Case Report: Human Pulmonary Infection by the Zoonotic *Metastrongylus salmi* Nematode. The First Reported Case in the Americas

Manuel Calvopina,^{1*} Henry Caballero,² Tatsushi Morita,³ and Masataka Korenaga⁴

¹Centro de Biomedicina, Carrera de Medicina, Universidad Central del Ecuador, Quito, Ecuador; ²Servicio de Terapia Intensiva, Hospital Oncológico Sociedad de Lucha Contra el Cáncer (SOLCA), Quito, Ecuador; ³Laboratory of Veterinary Parasitology, Nippon Veterinary and Life Science University, Musashino, Japan; ⁴Department of Parasitology, Kochi Medical School, Kochi University, Kochi, Japan

Abstract. Pulmonary metastrongylosis, a zoonotic disease found primarily in pigs, is caused by eight different species of the cosmopolitan nematode *Metastrongylus* genus. To date, only four human cases have been reported, all from Europe. Herein, a severe case of pulmonary infection caused by *Metastrongylus salmi* in an Ecuadorian man, with successful treatment with ivermectin, is described.

INTRODUCTION

Metastrongylus species (lungworms) are parasitic nematodes of the respiratory tract, where both domestic and wild pigs, and peccaries are found with highly prevalent infections.^{1–4} Human infections rarely occur, with only four cases to date described in the literature. These human cases, reported from Europe in the years of 1845, 1855, 1888, and 1956, were caused by *Metastrongylus elongatus*.^{1,5} The clinical symptoms of human infection are unknown, as they were not described in the previous reported cases. In pigs, an infection produces pneumonitis and bronchitis, which may be fatal in young animals, and dead worms may produce whitish nodular patches in the lungs.¹ An infection is acquired either by the ingestion of the infective third-stage larvae (L3) found in earthworms or after they accidentally escape from these annelids.¹ The *Metastrongylus* genus, comprising eight different species: *Metastrongylus apri* or *M. elongatus*, *Metastrongylus salmi*, *Metastrongylus pudendotectus*, *Metastrongylus confusus*, *Metastrongylus asymmetricus*, *Metastrongylus madagascariensis*, *Metastrongylus pulmonalis*, and *Metastrongylus tschicauricus*, are distributed worldwide.^{6,7} They usually present as mixed infections as reported in Florida, where feral swine were infected with *M. apri*, *M. salmi*, and *M. pudendotectus* with a prevalence of 94%, 76%, and 64%, respectively.³ In Ecuador, *M. salmi* has been reported infecting *Tayassu pecari* from the Amazon region.⁴ It was also found in domestic pigs from the province of Pichincha in the Andes region,⁸ as well as from the province of El Oro in the Pacific Coast region.^{9,10} For the treatment of pigs infected by *Metastrongylus* spp., the following drugs are recommended: ivermectin, doramectin, moxidectin, fenbendazole, or levamisole.¹¹

Reported here is the first human case of pulmonary metastrongylosis in Ecuador and the Americas, diagnosed by direct and microscopic observation of adult worms and eggs in bloody sputum, identified as *M. salmi*, and its response to ivermectin treatment.

CASE REPORT

A 63-year-old male, a resident of Puyo-Pastaza Province in the Amazon region, was admitted to the SOLCA hospital in Quito, where a year ago he was diagnosed with intestinal

Hodgkin's lymphoma (Burkitt's lymphoma) and received chemotherapy. Having been recently diagnosed with recurrent lymphoma because of the thickening of bowel loops shown in computed tomography (CT) scan, he was transferred from the Shell Hospital, arriving with fever and diarrhea. On hospital admission, he was febrile (38.4°C), malnourished, with oral herpes, but with no palpable lymphadenopathy. Pulmonary and cardiac auscultation were normal. Standard chest X-ray was reported as being normal. Edema of the lower limbs was present. He was experiencing six bowel movements daily with the stool characterized as liquid, abundant, and greenish in color. During this period, he received antibiotics (metronidazole and ciprofloxacin), upon which the fever and diarrhea subsided. The laboratory results showed a leukocytes count of 11,600/μL with 87% neutrophils and 13% lymphocytes, 180,000 platelets/μL, a hemoglobin of 13.6 g/L, a hematocrit value of 45.9%, and an erythrocyte sedimentation rate of 24/60. Stool examination was negative for pathogenic parasites. Screening for human immunodeficiency virus antigen and hepatitis B (by HbS antigen) were both negative.

