

Imaging of Eosinophilic Lung Diseases



Melissa Price, MD^a, Matthew D. Gilman, MD^a, Brett W. Carter, MD^b, Bradley S. Sabloff, MD^b, Mylene T. Truong, MD^b, Carol C. Wu, MD^{b,*}

KEYWORDS

- Eosinophilic pneumonia • Eosinophilic granulomatosis with polyangiitis
- Allergic bronchopulmonary aspergillosis • Hypereosinophilic syndromes

KEY POINTS

- The classic “photographic negative of pulmonary edema” pattern is only seen in a minority of patients with chronic eosinophilic pneumonia.
- Simple pulmonary eosinophilia is characterized by peripheral eosinophilia, minimal respiratory symptom, and transient pulmonary opacities.
- Eosinophilic granulomatosis and polyangiitis, formerly known as Churg-Strauss syndrome, typically occur in patients with history of asthma, allergic rhinitis, and/or sinusitis.
- Hyperdense mucus is pathognomonic for allergic bronchopulmonary aspergillosis.
- Drug-induced eosinophilic pneumonia can have clinical presentations and imaging features similar to acute eosinophilic pneumonia, chronic eosinophilic pneumonia, or rarely, eosinophilic granulomatosis and polyangiitis.

INTRODUCTION

Eosinophilic lung diseases encompass a varied group of pulmonary diseases that characteristically feature peripheral or tissue eosinophilia. The clinical presentation of these disorders varies markedly, and patients may be asymptomatic or experience life-threatening respiratory illness at the time of diagnosis.¹

Eosinophilic lung disease traditionally can be diagnosed when one of the following criteria are met: (1) peripheral eosinophilia in the presence of opacities on a chest radiograph, (2) surgical or transbronchial lung biopsy demonstrating tissue eosinophilia, or (3) increase in the percentage of eosinophils in bronchoalveolar lavage (BAL) fluid.²

Imaging findings, particularly with thin-section computed tomography (CT), can sometimes

suggest the diagnosis of an eosinophilic lung disease. In many cases, given the relatively rare nature and nonspecific clinical presentation of these diseases, the findings on CT may be the first clue to the diagnosis and may prompt further diagnostic workup. Alternatively, in patients with known peripheral eosinophilia, imaging can provide information regarding presence, severity, and distribution of pulmonary involvement, potentially narrow the differential possibilities, and serve as a guide for BAL or biopsy.

IMAGING PROTOCOLS

Standard chest CT protocol is preferably with thin slice thickness (<1.5 mm) and high spatial resolution image reconstruction algorithm.

The authors have nothing to disclose.

^a Department of Radiology, Massachusetts General Hospital, 55 Fruit Street, Founders 202, Boston, MA 02114, USA; ^b Department of Diagnostic Radiology, University of Texas MD Anderson Cancer Center, 1515 Holcombe Boulevard, Unit 1478, Houston, TX 77030, USA

* Corresponding author.

E-mail address: carolcwu@gmail.com

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DIAGNOSTIC CRITERIA

- Blood, tissue, or BAL fluid eosinophilia
- Pulmonary opacities

Acute Eosinophilic Pneumonia

The clinical diagnosis of acute eosinophilic pneumonia (AEP) is made in patients with an acute febrile illness lasting fewer than 5 days, hypoxemic respiratory failure, diffuse opacities on chest radiograph, and greater than 25% eosinophils in BAL fluid. Blood eosinophils may be normal or mildly elevated at initial presentation² but subsequently increase in the days after treatment.^{3,4} The absence of a concurrent infection is necessary for the diagnosis.^{2,5} Although the clinical presentation and imaging of findings of AEP may mimic acute respiratory distress syndrome (ARDS), the BAL fluid should demonstrate high neutrophils in ARDS.²

The cause of AEP has not been identified, but there is a reported association with cigarette smoking, particularly new-onset cigarette smoking.^{4,6-9} The illness has also been reported to occur after inhalation of toxins¹⁰ and use of certain medications.^{11,12}

The chest radiograph findings in patients with AEP vary and include bilateral septal thickening and patchy or diffuse opacities.^{4,13}

CT commonly shows ground-glass opacities, consolidation, interlobular septal thickening, bronchial wall thickening, and pleural effusions.¹⁴ A CT pattern of crazy-paving with thickening of the interlobular septa and intralobular lines in the setting of ground-glass opacities¹⁵ can be seen in patients with AEP¹⁴ (Fig. 1). When present, pleural effusions are most commonly bilateral. In most cases, there is no overall lung zone predominance in the cephalocaudal plane.^{14,16}

A peripheral distribution of the ground-glass and consolidative opacities has been described to occur in up to half of patients with AEP.¹⁴ Cardiomegaly is not a feature of the illness.¹⁷ In a minority of patients with AEP, lymphadenopathy may be observed at CT.¹⁶

AEP is extremely steroid responsive; however, there are patients who recover fully in the absence of corticosteroid treatment.¹⁸

Chronic Eosinophilic Pneumonia

Idiopathic chronic eosinophilic pneumonia (ICEP) is an uncommon entity with respiratory symptoms such as dyspnea and cough lasting more than 2 weeks. It is associated with alveolar eosinophilia 40% or greater at (BAL) differential cell count and/or blood eosinophilia 1000/mm³ or more. Other known causes of eosinophilic lung disease must be excluded. The disease affects women twice as often as men. Up to 50% patients with ICEP have a history of asthma.¹⁹ In distinction from eosinophilic granulomatosis with polyangiitis (EGPA) or hypereosinophilic syndrome (HES), patients with ICEP usually do not have extrathoracic manifestations.¹⁹

The classic radiographic finding has been described as the photographic negative of pulmonary edema with diffuse peripheral opacities and ill-defined margins.^{20,21} However, this classic radiographic pattern is seen in fewer than one-third of patients.²² The opacities usually do not have lobar or segmental distribution, can be unilateral or bilateral, and are often in an apical or axillary location without basilar involvement. These opacities can disappear and reappear in the exact same locations.²⁰ Pleural effusion is not commonly seen.

