23

Pneumonia Mimics

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Introduction

Although infectious pneumonitis is a common illness, known since antiquity, the diagnostic tools used to recognize it have advanced slowly. A positive blood culture, pleural fluid culture, or even a sputum culture with a heavy growth of a recognized pathogen confers varying degrees of confidence in recognizing bacterial pneumonia. However, culture confirmation of pneumonia is rare in patients with community-acquired pneumonia who are treated as outpatients, and 35% to 40% of patients with community-acquired pneumonia treated as inpatients fail to have a specific pathogen identified. Most physicians arrive at a clinical diagnosis based on a patient´s fever, respiratory symptoms, and abnormal chest roentgenogram. This leads to initiation of antibiotic therapy, and improvement with therapy is used as verification of the diagnosis. Unfortunately, the symptoms and signs of infectious pneumonia are mimicked by many noninfectious pulmonary disorders. This chapter discusses the differential diagnosis of the noninfectious entities that mimic pneumonia, identifies the clinical features that raise suspicion of their presence, and reviews the steps necessary for diagnosis.

Clinical Suspicion of Pneumonia Mimics

The disease pattern at presentation may raise an early suspicion of noninfectious mimics of pneumonia. For example, fever, new air space disease, and pulmonary symptoms in a patient just completing thoracic radiation for neoplasm would immediately raise the possibility of radiation pneumonitis, whereas the same patient receiving chemotherapy creates a suspicion of drug-induced pulmonary disease. Collagen vascular diseases and the granulomatous vasculitides commonly present as multisystem diseases, with affected patients exhibiting either skin rash, ocular inflammation, synovitis, renal disease, or central nervous system disease. Peripheral blood eosinophilia suggests eosinophilic pneumonia or the Churg-Strauss syndrome.

A patient's failure to respond to antibiotic therapy is the most common stimulus that pushes the clinician to consider noninfectious mimics of pneumonia. Symptomatic relief and roentgenographic improvement are both important facets of this therapeutic response. The rate of improvement with antibiotics is variable and it is difficult to precisely distinguish patients who are responding slowly from patients who are not responding. Radiographic progression and lack of symptomatic improvement after 1 week of antimicrobial therapy or lack of radiographic improvement after 2 weeks of treatment should raise the possibility of pneumonia mimics. Disease severity plays a strong role in the decision to consider pneumonia mimics. The seriously ill, hospitalized patient provides little or no margin for error diagnostically, and the search for noninfectious mimics of pneumonia should be initiated earlier in these patients than in less seriously ill patients.

Once a noninfectious mimic of pneumonia is suspected, the differential diagnosis is considered (Table 1). The illnesses listed in Table 1 all produce air space disease, fever, and pulmonary symptoms.

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TABLE 1. Noninfectious Mimics of Pneumonia

Pulmonary embolism
Pulmonary neoplasm
Obstructive endobronchial neoplasm with distal infection
Bronchoalveolar cell carcinoma
Lymphoma
Kaposi's sarcoma
Radiation pneumonitis
Bronchiolitis obliterans organizing pneumonia
Fibroproliferative phase of late adult respiratory distress syndrome
Collagen vascular disease
Systemic lupus erythematosus
Polymyositis and dermatomyositis
Mixed connective tissue disease
Drug-induced pulmonary disease
Hypersensitivity pneumonitis
Granulomatous vasculitis
Wegener's granulomatosis
Churg-Strauss syndrome
Acute/chronic eosinophilic pneumonia

Many chronic pulmonary syndromes, such as sarcoidosis, idiopathic pulmonary fibrosis, pneumoconioses, pulmonary alveolar proteinosis, and histiocytosis-X, are not listed. In patients with these diseases, the chronicity of the illness and lack of fever guides the clinician away from infectious pneumonia.

Pulmonary Embolism

Pulmonary embolism is a common disease in the United States, with 170,000 to 650,000 patients affected and 50,000 deaths annually (Dalen & Alpert, 1975; Bell & Simon, 1982; National Institutes of Health, 1986; Anderson et al., 1991). Underdiagnosis of pulmonary embolism is common (Goldhaber et al., 1982; Mercer & Talbot, 1985; Gross et al., 1988; Rubenstein et al., 1988). A missed diagnosis of pulmonary embolism has resulted in a mortality rate five to six times greater than that seen in patients promptly diagnosed.

Risk factors for pulmonary embolism, both inherited and acquired, have been well described (Coon, 1984; Moser, 1990; Raskob & Hull, 1990). Although inherited risk factors contributing to a hypercoagulable state are rare, acquired risk factors are not. The more common acquired risk factors include age, previous venous thromboembolism, prolonged immobility or paralysis, malignancy, congestive heart failure, estrogen use, trauma, pregnancy, obesity, and surgery.

Clinical Symptoms and Signs of Pulmonary Embolism

Every study addressing the difficulty in diagnosis of pulmonary embolism comments on the lack of specificity of the symptoms and signs of the disease. The most common symptoms are dyspnea, pleuritic chest pain, apprehension, and coughing. Any or all of these may result from a variety of cardiopulmonary disorders, including infectious pneumonia (Raskob & Hull, 1990). In one series of patients with acute pulmonary embolism, the classic symptom triad of hemoptysis, pleuritic chest pain, and dyspnea was noted in only 20% of patients (Wenger et al., 1972). The recent Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) study cited the difficulty of using symptoms to detect the presence of pulmonary embolism (PIOPED Investigators, 1990). The pattern of respiratory symptoms was the same for patients with angiographically proven pulmonary embolus and patients with a negative angiogram (Stein et al., 1991a). Clinical signs in pulmonary embolism are no more specific. Tachypnea, rales, tachycardia, increased intensity of the pulmonic component of the second heart sound, and fever may be present in some combination. The presence of fever with pulmonary embolism may direct initial clinical suspicion toward infectious pneumonia. Although fevers caused by pulmonary embolism are typically of low grade ($\leq$38.5°C) (Moser, 1990), elevations to 40°C may be seen in some patients (Murray et al., 1979).

Laboratory Tests in Pulmonary Embolism

The average peripheral leukocyte count at the time of hospital admission of febrile patients with pulmonary embolism was 11,600/mm^3 in one study (Murray et al., 1979). Among outpatients presenting to the emergency department with pleuritic chest pain and leukocytosis, approximately one third proved to have pulmonary embolism (Hull et al., 1988).

Arterial oxygenation is commonly measured in the evaluation of a patient suspected to have pulmonary embolism. Hypoxemia is common in major pulmonary embolism but is not universal. In the PIOPED study, the mean arterial PO_2 level in patients with pulmonary embolism was 70 ± 16 mm Hg, compared with 72 ± 18 mm Hg in those with similar symptoms but no embolism. Patients with pulmonary embolism had an A-a gradient of 37 ± 17 mm Hg compared to 35 ± 18 mm Hg for patients without embolism (Stein et al., 199la).

