Chapter 11
Parasitic Diseases of the Lung

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Introduction

Parasitic infection can be categorized into helminthic and protozoal infections. Although, there is a decreasing trend of parasitic infection worldwide due to improved socioeconomic conditions and better hygiene practices, the urbanization of the cities around the world, global climate changes, international traveling, and increasing numbers of immunocompromised individuals have expanded the population who is vulnerable to parasitic diseases [1]. The diagnosis of parasitic diseases of the respiratory system is relatively difficult because clinical manifestations and radiologic findings are non-specific. Therefore, high index of suspicion, travel history, and a detailed interrogation of personal hygiene are crucial for diagnosis of parasitic lung diseases. The helminthes can affect respiratory system in different phases of their life cycle. In this chapter, we discuss the clinical manifestations, radiographic, bronchoscopic and pathologic findings, and management of several helminthic and protozoal lung diseases. The term "pneumatodes" has been used to represent the group of parasites that affect airways and lungs. Some of the unique presentations of each parasite are also addressed which may be helpful to pulmonologist in managing these uncommon diseases (Tables 11.1 and 11.2).

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Table 11.1 Key features of protozoal infections of lung

Protozoal parasites	Endemic area	Mode of transmission	Presentation	Bronchoscopic evaluation	Treatment
- Pulmonary amebiasis	Worldwide	Ingestion	Fever, right upper quadrant abdominal pain, lung abscess, hepatobronchial fistula	Surgical lung biopsy shows *E. histolytica* trophozoites	Metronidazole
- Pulmonary leishmaniasis	Asia, Africa, and Central and South America	Sand fly-borne infection	Pneumonitis, pleural effusion, mediastinal lymphadenopathy	Transbronchial needle biopsy of a mediastinal lymph node showing histiocytes containing *L. donovani* organisms.	Pentavalent antimonials, liposomal amphotericin B, and miltefosine
- Pulmonary malaria	Tropical and subtropical areas	Mosquito-borne infection	Fever, cough, acute respiratory distress syndrome (ARDS)	N/A	Intravenous artesunate and artemisinin
- Pulmonary babesiosis	North America	*Ixodes* tick-borne infection	Fever, drenching sweats, acute respiratory distress syndrome (ARDS)	N/A	A combination of atovaquone plus azithromycin or clindamycin plus quinine
- Pulmonary toxoplasmosis	Worldwide	Ingestion	Generalized lymphadenopathy, interstitial pneumonia, diffuse alveolar damage	Histologic examination of lung biopsy can identify *T. gondii* tachyzoites in necrotic area	Pyrimethamine and sulfadiazine

Table 11.2 Main features of parasitic diseases of lung

Parasite	Infective form	Endemic area	Mode of transmission	Pulmonary presentation	Bronchoscopic evaluation	Treatment
Nematodes						
Ascariasis (*Ascaris lumbricoides*)	Eggs and larva	Asia, Africa, and South America	Ingestion	Eosinophilic pneumonia, cough, wheezing, dyspnea	Presence of parasite in the airways	Mebendazole and albendazole
Hookworm (*Ancyclostoma duodenale*) (*Necator americanus*)	Larva	Tropical and subtropical areas	Skin penetration	Eosinophilic pneumonia, cough, wheezing, dyspnea, alveolar hemorrhage	Presence of hookworm in sputum, a marked eosinophil predominance from BAL	Mebendazole and albendazole
Strongyloidiasis (*Strongyloides stercoralis*)	Filariform larvae	Tropical and subtropical areas	Skin penetration	Eosinophilic pneumonia, cough, wheezing, dyspnea, hyperinfection syndrome	Bloody bronchoalveolar lavage (BAL) and presence of parasite from BAL under microscopic examination	Ivermectin and albendazole
Syngamosis (*Mammomonogamus laryngeus*)	Eggs or adult worms	Asia, Africa, and South America	Ingestion	Foreign body-like lesion in bronchus nocturnal cough	Presence of parasite in the airways	Removal via bronchoscopy
Dirofilariasis (*Dirofilaria immitis*)	Larva	Tropical and subtropical areas	Mosquito-borne infection	Cough, chest pain, fever, dyspnea, mild eosinophilia, and lung nodules	Surgical lung biopsy	None (self-limited)

(continued)

Table 11.2 (continued)

Parasite	Infective form	Endemic area	Mode of transmission	Pulmonary presentation	Bronchoscopic evaluation	Treatment
Tropical pulmonary eosinophilia (*Brugia malayi*) (*Wuchereria bancrofti*)	Larva	Tropical and subtropical areas (South and Southeast Asia)	Mosquito-borne infection	Eosinophilic pneumonia, cough, wheezing, dyspnea, restrictive pattern on spirometry, decreased diffusion lung capacity	BAL shows eosinophils more than 50 % of the total cells	Diethylcarbamazine (DEC)
Visceral larva migrans (*Toxocara canis*) (*Toxocara catis*)	Larva	Worldwide	Ingestion	Eosinophilic pneumonia, episodic wheezing	N/A	Diethylcarbamazine (DEC)
Trichinella infection (*Trichinella spiralis*)	Larva	Worldwide	Ingestion	Cough, pulmonary infiltrates, dyspnea is due to respiratory muscles involvement	N/A	Mebendazole
Trematodes						
Schistosomiasis (*Schistosoma* spp)	Cercarial larvae	East Asia, South America, sub-Saharan Africa	Skin penetration	Pulmonary hypertension, and Katayama fever	An eosinophil predominance from BAL in the absence of parasites	Praziquantel
Paragonimiasis (*Paragonimus* spp)	Metacercaria (infective larvae)	Southeast Asia, South America, Africa	Ingestion of infested crustaceans	Fever, cough, hemoptysis, chest pain, and pleural effusion	Bronchial stenosis due to mucosal edema and mucosal nodularity	Praziquantel and triclabendazole