CT often shows bilateral subpleural consolidation and ground-glass opacities and can be associated

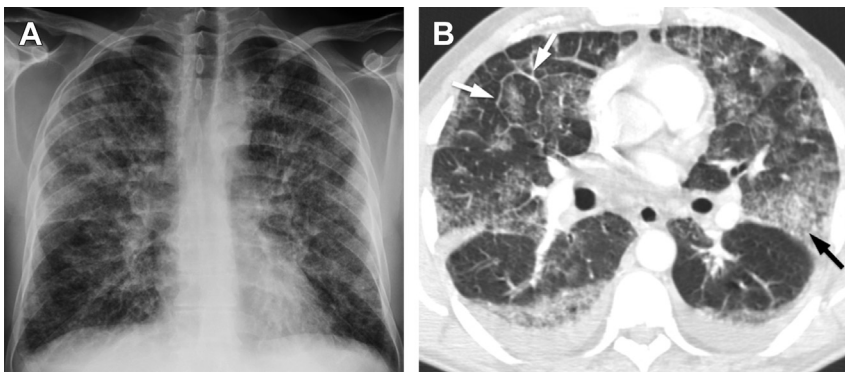


Fig. 1. AEP in a 41-year-old male firefighter who presented with severe dyspnea 6 days following a significant episode of occupational smoke inhalation. BAL specimen showed a heavy eosinophilic infiltrate with 36% eosinophils. (A) Chest radiograph shows patchy linear and nodular opacities. (B) CT demonstrates patchy ground-glass opacities (*black arrow*), interlobular septal thickening (*white arrows*), and small bilateral pleural effusions.

with enlarged mediastinal lymph nodes²³ (Figs. 2 and 3). In some cases, the peripheral nature of the opacities will not be apparent radiographically but are clearly demonstrated on CT.²⁴

Chronic eosinophilic pneumonia (CEP) is very steroid responsive, and the opacities have been shown to resolve within 7 to 10 days of initiation of corticosteroid therapy.²¹

Simple Pulmonary Eosinophilia

Simple pulmonary eosinophilia (SPE), which was originally described by Löffler in 1932, occurs in the presence of blood eosinophilia, transient opacities on chest radiograph, and minimal associated respiratory symptoms. The cause of SPE is frequently parasitic infection or a drug reaction, but approximately one-third of cases are idiopathic. SPE has also been reported to occur as incidental findings on follow-up CT of 0.95% of oncologic patients²⁵ and in 0.9% of asymptomatic individuals undergoing low-dose CT for lung cancer screening.²⁶

The plain radiographic findings of SPE are opacities with a nonsegmental peripheral distribution,²

which can be unilateral or bilateral.²⁷ These opacities can be fleeting or migratory²⁷ (Fig. 4).

CT usually demonstrates peripheral patchy consolidations with scattered ground-glass opacities that have an upper and mid lung zone predominance (Fig. 5). As with the radiographic findings, the CT imaging features of the illness are often fleeting and migratory. Some patients may also have discrete pulmonary nodules, and bronchial wall thickening is commonly seen.¹⁶ SPE and CEP have a similar pattern of distribution of opacities; however, the opacities in SPE often fluctuate over a period of days, whereas in CEP they persist for weeks to months.²⁴ In cases of SPE incidentally found during oncologic follow-up or screening, single or multiple pulmonary nodules with ground-glass halos are the most common findings. These lesions are reported to have lower lung zone predominance with peripheral distribution.^{25,26} These lesions can have mild to moderate uptake on fludeoxyglucose-PET²⁸ and mimic primary or metastatic neoplasm. In patients with these findings, correlation with blood eosinophil count and short-term follow-up CT may help obviate more invasive procedures.^{25,26,28}

