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Lung Manifestations of Chronic Infections: A Diagnostic Review

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Abstract

Introduction: The human pulmonary system can be affected by various infections, which can enter the lungs during the migration phase of their life cycle, travel there by embolic spread or direct invasion, or be a primary infestation or a feature of more generalized disease. These findings can mimic tuberculosis, sarcoidosis, or metastatic disease. This review aimed to identify radiological manifestations related to chronic bacterial, parasitic and viral infections.

Methods: A systematic review of the medical literature was conducted by searching PubMed up to January 2022 using the MeSH terms and keywords. The references of the retrieved articles were also manually searched. Only original papers in English or Italian discussing latent and post-primary TB imaging and diagnosis, with a focus on TB reactivation in patients receiving biologics, were included. The remaining papers were analyzed based on the relevance of their title or abstract.

Results: A total of 105 papers were identified in a literature review, of which 93 were initially excluded as not relevant based on their title or abstract. After further review, 12 papers were selected for inclusion. Previous research has found that chest radiography has a sensitivity of 73-79% and a specificity of 60-63% for detecting latent tuberculosis (TB) in high-risk populations. Eosinophilic lung diseases are a group of conditions characterized by an accumulation of eosinophils (a type of white blood cell) in the lungs.

Conclusions: There are several conditions that can cause transient pulmonary opacities or increased opacity in the lungs, including bronchiectasis, bronchial asthma, and bronchial granulomatosis. In order to accurately diagnose parasitic infections, it is important for healthcare providers to be familiar with the common parasites in their region.

Keywords: Infection, Pulmonary, Diagnosis, Parasites, Tuberculosis.

Introduction

Parasitic pneumonias and lung involvement caused by protozoa and helminths are common in tropical regions, but they are more rare in the western world and tend to affect immunocompromised individuals. In the United States, Toxoplasma gondii pneumonia is most often seen in people with AIDS. Pulmonary strongyloidiasis, which is caused by the roundworm Strongyloides stercoralis and is associated with chemotherapy or glucocorticoid treatment, is endemic in the south eastern United States [1]. Ascaris and hookworm infestations can also cause eosinophilia and pulmonary infiltrates during the larval migration stage. Eosinophilic lung diseases related to parasitic infestations are more common in tropical regions, while Entamoeba histolytica, Paragonimus, and Dirofilaria lung involvement is less common [2]. Malaria, which is caused by the protozoan parasites of the genus Plasmodium, is primarily transmitted by the bite of an infected female Anopheles mosquito. The four types of malaria are Plasmodium falciparum, Plasmodium malariae, Plasmodium vivax, and Plasmodium ovale. After being transmitted to humans, the parasites infect hepatocytes, entering a stage called the "human liver stage," which takes about 4.5 days for Plasmodium falciparum. Plasmodium vivax, one of the two forms of relapsing malaria that can infect humans, is most prevalent in Southeast Asia and South America, and has the ability to become dormant in the liver ("hypnozoite") and reactivate after months or years, leading to attacks of intraerythrocytic stage malaria even in the absence of mosquito bites. The human liver stage and human intraerythrocytic stage are asexual stages [2,3].

Parasitic diseases are a major cause of morbidity and mortality globally. The human pulmonary system can be affected by various parasites, which can enter the lungs during the migration phase of their life cycle, travel there by embolic spread or direct invasion, or be a primary infestation or a feature of more generalized disease. Hydatidosis, caused by the tapeworm Echinococcus granulosus, is one of the most geographically widespread zoonoses in the world, and treatment remains controversial [4]. Four species of Echinococcus are recognized, but the vast majority of human infestations are caused by E. granulosus. This organism is transmitted to humans in settings where other animals involved in its life cycle (such as dogs or sheep) are present. Humans may accidentally ingest E. granulosus eggs through direct contact with a final host (usually a dog) or by consuming food or fluids contaminated with feces containing the eggs. Its life cycle involves wild canines (definitive hosts) and mainly rodents (intermediate hosts). Domestic dogs and cats may also become infected and transmit the infection to humans [5]. E. multilocularis is more common in colder areas, such as the Arctic and some regions of Asia and western Europe. The primary location of alveolar hydatid cysts is the liver, and primary lung involvement is not described. However, E. multilocularis may initiate the formation of distant metastasis in the lung and other organs. E. vogeli and E. oligarthus are endemic to certain regions. Hydatid disease primarily affects the liver, and one of its potential local complications is transdiaphragmatic thoracic involvement. The lung can also be involved through haematogenous or lymphatic dissemination. The clinical presentation of hydatidosis of the lung depends on whether the cysts are intact or ruptured. Most intact hydatid cysts in pulmonary tissue are either noted as incidental findings or cause symptoms such as cough, dyspnea, or chest pain [6].

