a flulike illness featuring fever, chills, cough, dyspnea, and malaise that lasts for up to 24 hours (e.g., farmer's lung from exposure to thermophilic actinomycetes). Subacute and chronic HP may occur with repeated or prolonged lower-level antigen exposure, which results in chronic dyspnea and cough with eventual progression to pulmonary fibrosis (e.g., pigeon breeder's lung from exposure to avian droppings and other antigens).

The patient with acute HP may be febrile. Diffuse wheezes are common physical findings in acute HP, whereas crackles may be auscultated in chronic HP. Patients with chronic HP may have clubbing. Hypoxemia with exertion may occur in earlier stages of disease, progressing to hypoxemia at rest in chronic fibrotic HP. Pulmonary function tests usually show a restrictive pattern with abnormal gas exchange in subacute and chronic HP, although obstructive or mixed patterns are sometimes seen.

HP is characterized by nonspecific infiltrates in the middle and upper lung fields on chest radiographs, although chest radiographs may be normal in acute disease. CT scanning is more sensitive than chest radiography, revealing ground-glass opacities, centrilobular nodules, and mosaic attenuation and air trapping patterns resulting from airway obstruction. Chronic HP may have architectural distortion with traction bronchiectasis and honeycombing.

Emphysema occurs in some cases of advanced farmer's lung. BAL may demonstrate a lymphocytic alveolitis, with $CD4^+$ T-lymphocyte predominance. Patients with HP may have precipitating antibodies to the offending antigen, but serum precipitins are not sufficiently sensitive or specific for diagnosis, and the specific antigen may not be known or may not be tested for with standard test panels.

Diagnosis and Differential Diagnosis

An appropriate exposure, clinical history, BAL, and HRCT imaging findings can suggest the diagnosis, but a lung biopsy may be necessary for confirmation, especially in subacute and chronic HP. Transbronchial biopsy may be sufficient, but surgical lung biopsy can collect larger samples from different lung regions. The differential diagnosis includes acute viral infection in acute HP; in chronic HP, the differential includes other fibrosing lung diseases such as IPF, NSIP, and sarcoidosis.

Treatment

Clinical improvement often occurs in the hospital setting when patients are isolated from the offending antigen, and relapse may occur after discharge. This pattern of illness can point to the diagnosis of HP. Corticosteroids can relieve symptoms in the acute phase, but their long-term efficacy in chronic forms of the disease is less clear (level 3 evidence). Identification of the cause of HP is important because chronic disease management requires avoidance of exposure to the antigen, which can be financially or psychologically challenging for patients in the setting of occupational, pet, or residential exposures. For advanced HP with fibrosis, lung transplantation may be necessary.

Prognosis

The prognosis for HP varies. Acute HP usually has a good prognosis, but chronic HP can lead to end-stage pulmonary fibrosis and death.

SPECIFIC DISEASES

Pulmonary Langerhans Cell Histiocytosis

Definition and Epidemiology

Pulmonary LCH, formerly called *eosinophilic granuloma,* is a rare disease of young and middle-aged adults. It is characterized by an abnormal infiltration of Langerhans cells, which are dendritic cells, into the lung parenchyma. The disease almost always occurs in smokers.

Pathology

Pulmonary LCH results in the formation of cysts and nodules in the lungs. The accumulation of activated Langerhans cells results in stellate nodular infiltrates around the small airways, with eventual destruction and dilation of the airway walls, resulting in cystic changes in the lung parenchyma. Although a multisystem Langerhans cell disease related to clonal proliferation of Langerhans cells occurs in children, isolated pulmonary LCH in adult smokers does not appear to be a clonal neoplastic disorder.

Smoking may alter local immune signaling, attracting the Langerhans cells to the lungs, or it may cause local proliferation and increased survival of Langerhans cells in the lungs. Biopsy of the lung demonstrates multiple stellate lung nodules that may be cellular or fibrotic, containing Langerhans cells that stain for Cd1a and S100. Electron microscopy may reveal Birbeck granules, distinctive racquet-shaped structures in the Langerhans cells

Clinical Presentation

Patients may be asymptomatic or may exhibit constitutional symptoms, dyspnea on exertion, and cough, possibly with hemoptysis. Spontaneous pneumothorax may also occur. Chest imaging shows nodules that may be cavitary and cysts that predominate in the middle and upper lung zones. Pulmonary function tests show impaired diffusion capacity, and an obstructive or restrictive pattern may be seen.

Diagnosis and Differential Diagnosis

A specific diagnosis can be made with open lung biopsy. In the right clinical setting and with a typical HRCT, a biopsy may not be needed for a presumptive diagnosis. The differential diagnosis includes other cystic lung diseases, such as lymphangioleiomyomatosis, sarcoidosis, and smoking-related idiopathic pneumonias such as RB-ILD and DIP complicated by emphysema.

Treatment

The main treatment is tobacco cessation (level 3 evidence). Corticosteroids and cytotoxic agents are sometimes employed as adjunctive therapy (level 3). Lung transplantation may be considered in cases of advanced disease.

Prognosis

In contrast to systemic LCH, pulmonary LCH is not a neoplastic disorder, and spontaneous regression may occur with smoking cessation. Although some patients have a benign course, others develop progressive disease or complications such as pulmonary hypertension, which may be fatal.