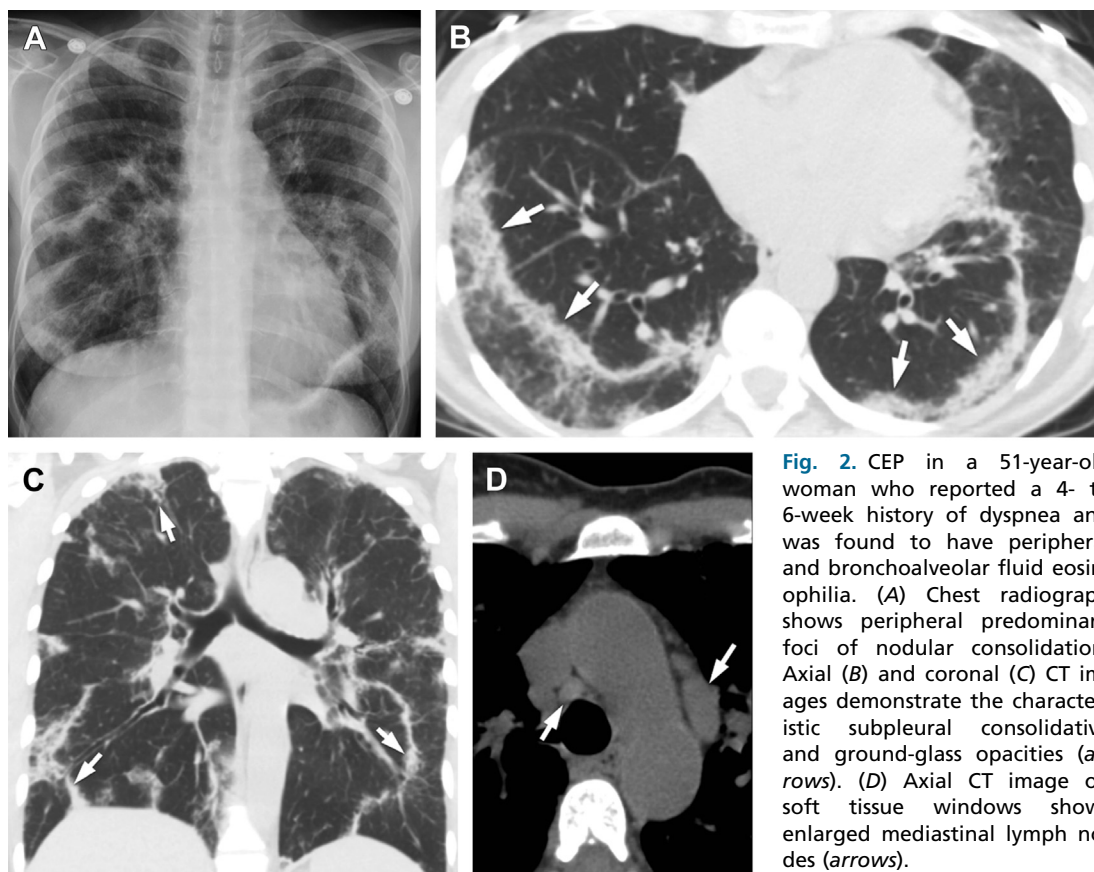


Fig. 2. CEP in a 51-year-old woman who reported a 4- to 6-week history of dyspnea and was found to have peripheral and bronchoalveolar fluid eosinophilia. (A) Chest radiograph shows peripheral predominant foci of nodular consolidation. Axial (B) and coronal (C) CT images demonstrate the characteristic subpleural consolidative and ground-glass opacities (arrows). (D) Axial CT image on soft tissue windows shows enlarged mediastinal lymph nodes (arrows).

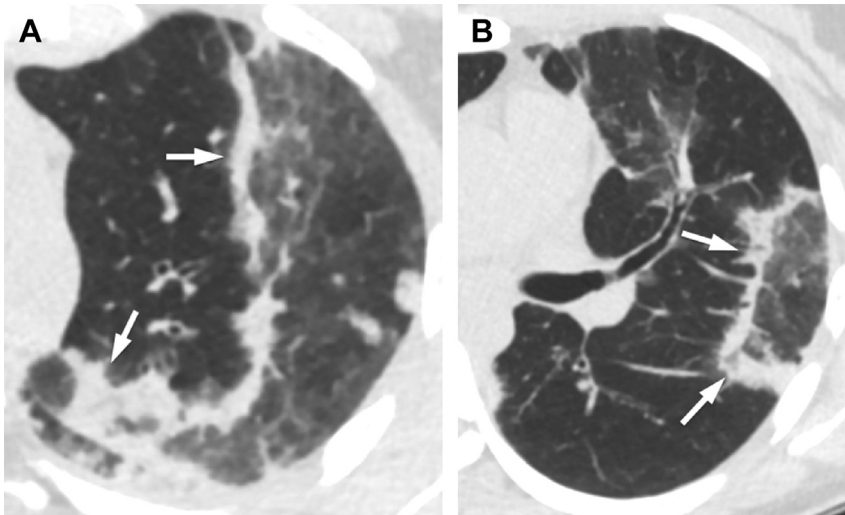


Fig. 3. A 31-year-old woman with CEP who initially presented with a chronic cough and had 71% eosinophils in BAL fluid. (A, B) CT images at 2 levels show peripheral ground-glass opacities and consolidation (arrows).

Individuals with idiopathic SPE often require no steroid therapy, and the pulmonary opacities and blood eosinophilia can often resolve within a month.²

Hyper eosinophilic Syndrome

HES is a rare group of diseases that is diagnosed when blood eosinophils are greater than $1500/\text{mm}^3$ for at least 6 months, there is evidence of organ dysfunction secondary to tissue infiltration by eosinophils, and there are no findings to suggest a parasitic, allergic, or other identifiable cause of the eosinophilia.²⁹ Additional subcategories have been identified, including primary HES, which occurs in the setting of clonal or neoplastic proliferation of eosinophils as well as secondary (reactive) HES, which is thought to be cytokine driven in response to a neoplastic or inflammatory condition.³⁰ HES is more common among men with a male-to-female ratio of 1.47:1 and has a median age at diagnosis of 52.5 years.³¹

In addition to hematologic abnormalities, cutaneous, neurologic, and cardiac involvement are common with HES.³² Cardiac involvement is the primary cause of mortality in patients with HES and may result in complete heart block, eosinophilic myocarditis, restrictive cardiomyopathy, ventricular thrombus formation, and sudden cardiac death.^{33,34} Pulmonary disease has been reported to occur in 40% of individuals with HES and can manifest as cough, dyspnea, and bronchospasm.³²

Radiographs may show no abnormalities in patients with HES. In some patients, nodular opacities³⁵ or reticular opacities will be visible on plain radiograph.²⁹

In individuals with HES and pulmonary involvement, CT often shows small nodules, frequently with a surrounding a ground-glass halo.³⁵ Patchy consolidation or ground-glass opacities may also be present, and pleural effusions are seen in a minority of cases.^{16,36} The nodules or opacities typically do not have a zonal predominance in the lungs. Interlobular septal thickening and bronchial

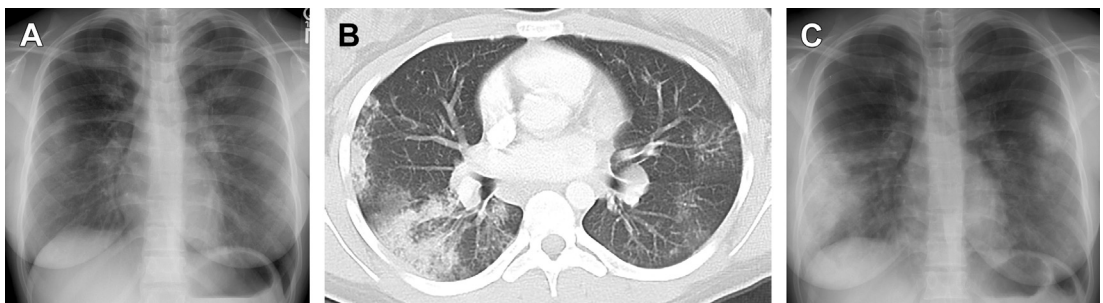


Fig. 4. Simple pulmonary eosinophilia in a 32-year-old woman with migratory opacities. (A) Initial chest radiograph shows bilateral multifocal consolidation. (B) CT demonstrates multifocal consolidation and ground-glass opacities. (C) Repeat chest radiograph 2 weeks later shows bilateral consolidation in a different distribution.