Chest radiographs of patients with paragonimiasis, a parasitic disease caused by the lung fluke Paragonimus, may show pleural lesions (such as pleural effusion, pneumothorax, empyema, and pleural thickening) or parenchymal lesions (such as patchy infiltration, nodular opacities, and fluid-filled cysts), or combinations of pleural and parenchymal lesions. On computed tomography (CT), paragonimiasis typically appears as single or multiple nodules in the pleura or lung parenchyma [7]. The clinical and radiological manifestations of paragonimiasis can resemble those of lung cancer, tuberculosis, mesothelioma, or metastatic malignancy, and the disease can mimic lung cancer on fluorodeoxyglucose positron emission tomography of

(FDG-PET). Immunodiagnostic testing can be helpful for diagnosis. Schistosomiasis, caused by blood flukes of the genus Schistosoma, is another parasitic disease. Three species – S. mansoni, S. japonicum, and S. haematobium – are responsible for the most frequent and clinically significant forms of the condition in humans. Once the cercaria (larval stage of the parasite) have penetrated the skin, they enter the bloodstream, migrate to the lung and liver, and eventually reach their target site, the portal vein (in the case of S. mansoni and S. japonicum) or the bladder [8]. Schistosomiasis can cause both acute illness (Katayama fever) and chronic manifestations. In the acute form of the disease, patients may present with shortness of breath, wheezing, and dry cough accompanied by fever, myalgia, headache, hepatosplenomegaly, and marked eosinophilia. In chronic schistosomiasis, embolization of eggs to the portal tracts leads to periportal fibrosis, portal hypertension, and portosystemic anastomoses [7,9]. Pulmonary involvement can occur during this phase, with ectopic migration of ova from the portal system to the pulmonary vascular bed. In the pulmonary vasculature, the eggs trigger a granulomatous response that results in fibrosis, pulmonary hypertension, and subsequent development of cor pulmonale. Vawda et al. described a patient with pulmonary schistosomiasis who presented with bilateral pneumothorax and had honeycombing in the lung parenchyma on CT. Radiology and CT may show small nodular lesions with ill-defined borders or, less commonly, a reticulonodular pattern or areas of diffuse, ground-glass increased opacity bilaterally in cases of pulmonary schistosomiasis. These findings can mimic tuberculosis, sarcoidosis, or metastatic disease [10]. This review aimed to identify radiological manifestations related to chronic bacterial, parasitic and viral infections.

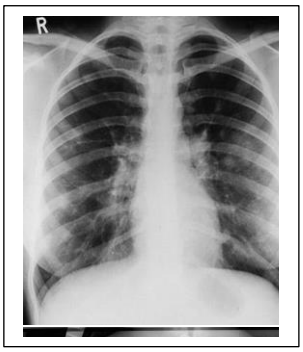
Methods

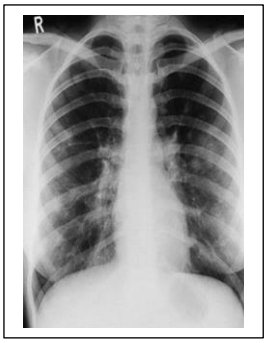
A systematic review of the medical literature was conducted by searching PubMed up to January 2022 using the MeSH terms "chest" or "thoracic" and "radiography" or "radiograph" or "x-rays" and "post primary tuberculosis" or "postprimary tuberculosis" or "post-primary tuberculosis" or "latent tuberculosis" or "tuberculosis reactivation" as keywords. Additional keywords used were "chest" or "thoracic" and "radiography" or "radiograph" or "x-rays" and "tumor necrosis factor-alpha" or "tumor necrosis factor-alpha antagonists" or "biologics." The references of the retrieved articles were also manually searched. Only original papers in English or Italian discussing latent and post-primary TB imaging and diagnosis, with a focus on TB reactivation in patients receiving biologics, were included. The remaining papers were analyzed based on the relevance of their title or abstract.

Results and discussion

A total of 105 papers were identified in a literature review, of which 93 were initially excluded as not relevant based on their title or abstract. After further review, 12 papers were selected for inclusion. Previous research has found that chest radiography has a sensitivity of 73-79% and a specificity of 60-63% for detecting latent tuberculosis (TB) in high-risk populations. Eosinophilic lung diseases are a group of conditions characterized by an accumulation of eosinophils (a type of white blood cell) in the lungs [11]. These diseases can be divided into two categories: those of unknown cause, such as simple pulmonary eosinophilia (SPE), acute eosinophilic pneumonia (AEP), chronic eosinophilic pneumonia (CEP), and idiopathic hypereosinophilic syndrome (IHS); and those of known cause, such as allergic bronchopulmonary aspergillosis (ABPA), bronchocentric granulomatosis (BG), parasitic infection, drug reaction, and eosinophilic vasculitis (allergic angiitis, granulomatosis).

Diagnostic criteria for eosinophilic lung diseases include the presence of asthma, eosinophilia in the blood, a positive skin test for Aspergillus antigens, elevated levels of immunoglobulin E (IgE) in the blood, and changes on chest radiography. A diagnosis can be confirmed by the presence of parasitic eggs in sputum, pleural fluid, or bronchoalveolar lavage fluid [12,13]. The presence of any abnormalities on chest radiography had a sensitivity of 0.97 and a specificity of 0.67 for detecting bacteriologically positive TB. The detection of enlarged lymph nodes in children has a sensitivity of 67% and a specificity of 59% [14]. The use of an additional lateral view of the chest could be





increase sensitivity by 1.8% and specificity by 2.5%. Chest CT has a sensitivity of 80% and a specificity of 89% for detecting active and inactive TB, respectively. Among patients with a high probability of TB infection, CT detected changes consistent with active TB in 32.7% of cases, while chest radiography missed 11 out of 21 cases of TB (1.1% of patients). CT showed changes consistent with latent TB infection in 52.9% of patients, including 8 out of 11 patients with negative TB skin tests and interferon-gamma release assays [15]. In the evaluation of eosinophilic lung diseases, the most important information is obtained from the patient's medical history and physical examination, including a thorough history of drug use.