(continued)

Table 11.2 (continued)

Parasite	Infective form	Endemic area	Mode of transmission	Pulmonary presentation	Bronchoscopic evaluation	Treatment
Cestodes						
Hydatid disease (*Echinococcus granulosus*)	Eggs	Worldwide (esp. Middle East)	Ingestion	Chest pain, cough, hemoptysis, pleural lesion, expectoration of cyst contents, and hypersensitivity reaction	Bronchoscopic examination reveals sac-like cyst in the airway	Surgical removal of cysts, followed by mebendazole and albendazole
Mesomycetozoea						
Rhinosporidiosis (*Rhinosporidium seeberi*)	Spores	South Asia	Ingestion of contaminated water	Strawberry-like, nasopharyngeal polyps, epistaxis, nasal congestion	Bronchoscopy revealed pinkish mulberry-like rhinosporidiosis mass in the airway	Therapeutic bronchoscopy and dapsone

Protozoal Parasites

Pulmonary Amebiasis

Entamoeba histolytica amebiasis occurs worldwide. Human becomes infected via feco-oral route by ingestion of mature *E. histolytica* cyst. Trophozoites invade the intestinal mucosa and enter the bloodstream which results in systemic infection. Invasive amebiasis is an emerging parasitic disease in human immunodeficiency virus (HIV)-infected patients [2]. Pleuropulmonary amebiasis occurs mainly by local extension from the amoebic liver abscess. Patients usually present with fever, right upper quadrant abdominal pain, chest pain, and cough. Lung abscess, hepatobronchial fistula, and pyopneumothorax can occur as complications from pleuropulmonary amebiasis. The radiographic findings are elevated right hemidiaphragm, hepatomegaly, and pleural effusion. Live trophozoites of *E. histolytica* can be found in sputum, pleural fluid, or lung biopsy. The presence of amoeba in the stool does not indicate active *E. histolytica* infection because there are two other non-pathologic *Entamoeba* species found in humans. A combination of serologic tests with detection of the parasite by antigen detection by polymerase chain reaction (PCR) is the most preferred approach to diagnosis [3]. Metronidazole is treatment of choice for invasive amoebiasis.

Pulmonary Leishmaniasis

Leishmania donovani is transmitted by various species of the sand fly and causes visceral leishmaniasis [4]. The endemic areas of leishmaniasis are Asia, Africa, and Central and South America. Pulmonary manifestations include pneumonitis, pleural effusion, and mediastinal lymphadenopathy [5]. Leishmania amastigotes can be found in the alveoli and mediastinal lymph node biopsy. Diagnosis of leishmaniasis is confirmed by the presence of the parasites in bone marrow aspirates or by the detection of PCR-amplified Leishmania. The treatment of choices includes pentavalent antimonials and liposomal amphotericin B. Oral miltefosine can also be used against visceral leishmaniasis [5].

Pulmonary Manifestations of Malaria

Plasmodium spp. are intra-erythrocytic protozoa, primarily transmitted by the Anopheles mosquito [6]. *Plasmodium falciparum* can cause cerebral malaria which may potentially fatal. The pulmonary manifestations range from dry cough to

severe and rapidly fatal acute respiratory distress syndrome (ARDS). The gold standard for the diagnosis of malarial infection is microscopic examination of stained thick and thin blood smears. Radiographic findings include lobar consolidation, diffuse interstitial edema, and pleural effusion. Mitochondrial PCR detection of Plasmodium DNA in saliva and urine has been described. However, this technology needs further validation [7]. Intravenous artesunate and parenteral artemisinin derivatives are effective treatments against *P. falciparum* in humans [8].

Pulmonary Babesiosis

Babesiosis is caused by hemoprotozoan parasites, *Babesia microti*, and *B. divergens* [9]. Ixodes scapularis is a vector of babesiosis. The symptoms are fever, drenching sweats, loss of appetite, myalgia, and headache. Splenic infarction and spontaneous splenic rupture have been reported in acute babesiosis [10]. In severe case, ARDS can occur after a few days after initiation of medical therapy. Chest radiography reveals bilateral infiltrates with pulmonary edema. Diagnosis is made by examination of a Giemsa-stained thin blood smear which shows tetrads inside the red blood cells (maltese cross formation). The two major antibiotic regimens consist of a combination of clindamycin and quinine or atovaquone and azithromycin. These regimens are orally given for 7–10 days [11]. Atovaquone plus azithromycin is preferred therapy.

Pulmonary Toxoplasmosis

Toxoplasmosis is caused by the protozoan parasite, *Toxoplasma gondii*. Cats are primary hosts of *T. gondii* [12]. Humans become infected by ingestion of parasitic cyst-contaminated undercooked food. The symptoms of toxoplasmosis are myalgia and generalized lymphadenopathy. Pulmonary toxoplasmosis has been reported with increasing frequency in HIV-infected patients. Pulmonary manifestations include interstitial pneumonia, diffuse alveolar damage, or necrotizing pneumonia [13]. Diagnosis of toxoplasmosis is based on the detection of the bradyzoites of *T. gondii* in body tissue (Fig. 11.1)**.** A real-time PCR-based assay in BAL fluid has been reported in HIV-positive patients. Toxoplasmosis can be treated with a combination of pyrimethamine and sulfadiazine for 3–4 weeks [14].