The electrocardiogram (ECG) is frequently abnormal in patients with pulmonary embolism, but again, the changes are nonspecific. Most common are depression of the ST segment and/or T-wave inversion (Stein et al., 1991a). The pattern of right axis shift and S1Q3T3 is uncommon (Raskob & Hull, 1990). The ECG may be useful in differentiating pulmonary embolism from myocardial infarction and pericarditis, although ST–T wave changes compatible with early myocardial infarction can be seen in some patients with pulmonary embolism (Moser, 1992).

Chest Radiography in Pulmonary Embolism

The PIOPED study showed that 84% of patients with pulmonary embolism have an abnormal chest radiograph (Stein et al., 1991a). The most frequent abnormalities seen were atelectasis and/or pulmonary consolidation (Stein et al., 1991; Urokinase Pulmonary Embolism Trial, 1973). Other common findings included pleural effusion, diaphragmatic elevation, and prominence of the central pulmonary vasculature. Pulmonary embolism with infarction may result in cavitation on a plain chest radiograph (Libby et al., 1985; Redline et al., 1985).

Pleural effusion is seen on the chest radiograph in up to 51% of patients with pulmonary embolism (Stein et al., 1991; Urokinase Pulmonary Embolism Trial, 1973; Bynum & Wilson, 1978). When present, the effusion almost always occupies less than one third of the hemithorax (Stein et al., 1991; Bynum & Wilson, 1978). The pleural effusion with pulmonary embolism is unilateral in 98% of patients and is associated with parenchymal consolidation in 55% (Bynum & Wilson, 1978). In 86% of patients, the effusion is seen as only costophrenic angle blunting on the chest radiograph (Stein et al., 1991a). Analysis of such effusions shows that a majority are exudates and contain a predominance of polymorphonuclear cells (Bynum & Wilson, 1976). A parapneumonic effusion has similar findings. Only 27% of effusions from pulmonary embolism are hemorrhagic (Bynum & Wilson, 1976).

Diagnosis

Ventilation–perfusion (V/Q) lung scanning is a cornerstone test for the diagnosis of pulmonary embolism (Stein et al., 1993; PIOPED Investigators, 1990). The PIOPED trial showed that the V/Q lung scan is both sensitive and, in some cases, specific for pulmonary embolism (PIOPED Investigators, 1990). Eighty-eight percent of patients with high probability scans had pulmonary embolism demonstrated on pulmonary angiogram. The combination of a high-probability lung scan and a high clinical suspicion of embolism was 96% specific for recognizing pulmonary embolization. This combination should lead to initiation of anticoagulation therapy without further testing.

Patients with prior cardiac or pulmonary disease are more likely to have indeterminate V/Q scans in the face of pulmonary embolism (Stein et al., 1991b). In the patient with suspected pulmonary embolism and a low or intermediate probability lung scan, the diagnostic sequence should be an ultrasound examination of the lower extremities looking for deep venous thrombosis and, if negative, intravenous pulmonary angiography. If this diagnostic sequence is used, pulmonary angiography will be required for approximately one third of patients suspected of having pulmonary embolism.

Spiral computed tomography (spiral CT) has been used to diagnose pulmonary embolism (Chintapalli et al., 1988). The diagnostic finding is an intraluminal filling defect caused by thrombus and the most common parenchymal finding is a neighboring wedge-shaped pleural-based parenchymal infiltrate (Chintapalli et al., 1988). Spiral CT reliably recognizes thromboembolism in large pulmonary vessels but misses disease in pulmonary arteries less than 2 mm in diameter (Gary et al., 1998; Coche et al., 1998; Remy-Jardin et al., 1997). Intravenous pulmonary angiography is recommended as the diagnostic standard.

Pulmonary Neoplasm

Endobronchial Obstruction

Fever is rarely a cardinal manifestation of lung cancer and when present strongly suggests a complicating infection. Pneumonia and lung abscesses both may develop distal to an obstructing endobronchial tumor and the infectious illness may prompt the patient to seek medical help. Small-cell lung cancer and squamous carcinoma typically occur centrally and are more likely to cause endobronchial obstruction (Hyde & Hyde, 1974). Some metastatic neoplasms, including malignant melanoma, adenocarcinoma of the breast and gastrointestinal tract, hypernephroma, and Kaposi's sarcoma, may cause metastatic endobronchial obstruction without apparent pulmonary parenchymal metastases. Abscesses also may develop within a necrotic tumor mass, usually a squamous cell or large-cell undifferentiated carcinoma.

Most neoplasms involving the lung appear on chest radiographs as single or multiple nodular densities. On occasion, lung cancer results in a parenchymal abnormality that may be difficult to distinguish radiographically from pneumonia. The failure of a presumed pneumonia to respond to antimicrobial agents often is the first clue to an underlying neoplastic process. Of particular importance is the presence of hilar or mediastinal adenopathy, which may not be apparent on standard chest radiographs but may be visualized with computed tomography (CT). Although intrathoracic adenopathy may occur with acute pneumonia, the prevalence of adenopathy is greater in patients with neoplasm.

Sputum cytology performed on a patient with pulmonary infection creates difficulties in interpretation. Atypical sputum cytology is common in the presence of bronchial or parenchymal pulmonary infection, and there can be false-positive results for malignancy. Fiber-optic bronchoscopy with transbronchial biopsy is required for accurate diagnosis.

Bronchoalveolar Carcinoma

Bronchoalveolar carcinoma (BAC) is a well-differentiated adenocarcinoma that originates in the pulmonary parenchyma. The tumor spreads by contiguous growth along alveolar surfaces and lymphatic routes (Edwards, 1984). Accepted diagnostic criteria for BAC include the absence of adenocarcinoma elsewhere, the absence of a central bronchogenic focus of tumor, tumor growth along alveolar walls with papillary projections into the alveolar air space, and preservation of the architecture of the interstitium (Liebow, 1960).

Recent evidence suggests that the incidence of BAC is increasing. A retrospective review found that the incidence of BAC relative to the total number of occurrences of lung cancers had increased from 5% to 24% between 1955 and 1990 (Barsky et al., 1994). Much of this increase has been noted in women. BAC has a lower male-to-female ratio than other lung cancer cell types. The association of this cell type with smoking is less than other cell types. BAC has an increased incidence in patients with fibrotic lung diseases such as idiopathic pulmonary fibrosis or scleroderma lung.

