Case Report: Ocular Gnathostomiasis in Venezuela Most Likely Acquired in Texas

Maria Alejandra Benavides,¹ Maria Belisa Baldo,¹ Shachar Tauber,² Sandra Fernandez Figueiras,³ Renzo Nino Incani,⁴ and Yukifumi Nawa^{5*}

¹Cornea Clinic, Ophthalmology Service, Centro Medico Docente La Trinidad, Caracas, Venezuela; ²Ophthalmic Research and Telemedicine Section, Ophthalmology and Optometry Mercy Clinic, Caracas, Venezuela; ³Section of Microbiology and Molecular Biology, Clinical Laboratory, Centro Medico Docente La Trinidad Caracas, Venezuela; ⁴Department of Parasitology, Faculty of Health Sciences, Universidad de Carabobo, Valencia, Venezuela; ⁵Tropical Diseases Research Centre, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand

Abstract. A 69-year-old male dentist in Caracas, Venezuela, was referred to our Cornea Clinic with a history of pain, photophobia, and blurred vision on his left eye. Routine biomicroscopic examination with a slit lamp showed a worm in the corneal stroma of his left eye. The worm was surgically removed and was identified morphologically as *Gnathostoma binucleatum*.

Gnathostomiasis is a representative fish-borne parasitic disease. Among 13 valid *Gnathostoma* species, five species have been proven to be human pathogens: four species (*Gnathostoma spinigerum*, *Gnathostoma hispidum*, *Gnathostoma doloresi*, and *Gnathostoma nipponicum*) in Asia and only one species, *Gnathostoma binucleatum*, in the Americas.¹ Although *Gnathostoma* species have a rather wide areas of distribution, human gnathostomiasis cases have been found in limited countries such as Thailand, Japan, Mexico, and Ecuador where people have the habit of consuming freshwater fish in raw or undercooked condition.^{1,2} Recent epidemiological surveys added several Southeast Asian countries such as Vietnam and Laos as endemic.¹ In addition, sporadic cases of gnathostomiasis have recently been reported from previously nonendemic countries such as Australia,³ Brazil,^{4,5} and Peru.⁶ The cases among travelers, not only those who have been to endemic countries⁷ but also to nonendemic African countries such as Botswana⁸ or Zambia,⁹ suggest much wider distribution of this parasite than we thought previously. In terms of clinical manifestations, the vast majority of gnathostomiasis patients presented with serpiginous eruptions or nodular migratory panniculitis on the skin.¹ Although the frequency is extremely low, *Gnathostoma* worms sometimes migrate into the eyes^{10–12} or central nervous system¹³ to cause deleterious illness. In Venezuela, when infectious disease consultants examined patients suffering from ocular parasitosis, they usually first consider *Onchocerca volvulus* infection, a filarial nematode parasite that causes cutaneous and ocular lesions¹⁴ and has long been known to be endemic in this country.¹⁵ Here, we report a case of ocular gnathostomiasis found in Venezuela. The patient has been to Texas, United States, for a holiday fishing trip and supposed to be infected by drinking unfiltered water from the rivers and lakes. This is the first ocular gnathostomiasis case in Venezuela and the 83rd reported case of ocular gnathostomiasis in the world.¹²

THE CASE

On July 27, 2016, a 69-year-old male Venezuelan dentist from Caracas was referred to the Cornea Clinic, Ophthalmology Service of the Centro Medico Docente la Trinidad, Caracas, Venezuela, because of pain, photophobia, and blurred vision of his left eye. About 1 month before, on June

2016, he had a traumatic corneal foreign body in his left eye as a consequence of polishing a dental implant. After removal of the corneal foreign body, he was treated with topical application of tobramycin and dexamethasone. Shortly after complete recovery from this accidental corneal injury, he traveled to Texas for vacation, where he went swimming in several natural pools and fishing and swimming in the Lake Conroe, near Houston, TX. During this holiday, although he did not consume freshwater fish dishes, he frequently drank unfiltered water from the rivers and lakes. On the third week in Texas, he began to suffer from photophobia, blurred vision, and swelling of the eyelid of his left eye. He returned to Venezuela and consulted an ophthalmologist who immediately referred the patient to our service.

