The Insidious Onset of Dyspnea and Right Lung Collapse in a 35-Year-Old Man*

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A 35-year-old man presented with 4-month history of cough, chest pain, and shortness of breath. There was no history of fever, hemoptysis, night sweats, weight loss, environmental/drug exposure, or foreign travel. He was a nonsmoker with no previous medical illness. Chest radiographic findings were reported as normal. He was treated with two courses of antibiotics and a cough suppressant. Over the next 2 months, his cough persisted and his weight decreased by 2 kg. A repeat chest radiograph showed partial collapse of right lower lobe. He was unable to produce sputum, and was started on empiric quadruple antituberculosis therapy. Just over 1 month later, central chest pain with worsening dyspnea developed. The chest radiograph now showed a complete collapse of the right lung. He was referred for further evaluation and management.

Physical Examination

On hospital admission, the patient was breathless at rest, with a respiratory rate of 28 breaths/min and pulse oxygen saturation of 82% on room air. He had a regular pulse of 102 beats/min, BP of 130/70 mm Hg, and body temperature of 37°C. He was of average build with no evidence of a multisystem disease, clubbing, or lymphadenopathy. Chest examination revealed tracheal shift to the right accompanied with reduced chest expansion, dull percussion note, and absent breath sounds on the right side. Findings of a left-sided chest examination were normal.

Laboratory and Radiographic Findings

Hemoglobin was 16.2 g/dL with hematocrit of 48.7%, mild leukocytosis of 12.5 × 10^3/µL with neutrophilia of 76%, and normal platelet count of 307 × 10^3/µL. Serum BUN, creatinine, electrolytes, coagulation, and albumin results were normal. Liver function test results were normal, except an elevated γ-glutamyltranspeptidase of 117 U/L. Arterial blood gases on oxygen (10 L/min by face mask) revealed pH 7.45; PaCO₂, 39 mm Hg; PaO₂, 83 mm Hg; HCO₃, 27.6, base excess, + 4.0; and oxygen saturation of 96.7%. A chest radiograph showed homogeneous opacification of right hemithorax with right-sided mediastinal shift suggestive of right lung collapse (Fig 1). A CT scan of the chest revealed a mass lesion completely occluding the right main bronchus protruding above the carina, causing complete collapse of the right lung (Fig 2). There was no mediastinal lymphadenopathy. The left lung, liver, and adrenals were normal.

Hospital Course

The patient was suspected to have a carcinoid tumor. In view of severe symptoms and hypoxia, patient was scheduled for urgent bronchoscopy with a view to resectional surgery if feasible. After induction of general anesthesia, a flexible fiberoptic bronchoscope was introduced. The trachea was normal. The right mainstem bronchus was completely occluded with a smooth polypoid lesion that was protruding 1 cm above the carina but was not

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attached to it. The left-sided bronchial tree was normal. It was decided to proceed with a right thoracotomy. A mass was identified protruding from the bronchus intermedius all the way up to carina.

There was no evidence of mass attachment to the proximal right mainstem bronchial stump or to the carina. There was no evidence of pleural or significant mediastinal involvement. Right pneumonectomy was performed.

What is your diagnosis?
Diagnosis: Inflammatory pseudotumor of the lung (synonyms: inflammatory myofibroblastic tumor, xanthomatous pseudotumor, fibrous xanthoma, plasma cell granuloma, xanthogranuloma, histiocytoma, plasma cell tumor)

Inflammatory pseudotumor of the lung is a benign growth of unknown etiology. It was first described by Brunn in 1939, but the name “pseudotumor” was espoused by Umiker in 1954 because of its propensity to mimic clinically and radiologically a malignant process.

Inflammatory pseudotumors arise through a non-neoplastic process due to an unregulated growth of inflammatory cells. The cause of this dysregulation is unknown but is postulated as an unchecked response to viral or bacterial antigens. Some authors believe that the tumor is a low-grade fibrosarcoma with inflammatory (lymphomatous) cells. The propensity of these tumors to occasionally be locally invasive, multifocal, and progress to malignancy supports this hypothesis. Immunohistochemical staining to differentiate monoclonal lines of B and T cells (lymphoma) from polyclonal mixtures of cell lines (pseudotumor) are helpful. In some cases, the pseudotumor develops at a site of inflammation secondary to infection or a surgical procedure, likely due to antigen-antibody complex deposition and an ensuing immune response. Organisms found in association with pulmonary pseudotumors include Mycoplasma, Nocardiae, and Actinomycetes.

