Two of a Kind*

Diverse Presentations of the Same Disease

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PATIENT 1

A 46-year-old woman with a history of mild, intermittent asthma, hypertension, and focal segmental glomerulosclerosis presented with progressive renal failure for the initiation of hemodialysis. She denied any pulmonary symptoms other than seasonal allergies. She denied fevers, cough, chest pain, or weight loss. She uses an albuterol inhaler less than twice per month. She has a 30-pack-year tobacco smoking history, and continues to smoke a half pack per day. She denied any recent travel or exposure to tuberculosis.

She was afebrile with a BP of 97/60 mm Hg, respiratory rate of 18 breaths/min, and a heart rate of 76 beats/min. Room air pulse oximetry was 97%. The physical examination was notable for scattered rhonchi in the right mid-lung field and for trace peripheral edema. There was no clubbing or lymphadenopathy. Laboratory studies demonstrated an elevated WBC count of 15,000/µL with 76% neutrophils, a hematocrit of 32%, and a creatinine level of 7 mg/dL.

Chest radiography showed a 2.7 × 2.0 cm, well-circumscribed nodule in the right middle lobe that was new compared with a radiograph obtained 2 years earlier (Fig 1). CT of the thorax confirmed that this was a lobulated nodule with air bronchograms (Fig 2). There was no calcification, cavitation, lymphadenopathy, or pleural disease.

The patient was initially treated with a 2-week course of levofloxacin for the possibility of a rounded pneumonia, but a follow-up chest radiograph demonstrated that the nodule was larger. The patient was then referred for video-assisted thoracoscopic surgery for removal of the nodule.

PATIENT 2

A 53-year-old man without a significant medical history presented with a nonproductive cough, fevers, and right-sided chest pain that had progressed over the past 2 months. He was treated with a course of levofloxacin by his primary care physician without improvement. A chest radiograph demonstrated a right-upper-lobe cavitary lesion, and the patient was

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Figure 1. Posteroanterior radiograph from patient 1 demonstrating a nodule in the right middle lobe adjacent to the diaphragm.
referred to our institution. He has a 40-pack-year smoking history and denied any tuberculosis exposure.

He was afebrile with a BP of 125/67 mm Hg, respiratory rate of 18 breaths/min, and heart rate of 71 beats/min. The chest was clear to auscultation, and the rest of his examination was normal. There was no lymphadenopathy. Purified protein derivative testing and sputum examination findings for acid-fast bacilli were both negative.

Chest radiography showed a cavitary lesion in the right upper lobe (Fig 3) that was confirmed by CT (Fig 4). This also demonstrated a thick rind around the lesion and subcentimeter pretracheal lymph nodes.

The patient initially underwent flexible bronchoscopy with lavage and transbronchial biopsies. Culture findings were negative, and biopsy specimens revealed bronchiolitis obliterans organizing pneumonia. This was thought to possibly be a secondary process, and the patient was referred for a CT-guided transthoracic biopsy and subsequent video-assisted thoracoscopic surgery for resection.

What pathologic process could account for both of these patients’ presentations?
Diagnosis: Inflammatory pseudotumors

Inflammatory pseudotumors of the lung are uncommon pathologic findings and account for < 1% of all pulmonary tumors. It is generally a benign histologic process, but can demonstrate characteristics that mimic malignant lesions, such as invasion of pleural, mediastinal, hilar, and vertebral structures. Recurrence and metastasis have also been reported. Inflammatory pseudotumors can arise in extrapulmonary sites such as the kidney, CNS, and stomach.

Pseudotumors can occur throughout all ages, but are more common in younger populations (< 40 years old) and are the most common pulmonary lesions in children. Male and female subjects are equally affected. Patients can be asymptomatic or have a variety of manifestations, including dyspnea, cough, fever, chest pain, hemoptysis, or wheezing. Radiographic appearances can vary. Most cases present as a peripheral nodule or mass with predilection for lower lobes. The nodules are usually well circumscribed and can be lobulated or smooth. Multiple tumors can also occur. Calcification and cavitiation occur rarely. Other findings include pleural thickening or effusions, hilar or mediastinal lymphadenopathy, and endobronchial lesions. Patients with locally invasive pseudotumors are more likely to be symptomatic.

No consistent identifiable risk factors have been reported. Pathologically, inflammatory pseudotumors are thought to originate from an organizing pneumonia. Symptoms consistent with a preceding infection occur in approximately one third of patients, but there is no clear information on time course after the infection or correlation of location between the infection and the subsequent tumor. Several reports linking infection to pseudotumors have included viral, bacterial, rickettsial, and fungal etiologies. Pseudotumors are categorized into three subtypes: organizing pneumonia, fibrous histiocytoma, and lymphoplasmacytic. Several features are common to all subtypes and include proliferation of spindle-shaped fibroblasts, granulomatous inflammation, lymphoid hyperplasia, fibrosis, and invasion of lymphocytes. Significant overlap among the three subtypes occurs. The organizing pneumonia subtype occurs with the greatest frequency and is characterized by intra-alveolar lymphohistiocytic inflammation and fibrosis with preserved alveolar architecture. The fibrous histiocytoma subtype is characterized by a proliferation of spindle cells in a storiform pattern with inflammatory cells at the periphery. In the lymphoplasmacytic subtype, plasma cells and lymphocytes predominate often with lymphoid aggregates. This is the least common of the subtypes. No distinct clinical or radiographic features have been described to differentiate the three subtypes.

Surgical resection is the treatment of choice. Needle biopsy or transthoracic biopsy are likely to show fibrosis or inflammation and may not exclude a malignant lesion. Corticosteroids have been used for treatment with report of decreased size or regression. No randomized controlled trials have been reported. Overall mortality is low, with an overall 5-year survival of 91% in one surgical series of 23 patients. Deaths were not directly related to the pseudotumor, but they have been reported rarely. The overall recurrence rate is unknown but can occur many years later.

Our patients had no antecedent symptoms to suggest respiratory infection. There is minimal information identifying risk factors for the development of an inflammatory pseudotumor. Identifying these risk factors would be unlikely to alter the clinical
course, because surgical resection would still be necessary for treatment and to exclude a malignant lesion.

**CLINICAL COURSE**

Both patients underwent surgical resection without complication. Pathologic findings are demonstrated in Figures 5, 6. No malignancy was found, and all stain and culture findings were negative for infectious etiologies. There has been no recurrence in either patient after 1-year of follow-up.

**CLINICAL PEARLS**

1. Inflammatory pseudotumors are rare, benign histologic lesions that can demonstrate aggressive behavior clinically.
2. Patients may be asymptomatic or present with symptoms suggestive of a respiratory infection.
3. Radiographic findings are usually a solitary nodule or mass, but can also demonstrate a variety of abnormalities, including pleural or endobronchial disease.
4. Preoperative diagnosis is rarely made, and the treatment of choice is surgical resection.
5. Steroids may be useful when surgery is contraindicated.

**SUGGESTED READING**


Maier HC, Sommers SC. Recurrent and metastatic pulmonary fibrous histiocytoma/plasma cell granuloma in a child. Cancer 1987; 60:1073–1076
