CHEST

Special Features

Parasites of the Air Passages

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Parasitic infestations affect millions of the world's population. Global immigration and climate change have led to changes in the natural distribution of parasitic diseases far removed from endemic areas. A broad spectrum of helminthic and protozoal parasitic diseases frequently affects the respiratory system. The wide varieties of clinical and radiographic presentations of parasitic diseases make the diagnosis of this entity challenging. Pulmonologists need to become familiar with the epidemiology, clinical presentation, pathophysiologic characteristics, and bronchoscopic findings to provide proper management in a timely fashion. This review provides a comprehensive view of both helminthic and protozoal parasitic diseases that affect the respiratory system, especially the airways. ***CHEST 2014; 145(4):883–895***

Abbreviations: BALF = BAL fluid; DEC = diethylcarbamazine; ELISA = enzyme-linked immunosorbent assay; PAH = pulmonary artery hypertension; TPE = tropical pulmonary eosinophilia

Helminthic and protozoal infestations cause significant morbidity and mortality worldwide. A decline in parasitic infestations has been observed in the past decade as a result of improved socioeconomic conditions and better hygiene practices. However, the rapid urbanization of cities around the world, global warming, international traveling, and increasing numbers of immunocompromised individuals have increased the vulnerability of the world population to parasitic diseases.[1] The diagnosis of parasitic diseases of the respiratory system is challenging because the clinical manifestations and radiologic findings are nonspecific. Thus, a high index of suspicion and detailed interrogation regarding travel history are critical. Most parasitic infestations of the respiratory system either involve the airways or require bronchoscopy for diagnosis. Helminthes can affect the airways during both the larval and the mature adult phases of their life cycle. The larvae can cause airway inflammation (paragonimiasis), whereas migration of the mature adult worms may cause mechanical obstruction of the airways (ascariasis). This article provides a comprehensive review of both helminthic and protozoal infestations, including clinical, radiographic, bronchoscopic, and pathologic manifestations, that may be helpful to pulmonologists in managing this important entity (Table 1).

Manuscript received September 1, 2013; revision accepted December 16, 2013.

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DOI: 10.1378/chest.13-2072

Nematodes

Nematodes, also known as roundworms, have a symmetrical, tube-like body with an anterior mouth and a longitudinal digestive tract.

Ascariasis

Ascaris lumbricoides is one of the most common parasitic infestations, affecting > 1 billion of the world's population and causing > 1,000 deaths annually.[1] *A lumbricoides* is transmitted via the feco-oral route. An Ascaris larva migrates to the lungs through either the lymphatics or the venules of the portal system. Larval ascariasis causes Löffler's syndrome, a concomitance of wheezing, pulmonary infiltrations, and eosinophilia.[2] It can cause alveolar inflammation, necrosis, and hemorrhage. Diagnosis of an ascariasis infestation during its larval phase is difficult. The sputum may show numerous eosinophils; stool examination, however, remains negative for eggs during the larval stage.[3] The diagnosis requires a high degree of suspicion. Occasionally,

the diagnosis can be confirmed by identifying larvae in the sputum. Solitary pulmonary nodules can also develop if the larva dies causing granulomatous inflammation.[4] Adult ascaris has been reported to cause airways obstruction in a child, producing a complete lobar collapse.[5] Mebendazole and albendazole are the most effective agents against ascariasis.

Ancylostomiasis (Hookworm Disease)