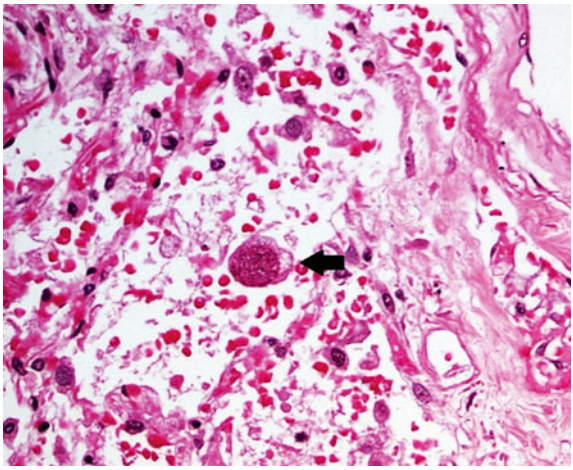

Fig. 11.1 Lung infected with *Toxoplasmosis gondii* (*arrow*) with diffuse alveolar damage (DAD) (H&E stain, ×100) (Courtesy of Danai Khemasuwan, MD, MBA, and Carol Farver, MD)

Helminthic Parasites

Nematodes (Roundworms)

Ascariasis

Ascaris lumbricoides is one of the most common parasitic infestations, affecting over a billion of the world's population causing more than thousand deaths annually [1]. *A. lumbricoides* is transmitted through the feco-oral route. Ascaris larvae migrate to the lungs via either the venules of the portal system or the lymphatic drainage. Larval ascariasis causes Löffler's syndrome, consisting of wheezing, pulmonary infiltrations, and a moderate eosinophilia [15]. The larvae can cause alveolar inflammation, necrosis, and hemorrhage. It is difficult to diagnose ascariasis infestation during its larvae phase. The sputum may show numerous eosinophils. However, stool examination usually yields negative results for eggs during larval stage because there is no reproducing adult ascaris in the host to produce eggs [16]. The diagnosis requires a high degree of suspicion. Occasionally, the diagnosis can be confirmed by identifying larvae in the sputum. Solitary pulmonary nodules (SPN) can also develop if the larva dies and evokes a granulomatous reaction [17]. Adult ascaris has been reported to cause airway obstruction in a child producing a complete lobar collapse [18]. Mechanical removal of ascaris through bronchoscopy is the management of choice. Mebendazole and albendazole are the most effective agents against ascariasis. The prognosis is excellent after eradication of ascariasis with anti-parasitic agents.

Ancylostomiasis (Hookworm Disease)

The common hookworms are *Ancylostoma duodenale* and *Necator americanus*. The latter is found in the parts of southern USA. Hookworm larvae enter human hosts via the skin, producing itching and local infection. *A. duodenale* larvae are also orally infective [19]. Hookworm infestation involves larval migration through the lungs via the bloodstream resulting in a hypersensitivity reaction. Patients usually present with transient eosinophilic pneumonia (Löffler's syndrome) [19]. Patients may ingest a large number of *A. duodenale* larvae and develop a condition known as Wakana disease. It is characterized by nausea, vomiting, dyspnea, cough, throat irritation, hoarseness, and eosinophilia [19]. Larval migration may also cause alveolar hemorrhage [20]. Similar to ascariasis, the diagnosis of a hookworm infestation during the larvae phase could be difficult. Computed tomography (CT) of the chest may reveal transient, migratory, patchy alveolar infiltrates [21]. Sputum examination may reveal occult blood, eosinophils, and, rarely, migrating larvae [22]. Bronchoscopic examination may reveal airway erythema and high eosinophil counts in bronchoalveolar lavage fluid (BALF) [23]. Patients can become profoundly anemic and malnourished. These manifestations may provide clinical clues to support the diagnosis. Anti-parasitic agents for hookworm are mebendazole and albendazole.

Strongyloidiasis

Strongyloides stercoralis is a common roundworm that is endemic throughout the tropical area, but also 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 gastrointestinal tract [24]. The larvae can reenter the circulatory system, returning to the lungs and causing autoinfection [24]. 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 [25]. The hallmarks of hyperinfection are exacerbation of gastrointestinal and pulmonary symptoms, and the detection of large number of larvae in stool and sputum [26]. Common pulmonary symptoms include wheezing, hoarseness, dyspnea, and hemoptysis. Chest X-ray usually demonstrates focal or bilateral interstitial infiltrates. Pleural effusions are present in 40 % of patients, and lung abscess is found in 15 % [27]. Diffuse alveolar hemorrhage is usually found in patients with disseminated strongyloidiasis. Adult respiratory distress syndrome (ARDS) may result as a reaction to the dead larvae. A massive migration of larvae through the intestinal wall can result in sepsis from gram-negative bacteria [26]. *Strongyloides* infestation can be potentially fatal if untreated.