As many as 45% of patients with BAC present with an asymptomatic peripheral lesion (Edwards, 1984). More extensive involvement may produce coughing, dyspnea, chest pain, cyanosis, hemoptysis, fever, and weight loss. A unique and characteristic feature of this neoplasm is profuse bronchorrhea, which has been reported in as many as one third of patients. Progressive restriction of lung capacity develops as the tumor extends to previously unaffected areas of the lungs. Severe hypoxemia may develop as a consequence of intrapulmonary shunting when the alveolar surface is filled with tumor infiltration while the circulation is unaffected (Fishman et al., 1974).

A study of 136 patients with BAC revealed that 30% had an area of consolidation on the chest roentgenogram at initial presentation (Hill, 1984). Seven percent of patients had a localized consolidation involving less than one lobe, while 33% presented with multifocal air space disease. Forty-three percent of patients had a single nodule or mass and 27% had multiple nodules. Pleural effusion was reported in 32% of cases (Hill, 1984). Multiple cystic spaces and cavitary infiltrates have been reported.

BAC requires a histologic diagnosis. Diagnostic material is best obtained by fiber-optic bronchoscopy (FOB) with both transbronchial biopsy

(TBBX) and bronchoalveolar lavage having a high diagnostic yield (Tao et al., 1986; Springmeyer et al., 1983). In some, a surgical lung biopsy via thoracoscopy or thoracotomy may be required (Greco et al., 1986).

BAC is managed in a manner similar to other non-small-cell lung cancers. If the tumor is localized, the preferred treatment is surgical removal. Treatment of multicentric or metastatic BAC is generally unsatisfactory. In this form, BAC is an aggressive malignancy with a poor prognosis and median survival of only 4 months in one series (Springmeyer et al., 1983). There are a few successful case reports of double lung transplantation (Etienne et al., 1997).

Hodgkin´s Lymphoma

Primary pulmonary Hodgkin's disease is a rare condition in which the lymphoma is restricted to the lung with no hilar or mediastinal lymph node involvement and no evidence of extrathoracic extent (Yousem et al., 1986). This occurs in less than 1% of patients with Hodgkin's disease and is more frequent in females (Berkman & Bruer, 1993). Some patients are asymptomatic but coughing is a frequent symptom. Weight loss, fever, and night sweats are present in up to 30% of patients (Yousem et al., 1986; Radin, 1990). Other symptoms include dyspnea, chest pain, hemoptysis, and fatigue. The chest radiograph most commonly shows nodules or masses, but may show an alveolar or reticulonodular infiltrate with air bronchograms. The nodules are often multiple and may cavitate. There are no CT scan findings specific for primary pulmonary Hodgkin´s disease (Yousem et al., 1986; Radin, 1990). The presence of B symptoms, bilateral and multilobar disease, cavitation, and advanced age are all associated with a poor prognosis. The diagnosis usually requires surgical lung biopsy. Reed-Sternberg cells must be present on an appropriate cellular background for diagnosis.

Secondary involvement of the lung with Hodgkin's disease is much more common than primary disease. Approximately 50% of patients show pulmonary parenchymal involvement at the time of presentation (Whitcomb et al., 1972). Three radiographic patterns have been described: nodular; bronchovascular-lymphangitic; and pneumonia-alveolar (Bailikian & Herman, 1979). Almost all patients with parenchymal disease will have associated mediastinal involvement and most will have evidence of extrathoracic disease.

Respiratory symptoms are frequently absent and pulmonary involvement is often discovered on screening radiography.

Non-Hodgkin's Lymphoma

Primary pulmonary non-Hodgkin's lymphoma is more common than primary pulmonary Hodgkin´s disease. However, secondary pulmonary involvement is less common than seen in patients with Hodgkin's disease. As many as 50% of patients have no symptoms. However, cough, chest pain, dyspnea, fever, night sweats, and weight loss all may occur (Li et al., 1990). The pattern of symptoms may relate to the specific cell type of the lymphoma (Colby & Yousem, 1985). The most common chest radiographic abnormality is sharply defined single or multiple nodules. Poorly defined single or multiple infiltrates also occur (Li et al., 1990; Turner et al., 1984).

Sixteen percent of patients with lymphoma develop pleural effusion in the course of their disease (Gabriel, 1965). Cytological examination of fluid removed by thoracentesis is nondiagnostic. Needle biopsy of the pleura or visibly directed thoracoscopic biopsy may establish the diagnosis (Berkman & Bruer, 1993).

The diagnosis of primary or secondary pulmonary lymphoma requires an adequate amount of tissue for examination. FOB with transbronchial biopsy is sometimes diagnostic, but most patients will require a surgical biopsy (Berkman & Bruer, 1993).

Lymphomatoid Granulomatosis

Lymphomatoid granulomatosis has recently been shown to be a B-cell neoplasm arising from Epstein-Barr virus (EBV)-infected cells. It may produce cough, dyspnea, chest pain, fever, night sweats, weight loss, and skin rash (Fauci et al., 1982). Males are affected more often than women. Typically, the chest radiograph shows multiple bilateral nodules that are frequently cavitary and are most often present in the middle or lower lobe

(Koss et al., 1986). Alveolar and interstitial infiltrates, pleural effusions, hilar adenopathy, and single nodules occur less often. The CT image is not specific.

Radiation Pneumonitis

Clinical Presentation

Radiation pneumonitis is the development of pulmonary infiltrates in a region of irradiated parenchyma accompanied by symptoms which may include fever, dyspnea, and nonproductive cough. The rate of development and severity of the radiation-induced changes are modified by a number of factors. These include the radiation dose, dose fractionation, total volume of lung irradiated, and the simultaneous use of certain chemotherapeutic agents (Phillips et al., 1975a,b). Coincidental discontinuation of corticosteroids may precipitate a severe case of radiation pneumonitis (Castellino et al., 1974; Parris et al., 1979; Pezner et al., 1984). The sequence of pathological events that occurs after pulmonary irradiation has been studied in detail (Gross, 1977; Smith, 1963; Coogle et al., 1986; Guzzon et al., 1993).

The clinical syndrome of radiation pneumonitis develops in only 5% to 15% of patients receiving thoracic radiation. When symptoms do develop, they typically start 1 to 3 months after the completion of therapy (Libshitz & Southard, 1974), but the range is from 2 weeks to 6 months after the completion of radiation therapy (Goldman & Enquist, 1975). A rule of thumb is to expect radiographic changes on the chest film 8 weeks after the delivery of 4000 rads, and 1 week earlier for each additional 1000 rads (Libshitz & Southard, 1974; Boyars, 1990). In general, the early onset of symptoms is indicative of a more serious illness and a protracted clinical course.

Nonproductive cough is often the earliest symptom. Later in the course, small amounts of sputum may be produced. Hemoptysis is unusual. The cardinal symptom of radiation pneumonitis is dyspnea. The onset is usually insidious, initially occurring with exertion. The dyspnea is progressive, and in severe cases may lead to respiratory failure (Boyars, 1990; Gracey, 1975). The degree of fever is variable, but may be $\geq 39°C$. Chest pain is usually musculoskeletal discomfort from cough. The patient may also complain of a sense of fullness in the chest or of a subjective limitation of inspiratory capacity.

