Pulmonary Capillariasis Miming Bronchial Carcinoma

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Abstract. Pulmonary capillariasis is a zoonotic disease caused by the cosmopolitan nematode *Capillaria aerophila*, which circulates among wild carnivorous and omnivorous mammals. Only 11 cases have been documented to date. We describe a cryptic case of pulmonary capillariasis in a Serbian woman that resembled a bronchial carcinoma.

INTRODUCTION

Pulmonary capillariasis in humans is a very rare event, with only 11 cases described to date. The etiologic agent, *Capillaria aerophila* (syn. *Euceleus aerophilus*, *Thominx aerophilus*), is a widespread nematode that parasitizes the trachea and mainly the bronchi of carnivorous mammals. The clinical symptoms of human infection are bronchitis, coughing, mucoid or blood-tinged sputum, fever, dyspnea, and eosinophilia. As a general rule, human pulmonary capillariasis is diagnosed by detecting eggs, which are characteristic, in sputum and/or feces. Herein, we describe the first human case of pulmonary capillariasis reported in Serbia, resembling a bronchial carcinoma, which was diagnosed with the support of serology.

CASE REPORT

A 68-year-old woman was admitted to the Institute for Pulmonary Diseases in Serbia with a productive cough with purulent expectorates, fatigue, and anal skin pruritus. One month earlier she had had mild fever (38°C), mild weight loss, and the same signs and symptoms observed on admission. At that time, her doctor diagnosed bronchopneumonia, and she was treated with antibiotics for 7 days (garamycin, 120 mg/d; azitromycine, 500 mg/d; ciprofloxacine, 1 g/d in two separated doses; and cephalor, 1.5 g/d in three doses). She showed no improvement, and on January 10, 2006, she was admitted to the above-mentioned institute. The woman had been living for many years in the countryside of Novi Sad (Serbia). In 1966, she had undergone an operative dilatation of the esophagus, after which she remained in good health.

On hospital admission, she had a body temperature of 37°C, a normal sinus rhythm, a blood pressure of 150/90 of mmHg, and a pulse of 80 beats/min. The leukocyte count was 11,300/mL, there were 48% neutrophils, 21% eosinophils, 26% lymphocytes, 5% monocytes, and 4,900,000 red blood cells/mL, hemoglobin was 138 g/L, hematocrit value was 0.394, there were 215,000 platelets/mL, and the sedimentation rate was 30/60. Antibiotic therapy was begun with azitromycine, 500 mg/d; cyprofloxacine, 1 g/d in two separated injections and the same signs and symptoms observed on admission. At that time, her doctor diagnosed bronchopneumonia, and she was treated with antibiotics for 7 days (garamycin, 120 mg/d; azitromycine, 500 mg/d; ciprofloxacine, 1 g/d in two separated doses; and cephalor, 1.5 g/d in three doses). She showed no improvement, and on January 10, 2006, she was admitted to the above-mentioned institute. The woman had been living for many years in the countryside of Novi Sad (Serbia). In 1966, she had undergone an operative dilatation of the esophagus, after which she remained in good health.

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Because the woman had a productive cough with purulent expectorates, sputum samples were examined (10 times between admission and February 2). A large number of preserved and degranulated eosinophils and Charcot-Leyden crystals were found. Sputum samples stained with Ziehl-Neelsen or cultivated for *Mycobacterium* were consistently negative.

An x-ray image revealed bilateral bronchopneumonic shadows, which were most intense in the right basal region (Figure 1A). The shadows were confirmed with computed tomography (CT) scan, appearing as spotted, partially confluent, nodular, and banding infiltrative lesions of the pulmonary parenchyma. Moreover, lymphadenopathy was detected in the retrocaval space near the tracheal carina with lymph nodes of up to 20 mm in diameter (Figure 1B). The clinical diagnosis was carcinoma in the right lateral bronchi.

In light of the CT scan and x-ray images, two bronchoscopies were performed at an 8-day interval. The first bronchoscopy showed that the larynx, the trachea, and its bifurcations and the left bronchus were normal, whereas on the right side, there was a white, soft tumor that blocked the lower lobe of the bronchus. A biopic specimen was collected. The specimen was necrotic, and it was not possible to identify the cell type or the nature of the inflammation. The Ziehl-Neelsen stain was negative. The second bronchoscopy revealed macro- and micro-tumors similar to the tumor observed with the first bronchoscopy, but many lemon-shaped parasite eggs with numerous eosinophils and Charcot-Leyden crystals were detected in the necrotic detritus. Histologic examination revealed well-preserved non-embryonated eggs, egg shells, and immature eggs with incomplete shells (Figure 2A). The lemon-shaped eggs were 64 × 29 μm in size and showed a double layered shell with radial striations on the outer shell and two polar plugs. No larval stage or adult parasites were found in the sputum, biopsy specimens, or stool. No egg was detected in the sputum or stool. An ultrasound showed that the liver and other abdominal organs were normal. On the basis of the egg morphology and size and the localization of the nematode in the bronchus, the worm was reasonably identified as a female belonging to the species *C. aerophila*.

