A 76-year-old man had a nodule, shown on a chest radiograph, in the lower lobe of the left lung. He denied any symptoms of fever, weight loss, cough, chest pain, or shortness of breath. His past medical history disclosed hypothyroidism and glaucoma. He had a 25 pack-year history of smoking but quit 30 years prior to onset of symptoms. Results of a physical examination were normal. The chest radiograph revealed a 2×3-cm nodule (Fig 1). Retrospectively, a chest roentgenogram 4 years prior (Fig 2) showed that the nodule was significantly smaller. A CT scan of the chest revealed a noncalcified, irregular, pleural-based mass containing air bronchogram (Fig 3). Blunting of the left costophrenic angle appeared to be due to scarring, with no evidence of a pleural effusion.

What is the diagnosis?
Diagnosis: Amyloidoma

Transbronchial biopsy of the tumor was nondiagnostic. An open thoracotomy revealed a 3-cm lung mass in the lower lobe of the left lung. Histopathologic studies indicated that the mass was comprised principally of an amorphous eosinophilic material surrounded by chronic inflammatory cells (Fig 4A). The walls of the surrounding alveolar septae and the bronchiolar walls were also thickened with this eosinophilic material. Visualization of the amorphous material stained with Bennhold’s Congo red stain under a polarizing microscope revealed the green birefringence that is characteristic of amyloid proteins (Fig 4B). Serum and urine protein electrophoresis were both within normal limits.

The differential diagnosis of a slowly growing lung nodule, defined as a rate of doubling in volume over a period of more than 1 year, includes hamartoma, sarcoid granuloma, carcinoid tumor,1 lipoma, and low-grade bronchogenic adenocarcinoma.2 Other rare causes in the lung include pseudolymphoma,3 bronchiolar adenomatosis,4 sclerosing hemangio- mas,5 intravascular bronchioloalveolar tumor,6 sali¬vary gland tumor metastases,7 and amyloidoma.

Amyloidosis is a term pertaining to a group of disorders having in common the extracellular accumulation of amyloid, an eosinophilic fibrillar protein arranged in a β-pleated sheet and exhibiting an apple-green birefringence under polarized light after Bennhold’s Congo red staining.8 The type of amyloid protein varies with the underlying cause and is useful for classifying amyloidosis. The two principal amyloid proteins are (1) AL, which is derived from κ or λ light chains and is associated with primary amyloidosis and with amyloidosis due to multiple myeloma and Waldenström’s macroglobulinemia, and (2) AA, a distinct protein produced by the proteolytic conversion of serum amyloid A protein, an acute phase reactant and associated with secondary amyloidosis, ie, amyloid secondary to chronic inflammatory and infectious diseases.9

The spectrum of pulmonary involvement by amy-
loid is protein. It may be localized or diffuse. Pulmonary involvement, comprised of microscopic deposits, in secondary amyloidosis usually is an incidental finding. In contrast, multiple myeloma-associated pulmonary amyloidosis is diffusely interstitial in nature. Respiratory disease is present in 30 to 90% of cases of primary amyloidosis and has a good prognosis if it is confined to the lungs but carries a median survival of approximately 1 year if it is associated with systemic amyloidosis.

Diffuse interstitial amyloidosis typically occurs in the setting of systemic amyloidosis associated with primary amyloidosis or plasma cell dyscrasia. The amyloid may be deposited in the interstitium and along the intima and media of arterioles and venules and in the alveolar-capillary basement membrane. This form of amyloidosis is characterized by progressive respiratory insufficiency and pulmonary hypertension.

Although tracheobronchial and nodular amyloidosis are of the AL amyloid type, they are generally not seen in association with systemic amyloidosis. Tracheobronchial amyloidosis may present either as an isolated endobronchial mass or as diffuse constricting submucosal plaques with obstructive signs and symptoms. The diffuse form of tracheobronchial amyloidosis is very difficult to treat; localized stenosis may be amenable to surgery or laser therapy.

Nodular pulmonary amyloidosis (amyloidoma) typically presents with a single nodule or, more commonly, with multifocal lesions in patients in their sixth decade. The nodules are slow-growing, may calcify over time, and are not associated with systemic disease. Although nodular amyloidosis usually is asymptomatic and is found incidentally, cases of atelectasis, secondary bronchiectasis due to an extraluminal obstruction of a bronchus, and massive multinodular involvement resulting in respiratory failure have been reported. Nodular amyloidosis cannot usually be differentiated clinically or radiographically from bronchogenic carcinoma. The diagnosis may be made by transbronchial biopsy although the nodular amyloid is often surgically removed to rule out a malignancy. Although cases have been reported of transbronchial biopsies of amyloid without bleeding complications, the risk of significant hemorrhage is likely to be higher than it is for most solid tumors. Grossly, the nodules are firm and gray or pale tan in color. Larger lesions may cavitate or have focal areas of hemorrhage, necrosis, fibrosis, or calcium deposition. Histologically, the nodules are comprised of irregular masses of amyloid interspersed with areas of fibrosis. Chronic inflammatory cells, including lymphocytes, plasma cells, histiocytes, and multinucleated giant cells, surround the amyloid nodule. At the periphery of the nodule, amyloid may be present in the walls of small blood vessels, bronchioles, and alveolar septae. Recurrence is rarely following surgical removal of an amyloidoma and the overall prognosis is very good.

References