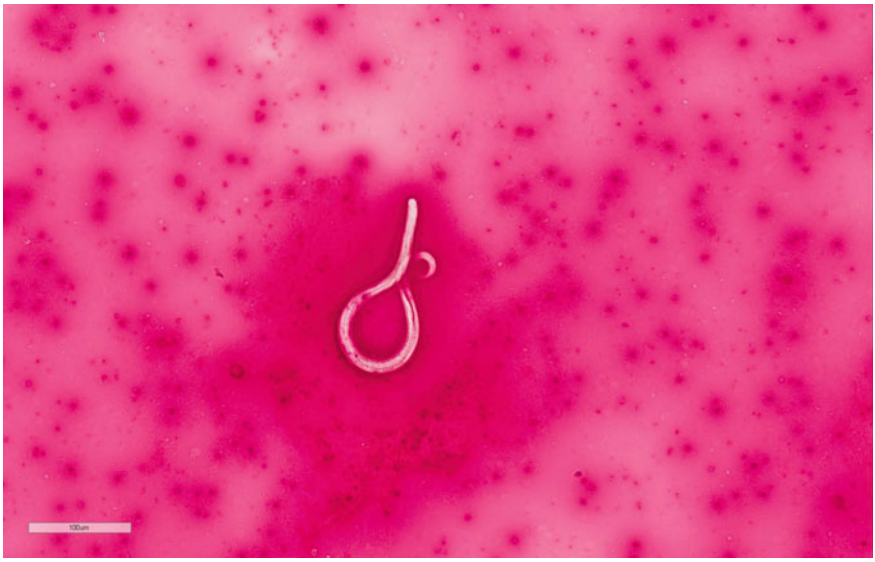

Fig. 11.2 Strongyloides larvae from BAL (H&E stain, 200×) (Courtesy of Danai Khemasuwan, MD, MBA, and Carol Farver, MD)

The diagnosis can be confirmed by the presence of larvae in the stool, duodenal aspirate, sputum, pleural fluid, BAL fluid, or lung biopsies (Figs. 11.2 and 11.3) [28]. The sensitivity of a stool exam for ova and larvae is 92 % when performed on three consecutive samples [29]. Enzyme-linked immunosorbent assay (ELISA)

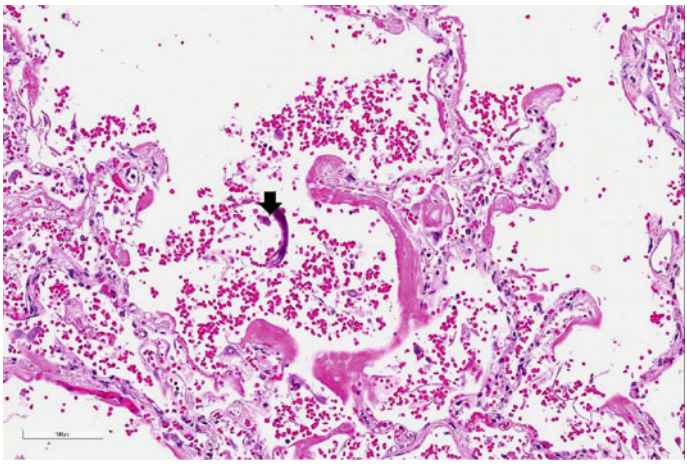

Fig. 11.3 Strongyloides larvae (*arrow*) present in alveolar space in lung with diffuse alveolar damage (DAD); (H&E stain, 400×) (Courtesy of Danai Khemasuwan, MD, MBA, and Carol Farver, MD)

measures IgG responses to the Strongyloides antigen. However, false-negative results can occur during acute infection as it takes 4–6 weeks to mount the immune response [30]. ELISA is sensitive but non-specific due to cross-reactivity with filarial infestations [28]. Oral ivermectin remains the treatment of choice for uncomplicated Strongyloides infection. In case of disseminated disease, a reduction of immunosuppressive therapy is recommended besides treatment with ivermectin [26, 31].

Syngamosis

Nematoda of the genus *Mammomonogamus* affect the respiratory tract of domestic mammals. Human is rarely become infested via respiratory tract. Most cases of human syngamosis are reported from tropical areas, including South America, the Caribbean, and Southeast Asia [32]. The life cycle is not completely known. Two hypotheses have been proposed in regard to 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 [33]. An alternative hypothesis is that the 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) [34]. The diagnosis is usually made by flexible bronchoscopy or when the worms are expelled after vigorous coughing. The removal of parasites through bronchoscopy is sufficient to improve the symptoms. There are no studies to support the effectiveness of antihelminthic drugs. However, they may be considered as an adjunct in the treatment [34, 35].

Dirofilariasis

Dirofilaria immitis is the filarial nematode that primarily infects dogs. Humans are considered accidental hosts since *D. immitis* is not able to mature to an adult form. The endemic areas of dirofilariasis are Southern Europe, Asia, Australia, and America. *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 arteries. The worm dies as a result of the inflammatory response and evokes granuloma formation [36]. A majority of patients with pulmonary dirofilariasis are asymptomatic. However, some patients may develop cough, hemoptysis, chest pain, fever, dyspnea, and mild eosinophilia $\sim$5 %) [37]. A peripheral or a pleural-based SPN is a typical presentation. The nodule may show increased fluoro-deoxy-glucose (FDG) avidity on a positron emission tomography (PET) scan [38, 39] and is often confused with malignancy. Calcification occurs within only 10 % of these nodules. CT may show

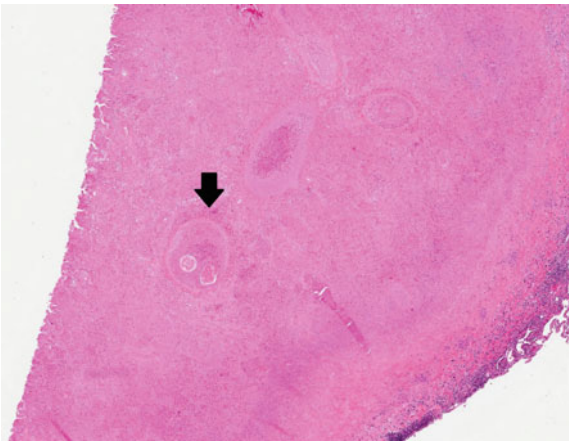

Fig. 11.4 A presence of Dirofilaria worms within pulmonary artery and causing pulmonary infarction (H&E stain, 27×) (Courtesy of Danai Khemasuwan, MD, MBA, and Carol Farver, MD)

a branch of pulmonary artery entering the nodule [40]. Serology has poor specificity due to cross-reactivity with other helminthes. The diagnosis is established by identifying the worm in the excised lung tissue (Figs. 11.4 and 11.5)**.** In patients with high risk of cancer, these lung nodules may be confused with malignancy. Needle biopsy and brushings are usually non-diagnostic due to the small sample size. The condition is self-limiting and does not require any specific treatment [37].