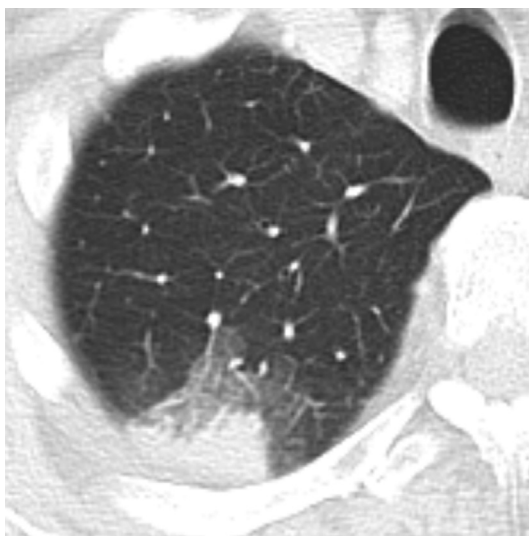


Fig. 5. Simple pulmonary eosinophilia in a 65-year-old man with peripheral eosinophilia. CT image shows right upper lobe subpleural nodular opacity with ground-glass halo, which improved spontaneously on follow-up imaging performed 4 weeks later.

wall thickening are commonly seen at CT.¹⁶ Intra-thoracic lymphadenopathy has been reported to occur in 12% to 33% of patients with HES.^{16,36}

Treatment for lung involvement in HES includes corticosteroids often with an additional agent such as hydroxyurea, imatinib, interferon- α , or mepolizumab.³⁶

Eosinophilic Granulomatosis with Polyangiitis (Churg-Strauss)

EGPA is a small-vessel antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis with blood and tissue eosinophilia, which typically occurs in patients with asthma.^{37,38} This disorder was previously known as Churg-Strauss syndrome, but the nomenclature was changed at the 2012 Revised International Chapel Hill Consensus Conference to highlight the histopathologic features of the disease.³⁸ In patients with EGPA, there is necrotizing granulomatous inflammation affecting the respiratory tract, necrotizing vasculitis, and eosinophilic organ infiltration.³⁹ ANCA is more frequently present in patients with glomerulonephritis.³⁸ Most affected patients are between 40 and 60 years of age.³⁵ Over the years, various diagnostic criteria have existed without widespread consensus.⁴⁰ The latest American College of Rheumatology criteria for the diagnosis of EGPA are listed in **Box 1**.⁴¹

EGPA usually occurs in 3 sequential phases. The first or allergic phase involves development of

Box 1 **American College of Rheumatology classification criteria**

- Asthma
- Eosinophilia (>10% on differential white blood cell count)
- Mononeuropathy or polyneuropathy
- Nonfixed pulmonary infiltrates
- Paranasal sinus abnormalities
- Extravascular eosinophils

4 out of 6 criteria = sensitivity of 85% and specificity of 99.7%

Data from Masi AT, Hunder GG, Lie JT, et al. The American College of Rheumatology 1990 criteria for the classification of Churg-Strauss syndrome (allergic granulomatosis and angiitis). *Arthritis Rheum* 1990;33(8):1094–100.

asthma, allergic rhinitis, and sinusitis. The second or eosinophilic phase is marked by an increase in peripheral eosinophilic count and eosinophilic infiltration of lungs, heart, or gastrointestinal system. Finally, the vasculitis phase is associated with necrotizing vasculitis resulting in purpura or neuropathy and constitutional symptoms such as fever, malaise, and weight loss.³⁹

The most common radiographic finding in EGPA is bilateral nonsegmental multifocal consolidation. Diffuse reticulonodular opacities and bronchial wall thickening can also be seen. Less commonly, discrete pulmonary nodules may be visible.⁴²

Common CT findings observed with EGPA include small (<10 mm) centrilobular nodules, ground-glass opacities, consolidation, and bronchial wall thickening⁴³ (**Fig. 6**). There is no overall zonal predominance. Pleural effusions occur in a minority of patients. Lymphadenopathy has been reported to present in approximately 25% of patients with EGPA.¹⁶ EGPA is associated with increased risk of thromboembolic events including pulmonary embolism.^{44,45} Therefore, if a contrast-enhanced CT is performed, an effort should be made to look for incidental pulmonary emboli.

Depending on the severity of disease, treatment usually involves corticosteroids with or without cyclophosphamide. Azathioprine or methotrexate can be used for maintenance therapy after remission has been achieved. Relapse occurs in approximately 25% to 30% of patients.^{39,45}

Allergic Bronchopulmonary Aspergillosis

Allergic bronchopulmonary aspergillosis (ABPA) occurs mostly in patients with asthma or cystic fibrosis. *Aspergillus* is ubiquitous fungus in the