The most common hookworms are *Ancylostoma duodenale* and *Necator americanus*. The latter is found in parts of the southern United States. Hookworm larvae enter human hosts via the skin, producing itching and local infection. The larvae are also infective via the oral route.[6] Hookworm infestations involve larval migration through the lungs via the bloodstream, resulting in a hypersensitivity reaction. Patients usually present with transient eosinophilic pneumonia (Löffler's syndrome).[6] If the patient ingests a large number of larvae, he/she may develop a condition known as "Wakana disease," characterized by nausea, vomiting, dyspnea, and eosinophilia. This clinical picture represents a severe hypersensitivity-like reaction to *A duodenale*.[6] Larval migration may also cause alveolar hemorrhage.[7] Similar to ascariasis, the diagnosis of a hookworm infestation during the larvae phase could be difficult to make. CT scanning of the chest may reveal transient, migratory, patchy alveolar infiltrates.[8] Sputum examination may reveal occult blood, eosinophils and, rarely, migrating larvae (Fig 1A).[9] Bronchoscopic examination may reveal airway erythema and high eosinophil counts in BAL fluid (BALF).[10] Patients can become profoundly anemic and malnourished. These manifestations may provide clinical clues to support the diagnosis. The antiparasitic agents for hookworm are mebendazole and albendazole.

Strongyloidiasis

Strongyloides stercoralis is a common roundworm that is endemic throughout the tropics but is found worldwide in all climates. Infective filariform larvae can penetrate the skin and infect human hosts. The larvae migrate through the soft tissues and enter the lungs via the bloodstream. A majority of roundworms migrate up the bronchial tree to the pharynx and are swallowed, entering the GI tract.[11] The larvae can reenter the circulatory system, returning to the lungs and causing autoinfection.[11] The life cycle of *Strongyloides* can be completed entirely within one host. The term "hyperinfection syndrome" describes the presentation of sepsis from enteric flora, mostly in immunocompromised patients.[12] The hallmarks of hyperinfection are an exacerbation of GI and pulmonary symptoms and the detection of more larvae in the stool and sputum.[13] Common pulmonary symptoms include wheezing, hoarseness, dyspnea, and hemoptysis. A chest radiograph usually demonstrates focal or bilateral interstitial infiltrates. Pleural effusions are present in 40% of patients, and lung abscess is found in 15%.[14] Diffuse alveolar hemorrhage is usually found in patients with disseminated strongyloidiasis. ARDS may result as a reaction to the death of the organisms. Migration of a massive number of larvae through the intestinal wall can result in sepsis, because larvae may convey gram-negative bacteria into the bloodstream.[13]

The diagnosis can be confirmed by the presence of larvae in the stool, duodenal aspirate, sputum, pleural fluid, or BALF or lung biopsy specimens (Figs 1B, 1C).[15] The sensitivity of a stool examination for ova and larvae is 92% when performed on three consecutive samples.[16] An enzyme-linked immunosorbent assay (ELISA) measures IgG responses to the *Strongyloides* antigen. However, false-negative results can occur during acute infection because it takes 4 to 6 weeks to mount the immune response.[17] The ELISA is sensitive but nonspecific because of cross-reactivity with filarial infestations.[15] Oral ivermectin remains the treatment of choice for uncomplicated *Strongyloides* infestation.[13,18]

Syngamosis

Nematoda of the genus *Mammomonogamus* affect the respiratory tract of domestic mammals. Occasionally, however, humans can become infested via the respiratory tract. Most cases of human syngamosis are reported from tropical areas, including South America, the Caribbean, and Southeast Asia.[19] Two hypotheses have been proposed regarding its life cycle. One is that humans become infested via the ingestion of food or water contaminated with larvae or embryonated eggs. The larvae complete the life cycle in the pulmonary system, and the adult worms migrate to the central airways as the preferred site of infection.[20] An alternative hypothesis is that patients are infected by the adult worms present in contaminated food or water. This mode of transmission is supported by its short incubation period (6-11 days).[21] The diagnosis requires flexible bronchoscopy unless the worms are expelled through vigorous coughing (Fig 1D). The removal of parasites through bronchoscopy is sufficient to improve symptoms. To date, no studies have supported the effectiveness of antihelminthic therapy.[21,22]

Dirofilariasis

Dirofilaria immitis is the filarial nematode that primarily infects dogs. Humans are considered accidental hosts because *D immitis* is unable to mature to an adult form. *D immitis* is transmitted to humans by mosquitoes harboring infective third-stage larvae. The larva travels to the right ventricle and develops into an immature adult worm. It is then swept into the pulmonary