On visual examination, his best-corrected visual acuity (BCVA) were as follows: right eye: 20/30 and left eye: 20/60. Biomicroscopic examination with a slit lamp revealed that his right eye had moderate nuclear sclerosis of the lens. His left eye had remarkable changes with an edematous upper eyelid, ptosis, and hyperemic conjunctivae. The most striking finding was the presence of a live worm measuring about 3.0 mm in length and 0.3 mm in maximum width in the corneal stroma associated with coarse corneal stromal edema and pigmented endothelitis (Figure 1A). His intraocular pressure was 18 mm of Hg in both the eyes. The fundus of both the eyes was within normal range. Ocular computed tomography (CT) of the left anterior segment revealed the presence of an encapsulated organism in the anterior half of the cornea stroma (Figure 1C). General examinations for systemic infection or pathology were almost within normal limits, with slight leukocytosis (10,000/mm³) and normal eosinophil count (3.4%).

On the next day, the worm remained in the same location (Figure 1B) and the patient underwent urgent partial thickness keratectomy and lamellar keratoplasty under local anesthesia (Figure 2A). The worm (Figure 2B) was removed completely without rupture of the surrounding capsule. The worm was sent immediately to the microbiology laboratory of our institution to take a live video of the moving worm for identification of the species.

A partial thickness graft was not performed because of the following two reasons: 1) severe inflammation of the borders of the resected tissue, which might be deleterious for the graft survival, and 2) sufficient residual corneal bed thickness (373–420 µm) for the spontaneous healing (Figure 2C). To suppress inflammation and to facilitate spontaneous healing of cornea, we prescribed moxifloxacin ophthalmic drops every 6 hours and Lotefsoft® (lotepredonol 0.5% suspension; Poen Laboratory, Bermudez, Argentina) every 8 hours. In addition,

* Address correspondence to Yukifumi Nawa, Tropical Diseases Research Centre, Faculty of Medicine, Khon Kaen University, Khon Kaen 40002, Thailand. E-mail: yukinawa@kku.ac.th

FIGURE 1. A *Gnathostoma* third-stage larva encysted in the corneal stroma. Biomicroscopic observation on the first (A) and second (B) day of visit to our clinic. Note that the larva is remaining in the same position in the cornea. Anterior segment tomography revealed that the larva is in the corneal stroma of the left eye of the patient. Stereoscopic view of the removed larva is shown (C). This figure appears in color at www.ajtmh.org.

an oral cycle of 400 mg of albendazole every 12 hours was given for 10 days for systemic prophylaxis.

Photographs and videos of the worm were studied at the Microbiology and Molecular Biology, Centro Medico Docente La Trinidad, Caracas, and the pictures of the parasite were sent to Dr. Kittisak Sawanyawisuth, Department of Medicine, Faculty of Medicine, Khon Kaen University, Thailand, for morphological identification of the parasite. As shown in Figure 3, the parasite has a distinct head bulb equipped with four rows of single-pointed hooklets with an oblong base. The number of hooklets on each row was > 40. The cylindrical body was covered with more than 200 rows of transverse single-pointed spines, of which size and number gradually diminished toward the distal end of the worm. From those characteristics, the parasite was identified as the advanced third-stage larva of *G. binucleatum*.

In the follow-up examinations, the BCVA of the left eye of the patient recovered to 20/40. A low maintenance dose of steroid (Lotesoft®) was prescribed for residual astigmatism of five diopters of his left eye. Although we had scheduled phacemulsification of the cataract of his right eye on September 2016, he was lost from our follow-up. When the patient came back on February 2017, he had stopped the steroid drops and has BCVA 20/80 of his left eye with a central haze, corneal endothelitis, and cataract.

The patient was admitted to the hospital on February 14, 2017 because of high fever, confusion with left hemiparesis, and hypoalgesia. Abdominal palpation revealed hepatosplenomegaly. Laboratory data on admission revealed leukocytosis ($21,410/\text{mm}^3$) with moderate eosinophilia (11.5%). One week later, white cell count elevated up to $28,000/\mu\text{L}$ with marked eosinophilia of 45%. Mild increase of transaminases was recognized. The lumbar puncture showed normal opening pressure with clear cerebrospinal fluid (CSF).