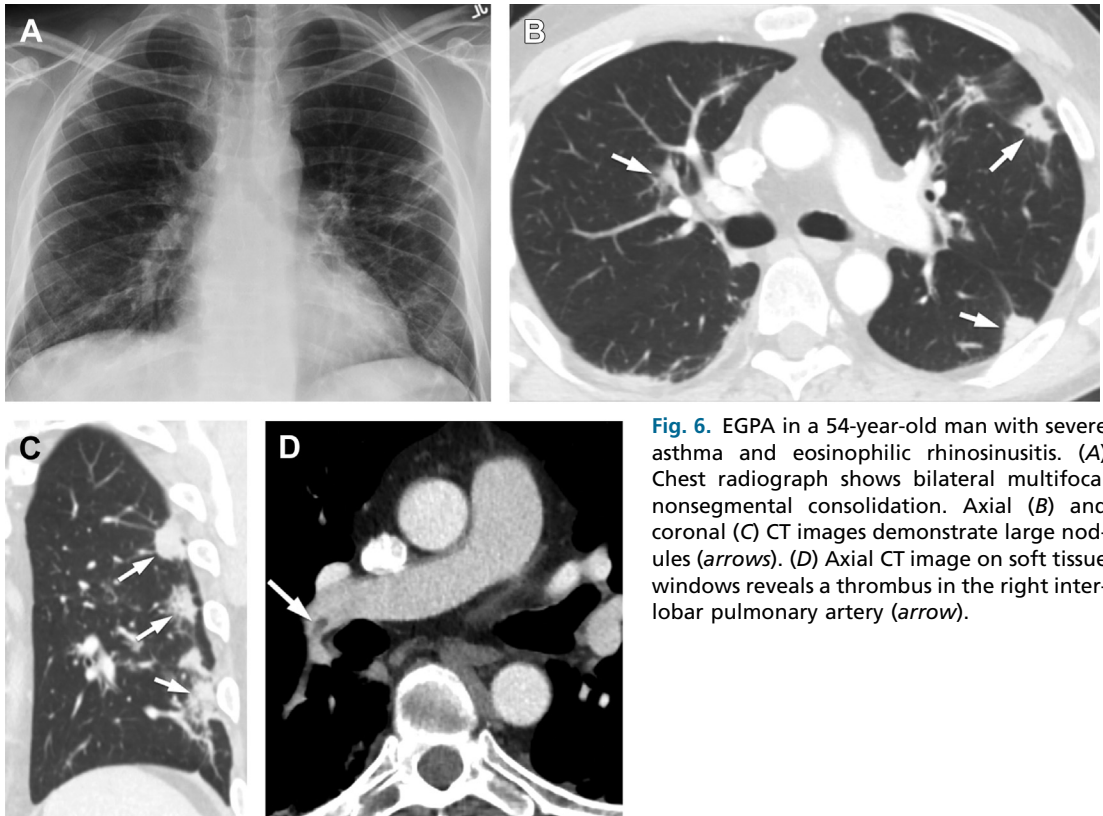


Fig. 6. EGPA in a 54-year-old man with severe asthma and eosinophilic rhinosinusitis. (A) Chest radiograph shows bilateral multifocal nonsegmental consolidation. Axial (B) and coronal (C) CT images demonstrate large nodules (arrows). (D) Axial CT image on soft tissue windows reveals a thrombus in the right interlobar pulmonary artery (arrow).

environment, and *Aspergillus fumigatus* is the most common pathogenic species in humans. It is thought that poor airway clearance in patients with asthma or cystic fibrosis allows noninvasive growth of *Aspergillus*, followed by hypersensitivity response in certain susceptible individuals, leading to airway injury in ABPA. Patients present with wheezing, dyspnea, cough, and hemoptysis. Occasionally patients will expectorate airway casts consisting of thick mucus and hyphae. Systemic symptoms such as fever, malaise, and weight loss are often reported. The combination of elevated serum *Aspergillus* immunoglobulin E (IgE) and positive skin testing is the most sensitive for making the diagnosis.⁴⁶ Allergic bronchopulmonary mycosis (ABPM) is a term used to describe patients who present with clinical features similar to ABPA caused by other fungi or yeasts.⁴⁷

Radiographic findings of ABPA include consolidation, bronchial wall thickening, bronchiectasis, and mucoid impaction (tubular or gloved finger shadows).⁴⁸

Classically, ABPA is associated with central or peripheral bronchiectasis and high-attenuation mucoid impaction on CT.⁴⁹ High-attenuation

mucus, which has been described as mucus plug that is visually denser than paraspinous skeletal muscle⁵⁰ or quantitatively with CT density greater than 70 HU,⁵¹ is presumed to be due to calcium or metallic ions within the mucus. Although hyperdense mucus is a distinguishing CT feature of ABPA not seen in other entities associated with bronchiectasis and mucus plugging, it is present in only 28% to 36% of patients with ABPA.^{50–52} The presence of high-attenuation mucoid impaction has been reported to correlate with higher peripheral eosinophil counts, serum total and *Aspergillus*-specific IgE levels,^{49,51} and higher relapse rate.⁴⁹ Bronchiectasis in ABPA is often central, with predilection for the upper and middle lobes⁵⁰ (Fig. 7). The absence of bronchiectasis, however, should not prevent the diagnosis of ABPA in patients with other suggestive clinical findings. Bronchiectasis may not be present during the early stage of ABPA.^{46,50,53} Other CT findings include consolidation, centrilobular nodules, and tree-in-bud opacities.⁵⁰

Treatment is necessary to prevent further airway damage and decline in pulmonary function. Corticosteroids are used as first-line treatment for ABPA. The addition of antifungal agents has

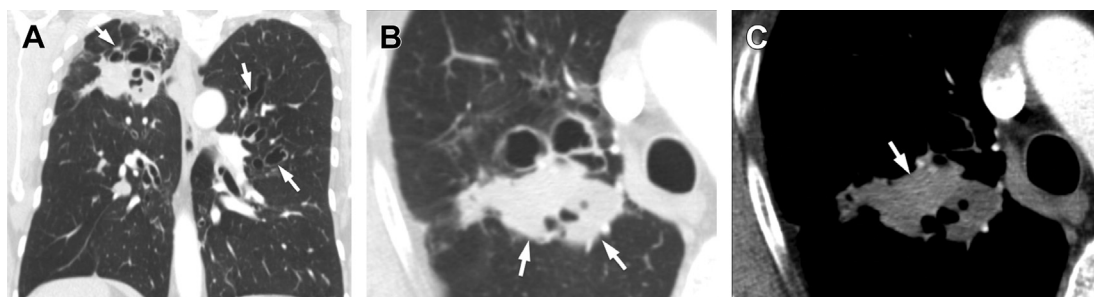


Fig. 7. ABPA in a 51-year-old woman with markedly elevated IgE levels treated with omalizumab, voriconazole, and chronic oral and inhaled corticosteroids. (A) Coronal CT image shows upper lobe predominant cystic and varicose bronchiectasis (arrows) with mucoid impaction and bronchial wall thickening. (B) CT image demonstrates mucus filling bronchiectatic airways in the right upper lobe (arrows). (C) A CT image at the same level on soft tissue windows shows the impacted area to have areas of internal high attenuation (arrow).