On physical examination, the signs of radiation pneumonitis are usually minimal. Atrophy, telangiectasia, and brawny induration over the radiation ports is common (Smith, 1963). However, the severity and extent of the skin change does not correlate with the presence or absence of underlying pneumonitis. Evidence of consolidation in the area of pneumonitis may be appreciated during the physical examination. Moist crackles may be heard, and rarely a pleural friction rub.

Imaging

The earliest chest radiographic changes include parenchymal ground-glass opacification, creating a diffuse haze and indistinctness of the normal pulmonary markings over the irradiated area (Gross, 1977; Libshitz & Southard, 1974; Guzzon et al., 1993; Davis et al., 1992). With mediastinal irradiation, the haziness causes the mediastinal contours to become indistinct or blurred. Later, the chest radiograph may show nodular infiltrates or dense consolidation of the irradiated field. Air bronchograms are usually present (Gross, 1977; Libshitz & Southard, 1974; Guzzon et al., 1993; Davis et al., 1992).

Pleural effusions are sometimes associated with radiation pneumonitis. Such effusions almost always appear within 2 to 6 months after the completion of treatment (Libshitz & Southard, 1974a; Bachman & Macken, 1959; Bate & Guttman, 1957). They are rarely large, usually do not give rise to symptoms, and may persist for years. Although the radiographic changes of radiation pneumonitis may sometimes resolve completely, progression to fibrosis is the usual sequence. With fibrosis, the radiographic appearance changes to streaky opacities radiating from the area of pneumonitis with contraction of lung volume. The cardinal feature of radiation-induced changes on chest radiographs is the sharp borders of the densities corresponding to the margins of the radiation port. The boundaries disregard normal anatomic lung divisions. In a few

cases, extensive changes beyond the field of irradiation have been observed (Bennett et al., 1969).

Recently, CT has found use in the detection of acute radiation pneumonitis (Libshitz & Shuman, 1984). The most characteristic feature of radiation-induced change is its confinement within the irradiated field. The CT patterns in the affected lung include (1) ground-glass opacification corresponding to alveolitis and early interstitial pneumonitis; and (2) homogeneous consolidation corresponding to interstitial pneumonitis with accumulation of desquamated alveolar cells and protein-rich fluid within the alveoli (Libshitz & Shuman, 1984; Ikezoe et al., 1988, 1990). CT can detect changes that are not visible on conventional chest radiography. It is also more specific than chest radiography in the diagnosis of radiation-induced lung injury as the straight-edge effect is clearly seen on CT scans.

Diagnosis/Treatment

Any patient who has received more than 4000 rads of radiation therapy should be suspected of having radiation pneumonitis, especially if there has been a history of concurrent treatment with certain cytotoxic chemotherapeutic agents, or recent discontinuation of steroids. Radiation pneumonitis has an insidious onset, over days or possibly weeks. Laboratory data are rarely helpful in the diagnosis. A peripheral polymorphonuclear leukocytosis may be present, and the erythrocyte sedimentation rate may be elevated (Gross, 1977).

FOB and its attendant procedures (bronchoalveolar lavage, quantitative brush culture, and transbronchial biopsies) should be done. Bronchoalveolar lavage cell populations in radiation pneumonitis are nonspecific, but typically show a significant increase in the lymphocytes (Gibson et al., 1988; Roberts et al., 1993; Massilta et al., 1993). Transbronchial biopsy may be helpful in excluding tumor and infection, but is not specific for radiation pneumonitis. Surgical lung biopsy is rarely necessary. Radiation pneumonitis usually responds rapidly to 40 mg of prednisone daily with prompt defervescence and radiographic improvement in 1 to 2 weeks. Once infection and tumor are excluded by FOB, the next step should be a trial of corticosteroid therapy.

Bronchiolitis Obliterans Organizing Pneumonia

Clinical Presentation

The taxonomy of bronchiolitis obliterans organizing pneumonia (BOOP) is confusing. BOOP may be interpreted as a distinct histologic picture occurring at a specific time in the continuum of lung parenchymal damage and subsequent repair. BOOP is characterized by myxoid fibrous tissue polyps filling the lumen of bronchioles, and adjacent alveoli with coincident organizing intra-alveolar exudate. This histologic response is a sequela of multiple illnesses including infectious pneumonia, collagen vascular disease, toxic fume exposure, and drug-induced parenchymal lung disease. BOOP is associated with a consistent clinical pattern which includes a symptom duration of weeks to months, fever, and prompt improvement with corticosteroid therapy. The syndrome of fibroproliferative phase of late adult respiratory distress syndrome (ARDS) is included in this discussion of BOOP because of its similar histology and clinical features.

Men and women are affected equally. There is no relationship to smoking. A flu-like illness, fever, and increased sedimentation rate occur in 30% to 50% of patients (Alegre-Martin et al., 1991; Flowers et al., 1992; Yamamoto et al., 1992). Coughing is common, dyspnea is variable, and wheezing and hemoptysis are rare. Auscultation reveals crackles in two thirds of patients and finger clubbing is usually absent (Epleret al., 1985). Pulmonary function tests show a decreased vital capacity, normal flow rates, and a decreased diffusing capacity.

Bilateral patchy infiltrates are the most common radiographic finding. Cavities (Epler et al., 1985; Alegre-Martin et al., 1991) and effusions are rare. Chest CT will show that these patchy infiltrates are typically peripheral. Some patients may show focal nodular or mass-like opacities that have either a traversing air bronchogram or penetrating pulmonary vessel (Bouchardy et al., 1993).

Bronchoalveolar lavage in idiopathic BOOP usually shows an increase in all inflammatory cells. Costabel et al. (1992) noted an increase in lymphocytes, neutrophils, and eosinophils. Yamamoto et al. (1992) found a predominance of lymphocytes,

sometimes as high as 80% to 95% and a decrease in the CD4/CD8 ration to ≤ 1.0.

Diagnosis/Treatment

Histologic diagnosis usually requires a surgical lung biopsy (Epler et al., 1985). Occasionally, a transbronchial biopsy may be enough to establish the diagnosis (Azzam et al., 1993). In many patients, a typical clinical presentation, failure to demonstrate infection, granuloma or neoplasm by FOB with bronchoalveolar lavage, and rapid improvement with corticosteroids (within 1 week) are sufficient to establish a clinical diagnosis.