Six days after admission, the patient developed a productive cough with a bloody thick sputum, fatigue, chest pain, and progressive dyspnea. Sputum samples were examined. Macroscopically, dozens of worms were seen; filiform in shape, brownish in color, measuring from 10 to 30 mm in length (Figure 1). Several female and male worm specimens were clarified in lactophenol solution and identified as to the genus and species by utilizing documented morphological characteristics.^{2,6,7} With the females, measuring from 15 to 30 mm, the caudal end was a finger-like tail, with the vulva situated just anterior to the anus, and several eggs in their uteri. For the males, measuring from 10 to 18 mm, the bursa copulatrix was relatively small with doubled dorsal rays; the spicule measured 1,940 μm long and the gubernaculum was 50 μm long (Figure 2). Furthermore, a head of a female was processed for scanning electron microscopic observation with JSM-6380LV (JEOL, Tokyo, Japan) showing a rudimentary buccal cavity and a mouth surrounded by two lateral trilobed lips (Figure 3). Thick-shelled, hyaline eggs were also observed microscopically in the sputum, measuring 45 to 55 by 30 to 40 μm. They were all unembryonated, showing different shapes; some were round and others were spherical. On the basis of these morphological characteristics, the worms were identified as *M. salmi* Geddoelst 1923. Extraction of genomic DNA for molecular phylogenetic analysis was unsuccessful, probably because the specimens had been fixed in formalin. Sputum samples were also examined for pathogenic bacteria,

*Address correspondence to Manuel Calvopina, Centro de Biomedicina, Universidad Central del Ecuador, Iquique N14-121 y Sodiro, Quito, Ecuador. E-mail: manuelcalvopina@gmail.com

FIGURE 1. Adult female and male *Metastrongylus salmi* worms observed in a sample of bloody and dense sputum of our patient.

Paragonimus spp., *Mycobacterium*, and fungus but with negative results. At this time, an X-ray image showed several and bilateral bronchopneumonic shadows with bilateral pleural effusion and effacement of costophrenic and cardiophrenic angles. The shadows were mainly in basal regions and pleural effusions were confirmed by CT scan. Antihelminthic therapy was initiated with ivermectin, 400 µg/kg/day, for two consecutive days. Three days later, all pulmonary symptoms had disappeared and no worms/eggs were seen in sputum specimens. Unfortunately, 7 days later, the patient expired, after having developed septic shock with neurological complications probably due to his metastatic lymphoma and/or bacterial or mycotic nosocomial infection. The adult worms are maintained in the Centro de Biomedicina, Quito, Ecuador, for future studies.

DISCUSSION

The present case demonstrated that *M. salmi* can infect humans; whereas the previous cases were by *M. elongatus*. Also, a pulmonary infection can produce severe pulmonary

FIGURE 2. Bursa of a *Metastrongylus salmi* male showing doubled dorsal rays, spicules, and gubernaculum. Scale = 50 µm.

FIGURE 3. Picture of scanning electron microscope showing the lateral trilobed lips characteristic of *Metastrongylus* spp. Scale = 10 µm.

distress with bilateral pleural effusion, cough with bloody dense sputum, fatigue, and progressive dyspnea. This is the first human case diagnosed in the Americas. To date, only four human cases have been published; all four from Europe. The reported cases involved a 6-year-old boy, an adult,¹² and two from Romania; a pork vendor and a male adult.^{5,13} The first three cases were reported more than 128 years ago and the last one, about 60 years ago. Human infection seems to be very rare, probably because the source of infection is by ingestion of earthworms, the intermediate host, carrying the L3 infective larvae or by the mucus secretions of an infected earthworm.¹ Another reason could be *Metastrongylus* adults and eggs can be misdiagnosed as other parasites, which is what initially occurred in our case, when it was diagnosed as *Strongyloides stercoralis*, even those nematodes have different size.

Several veterinary practitioners advocate that the *Metastrongylus* nematode can pose a potential risk for human infection since this genus is distributed worldwide, infecting both wild and domestic swine, with a high prevalence of infection.^{2-4,6,14} Other animals such as sheep, cattle, deer, and other ruminants are less commonly infected.¹ In Ecuador, infection in swine has been reported from the three geographical regions. In the Amazon region, from where our patient originated, *T. pecari* has been shown to have a 30% infection rate with *M. salmi*.⁴ This is the same species that was identified in the patient.

There is no available information regarding drug treatment of human metastrongylosis. For *Metastrongylus* infection in pigs, independent of the species involved, avermectins and benzimidazoles derivatives are recommended.¹¹ Oral ivermectin, when administered to our patient, showed to be very effective; clearing the adult parasites and eggs within 3 days of treatment.