A white blood cell differential count is also important in this evaluation. Pulmonary function tests and bronchoalveolar lavage (BAL) may also be useful in certain cases. Open lung biopsy may be necessary to confirm certain conditions, but is generally not required for the diagnosis of others. Acute eosinophilic pneumonia (AEP) is a distinct type of eosinophilic lung disease that is more common in women and is characterized by a restrictive pattern on pulmonary function tests and a high percentage of eosinophils in the BAL fluid [16]. Chronic eosinophilic pneumonia and idiopathic hypereosinophilic syndrome may be difficult to distinguish from each other and from other conditions, but CT imaging can help differentiate between them. Differentiation between Churg-Strauss syndrome and chronic eosinophilic pneumonia is important in patients with peripheral eosinophilia and pulmonary abnormalities, and CT imaging can assist in this distinction. Allergic bronchopulmonary aspergillosis is thought to be caused by allergic reactions to the fungus Aspergillus [17]. In order to accurately diagnose parasitic infections, it is important for healthcare providers to be familiar with the common parasites in their region. Lumbricoides was a common cause of pulmonary opacities in Loeffler's patients. Infestation with Clonorchis can cause pulmonary opacities in the form of single or multiple migrating nodules, and high levels of IgE and IgG in the serum and bronchoalveolar lavage (BAL) fluid may be present. In some cases, discontinuing the medication causing drug-induced eosinophilic lung disease can improve symptoms, but corticosteroids may be necessary in severe or persistent cases. Churg-Strauss syndrome can be diagnosed if the patient has asthma, eosinophilia greater than 10% of the white blood cell differential count, neuropathy, migratory or transient pulmonary opacities, paranasal sinus abnormalities, and extravascular eosinophils revealed on biopsy.Mycoplasma is the most common cause of pneumonia in people over the age [18]. This type of pneumonia is characterized by infiltration of the alveoli with neutrophils and mononuclear cells, as well as fibrin and edematous fluid. The first phase of this disease is marked by active hyperemia and engorgement of the arterial blood vessels, with the accumulation of fibrin and exudative cells.

Other radiographic features may include lobar consolidation or pseudo-consolidation, atelectasis, bilateral parahilar peribronchial opacities resembling butterfly wings, a bilobar reticular pattern, pleural and pericardial effusion, and hilar lymphadenopathy. CT scans are more effective than chest radiographs at detecting lobar lesions such as cavitary necrosis, early abscess formation, chest tube placement, fluid loculation, empyema, bronchopleural fistulas, and pericardial effusions [17]. In this disease, the centrilobular opacities may coalesce, resulting in focal areas of bronchopneumonia, and the nodules that heal may leave behind residual granulomata that calcify. Infection of the liver is the primary site of infection in 75% of patients with this disease. Studies have shown that asthma exacerbations are more likely to test positive for viruses than COPD exacerbations, with PCR detecting viruses in 80-85% of children and 60-80% of adults [15,19]. The most common viruses found in these studies were rhinovirus, influenza, RSV, and corona virus, though there was some variation based on season, location, and age group. In

a study of 100 adults with CF, rhinovirus was the most common virus detected (72.5%), followed by metapneumovirus (13.2%) and adenovirus (4.1%). Influenza, RSV, and PIV together accounted for only 10.6% of viral isolates [20,21]. Infants with CF who developed respiratory symptoms due to RSV infection had a reduction in lung function, but there was no significant association between viral infection and accelerated lung function decline in adults with CF. A recent study combining pediatric and adult populations found that 68% of adult and 72% of pediatric exacerbations were virus-positive. In a study of 54 pediatric patients, those with an influenza virus-positive exacerbation had a larger decline in lung function (26%) compared to those with other types of viruses (6%) [23,24].

Conclusions

There are several conditions that can cause transient pulmonary opacities or increased opacity in the lungs, including bronchiectasis, bronchial asthma, and bronchial granulomatosis (BG). BG is a rare disorder characterized by inflammation of the bronchial and bronchiolar epithelium, and can be accompanied by asthma and tissue eosinophilia. Parasitic infections can also cause pulmonary opacities and eosinophilia, such as schistosomiasis, a helminthic infection found in tropical and subtropical regions, can cause granuloma formation and fibrosis in the lungs, leading to obliterative arteriolitis and pulmonary hypertension. Acute schistosomiasis is commonly seen in nonimmune travelers, while chronic and recurrent infection occurs in those living or traveling in endemic areas.

Conflict of interests

The authors declared no conflict of interests.

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