Prednisone is the treatment of choice for BOOP. The recommended dose is 40 mg daily for 2 weeks, with the dose reduced in 5- to 10-mg increments every 2 weeks. A maintenance dose of 10 to 20 mg daily is continued for at least 3 months. Fifty percent of patients show complete roentgenographic clearing by 2 weeks. Less than 3 months of steroid therapy is frequently followed by relapse. Normalization of the chest radiograph is seen in 65% to 80% of patients treated (Epler et al., 1985; Costabel et al., 1992; Yamamoto et al., 1992). The mortality is approximately 5% (Epler et al., 1985; Yamamoto et al., 1992). Patients with progressive disease despite therapy with 40 mg prednisone daily have a poor prognosis. Cytoxan and other cytotoxic agents are not of proven benefit.

The Fibroproliferative Phase of Late Adult Respiratory Distress Syndrome

The ARDS is a clinical entity characterized by acute, diffuse injury to the endothelial and epithelial surface of the lung that leads to respiratory failure. The fibroproliferative phase of late ARDS refers to a time of lung repair resulting in BOOP histology. Clinical experience has suggested benefit from systemic corticosteroids in some patients with this late fibroproliferative syndrome. The conundrum is to recognize this period of fibroproliferative repair in a patient population frequently too sick for surgical lung biopsy. Corticosteroids at other points in the ARDS disease continuum are of no value.

The chest roentgenogram of fibroproliferative ARDS is characterized by a patchy, dense consolidation progressing to a more diffuse, hazy, less dense, air space pattern (Winer-Muram et al., 1993, 1994). These less dense opacities have a diffuse, ground-glass appearance when imaged with CT.

A study of 13 ARDS patients with histologically proven lung parenchymal fibroproliferation showed a bronchoalveolar lavage fluid with a high percentage of neutrophils and elevated albumin concentration (Meduri et al., 1994). Most patients had fever $>38.8°C$ and leukocytosis, and their illness mimicked nosocomial pneumonia. Progression of fibroproliferation to pulmonary fibrosis produced respiratory death in 15% to 40% of ARDS patients (Zapol et al., 1979; Montgomery et al., 1985; Suchyta et al., 1992).

Collagen Vascular Disease

Systemic Lupus Erythematosus

Systemic lupus erythematosus (SLE) has a prevalence of 15 to 50 per 100,000 population in urban areas of the United States (Fessel, 1974). It is the most likely collagen vascular disease to mimic pneumonia. Lupus-associated pneumonitis has been reported to occur in 1% to 4% of individuals with SLE, with more severe pulmonary disease appearing in younger patients (Weidemann & Mathay, 1989; Cervera et al., 1993).

The syndrome of acute lupus pneumonitis can occur either in patients with chronic or newly diagnosed SLE. Patients present with fever, cough, dyspnea, tachycardia, tachypnea, and hypoxemia (Orens et al., 1994). The chest x-ray shows parenchymal disease which can be unilateral or bilateral (Orens et al., 1994). Effusions from coincident pleural involvement may be present (Good et al., 1983). Infection has to be ruled out before immunosuppressive therapy can be started. FOB with protected specimen brush quantitative culture and bronchoalveolar lavage should be considered early. Transbronchial biopsy will show only nonspecific inflammation in the majority of cases. Pulmonary hemorrhage is a well-recognized complication of SLE pneumonitis. When hemorrhage occurs, the mortality may be as high as 70% (Leatherman et al., 1984). The presence of antiphospholipid antibodies in SLE are associated with an increased incidence

of thromboembolism (Love & Santoro, 1990). In patients with SLE, the prevalence for lupus anticoagulant was 34% and anticardiolipin antibody 44% (Love & Santoro, 1990).

The most characteristic laboratory abnormality is an antinuclear antibody liter ≥ 1:160 which is found in 96% of patients with SLE. The diagnostic serologic finding is an elevation of the percent DNA binding to >15%. SLE pneumonitis is diagnosed when there is an appropriate clinical syndrome and diagnostic serologic tests are positive in the absence of infection and pulmonary edema secondary to congestive heart failure or renal failure. Lupus pneumonitis usually responds rapidly to the administration of prednisone, 1 mg/kg/day. Occasionally, symptoms will recur and azathioprine or cyclophosphamide may have to be used.

Polymyositis and Dermatomyositis

The incidence of polymyositis (PM) and dermatomyositis (DM) is estimated to be 2 to 3 patients per 100,000 population. Women are affected twice as often as men. The most common presentation is an insidious progression of muscular weakness, muscle pain (20% of patients), and dysphagia. The skin changes of dermatomyositis include erythema, maculopapular eruption, eczematous dermatitis, and rarely, exfoliative dermatitis. PM and DM are associated with neoplasia in 8% of cases.

The incidence of lung disease in patients with PM and DM has been reported as high as 45% (Sandbank et al., 1966). Pulmonary involvement has been estimated to precede muscle disease in at least one third of the reported cases and is not correlated with the severity of extrapulmonary manifestations (Weidemann & Matthay, 1989; Dickey & Myers, 1984). Pulmonary symptoms include nonproductive cough and insidiously progressive dyspnea. Fevers may be present and are usually associated with a more acute onset of symptoms (Weidemann & Matthay, 1989). Rales are common, but clubbing is absent (Dickey & Myers, 1984). X-ray findings are most often bilateral, parenchymal infiltrates predominant in the lower lobes (Tazelaar et al., 1990). Pulmonary function testing shows mild to severe decreases in total lung capacity and diffusing capacity (Tazelaar et al., 1990).

The presence of air space disease in a patient with PM or DM raises the possibility of noninfectious inflammation. FOB should be performed to exclude infection and tumor. In a patient with PM or DM that presents with pulmonary infiltrates, a search for skin rash or muscle weakness, including dysphagia, should be undertaken, and serum creatine phosphokinase measured. Electromyography and/or muscle biopsy should be performed in suspect cases. Lung biopsy is nonspecific and does not add materially to FOB in managing these patients.

Mixed Connective Tissue Disease

Mixed connective tissue disease shares clinical characteristics with SLE, progressive systemic sclerosis, PM and DM, and rheumatoid arthritis. Pulmonary disease is common, occurring in up to 85% of patients (Sullivan et al., 1984). Pulmonary involvement can manifest as pneumonitis, severe interstitial disease, pulmonary hypertension, pulmonary embolism, pulmonary hemorrhage, and/or diaphragmatic dysfunction.

Drug-Induced Pulmonary Disease

Patients with drug-induced pulmonary disease frequently present with fever. When fever and infiltrate occur acutely, the illness mimics infection. Table 2 lists most of the drugs known to cause diffuse lung injury (Winterbauer & Hammar, 1988). The clinical presentation begins with fever, followed by nonproductive cough and dyspnea. These symptoms may precede x-ray changes. Anorexia and weight loss are common. The physical examination has few abnormalities. Clubbing is absent. Auscultation of the lungs may be normal or disclose crackles. The chest x-ray may be normal at the onset of symptoms, but then progress in an asymmetrical fashion. The infiltrates frequently localize to one area, mimicking a pneumonia. The progression of pulmonary infiltrate is insidious. A high-resolution CT scan helps to define the parenchymal disease but has little diagnostic specificity. The histology of drug-induced diffuse lung disease is varied and nonspecific. The changes seen include alveolitis, granulomata, myxoid fibroproliferative change, bronchiolitis, and interstitial fibrosis. Vasculitis is rare.