been shown to be useful. Omalizumab, an antibody to IgE, has also been introduced.⁴⁷ Patients are followed with serial assessment of total serum IgE level.^{46,47}

Parasitic Infection

Eosinophilic pneumonia (EP) related to parasitic infection has been postulated to be a result of a combination of direct invasion and allergic reaction.⁵⁴ The prevalence and type of parasitic infection-related EP vary according to geographic locations. However, because of growing international travel and migration, these diseases are increasingly reported in nonendemic areas. Knowledge of world distribution of common parasites and the patient travel history is helpful in establishing the diagnosis. Some of the more common causes of parasitic eosinophilic diseases are detailed in later discussion.

Transient eosinophilic pulmonary pneumonia (Löffler syndrome)

Worldwide, the most common causes of transient eosinophilic pulmonary pneumonia (Löffler syndrome) are *Ascaris lumbricoides*, *Ancylostoma duodenale*, and *Necator americanus*. *Strongyloides stercoralis* is less common but is seen in the southeastern United States⁵⁵ and Puerto Rico.⁵⁶ Its ability to reproduce within the human hosts (autoinfection) can lead to prolonged disease and severe hyperinfection in immunocompromised individuals such as those on steroids or with human immunodeficiency virus infection.^{56–58} Pulmonary symptoms in these parasitic infections are caused by hypersensitive response to larval migration through the lungs. Patients can be asymptomatic or present with fever, cough, dyspnea, and hemoptysis, with severity correlated to parasitic burden. Blood and sputum

eosinophilia is common.⁵⁵ The course tends to be self-limited.

Most common imaging findings are transient, migratory areas of consolidation.⁵⁹ Other findings include reticular or reticulonodular opacities, miliary nodules, and pleural effusions.^{55,58,60} Pulmonary cavitation and abscess formation have also been reported with *Strongyloides*.^{61,62}

Treatment is specific to the underlying parasitic infection.

Tropical pulmonary eosinophilia

Tropical pulmonary eosinophilia, a syndrome that results from immunologic response to filarial infection by *Wuchereria bancrofti* and *Brugia malayi*, is predominantly seen in the tropical and subtropical regions. It is the most serious parasitic eosinophilic lung disease.⁵⁵ Patients typically present with cough, dyspnea, and nocturnal wheezing, mimicking acute or refractory asthma. Marked peripheral eosinophilia is the norm with absolute blood eosinophil counts usually exceeding 3000 cells per cubic millimeter.^{55,63} In the acute phase, interstitial eosinophilic infiltration occurs, and more chronically, interstitial fibrosis can develop.⁶³

Radiographic findings of diffuse bilateral reticular or reticulonodular opacities have been described.^{64–66} Bronchiectasis, air-trapping, and mediastinal lymphadenopathy can be seen on CT.⁶⁶

Treatments include diethylcarbamazine, ivermectin, albendazole, and/or steroids. Because of the potential for relapses and persistent chronic inflammation and lung injuries, some patients require prolonged treatment.^{55,63}

Echinococcosis

Echinococcus granulosus is mainly found in South and Central America, sub-Saharan Africa, Russia, and China and around the Mediterranean Sea. *Echinococcus multilocularis* is endemic in parts of

the United States, Canada, China, Northern Japan, and Europe. Humans are infected by eggs excreted in canine feces, and the larvae subsequently travel to the lungs and/or liver.⁶² Peripheral eosinophilia is not always present. Patients with pulmonary involvement can be asymptomatic or present with cough, pain, fever, or hemoptysis.^{55,67,68}

Echinococcosis usually presents as a solitary cyst in the lung, which usually appears as a sharply defined round or oval opacity on radiograph. Approximately 20% to 30% of patients have multiple pulmonary cysts.⁶² A fluid-filled cyst with internal daughter cysts can be seen on CT. The water lily sign is seen when detached endocyst membrane floats within the pericyst. The cyst can also be completely air-filled (Fig. 8), referred to as the dry cyst sign, when it ruptures into an airway and expels its fluid content.⁶⁹ The cyst wall can calcify over time. Complications such as pneumothorax or empyema can also be observed on radiography or CT.^{67,68}

Treatment options include surgical resection and/or albendazole.^{67,68}

Paragonimiasis

Paragonimus westermani, endemic in Southeast Asia, can be contracted by ingestion of incompletely cooked freshwater crabs or crayfish. There are reported cases in the United States from ingestion of live crabs in sushi.⁷⁰ There are a few other species that are known to cause human infection.⁵⁵

In the early stage of pleuropulmonary paragonimiasis, pneumothorax, hydropneumothorax, focal consolidation, and linear opacities are caused by migration of juvenile worms. Findings of thin-walled cysts, subpleural nodules (Fig. 9), masslike consolidation, bronchiectasis, and pleural thickening occur later in the disease process.^{71,72} Compared with other parasitic infections, internal hypoattenuation or cavity within pulmonary lesions

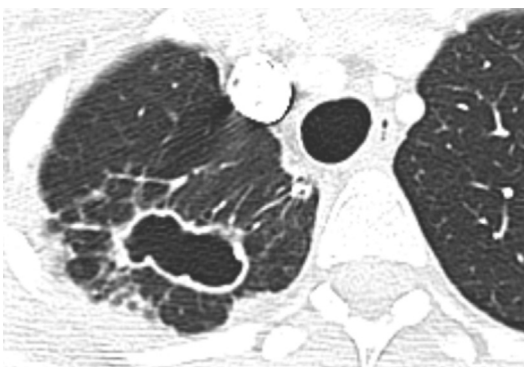


Fig. 8. Echinococcal cyst in a 31-year-old woman from South Africa. CT shows a lobulated air-containing cyst. The patient was treated with albendazole, and the cyst remained stable on subsequent CT.