With domestic pigs being raised extensively in periurban and more so in rural areas of developing countries, along with the vast number of wild swine population and the knowledge that most species of earthworms can serve as intermediate host, the occurrence of human cases of metastrongylosis could increase. Finally, we would like to encourage physicians and laboratory technicians to consider the importance of including pulmonary *Metastrongylus* spp.

infection in the differential diagnosis of patients presenting with bloody sputum. This case clearly shows how a parasitological diagnosis and species identification can be easily made by observing their different features under a light microscopy.

Received March 30, 2016. Accepted for publication May 21, 2016.

Published online July 5, 2016.

Authors' addresses: Manuel Calvopina, Centro de Biomedicina, Carrera de Medicina, Universidad Central del Ecuador, Quito, Ecuador, E-mail: smcalvopina@uce.edu.ec. Henry Caballero, Servicio de Terapia Intensiva, Hospital Oncológico Sociedad de Lucha Contra el Cáncer (SOLCA), Quito, Ecuador, E-mail: hcaballero2000@hotmail.com. Tatsushi Morita, Laboratory of Veterinary Parasitology, Nippon Veterinary and Life Science University, Musashino, Japan, E-mail: t-morita@nvlu.ac.jp. Masataka Korenaga, Department of Parasitology, Kochi Medical School, Kochi University, Kochi, Japan, E-mail: korenaga@kochi-u.ac.jp.

REFERENCES

1. Beaver PC, Jung RC, Cupp EW, 1984. *Clinical Parasitology*, 9th edition. Philadelphia, PA: Lea and Febiger, 291–292.
2. Morita T, Haruta K, Shibata-Haruta A, Kanda E, Imai S, Ike K, 2007. Lung worms of wild boars in the western region of Tokyo, Japan. *J Vet Med Sci* 69: 417–420.
3. Forrester DJ, Porter JH, Belden RC, Frankenberger WB, 1982. Lungworms of feral swine in Florida. *J Am Vet Med Assoc* 181: 1278–1280.
4. Amunárriz M, 1984. *Salud y Enfermedad. Patología en la Región amazónica Ecuatoriana*. Navarre, Spain: CICAME, 45–48.
5. Miloshev B, 1956. Case of triple infection with *Metastrongylus elongatus*, *Thaeniarrhynchus saginatus* and *Enterobius vermicularis* [in Bulgarian]. *Suvr Med (Sofia)* 7: 94–97.
6. Gassó D, Rossi L, Mentaberre G, Casas E, Velarde R, Nosal P, Serrano E, Segales J, Fernandez-Llario P, Feliu C, 2014. An identification key for the five most common species of *Metastrongylus*. *Parasitol Res* 119: 3495–3500.
7. Noda R, 1973. A new species of *Metastrongylus* (Nematoda) from a wild boar with remarks on other species. *Bull Univ Osaka Pref Ser. B* 25: 21–29.
8. Teuscher E, Komijn RE, Alvarez R, 1968. Tetramisol en cerdos: ensayos efectuados en el Ecuador con animales naturalmente infestados por *Metastrongylus* y otros nematodos. *Zbl Vet Med Reihe B* 16: 60–66.
9. Monar JP, 2005. *Prevalencia de Metastrongylus en cerdos faenados en el camal municipal del cantón Machala provincia de El Oro (Tesis de pregrado)*. Machala, Ecuador: UTMACH, Unidad Académica de Ciencias Agropecuarias, 1–78.
10. Márquez WH, 2008. *Prevalencia de Metastrongylus en cerdos faenados en el matadero municipal del cantón Pasaje (tesis de pregrado)*. Machala, Ecuador: UTMACH, Unidad Académica de Ciencias Agropecuarias, 1–83.
11. Merck Sharp and Dohme Corp, 2009–2015. *Recommended Treatment for Lungworms*. Kenilworth, NJ: Merck and Co., Inc.
12. Rainey G, 1855. Entozoon found in the larynx. *Trans Pathol Soc London* 6: 370–372.
13. Chatin JCM, 1888. Strongle Paradoxal Chez L'homme. *Bull Acad Med Paris* 52: 482–491.
14. Solaymani-Mohammadi S, Mobedi I, Rezaian M, Massoud J, Mohebbi M, Hooshyar H, Ashrafi K, Rokni MB, 2003. Helminth parasites of the wild boar, *Sus scrofa*, in Luristan province, western Iran and their public health significance. *J Helminthol* 77: 263–267.