TABLE 2. Pharmacologic Agents That Cause Diffuse Pulmonary Injury[a]

Cytotoxic drugs	Noncytotoic drugs	
Antiobiotics	Antibacterial agents	Nonsteroidal anti-inflammatory agents
Bleomycin	Nitrofurantoin	Phenylbutazone
Mitomycin	Amphotericin B	Sulindac
Neocarzinostatin	Sulfasalazine	Naproxen
Alkylating agents	Pyrimethamine	Azapropazone
Busulfan	Sulfadimethoxine	Fenbufen
Cyclophosphamide	Penicillin	Antiarrhythmic agents
Melphalan	Ampicillin	Amiodarone
Nitrosoureas	Cephadrine	Lidocaine
Carmustine (BCNU)	Metronidazole	Tocainide
Semustine (methyl-CCNU)	Isoniazid	Miscellaneous
Lomustine (CCNU)	*p*-aminosalicylic acid	Gold salts
Chlorozotocin	Analgesics	Penicillamine
Antimetabolites	Acetylsalicylic acid	Colchicine
Methotrexate	Opiates	Chlorpropamide
Azathioprine	Heroin	Imipramine
Mercaptopurine	Propoxyphene	Methylphenidate
Cytosine arabinoside	Methadone	Hydralazine
Miscellaneous	Sedatives	Dantrolene
Procarbazine	Ethchlorvynol	Cromolyn
VM-26	Chlordiazepoxide	Captopril
Vinblastine	Anticonvulsants	L-Tryptophan
Vindesine	Diphenylhydantoin	Crack cocaine
	Carbamazepine	Diuretics
	Beta-blocking agents	Hydrochlorothiazide
	Nadolol	Major tranquilizers
	Practolol	Haloperidol
	Pindolol	Fluphenazine
	Propranolol	

[a]Modified from Winterbauer & Hammar, 1988.

FOB should be performed in patients suspected of having drug-induced parenchymal lung disease to eliminate the possibilities of tumor and infection. The bronchoalveolar fluid reveals an increase in either neutrophils and/or lymphocytes. Lymphocyte subset analysis shows a predominance of T cells, frequently with a CD4/CD8 ratio < 1.

Hypersensitivity Pneumonitis

Clinical Presentation

Hypersensitivity pneumonitis is a diffuse parenchymal inflammatory disease caused by repeated inhalation of organic dusts containing protein particles of animal or plant origin (Ramazzini, 1940). Although many people are exposed to these antigens, only a few develop disease (Table 3). For example, in some farming communities, the prevalence of farmer's lung, the most common type of extrinsic allergic alveolitis, ranges from 1% to 8% of the population (Grant et al., 1972). This low incidence contrasts with that of pigeon-breeder´s disease, which occurs in 6% to 15% of those who raise pigeons (Reed et al., 1965).

Typical symptoms include cough, fever, tightness of the chest, malaise, and body aches (Sharma, 1991). These symptoms appear 8 to 24 hours after the most recent exposure to the offending antigen (Sharma, 1991). Many patients are unaware of a relationship between their symptoms and a specific exposure. Occasionally, the symptom complex is mistaken for an episode of flu or walking pneumonia. Expectoration is scanty and hemoptysis is rare. Examination of the lungs reveals fine crackles. The attack usually lasts 12 to 48 hours.

The chest x-ray may be normal at this stage. A

TABLE 3. Agents Associated with Hypersensitivity Pneumonitis[a]

Disease	Antigen	Source
Related to agriculture		
Farmer's lung	Thermophilic *Actinomyces*	Moldy hay, grain
Bagassosis	Thermophilic *Actinomyces*	Moldy bagasse (sugar cane)
Malt worker's lung	*Aspergillus fumigatus* or *A. clavus*	Moldy barley
Mushroom worker's lung	Thermophilic *Actinomyces*	Mushroom compost
Cheese washer's lung	*Penicillium casei*	Moldy cheese
Coffee worker's lung	Coffee bean dust	Coffee beans
Miller's lung	*Sitophilus granarius* (wheat weevil)	Infested wheat flour
Fish meal worker's lung	Fish meal dust	Fish meal
Compost lung	*Aspergillus*	Compost
Streptomyces albus EAA	*Streptomyces albus*	Contaminated fertilizer
Potato riddler's lung	Thermophilic *Actinomyces*, *Micropolyspora faeni*, *Thermoactinomyces vulgaris*, *Aspergillus* sp.	Moldy hay around potatoes
Tobacco worker's disease	*Aspergillus* sp.	Mold on tobacco
Winegrower's lung	*Botrytis cinerea*	Mold on grapes
Lycoperdonosis	Puffball spores	*Lycoperdon* puffballs
Related to animals		
Bird fancier's, breeder's, or handler's lung	Bird proteins, all types	Avian droppings or feathers
Pituitary snuff taker's lung	Animal proteins	Pituitary snuff
Furrier's lung	Animal fur dust	Animal pelts
Japanese summer house EAA	*Trichosporon cutaneum*	House dust, bird droppings
Related to contaminated water		
Humidifier or air conditioning lung	*Aureobasidium pullulans* or other microorganisms	Contaminated water in system
Sauna taker's lung	*Aureobasidium* sp.	Sauna water
Hot tub lung	*Cladosporium* sp.	Mold on ceiling
Tap water lung	Unknown	Contaminated tap water
Cephalosporium EAA	*Cephalosporium*	Contaminated basement sewage
Related to wood products		
Sequoiosis	*Aureobasidium*, *Graphium* sp.	Redwood sawdust
Woodworker's lung	Wood dust, *Alternaria*	Oak, cedar, and mahogany dust
Maple bark disease	*Cryptostroma corticale*	Maple bark
Suberosis	Cork dust mold	Cork dust
Woodman's disease	*Penicillium* sp.	Oak and maple trees
Wood trimmer's disease	*Rhizopus* and *Mucor* sp.	Contaminated wood trimmings
Thatched roof disease	*Saccharomonospora viridis*	Dried grasses and leaves
Familial EAA	*Bacillus subtilis*	Contaminated wood dust
Related to chemicals		
Chemical worker's lung	Isocyanates	Polyurethane foam, varnish, lacquer
Laboratory worker's EAA	Male rat urine	Laboratory rat
Pauli's EAA	Pauli's reagent	Laboratory reagent
Detergent worker's disease	*Bacillus subtilis* enzymes	Detergent

EAA, extrinsic allergic alveolitis
[a]Modified from Richerson et al., 1989.

study of mushroom worker's lung showed only 8% had an abnormal chest x-ray initially (Stolz et al., 1976). The initial radiograph changes are bilateral ground-glass haziness with loss of definition of the pulmonary vessels, fine nodular shadows varying from 1 mm to 4 mm in diameter, and reticular shadows. High-resolution CT is more sensitive than plain chest roentgenogram in demonstrating the disease. The diffuse ground-glass pattern seen is suggestive of but not specific to hypersensitivity pneumonitis.