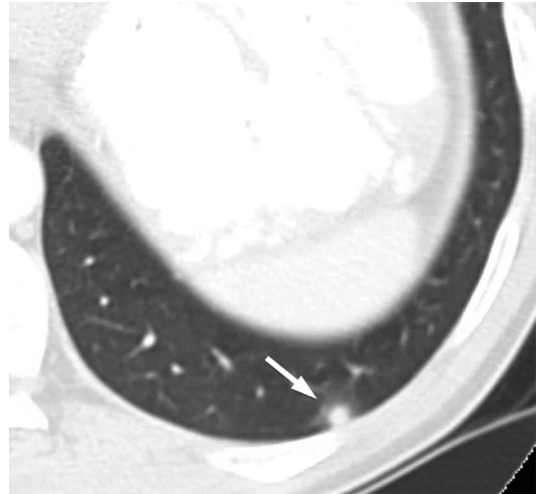


Fig. 9. Paragonimiasis in a 51-year-old Brazilian man with a history of gastric adenocarcinoma with peritoneal metastases. CT shows a 5-mm nodule in the left lower lobe with minimal surrounding ground-glass opacity (arrow), which was initially interpreted as suspicious for metastasis. The patient underwent a wedge resection of the nodule, which revealed necrotizing granulomatous inflammation due to degenerative trematodes with morphologic features of the *Paragonimus* species.

and perilesional centrilobular nodules occur more frequently in paragonimiasis.⁷³ Associated ascites, intraperitoneal or abdominal wall nodules, and low-attenuation hepatic lesions have also been reported.⁷⁴ Because nodules and masslike consolidation are frequent findings, pleuropulmonary paragonimiasis can mimic lung cancer as well as tuberculous or fungal infection.

Patients usually respond well to praziquantel or triclabendazole.⁵⁵

Toxocariasis

Toxocariasis occurs worldwide, particularly in the tropics, and is caused by *Toxocara canis* or *Toxocara cati*.⁵⁵ Human infection occurs as the result of ingestion of embryonated eggs from soil or uncooked liver of cows, pigs, lambs, and chickens. The parasite larvae migrate to and invade various organs, including the liver, lung, and brain.⁷⁵ Patients can be asymptomatic or present with cough, dyspnea, or hemoptysis.

CT findings include ground-glass opacities, solid nodules, consolidation, and linear opacities with subpleural and lower lung predominance.⁷⁵ In one study, it was noted that a nodule with a ground-glass halo was more common in toxocariasis patients with eosinophilia than in those with normal eosinophil levels. Focal ground-glass opacity was more common in the normal eosinophil group.⁷⁶

Patients can be treated with mebendazole, thia-bendazole, or diethylcarbamazine with or without a short course of steroids.⁵⁵

Drug- and Toxin-induced Eosinophilic Pneumonia

Multiple medications and toxins have been reported to cause EP. Drug- or toxin-induced EP is indistinguishable from idiopathic acute or CEP by symptoms, imaging, or histopathologic criteria. The diagnosis is based on temporal relationships of clinical signs and symptoms with recent use of or exposure to an associated causative agent. Resolution of symptoms with cessation of exposure is key to the diagnosis. Recurrence of the condition with re-exposure, although helpful in confirming the diagnosis, is usually not necessary and can be potentially dangerous.⁷⁷

Nonsteroidal anti-inflammatory drugs (NSAIDs) and antibiotics such as nitrofurantoin^{78–80} and dapsone^{81,82} are some of the medications that most commonly cause EP. Antidepressants^{12,83} and cardiovascular medications such as angiotensin conversion enzyme inhibitors^{84,85} and β -blockers⁸⁶ have also been implicated. Oxaliplatin, an alkylating agent usually used in treatment of colorectal cancer, has been reported to cause EP.⁸⁷ Although most medications cause acute or chronic EP, zafirlukast, a leukotriene inhibitor used to treat asthma, is associated with EGPA.⁸⁸ It is unclear whether the medication induces vasculitis or its use allows steroid withdrawal and unmasking of the underlying vasculitis.^{89,90} An extensive list of medications associated with EP can be found online at <http://www.pneumotox.com>, maintained by Department of Pulmonary and Intensive Care University Hospital Dijon France.⁹¹ An abbreviated list of more commonly encountered medications associated with EP is provided in **Box 2**.

Imaging findings of drug-induced EP are similar to idiopathic forms of EP. Consolidation and ground-glass opacities (**Fig. 10**) with predominantly upper lung and peripheral distribution are the most common findings. The reversed halo sign (ground-glass opacity surrounded consolidation), small nodules, septal thickening, and reticulation are less common.⁹²

Various toxin-induced EPs have been described. Cigarette smoking has been reported to cause AEP, usually in individuals who recently started smoking, restarted smoking, or have increased the quantity of cigarettes smoked.^{8,93,94} High-level dust exposure, such as in the case of a firefighter exposed to World Trade Center dust

Box 2

Medications associated with eosinophilic pneumonia

Antibiotics

- Nitrofurantoin
- Daptomycin
- Dapsone
- Minocycline

NSAIDs (Cardiovascular medications)

- Amiodarone
- ACE inhibitor
- β -Blocker

Antidepressants

- Amitriptyline
- Velafaxine
- Fluoxetine

Anticonvulsants

- Phenytoin
- Carbamazepine

Others

- Mesalazine

Abbreviations: ACE, angiotensin converting enzyme; NSAIDs, nonsteroidal anti-inflammatory drugs.