Biochemical analysis of CSF was normal, but cytology revealed eosinophilic pleocytosis. His electroencephalogram was normal. Computed tomography and gadolinium-enhanced magnetic resonance imaging (MRI) did not reveal the presence of any structural lesions in the central nervous system. One more week later, the patient still had leukocytosis ($18,500/\text{mm}^3$) with eosinophilia (25%). These findings strongly suggest possible eosinophilic meningitis due to migration of *Gnathostoma* larva. Further workup revealed an abdominal aortic aneurism with mural thrombosis and a upper left renal tumor on abdominal ultrasound. We were unable to follow this patient any further.

DISCUSSION

Gnathostomiasis is an emerging fish-borne zoonosis in Latin America, with reported prevalence in Mexico and Ecuador since the 1970s.^{1,2} In addition, few sporadic indigenous gnathostomiasis cases have been reported from several South American countries¹⁶ such as Brazil,^{4,5} Peru,⁶ Argentina,¹⁷ and Colombia.¹⁸ Nevertheless, not much attention has been paid for gnathostomiasis in Venezuela, until recent report of an indigenous case of cutaneous gnathostomiasis in a 25-year-old man who went to Apure State for game fishing and consumed a raw freshwater fish.¹⁹ Similar to the present case, the first gnathostomiasis case in Colombia¹⁸ was a 63-year-old male international traveler with a recent history of travel to the United States. Game fishing, especially in angling spots in United States, seems to be an important risk factor for gnathostomiasis.

In terms of clinical manifestation, skin lesions such as serpiginous eruption or nodular migratory eosinophilic panniculitis are the most common symptom of gnathostomiasis.¹ Ocular involvement is rather rare, but still more than 80 cases have been reported sporadically, mostly from the endemic

FIGURE 2. Extirpation of the *Gnathostoma* larva by lamellar keratoplasty. Biomicroscopic view of the corneal stroma shortly after lamellar keratoplasty (A), a live *Gnathostoma* larva after surgical removal (B), and corneal topography (C) 24 hours (left) and 6 months (right) after lamellar keratoplasty showing good recovery of the cornea. This figure appears in color at www.ajtmh.org.

areas^{11,12} and the present case was listed as the 83rd case.¹² In the present study, the patient developed eosinophilic meningitis after surgical removal of the worm from his left eye, suggesting infection with multiple larvae. Infection with multiple larvae is rare but there are some cases in highly endemic area such as Thailand.²⁰

Human infection with *Gnathostoma* larvae occurs mainly by ingesting raw or undercooked fish.¹ In the present study, however, the patient has been to Texas for a holiday fishing and swimming, but declared not having consumed raw fish dishes. Instead, he drank unfiltered water of the rivers and lakes almost every day before developing cutaneous and ocular symptoms while he was still there. He did not do such behavior while he was in Venezuela. *Gnathostoma* infections via unfiltered drinking water contaminated with *Cyclops* carrying *Gnathostoma* larvae have been reported.^{21,22}

The *Gnathostoma* worm removed from his left eye was identified morphologically as a third-stage larva of *G. binucleatum*. Although it remains uncertain whether *G. binucleatum* is present in Texas, this species is widely distributed in Mexico and several countries in South America,²³ and it is the only proven species to

cause human gnathostomiasis in the Americas.^{1,2,16} Thus, it is not surprising that this species is in fact endemic in southern parts of United States where many famous fishing game spots are present. Epidemiological surveys for the prevalence of *G. binucleatum* in freshwater fish in southern United States are urgently necessary to prevent human infections.