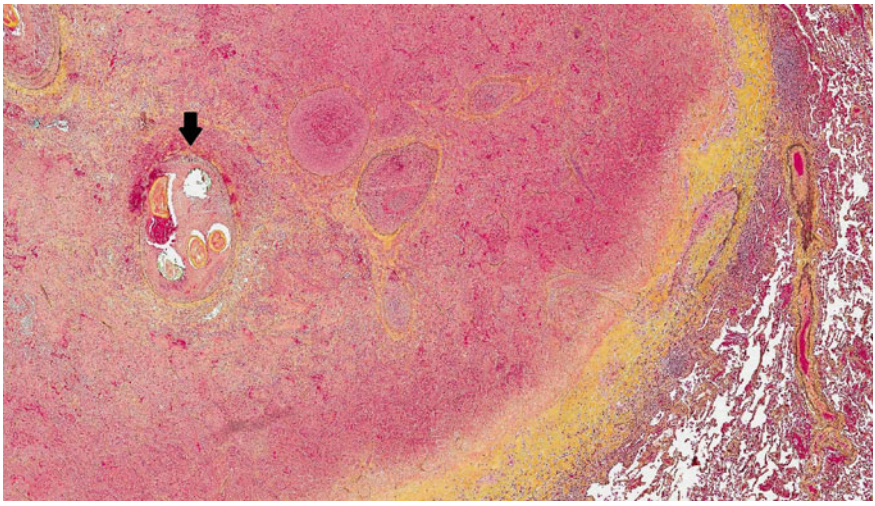

Fig. 11.5 Cross sections of a coiled Dirofilaria worms (*arrow*) within involved artery causing surrounding infarction of lung tissue. Note the smooth cuticle (Movat stain, 30×) (Courtesy of Danai Khemasuwan, MD, MBA, and Carol Farver, MD)

Tropical Pulmonary Eosinophilia

Tropical pulmonary eosinophilia (TPE) is a syndrome of immunologic reaction to microfilaria of the lymphatic-dwelling organisms *Brugia malayi* and *Wuchereria bancrofti*. It is a mosquito-borne infestation. The larvae reside in the lymphatics and develop into mature adult worms. The endemic areas of TPE are in the tropical and subtropical regions of South and Southeast Asia. Travelers from non-endemic areas are at risk of developing TPE because they do not have natural immunity against microfilaria compared with subjects living in endemic area. The microfilariae are released into the circulation and may be trapped in the pulmonary circulation [41]. Trapped microfilariae demonstrate a strong immunogenicity and trigger anti-microfilarial antibodies, resulting in asthma-like symptoms. The hallmark of TPE is a high absolute eosinophil count (5000–80,000/mm^3) [42]. The radiologic features include reticulonodular opacities predominantly in the middle and the lower lung zones, miliary mottling, and predominant hila with increased vascular markings at the bases [43]. Chest CT may demonstrate bronchiectasis, air trapping, calcification, and mediastinal lymphadenopathy [44]. Pulmonary functions indicate a restrictive defect with mild airway obstruction [42]. BAL fluid may contain numerous eosinophils. Occasionally, microfilaria can be identified on brushings or biopsies [45]. The chronic phase of TPE may lead to progressive and irreversible pulmonary fibrosis [41].

The standard treatment for TPE is diethylcarbamazine (DEC). Patients usually show improvement within 3 weeks. However, many patients may be left with a mild form of interstitial lung disease and diffusion impairment on pulmonary function tests [46]. Concomitant use of corticosteroid may have a role in TPE. However, a clinical trial is required to determine the proper dose and duration of DEC therapy.

Toxocariasis

Toxocara canis and *Toxocara cati* are roundworms that primarily affect the dog and cat, respectively. These roundworms are common parasites that cause visceral larva migrans and eosinophilic lung disease in humans. Toxocariasis is transmitted to humans via ingestion of food that is contaminated with parasite eggs. The larvae can migrate throughout the host's body, including the lungs [5]. The pathologic manifestations of visceral larva migrans are due to a hypersensitivity response to the migrating larvae. Visceral larva migrans can present with fever, cough, wheezing, seizures, and anemia. Examination features include general lymph node enlargement, hepatomegaly, and splenomegaly. Leukocytosis and severe eosinophilia are demonstrated in a peripheral smear. Chest X-ray reveals pulmonary infiltrates with hilar and mediastinal lymphadenopathy. Bilateral pleural effusion can occur [47]. Non-cavitating pulmonary nodules have also been reported [48]. The diagnosis of

toxocariasis is established by an ELISA for the larval antigens [49]. The treatment of choice is DEC; however, DEC may exacerbate the inflammatory reactions due to killing of larvae. Thus, it is advised to use corticosteroid along with DEC to ease the inflammatory response [5].