In some patients, repeated exposure leads to chronic illness and pulmonary fibrosis. The clinical episodes are less dramatic and the patient experi-

ences only progressive dyspnea with or without coughing. Cyanosis may occur. Finger clubbing is rare. Ultimately, chronic irreversible pulmonary fibrosis may lead to polycythemia and cor pulmonale. This stage is characterized by chronic diffuse interstitial fibrosis with coarse reticulonodular infiltrates, especially in the upper- and mid-lung zones. The lungs shrink and show traction bronchiectasis. Selective upper-lung volume loss was found in 46% of patients in one study (Hapke et al., 1968).

Diagnosis/Treatment

The diagnosis depends on the history of exposure to a recognized antigen, the presence of specific serum precipitating antibodies to the antigen, intermittent or recurrent symptoms, bronchoalveolar lavage fluid demonstrating lymphocytosis with a CD4/CD8 ratio <1, and a good response to antigen avoidance and/or corticosteroids. Skin tests are of no value. Inhalational challenge with the offending antigen is diagnostic, but rarely necessary, and may be dangerous. Such tests should be performed only by experts in the technique. The potential dangers of challenge combined with lack of commercially available standardized antigens preclude routine use of the technique. Avoidance of exposure followed by absence of symptoms may be evidence of cause and effect. In the rare situation where the diagnosis remains obscure, open-lung biopsy could be performed.

The most important treatment is avoidance of the antigen. Minor symptoms can be treated with anti-inflammatory drugs and bronchodilators. In severe cases, corticosteroids for 2 to 4 weeks can achieve resolution of clinical, functional, and radiological findings. A small number of patients will develop cor pulmonale from progressive parenchymal fibrosis.

Granulomatous Vasculitis

Wegener´s Granulomatosis

Wegener's granulomatosis (WG) consists of a triad of (1) necrotizing granulomatous inflammation and vasculitis involving the upper and lower respiratory tract, (2) a generalized vasculitis affecting arteries and veins, and (3) glomerulonephritis. Classic Wegener's granulomatosis commonly presents with upper respiratory tract disease which may include destructive lesions of the nasal septum, sinusitis, chronic otitis media, and occasionally laryngitis. The most frequent lower respiratory tract symptoms are cough, chest pain, dyspnea, and occasionally hemoptysis. Patients with Wegener´s granulomatosis are often febrile and may have arthralgias, skin rashes, conjunctivitis, pericarditis, and central nervous system disease.

These patients characteristically have a high erythrocyte sedimentation rate, leukocytosis, elevated serum IgG and IgA levels, a low titer rheumatoid factor, and occasionally cryoglobulins in their serum. An initial presentation with renal failure is relatively uncommon, although an abnormal urinary sediment is a common finding. Chest radiographs most frequently show multiple well-demarcated peripheral nodules, but multiple patterns can be seen, including segmental or lobar consolidalion and diffuse reticulonodular infiltrates.

The diagnosis of Wegener's granulomatosis was advanced significantly with recognition of antineutrophil cytoplasmic autoantibodies (ANCAs). These antibodies react against lysosomal enzymes present in myeloid cells (Goldschmeding et al., 1989). Using indirect immunofluorescent techniques on alcohol-fixed neutrophils, two types of immunofluorescent staining patterns have been identified: (1) a pattern in which the staining is predominantly in a cytoplasmic distribution (Anti-PR-3); and (2) a perinuclear fluorescent pattern which is an artifact of ethanol fixation that results in rearrangement of positively charged granules around and on negatively charged nuclear membrane (anti-MPO). PR-3 antibodies recognize a soluble 29-kd serine protease (proteinase-3) in the lysosomal granules of neutrophils and monocytes (Jennette et al., 1990). MPO antibodies recognize other lysosomal antigens, including myeloperoxidase, elastase, cathepsin-G, lactoferrin, and lysozyme (Roberts, 1992). Anti-PR-3 has a high specificity for Wegener´s granulomatosis (Specks & Homburger, 1994). Anti-MPO has been observed in a wide spectrum of disease, including inflammatory bowel disease, autoimmune liver disease, and rheumatoid arthritis (Gal et al., 1994).

Diagnosis

The diagnosis of WG is established when a characteristic clinical syndrome is accompanied by typical pathologic features on a biopsy specimen. The American College of Rheumatology criteria for WG is a patient with vasculitis (tissue or angiographically demonstrated) and any two of the following four findings: (1) painful or painless oral ulcers or purulent or bloody nasal discharge; (2) chest radiograph showing the presence of nodules, fixed infiltrates, or cavities; (3) microhematuria (> five red blood cells per high power field) or red cell casts in urine sediment; and (4) histologic changes showing granulomatous inflammation within the wall of an artery or in the perivascular or extravascular area (Gaulard et al., 1988). These criteria had a sensitivity of 88% and specificity of 92% in recognizing WG (Gaulard et al., 1988). ANCA was not used in developing these criteria. The presence of anti-PR-3 appears to be a highly specific and moderately sensitive marker of WG, and when present in a patient with typical clinical features it may obviate the need for histologic confirmation.

For histologic confirmation an open-lung biopsy is the procedure of choice. The patchy nature of the infiltrate makes diagnosis difficult. The kidney is a poor site to sample for it rarely yields diagnostic histology. Biopsy of an upper airway lesion can confirm WG, but nonspecific inflammation does not rule out the diagnosis.

Treatment

The best treatment for WG currently is oral cyclophosphamide (2 mg/kg/day) and prednisone (initially 1 mg/kg/day) (Fauci et al., 1983; Guinee et al., 1994). Among patients who achieve remission after receiving standard therapy, conversion from daily to alternate-day prednisone usually occurs at approximately 3 months (Hoffman et al., 1992). Cyclophosphamide should be continued for at least one full year after the patient is in complete remission (Fauci et al., 1983; Hoffman et al., 1992). This treatment results in marked improvement or partial remission in 91% of patients and complete remission in 75% of patients (Hoffman et al., 1992). Although some patients achieve complete remission within a few months, the median time to achieve remission is 12 months (Hoffman et al., 1992).

