminthiasis in general are extremely rare in United States. As a result, physicians in the United States do not routinely consider parasitic infections in the differential diagnosis of meningoencephalitis and it is unlikely that halicephalobiasis would be in the differential diagnosis even if other helminthic infections were considered. This feature is complicated by the fact that there are no easy screening or confirmatory tests for parasitic meningoencephalitis and a definitive diagnosis of halicephalobiasis is difficult to confirm in the absence of accessible lesions for biopsy. Although extremely uncommon, clinicians may wish to entertain a diagnosis of *Halicephalobus* infection, especially in rapidly progressing neurologic cases in which other possible infections have been ruled out. Unfortunately, at present, arriving at a definitive diagnosis has only been possible postmortem.
REFERENCES