Data from Bonniaud Ph, Baudouin N, Fanton A, et al. The drug-induced respiratory disease website. Dijon (France): Department of Pulmonary Medicine and Intensive Care University Hospital; 2016. Available at: <http://www.pneumotox.com/>.

consisting of silicates,¹⁰ has also been reported to cause AEP. Crack cocaine inhalation has been reported to result in AEP,^{95,96} eosinophilic pleural effusion,⁹⁷ and EGPA.⁹⁸

Similar to idiopathic forms of AEP, CEP, and EGPA, corticosteroids are helpful in severe cases of drug- or toxin-induced eosinophilic lung diseases.⁷⁷

RADIATION-INDUCED EOSINOPHILIC PNEUMONIA

There are reports of EP in women who received radiation therapy for breast cancer. These patients usually had a history of asthma and/or allergies and presented within 1 year of radiation treatment.^{99,100} In one case, the patient developed CEP 6 years after completion of radiation treatment.⁹⁹ Pulmonary opacities can be seen in the irradiated lung or bilaterally (**Fig. 11**). It is postulated that the radiation causes an initial

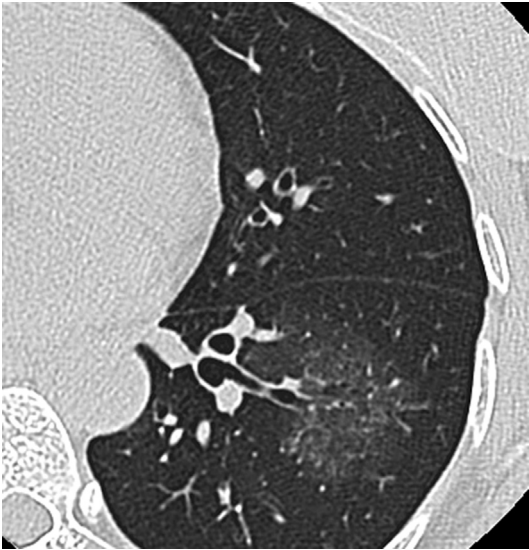


Fig. 10. Drug-induced EP in a 34-year-old woman who developed peripheral eosinophilia shortly after initiation of fluoxetine for treatment of depression. CT shows left lower lobe focal ground-glass opacity, which resolved after steroid treatment.



Fig. 11. Radiation-induced EP in a 72-year-old woman with a history of asthma and bilateral breast cancer who presented with cough, dyspnea, wheezing, and peripheral eosinophilia 3 months after completion of radiation treatment. CT image demonstrates bilateral nodular ground-glass opacities outside of the radiation field. The diagnosis of EP was confirmed after BAL showed elevated eosinophils in the lavage fluid and absence of pulmonary infection.

lymphocytic priming, which, when followed by antigenic stimulation, leads to development of CEP. The patients in reported cases had good response to systemic steroids.

DIFFERENTIAL DIAGNOSIS

- Infection
 - Bacterial
 - Mycobacterial
 - Fungal
- Organizing pneumonia
- Pulmonary alveolar hemorrhage
- Sarcoidosis
- ARDS
- Lung cancer
- Lymphoma

PEARLS, PITFALLS, VARIANTS

CT shows peripheral (subpleural) distribution of pulmonary opacities in CEP to better advantage than chest radiograph.

EGPA is associated with increased risk of pulmonary embolism, and efforts should be made to look for incidental pulmonary emboli if the chest CT was performed with intravenous contrast.

Hyperdense mucus is pathognomonic for ABPA.

WHAT THE REFERRING PHYSICIAN NEEDS TO KNOW

1. The distribution of pulmonary opacities to guide potential BAL or biopsy
2. Incidental nodules with ground-glass halos in patients with peripheral eosinophilia may represent SPE, and short-interval follow-up CT may help obviate more invasive procedures
3. The presence of hyperdense mucus in patients with ABPA because it can be associated with higher relapse rate

SUMMARY

Eosinophilic lung diseases can have a wide range of clinical presentations, which are often nonspecific. However, when certain clinical information (such as underlying asthma, travel history, or recent exposure to medications) is combined with the imaging characteristics (such as peripheral, upper lobe pulmonary opacities, or hyperdense mucus), differential diagnoses can be narrowed. Awareness of these uncommon entities allows radiologists to suggest these diagnoses in the appropriate situations. The main clinical and imaging features of various eosinophilic lung diseases are summarized in **Table 1**.

Table 1
Summary of clinical and imaging features of eosinophilic lung diseases

Eosinophilic Lung Disease	Clinical Feature	Imaging Feature
Acute EP	Acute onset fever, dyspnea	GGO, consolidation
Chronic EP	Subacute respiratory symptoms	Peripheral upper lobe predominant opacities
	Absence of extrapulmonary involvement	Photonegative of pulmonary edema
Simple pulmonary eosinophilia	Peripheral eosinophilia Minimum symptoms	Single or multiple pulmonary nodules with GG halos Transient GGO, consolidation
Hypereosinophilia syndrome	Marked peripheral eosinophilia Cutaneous, neurologic, or cardiac involvement	Pulmonary nodules with GG halos, consolidation, GGO
EGPA	Asthma, allergic rhinitis, sinusitis ANCA	GGO, consolidation, centrilobular nodules
ABPA	Asthma or cystic fibrosis <i>Aspergillus</i> -specific serum IgE	Bronchiectasis Hyperdense mucus
Parasitic infection	Travel to endemic region	Nodules, consolidation, subpleural linear opacities
Drug- or toxin-induced EP	Recent exposure to drug or toxin Improvement with cessation of exposure	Can be similar to AEP, CEP, or EGPA
Radiation-induced EP	Radiation treatment	Opacities outside of radiation field

Abbreviations: GG, ground-glass; GGO, ground-glass opacities.

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