Churg-Strauss Syndrome

Patients with Churg-Strauss Syndrome (CSS) have a triad of asthma, blood eosinophilia, and systemic vasculitis (Churg & Strauss, 1951). The central/peripheral nervous system and gastrointestinal tract are common extrathoracic sites of involvement. Three clinical phases of CSS have been postulated (Lanham et al., 1984). The first is a prodromal allergic phase, which may persist for years, consisting of allergic rhinitis, nasal polyposis, and asthma. The second phase is characterized by the onset of peripheral blood and tissue eosinophilia, frequently causing a syndrome resembling Löffler's syndrome, or chronic eosinophilic pneumonia. The eosinophilic infiltrative disease may remit and recur over years before the third phase, consisting of systemic vasculitis, is reached. Men and women are equally affected. Chest radiographs usually show pulmonary infiltrates that are patchy and sometimes transient, although occasionally large and small noncavitary nodules or diffuse pulmonary infiltrates are seen. Pleural effusions occur in about one third of the patients, and hilar lymph node enlargement has also been noted. In some patients, angiograms show hepatic or renal aneurysms resembling those seen in polyarteritis nodosa.

There is often a significant elevation in IgE level, and it may correlate with disease activity. Low titers of rheumatoid factor have also been noted, and most patients have an elevated erythrocyte sedimentation rate and mild anemia. Complement levels are usually in the normal range.

Diagnosis

The histologic triad of tissue infiltration with eosinophils, necrotizing vasculitis, and extravascular granuloma formation does not need to be present if one or more of these features are documented in patients with typical clinical features (Lanham et al., 1984). The American College of Rheumatology developed six diagnostic criteria for the diagnosis of CSS in a patient with documented vasculitis: (1) asthma, (2) eosinophilia >10% on differential

white blood cell count, (3) mononeuropathy (including multiplex) or polyneuropathy, (4) nonfixed pulmonary infiltrates on roentgenography, (5) paranasal sinus abnormality, and (6) biopsy containing a blood vessel with extravascularеosinophils (Masi et al., 1990). The presence of four or more of these criteria in a patient with documented vasculitis yielded a sensitivity of 85% and a specificity of 99% in recognizing CSS (Masi et al., 1990). In a patient with well-documented systemic vasculitis the combination of asthma, eosinophilia >10% on differential white blood cell count, and history of documented allergy (allergic rhinitis, food or contact hypersensitivity) other than asthma or drug sensitivity was 95% sensitive and 99% specific for CSS (Masi et al., 1990). In cases of suspected CSS, extrathoracic biopsy sites such as skin, gastrointestinal tract, or peripheral nerve should be considered prior to lung biopsy.

Treatment

CSS responds well to steroids. Allergic symptoms and eosinophilia improve rapidly with the vasculitic component requiring treatment for several weeks to subside. A short time interval from onset of asthma to development of vasculitis is associated with a worse prognosis (Chumbley et al., 1977; Lanham et al., 1984). Asthma usually persists after the resolution of the vasculitic illness with corticosteroids. The therapy of choice is prednisone with an initial dose of 1 mg/kg/day until a clinical response is attained. At that point the dose is tapered. Some patients will require the addition of oral cyclophosphamide at a dose of 2 mg/kg/day (Leavitt & Fauci, 1986).

Chronic Eosinophilic Pneumonia

Clinical Presentation

Women are affected by chronic eosinophilic pneumonia twice as often as men, with a peak incidence in the third decade of life. Preexisting atopic disease occurs in 50% of patients, with asthma being the most common manifestation. Asthma typically exists for years prior to symptoms of chronic eosinophilic pneumonia. Many patients are cigarette smokers. Most patients will present with a subacute respiratory illness of approximately 6 months' duration, with symptoms of nonproductive cough (90%), dyspnea (57%), fever (87%), and weight loss (57%) (Matsuse et al., 1997). The pathologic changes seen on open-lung biopsy are an intra-alveolar accumulation of eosinophils and histiocytes (Jederlinic et al., 1988).

Diagnosis/Treatment

Peripheral pulmonary infiltrates, an increase in blood eosinophils, bronchoalveolar lavage fluid eosinophilia, and transbronchial biopsy showing an eosinophilic parenchymal infiltrate are strongly supportive of chronic eosinophilic pneumonia. The presence of >30% eosinophils in the bronchoalveolar lavage cell differential is consistent with, although not diagnostic of, chronic eosinophilic pneumonia, but parenchymal infiltration with eosinophils on transbronchial biopsy is diagnostic. An open-lung biopsy is rarely needed (Carrington et al., 1969).

These patients usually respond promptly and completely to corticosteroids. Their response to low-dose corticosteroids is so dramatic that 10 mg of prednisone daily has been suggested as a therapeutic trial. If chronic eosinophilic pneumonia is present, there should be a dramatic, immediate response, usually within 3 to 5 days. Therapy of at least 6 months duration is often required to avoid relapse.

Summary

Infectious pneumonia and noninfectious pneumonia mimics frequently have overlapping symptom complexes and chest roentgenographic patterns. The initial evaluation of such patients should include a careful search for extrathoracic disease manifestations, exposure to hypersensitivity antigens, and recent medications, as well as recognition of risk factors for venous thrombosis/pulmonary embolism. Failure of the patient to respond to antibiotic therapy frequently is the first clue to the presence of a pneumonia mimic. Patients who demonstrate roentgenographic progression and fail to show symptomatic improvement after 1 week of

antimicrobial therapy or roentgenographic improvement after 2 weeks of treatment should be evaluated for mimics of pneumonia.

The diagnostic sequence to search for pneumonia mimics does not lend itself to a simple algorithm. Patients with multi-system disease should have serologic testing to check for collagen vascular disease and Wegener´s granulomatosis. The recommended diagnostic sequence for pulmonary embolism is ultrasound of the lower extremities (to detect deep venous thrombosis), ventilation–perfusion lung scans, and pulmonary angiography. Anticoagulation may be started at any point along the three-test sequence depending on the results. Imaging techniques are of limited help in the diagnosis of mimics of pneumonia. The exceptions are a thoracic CT scan which may be helpful in recognizing radiation pneumonitis by defining the sharp borders of the radiodensities corresponding to the margins of the radiation port, the high-resolution CT ground-glass appearance of hypersensitivity pneumonitis, and pulmonary angiograph for pulmonary embolism. FOB with bronchoalveolar lavage, transbronchial biopsy, and cultures for multiple pathogens should be done in many patients suspected of having pneumonia mimics. A surgical lung biopsy will be necessary in only a small fraction of patients. Recognition of pneumonia mimics is imperative. Most of the diseases described show a good response to appropriate therapy. The therapies used are widely disparate and proper selection requires accurate diagnosis.

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