CHRONIC EOSINOPHILIC PNEUMONIA

In contrast to acute eosinophilic pneumonia, chronic eosinophilic pneumonia is a more indolent syndrome that is characterized by pulmonary infiltrates and eosinophilia in both the tissue and blood. Most patients are female nonsmokers with a mean age of 45, and patients do not usually develop the acute respiratory failure and significant hypoxemia appreciated in acute eosinophilic pneumonia. Similar to EGPA, a majority have asthma, with many having a history of allergies.

Patients present with a subacute illness over weeks to months, with cough, low-grade fevers, progressive dyspnea, weight loss, wheezing, malaise, and night sweats, and a chest x-ray with migratory bilateral peripheral or pleural-based opacities. Although this "photographic negative pulmonary edema" appearance on chest x-ray and chest CT is pathognomonic of chronic eosinophilic pneumonia, less than 25% of patients present with this finding. Other radiographic findings include atelectasis, pleural effusions, lymphadenopathy, and septal line thickening.

Almost 90% of patients have peripheral eosinophilia, with mean eosinophil counts of over 30% of total white blood cell count. BAL eosinophilia is also an important distinguishing feature with mean BAL eosinophil counts of close to 60%. Both peripheral and BAL eosinophilia are very responsive to treatment with corticosteroids. Other laboratory features of chronic eosinophilic pneumonia include increased ESR, C-reactive protein, platelets, and IgE. Lung biopsy is also often not required to establish a diagnosis, but may show accumulation of eosinophils and histiocytes in the lung parenchyma and interstitium, as well as cryptogenic organizing pneumonia, but with minimal fibrosis. Nonrespiratory manifestations are uncommon, but arthralgias, neuropathy, and skin and GI symptoms have all been reported; their presence may suggest EGPA or hypereosinophilic syndrome. Another similarity is the rapid response to corticosteroids with quick resolution of peripheral and BAL eosinophilia and improvement in symptoms. In contrast to acute eosinophilic pneumonia, though, over 50% of patients relapse, and many require prolonged courses of corticosteroids for months to years.

EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS (EGPA)

Previously known as allergic angiitis granulomatosis or Churg-Strauss syndrome, this complex syndrome is characterized by eosinophilic vasculitis that may involve multiple organ systems including the lungs, heart, skin, GI tract, and nervous system. Although EGPA is characterized by peripheral and pulmonary eosinophilia with infiltrates on chest x-ray, the primary features that distinguish EGPA from other pulmonary eosinophilic syndromes are the presence of eosinophilic vasculitis in the setting of asthma and involvement of multiple end organs (a feature it shares with hypereosinophilic syndrome). Although perceived to be quite rare, in the last few years, there has appeared to be an increased incidence of this disease, particularly in association with various asthma therapies.

The primary features of EGPA include asthma, peripheral eosinophilia, neuropathy, pulmonary infiltrates, paranasal sinus abnormality, and presence of eosinophilic vasculitis. It typically occurs in several phases. The prodromal phase is characterized by asthma and allergic rhinitis, and usually begins when the individual is in his or her twenties or thirties, typically persisting for many years. The eosinophilic infiltrative phase is characterized by peripheral eosinophilia and eosinophilic tissue infiltration of various organs including the lungs and GI tract. The third phase is the vasculitic phase and may be associated with constitutional signs and symptoms including fever, weight loss, malaise, and fatigue. The mean age at diagnosis is 48 years, with a range of 14 to 74 years; the average length of time between diagnosis of asthma and vasculitis is 9 years.

Similar to other pulmonary eosinophilic syndromes, constitutional symptoms are very common in EGPA and include weight loss of 10–20 lb, fevers, and diffuse myalgias and migratory polyarthralgias. Myositis may be present with evidence of vasculitis on muscle biopsies. In contrast to the eosinophilic pneumonias, EGPA involves many organ systems including the lungs, skin, nerves, heart, GI tract, and kidneys.

Symptoms and Clinical Manifestations • ***RESPIRATORY*** Most EGPA patients have asthma that arises later in life and in individuals who have no family history of atopy. The asthma can often be severe, and oral corticosteroids are often required to control symptoms but may lead to suppression of vasculitic symptoms. In addition to the more common symptoms of cough, dyspnea, sinusitis, and allergic rhinitis, alveolar hemorrhage and hemoptysis may also occur.

NEUROLOGIC Over three-fourths of EGPA patients have neurologic manifestations. Mononeuritis multiplex most commonly involves the peroneal nerve, but also involves the ulnar, radial, internal popliteal, and occasionally, cranial nerves. Cerebral hemorrhage and infarction may also occur and are important causes of death. Despite treatment, neurologic sequelae often do not completely resolve.

DERMATOLOGIC Approximately half of EGPA patients develop dermatologic manifestations. These include palpable purpura, skin nodules, urticarial rashes, and livedo.

CARDIOVASCULAR Granulomas, vasculitis, and widespread myocardial damage may be found on biopsy or at autopsy, and cardiomyopathy and heart failure may be seen in up to half of all patients but are often at least partially reversible. Acute pericarditis, constrictive pericarditis, myocardial infarction, and other electrocardiographic changes all may occur. The heart is a primary target organ in EGPA, and cardiac involvement often portends a worse prognosis.

GI GI symptoms are common in EGPA and likely represent an eosinophilic gastroenteritis characterized by abdominal pain, diarrhea, GI bleeding, and colitis. Ischemic bowel, pancreatitis, and cholecystitis have also been reported in association with EGPA and usually portend a worse prognosis.

RENAL Renal involvement is more common than once thought, and approximately 25% of patients have some degree of renal involvement. This may include proteinuria, glomerulonephritis, renal insufficiency, and rarely, renal infarct.

Lab Abnormalities Systemic eosinophilia is the hallmark laboratory finding in patients with EGPA and reflects the likely pathogenic role that the eosinophil plays in this disease. Eosinophilia greater than 10% is one of the defining features of this illness and may be as high as 75% of the peripheral white blood cell count. It is present at the time of diagnosis in over 80% of patients but may respond quickly (often within 24 h) to initiation of systemic corticosteroid therapy. Even in the absence of systemic eosinophilia, tissue eosinophilia may be present.

Although not specific to EGPA, ANCAs are present in up to two-thirds of patients, mostly with a perinuclear staining pattern. Nonspecific lab abnormalities that may be present in patients with EGPA include a marked elevation in ESR, a normochromic normocytic anemia, an elevated IgE, hypergammaglobulinemia, and positive rheumatoid factor and antinuclear antibodies (ANA). Although BAL often reveals significant eosinophilia, this may be seen in other eosinophilic lung diseases. Similarly, PFT often reveals an obstructive defect similar to asthma.

Radiographic Features Chest x-ray abnormalities are extremely common in EGPA and consist of bilateral, nonsegmental, patchy infiltrates that often migrate and may be interstitial or alveolar in appearance. Reticulonodular and nodular disease without cavitation can be seen, as can pleural effusions and hilar adenopathy. The most common CT findings include bilateral ground-glass opacity and airspace consolidation that is predominantly subpleural. Other CT findings include bronchial wall thickening, hyperinflation, interlobular septal thickening, lymph node enlargement, and pericardial and pleural effusions. Angiography may be used diagnostically and may show signs of vasculitis in the coronary, central nervous system, and peripheral vasculature.

Treatment and Prognosis of EGPA Most patients diagnosed with EGPA have previously been diagnosed with asthma, rhinitis, and sinusitis, and have received treatment with inhaled or systemic corticosteroids.