In addition to the ocular lesion in his left eye, our patient suffered a stroke with left hemiparesis and hypoalgesia associated with hyper eosinophilia (45%) at about 7 months after the diagnosis of ocular gnathostomiasis. Since his CSF examination, data were within normal ranges except for eosinophilic pleocytosis, and radio-imaging with CT and MRI did not reveal any obvious lesions in brain parenchyma; eosinophilic meningitis due to migration of larval *Gnathostoma* was highly likely present in this case. Unfortunately, we were unable to follow this patient any further because his systemic condition turned serious and required extensive care. In gnathostomiasis, definite diagnosis by direct detection of pathogen is difficult and ocular gnathostomiasis like this case is rather exceptional because almost all ocular cases were diagnosed by morphological identification of surgically

FIGURE 3. Closed-up view of *Gnathostoma* larva showing characteristic features of the four rows of hooklets on the head bulb and the cuticular spines covering the body surface. This figure appears in color at www.ajtmh.org.

removed worms. In general, apart from ocular case, most of the gnathostomiasis cases have been diagnosed by the combination of clinical features and immunodiagnosis, although some cautions are required for the identification of causative species.²⁴ Because involvement of the central nervous system is rare but sometimes fatal,¹³ specific antibody detection in CSF and serum would be helpful for differential diagnosis of eosinophilic meningitis or cerebral hemorrhage with eosinophilia.^{1,13}

In conclusion, although gnathostomiasis is not a common parasitic disease in Venezuela, this case together with the recent report of indigenous cutaneous gnathostomiasis in this country raises an alert for clinicians to pay attention on this disease in differential diagnosis. A recent ingestion of raw fish dishes or drinking unfiltered water highlights the importance of considering infection with *Gnathostoma* in the differential diagnosis of related pathology.

Received June 11, 2018. Accepted for publication July 4, 2018.

Published online August 20, 2018.

Acknowledgments: We thank Kittisak Sawanyawisuth, Department of Medicine, Faculty of Medicine, Khon Kaen University, Thailand, for the identification of *Gnathostoma* species.

Authors' addresses: Maria Alejandra Benavides and Maria Belisa Baldo, Cornea Clinic, Ophthalmology Service, Centro Medico Docente La Trinidad, Caracas, Venezuela, E-mails: mabenavides@

me.com and mbbaldo@gmail.com. Shachar Tauber, Ophthalmic Research and Telemedicine Section, Ophthalmology and Optometry Mercy Clinic, Caracas, Venezuela, E-mail: shachar.tauber@mercy.net. Sandra Fernandez Figueiras, Sección de Microbiología, Laboratorio de Microbiología y Biología Molecular, Centro Medico Docente La Trinidad, Caracas, Venezuela, E-mail: sandra_fernandez_inhrr@yahoo.com. Renzo Nino Incani, Department of Parasitology, Faculty of Health Sciences, Universidad de Carabobo, Valencia, Venezuela, E-mail: rmncani@gmail.com. Yukifumi Nawa, Tropical Diseases Research Center, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand, E-mail: yukinawa@kku.ac.th.