Trichinella Infection

Trichinella spiralis is the most common Trichinella species that infects humans. Trichinella is a food-borne disease from undercooked pork containing larval trichinellae. In addition to the pork meat, wild animals such as bear meat may also contain *T. spiralis* [50]. The larvae migrate and reside in the gastrointestinal tract until they develop into an adult form. Fertilized female worms release first-stage larvae into the bloodstream and the lymphatics [51]. Pulmonary involvement, although uncommon, produces shortness of breath and pulmonary infiltrates. Dyspnea is due to parasitic invasion of the diaphragm and the accessory respiratory muscles [39]. The diagnosis is confirmed by muscle biopsy, which may demonstrate *T. spiralis* larvae. An ELISA using anti-*Trichinella* IgG antibodies can confirm the diagnosis in humans [52]. A 2-week course of mebendazole with analgesics and corticosteroids is the recommended treatment [51].

Trematodes (Flatworms)

Schistosomiasis

Five schistosomes species cause disease in humans: *Haematobium, Mansoni, Japonicum, Intercalatum*, *and Mekongi* [21]. The endemic area for *S. haematobium* and *S. mansoni* are sub-Saharan Africa and South America, and for *S. japonicum*, Far East [21]. Schistosomiasis is the second most common cause of mortality among parasitic infections after malaria worldwide [1]. *S. haematobium* resides in the urinary bladder, while *S. mansoni* and *S. japonicum* reside in the mesenteric beds [5]. Humans become infested through the skin from a contact with fresh water containing *Schistosomal* cercaria (infective larva). After the cercariae have penetrated the skin, they migrate to the lung and the liver. There are several case reports of acute schistosomiasis (Katayama fever) among travelers with history of swimming in Lake Malawi and rafting in sub-Saharan Africa [53].

In acute schistosomiasis, patients present with dyspnea, wheezing, dry cough, abdominal pain, hepatosplenomegaly, myalgia, and eosinophilia [54]. Patients experience shortness of breath due to an immunologic reaction to antigens released by the worms. The level of circulating immune complexes correlates with symptoms and with the intensity of infection.

In chronic schistosomiasis, embolization of the eggs in the portal system causes periportal fibrosis and portal hypertension. Pulmonary involvement can occur as a result of the systemic migration of parasitic eggs from the portal system. The eggs trigger an inflammatory response that leads to pulmonary artery hypertension and subsequent development of cor pulmonale in 2–6 % of patients [55]. Apoptosis of the endothelial cells in the pulmonary vasculature plays a role in the pathogenesis of schistosomal-associated cor pulmonale [56]. Chest X-ray and CT may show diffuse reticulonodular pattern or ground-glass opacities [57]. In the acute phase, BALF may reveal eosinophilia in the absence of parasites. The diagnosis is confirmed by microscopic examination of stool and urine or by rectal biopsy. However, the sensitivity of these tests is low for an early infection. ELISA can be used as a screening test and is confirmed by enzyme-linked immunoelectrotransfer blot. These tests become positive within 2 weeks after the infestation. Schistosomal ova can be found in the lung biopsy specimen.

Acute schistosomiasis is treated with praziquantel. The treatment is repeated within several weeks since it has no antihelminthic effect on the juvenile stages of the parasites [58]. Acute pneumonitis can be observed 2 weeks after the treatment, which is believed to be related to lung embolization of adult worms from the pelvic veins [59]. Patients with schistosomal-associated pulmonary arterial hypertension (PAH) can be treated with PAH-specific therapy along with anti-parasitic medications [59].

Paragonimiasis

Paragonimus species, including *westermani,* cause paragonimiasis that usually involves the lungs. Infection of *paragonimus* species is geographically distributed in Southeast Asia, African, and South America. The mode of transmission is ingestion of the metacercaria (infective larvae) from undercooked crustaceans. Undercooked meat of crab-eating mammals (wild boars and rat) can infect humans as indirect route of transmission [60]. The larvae penetrate the intestinal wall, migrating through the diaphragm and the pleura, into the bronchioles [61]. The eggs are produced by the mature adult worms which are expelled in the sputum or swallowed and passed with the stool. Typically acute symptoms include fever, chest pain, and chronic cough with hemoptysis [62]. Pleural effusion and pneumothorax may be the first manifestation during the migration of the juvenile worms through the pleura. Chest X-ray demonstrates patchy infiltrates, nodular opacities, pleural effusion, and fluid-filled cysts with ring shadows [5]. Chest CT may reveal a band-like opacity abutting the visceral pleura (worm migration tracks), bronchial wall thickening, and centrilobular nodules. Bronchoscopic examination may reveal airway narrowing from mucosal edema [63]. Lung biopsy may show chronic eosinophilic inflammation. The diagnosis is confirmed by the presence of eggs or larvae in the sputum sample or BALF. The pleural fluid, when present, is an exudate with eosinophilia, mostly sterile, without the presence of any organisms

[64]. Eosinophilia and elevated serum IgE levels are observed in more than 80 % of infected patients [5]. Serological tests with ELISA and a direct fluorescent antibody (DFA) are highly sensitive and specific for establishing the diagnosis [65]. Praziquantel and triclabendazole are the treatments of choice with a high cure rate of 90 and 98.5 %, respectively [5].

Cestodes

Echinococcosis

Echinococcus granulosus and *E. multilocularis* are the parasite species that cause hydatid disease in humans. *E. granulosus* is endemic in sheep-herding areas of the Mediterranean, Eastern Europe, the Middle East, and Australia. An estimated 65 million individuals in these areas are infected [1]. Humans become accidental hosts either by direct contact with the primary hosts (usually dogs) or by the ingestion of food contaminated with feces containing parasite eggs [5]. The larvae reach the bloodstream and lymphatic circulation of intestines and migrate to the liver which is the main habitat in human host. Two different presentations of echinococcosis are as follows: (a) cystic hydatidosis and (b) alveolar echinococcosis.