To confirm the diagnosis, the serum sample was tested by an immunfluorescent antibody test (IFAT) using, as antigens, histologic sections from the trachea of a cat that was naturally and heavily infected with *C. aerophila*. In brief, the tracheal tissue was fixed in Bouin solution (saturated picric acid in water, formaline, and acetic acid, 30:10:2) and embedded in paraffin, according to routine histologic procedure. Sections of 5 μm were mounted on glass slides. The serum was diluted from 1:20 to 1:160, incubated in a moist chamber for 30 min-

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utes, rinsed with phosphate-buffered saline (PBS), and incubated with anti-human IgG fluorescein isothiocyanate (FITC) conjugate (Institute INEP, Belgrade, Serbia); it was rinsed again with PBS, mounted in PBS–glycerin, and examined by a UV microscope (DMLB; Leica, Wetzlar, Germany). The patient serum was positive up to 1:80 dilution. After UV examination, slides were stained with hematoxylin and examined at 100–1,000 magnifications by light microscopy. In the worm sections, the most fluorescent structures were the ovarian tissue and the eggs (Figure 2B). A serum sample from a child infected with *Toxocara* sp. was used as control. No cross-reaction was observed.

On February 3, antihelminthic therapy was started with mebendazole (5 mg/kg/d for 6 days) and albendazole (15 mg/kg/d for 20 days). The eosinophil count slowly decreased. On Day 6 of treatment, the leukocyte count was 8,100/mm$^3$ (58% neutrophils, 12% eosinophils, 26% lymphocytes, and 4% monocytes). On February 17, the woman was discharged from the hospital and was followed as an outpatient until March 28, when the leukocyte count returned to normal.

**DISCUSSION**

*Capillaria aerophila* is a nematode worm of the superfamily Trichinelloidea. Adult male worms are up to 25 mm in length and 62 μm in width; adult females are up to 32 mm in length and 105 μm in width. In natural hosts, adult worms are localized in the mucosa of the trachea and bronchi, where they cause respiratory symptoms in heavily infected animals. Females excrete non-embryonated ova, which are deposited in the lungs, are coughed up, swallowed, and passed in the feces. Under favorable climatic conditions, the larvae develop in the eggs in the soil. The eggs may be ingested by earthworms,
where they hatch, and ingestion of earthworms can result in infection in animals. Infection may also be transmitted directly by the ingestion of embryonated eggs, which may have been the mode of transmission for the case described herein (e.g., consumption of vegetables not sufficiently washed). Once in the host, the larvae migrate to the lungs and invade the mucosa. Although the migration route is not known, it has been speculated that the larvae reach the respiratory tree through the blood and lymphatic vessels.7

Capillaria aerophila shows a cosmopolitan distribution in both domestic mammals (dog and cat) and wild mammals (e.g., wolf, coyote, red fox, arctic fox, raccoon dog, marten, badger, ferret, wild cat, opossum, and hedgehog), with the prevalence differing according to both host species and region.8–12 Ten free-living house cats of Novi Sad city (Serbia) were tested by scraping the tracheal surface; adult worms (both males and females with eggs) of C. aerophila were detected in all the animals. Three of these cats also harbored Aelurostrongylus abstrusus larvae (Dušan Lalošević, unpublished data).

Pulmonary capillariasis in humans has been documented in Russia and the Ukraine (eight cases), Morocco (one case), Iran (one case), and France (one case).1,2,4,13–15 Because a very limited number of human infections have been documented, the incubation period is unknown, although some authors believe that it could be similar to the prepatent period in animals (i.e., 25–40 days).7 With regard to the treatment of human infection, benzimidazole derivatives are generally used to treat nematode infection. In the past, thiabendazole was used, yet because of the side effects, it has been replaced by mebendazole and albendazole, which in this case were shown to be effective.

In the case described, the presence of C. aerophila eggs in the bronchial biopsy suggests that the worm's died in the bronchi, and the tumor-like lesion was the abscess caused by the parasite. The case report of Semenova and Barabashkina16 was characterized by an abundant mucopurulent expectoration rich in C. aerophila eggs.

The increasing number of foxes and of stray dogs and cats living in urban areas could increase the occurrence of pulmonary capillariasis. This case clearly showed how diagnosis is difficult and that misdiagnoses such as pulmonary carcinoma can be made.

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REFERENCES