REFERENCES

- Nawa Y, Maleewong W, Intapan PM, Díaz-Camacho SP, 2015. *Gnathostoma*, Chapter 21. Xiao L, Ryan U, Feng Y, eds. *Biology of Food-Borne Diseases*. Boca Raton, London, New York: CRC Press, Taylor & Francis, 405–426.
- Waikagul J, Diaz Camacho SP, 2007. Gnathostomiasis. Murrell KD, Fried B, eds. *World Class Parasites, Vol. 11, Food-Borne Parasitic Zoonoses: Fish and Plant-Borne Parasites*. New York, NY: Springer, 235–261.
- Jeremiah CJ, Harangozo CS, Fuller AJ, 2011. Gnathostomiasis in remote northern Western Australia: the first confirmed cases acquired in Australia. *Med J Aust* 195: 42–44.
- de Sousa Vargas TJ, Kahler S, Dib C, Cavaliere MB, Jeunon-Sousa MA, 2012. Autochthonous gnathostomiasis, Brazil. *Emerg Infect Dis* 18: 2087–2089.
- Chaves CM, Chaves C, Zoroquiain P, Belfort R Jr., Burnier MN Jr., 2016. Ocular gnathostomiasis in Brazil: a case report. *Ocul Oncol Pathol* 2: 194–196.
- Maco V, Bravo L, Marcos LA, 2016. Recurrent abdominal panniculitis in a Peruvian man. *Int J Dermatol* 55: 1057–1059.
- Diaz JH, 2015. Gnathostomiasis: an emerging infection of raw fish consumers in *Gnathostoma* nematode-endemic and non-endemic countries. *J Travel Med* 22: 318–324.
- Herman JS, Wall EC, van Tulleken C, Godfrey-Faussett P, Bailey RL, Chiodini PL, 2009. Gnathostomiasis acquired by British tourists in Botswana. *Emerg Infect Dis* 15: 594–597.
- Hale DC, Blumberg L, Frean J, 2003. Case report: gnathostomiasis in two travelers to Zambia. *Am J Trop Med Hyg* 68: 707–709.
- Otranto D, Eberhard ML, 2011. Zoonotic helminths affecting the human eye. *Parasit Vectors* 4: 41.
- Nawa Y, Katchanov J, Yoshikawa M, Rojekkittikhun W, Dekumyoy P, Kusolusuk T, Wattanakulpanich D, 2010. Ocular gnathostomiasis: a comprehensive review. *J Trop Med Parasitol* 33: 77–86.
- Nawa Y, Yoshikawa M, Sawanyawisuth K, Chotmongkol V, Figueiras SF, Benavides M, Diaz-Camacho SP, 2017. Ocular gnathostomiasis—update of earlier survey. *Am J Trop Med Hyg* 97: 1232–1234.
- Katchanov J, Sawanyawisuth K, Chotmongkol V, Nawa Y, 2011. Neurognathostomiasis, a neglected parasitosis of the central nervous system. *Emerg Infect Dis* 17: 1174–1180.
- Cordero-Moreno R, 1973. Etiologic factors in tropical eye diseases. *Am J Ophthalmol* 75: 349–364.
- Convit J, Schuler H, Borges R, Olivero V, Domínguez-Vázquez A, Frontado H, Grillet ME, 2013. Interruption of *Onchocerca volvulus* transmission in northern Venezuela. *Parasit Vectors* 6: 289.
- Eiras JC, Pavanelli GC, Takemoto RM, Nawa Y, 2017. Fish-borne nematodiasis in South America: neglected emerging diseases. *J Helminthol* Oct 25: 1–6. doi: 10.1017/S0022149X17001006. [Epub ahead of print].
- Kaminsky CA, De Kaminsky AR, Costantini SE, Abulafia J, 1989. Eosinophilic migratory nodular panniculitis (human gnathostomiasis) [in Spanish]. *Med Cutan Ibero Lat Am* 17: 158–162.
- Jurado LF, Palacios DM, López R, Baldión M, Matijacevic E, 2015. Gnathostomiasis cutánea, primer caso confirmado en Colombia. *Biomedica* 35: 462–470.
- Guinand PP, 2017. Gnathostomiasis at the Venezuelan plains: first case reported. *J Am Acad Dermatol* 76: AB147.

20. Daengsvang S, 1980. *A Monograph on the Genus Gnathostoma and gnathostomiasis in Thailand*. Tokyo, Japan: Southeast Asian Medical Information Center (SEAMIC), International Medical Foundation of Japan.
21. Subhedar V, Nandedkar S, Jain M, Bajpai T, 2014. Gnathostomiasis: a rare case of cutaneous creeping eruptions. *Indian J Dermatopathol Diagn Dermatol* 1: 32–34.
22. Pal M, Seid H, Giro B, Wakjira B, Abdo J, 2013. Gnathostomiasis—an emerging nematodal zoonotic disease. *Int J Livest Res* 3: 12–17.
23. Bertoni-Ruiz F, Lamothe Argumedo MR, García-Prieto L, Osorio-Sarabia D, León-Régagnon V, 2011. Systematics of the genus *Gnathostoma* (Nematoda: Gnathostomatidae) in the Americas. *Rev Mex Biodivers* 82: 453–464.
24. Neumayr A et al., 2016. Cross-reactivity pattern of Asian and American human gnathostomiasis in western blot assays using crude antigens prepared from *Gnathostoma spinigerum* and *Gnathostoma binucleatum* third-stage larvae. *Am J Trop Med Hyg* 95: 413–416.