In most cases, lung hydatidosis is a single cyst (72–82 %). An echinococcal infection becomes symptomatic after 5–15 years, secondary to local compression or dysfunction of the affected organ. Pulmonary cysts expand at a slower rate of 1–5 cm per year than liver cysts, and calcification of the cyst is less common [66]. Pulmonary symptoms from the intact cyst include cough, fever, dyspnea, and chest pain. The cyst may rupture into a bronchus and cause hemoptysis and/or expectoration of cystic fluid containing parasitic components (hydatoptysis) which is considered a pathognomonic finding of cyst rupture [67]. The patients may present with hydropneumothorax or empyema. Occasionally, a ruptured cyst can cause an anaphylactic-like reaction and pneumonia [21]. Cystic hydatidosis is diagnosed by chest radiography which demonstrates a well-defined homogenous fluid-filled round opacity. Ruptured cysts may demonstrate an empty cavity, but it is more usual to have characteristic features such as air crescent, pneumocyst, and floating membrane ("water lily sign") (Fig. 11.6) on radiologic examination [68]. The "meniscus" or "crescent" sign and Cumbo's sign (onion peel) have also been described. Thoracic ultrasonography may be useful to confirm the cystic structure, demonstrating the characteristic double-contour (pericyst and parasitic membrane endocyst) of intact cysts. Daughter cysts are also occasionally observed in pulmonary hydatidosis [68]. Bronchoscopic examination reveals sac-like cysts in the airway (Fig. 11.7). Bronchoscopic extraction of the hydatid cyst is possible; however, there is a risk of cyst rupture. Therefore, it should be considered on a case-by-case basis. Serological tests are more sensitive in patients with liver

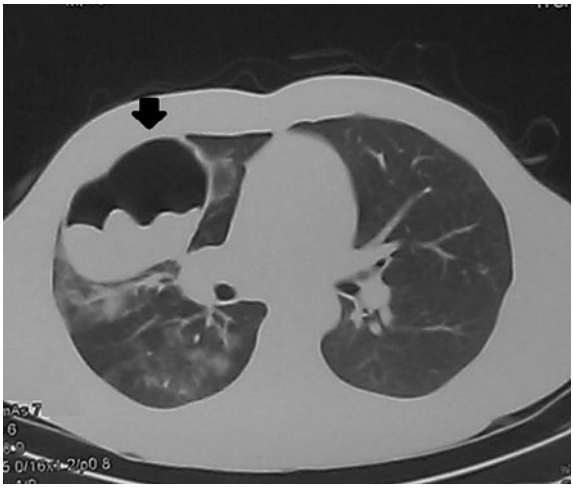

Fig. 11.6 Water lily sign (CT scan obtained at level of right middle lobe shows ruptured hydatid cyst. After rupture and discharge of cyst fluid into pleural cavity, endocyst collapses, sediments, and floats in remaining fluid at bottom of original cyst) (Courtesy by Farid Rashidi, MD)

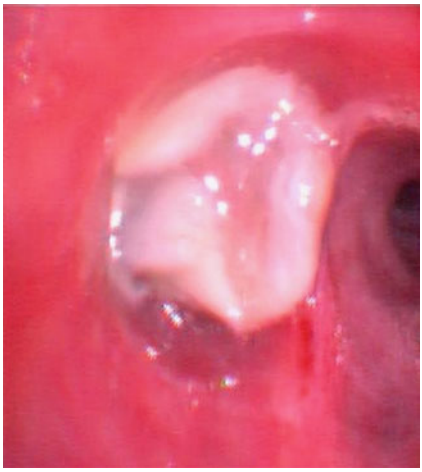

Fig. 11.7 Protruded hydatid cyst from left lower lob (LLL) bronchus (Courtesy by Farid Rashidi, MD)

involvement (80–94 %) than with lung hydatidosis (65 %) [5]. Hydatid cyst rupture can increase sensitivity of serological tests to be more than 90 % [67]. Surgical resection of the cysts is the main treatment of pulmonary hydatidosis and aims to remove the intact hydatid cyst and treat associated parenchymal and bronchial disease. The principle of surgery is to preserve as much as lung tissue as possible. Lung parenchyma around a hydatid cyst is often affected by the lesion and may show chronic congestion, hemorrhage, and interstitial pneumonia. These inflammatory changes in the lung tissue often resolve after surgery [69]. Spillage of hydatid fluid must be avoided to prevent secondary hydatidosis. After complete removal of hydatid cyst, the cavity needs to be irrigated with hypertonic saline solution and it is obliterated with separate purse-string sutures. Surgical specimens may reveal echinococcus cyst fragments (Figs. 11.8 and 11.9).

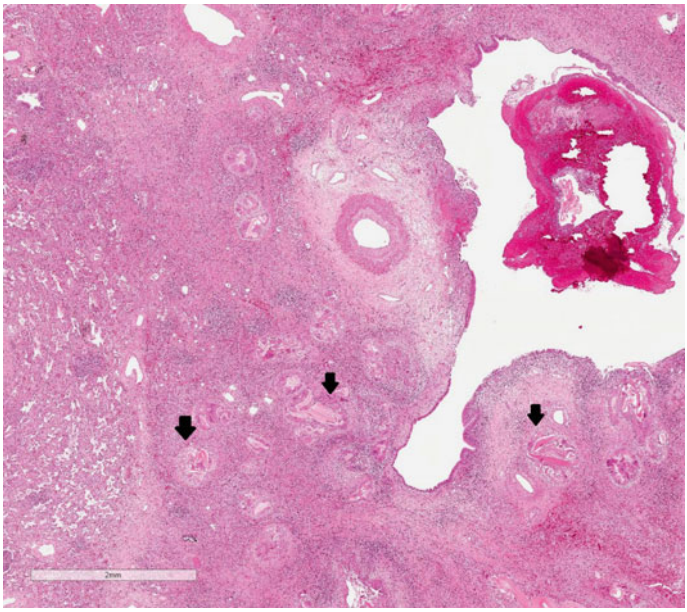

Fig. 11.8 Echinococcus cyst fragments in lung biopsy. The *arrows* highlight the collapsed chitinous layer of a death hydatid cyst. (H&E stain, ×15) (Courtesy of Danai Khemasuwan, MD, MBA, and Carol Farver, MD)