Histopathologically, the lesions are divided into three types based on the predominant feature: (1) organizing pneumonia pattern; (2) fibrous histiocytic pattern, which is the most common and is characterized by spindle shaped myofibroblasts arranged in whorls, and (3) lymphohistiocytic pattern. Pseudotumors of the lung are uncommon lesions. The incidence reported in the literature ranges from 0.04 to 0.7% of all lung masses. Pseudotumors can occur at any age (range, 1 to 77 years), with a peak incidence in the second and third decades. There is no apparent sex predilection. Inflammatory pseudotumor is the most common primary lung mass in children, constituting approximately 50% of all benign intrapulmonary tumors seen in the pediatric population.

In two case series, with a total of 81 patients, up to 40% of cases were asymptomatic and the tumor was seen as an incidental finding during chest radiography performed for other reasons, e.g., routine examination. Nearly 15% presented with symptoms of lower respiratory infection. Symptoms related to endobronchial obstruction included cough, dyspnea, chest pain, hemoptysis, and wheezing. Constitutional symptoms such as weight loss, fever, or fatigue are related to production of cytokines, especially interleukin-1, by the pseudotumor.

Although the lung is the most frequent site of origin, inflammatory pseudotumors have been reported from orbital, cardiac, GI, hepatic, nervous system, and renal sites. The most frequent is orbital, comprising 6% of all orbital lesions. Other sites are rare.

On chest radiography, a solitary, well-demarcated, sometimes lobulated, coin lesion in the periphery of the lung, frequently in the lower lobes, is the most typical image. The diameter ranges from 1 to 10 cm. Fifteen percent demonstrate calcification, < 10% have an ipsilateral effusion, 8 to 14% have atelectasis (due to constriction and tapering of the vessels and bronchi), and in < 7% hilar or mediastinal adenopathy is present. Cavitation rarely occurs. On CT scans, inflammatory pseudotumors have a variable and nonspecific appearance, but most commonly demonstrate heterogeneous attenuation and enhancement. Few reports describe these lesions on MRI with a heterogeneous intermediary signal on T1-weighted images and a high signal on T2-weighted images. On MRI, no specific pattern of contrast enhancement is reported.

The therapeutic approach is problematic because a firm diagnosis is established only after studying the excised tissue. 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. In a series of 23 patients with inflammatory pseudotumor, two distinct types were identified by the presence or absence of local invasion. The first type, noninvasive inflammatory pseudotumor, is more likely to occur in an asymptomatic patient and is characterized by a small lesion that does not invade surrounding structures and is easily removed by wedge resection. The second type is the invasive inflammatory pseudotumor of the lung, which occurs in younger patients who usually have systemic symptoms of fever, fatigue, or weight loss. The tumor may require a lobectomy or pneumonectomy with concomitant chest wall resection.

Radiation has been reported to be successful in some patients. Chemotherapy with cyclosporine, methotrexate, azathioprine, or cyclophosphamide has not been effective. Response to corticosteroids in inflammatory pseudotumor of the lung is unpredictable.

Overall prognosis of this tumor is excellent; reported 5-year, 8-year and 10-year survivals are 91.3%, 91.3%, and 77% respectively. The tumor appears to follow a benign course, with problems arising only when it lies in or spreads to a vital structure. Recurrence rates after resection are low at 4% and occur at sites of incomplete resection.
Follow-up

The most crucial aspect of management was to determine the involvement of carina and the nature of mass lesion. In view of the marked dyspnea and significant hypoxia, fiberoptic bronchoscopy under controlled ventilation was chosen for further evaluation. Once the carina and right mainstem were found to be free of tumor, a decision to proceed to lung resection (lobectomy or pneumonectomy) was reached.

The tumor was grayish white in color, firm in consistency, and measuring $4 \times 2.5 \times 1.5$ cm in maximum dimensions. Histology revealed proliferating myofibroblasts with sheets of lymphocytes and plasma cells (Fig 3). There was extensive surface ulceration and granulation tissue. All sampled lymph nodes were benign, and resection margins were clear. The dependant lung had areas of bronchiectasis and consolidation. All microbiological cultures (bacterial, fungal, and tuberculous) were negative.

The postoperative course was uneventful. By discharge on the fifth postoperative day, the patient was mobilized and had a room air saturation of 94%. At 6-month follow-up, the patient remained well with normal functional activity.

Clinical Pearls

1. Inflammatory pseudotumors of the lung are benign tumors with a peak incidence in the second and third decades. They are the most common primary lung tumors in children.
2. Local invasion may occur with significant morbidity.
3. A diagnosis is established only after resection of the tumor.
4. Surgical resection is the treatment of choice.
5. Prognosis is excellent after complete excision. The postoperative recurrence rate is low at 4%, and occurs at sites of incomplete resection.

Suggested Readings

Dehner LP. The enigmatic inflammatory pseudotumors: the current state of our understanding, or misunderstanding. J Pathol 2000; 192:277–279