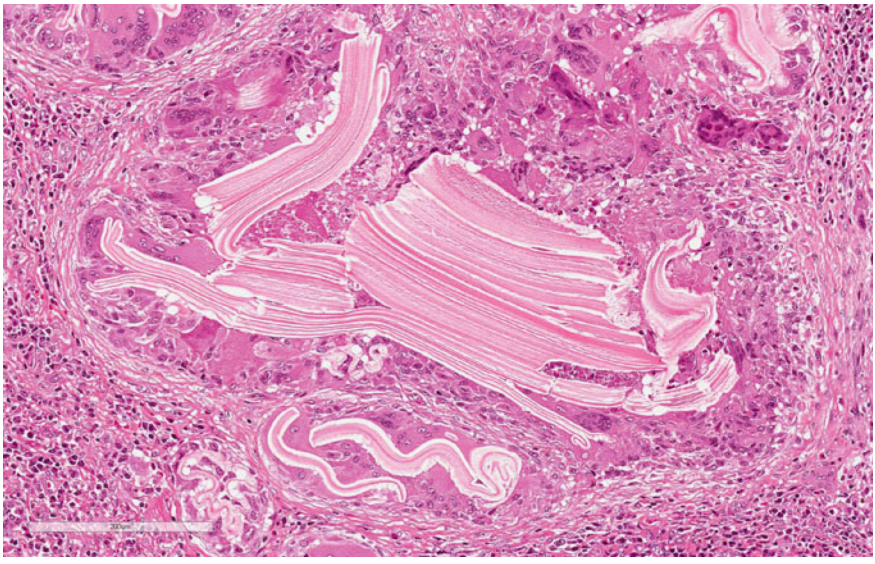

Fig. 11.9 Echinococcus cyst fragments in lung biopsy. The fragmented echinococcus cyst with collapse chitinous layer resides within granulomatous reaction. (H&E stain, ×180) (Courtesy of Danai Khemasuwan, MD, MBA, and Carol Farver, MD)

Medical therapy may have a role in poor surgical candidates and when there is intra-operative spillage of fluid from hydatid cyst. Antihelminthic agents, such as mebendazole or albendazole, have shown only 25–34 % cure rates [70]. The disadvantage of antihelminthic therapy is that it may weaken the cyst wall and increases the risk of spontaneous rupture. In addition, if the parasite dies due to the drug, the cyst membrane may remain within the cavity and lead to secondary complications, including infections [71]. Percutaneous treatment by puncture, aspiration, injection, and re-aspiration (PAIR) has rarely been used in pulmonary cysts because of the risk of anaphylactic shock, pneumothorax, pleural spillage, and bronchopleural fistulae [72].

Pulmonary alveolar echinococcosis is a rare but severe and potentially fatal form of echinococcosis. This form is restricted to the Northern Hemisphere. The liver is the first target for the parasite, with a long, silent incubation period. Pulmonary involvement results from either dissemination or the direct extension of the hepatic echinococcosis with intrathoracic rupture through the diaphragm into the bronchial tree, pleural cavity, or mediastinum. Chest X-ray or CT may aid in the diagnosis. ELISA and indirect hemagglutination assay are available and offer early detection in endemic areas. Radical resection of localized lesions is the only curative treatment yet and is rarely possible in invasive and disseminated disease. Mebendazole and albendazole can be used, but the required treatment duration needs is a minimum of 2 years after the radical surgery [73].

Mesomycetozoea

Rhinosporidiosis

Rhinosporidiosis is a chronic granulomatous infectious disease caused by *Rhinosporidium seeberi*. Recent molecular studies have categorized class Mesomycetozoea at the border of animal–fungal kingdom [74]. The infection is endemic in South Asia [75]. Patients usually presents with polypoidal lesions which are friable and have a high risk of bleeding during resection and high tendency of recurrence. The common sites of presentation are nose and nasopharynx. However, lesions can involve tracheobronchial tree which may lead to partial or complete airway obstruction [76]. There are only three case reports of bronchial involvement which all of them are reported from South Asia. CT is the preferred imaging technique since it offers details of the extension of disease. Bronchoscopic management plays a major role in bronchial involvement of rhinosporidiosis. The mass can completely cauterized with bronchoscopic snare and excised mass can be removed by the basket. Microscopic examination of the resected specimen demonstrated bronchial subepithelium with sporangia filled with small round endospores. The bleeding can be controlled by cauterization. Dapsone is the only

medication found to arrest the maturation of the sporangia, but the lesion may recur after months or years [77]. Thus, follow-up bronchoscopy is recommended to monitor early signs of recurrence.

Conclusion

Global warming, international travel, and immigration has changed the old paradigm of natural distribution of helminthic and protozoal infestations which have been dominant mainly in the tropical and subtropical areas. In addition, the increasing use of immunosuppressive drugs and increasing organ transplantations also result in resurgence of parasitic lung infections worldwide. Therefore, it is important for pulmonologists to recognize the epidemiology, life cycles, clinical presentation, laboratory diagnosis, and treatments of these "pneumatodes" in order to make the proper management in these patients.

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