Lung Masses in a 70-Year-Old Man*

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A 70-year-old man presented with progressive mild dyspnea on exertion, cough, and low-grade fevers. He had a long history of atrial fibrillation, recurrent despite multiple cardioversions, and antiarrhythmics, and was currently rate controlled with amiodarone, 200 mg po tid. He also had a history of coronary artery disease documented by coronary angiography, asthma, and prior transurethral resection of prostate for benign prostatic hyperplasia. He was a lifelong nonsmoker with no occupational exposures.

Physical examination revealed an elderly man in no acute distress. Heart rate was 82 beats/min, BP was 150/80 mm Hg, respiratory rate was 16 breaths/min, and temperature was 37.1°C. Auscultation of the chest revealed mildly diminished breath sounds with otherwise normal lungs. The remainder of the physical examination was normal. Laboratory data were unremarkable, with a normal CBC, serum chemistry and liver function test results, and erythrocyte sedimentation rate.

The chest radiograph (not shown) demonstrated a hazy mass at the peripheral aspect of the right lung base. The cardiac size was normal. CT scan of the thorax revealed subcarinal lymph node enlargement (Fig 1) and masses in the left upper, left lower, right lower, and right middle lobes (Fig 2), each approximately 1 cm in size. There was focal ground-glass opacity in the azygoesophageal recess (Fig 3).

At bronchoscopy, there was no evidence of endobronchial lesions. Bronchial washings were negative for acid-fast bacilli and fungi, with rare atypical keratinizing squamous cells.

What is the diagnosis?
Figure 2. CT scan on the same date as in Figure 1, with lung window photography, reveals bilateral lung masses. On soft-tissue windows (not shown), masses had attenuation roughly the same as that of muscle.

Figure 3. Initial CT scan, again with lung window photography but more cephalad than Figure 2, demonstrates focal ground-glass opacity in the azygosophaged recess.
Diagnosis: Amiodarone-induced pulmonary toxicity

CT-guided percutaneous fine-needle aspiration of a right lung mass was performed, and revealed foamy histiocytes, type II pneumocytes, and fragments of benign soft tissue without malignant cells. These findings were believed to be consistent with amiodarone pulmonary toxicity, and the drug was discontinued. The patient was followed up with serial CT scans. The subsequent scans demonstrated complete resolution of the parenchymal masses, ground-glass opacity, and subcarinal lymph node enlargement over a 10-month period of time.

Amiodarone is an iodinated benzofuran derivative used in the treatment of a wide range of supraventricular and ventricular dysrhythmias. It has a variety of side effects, with reported ocular, neurologic, cutaneous, thyroid, hepatic, and pulmonary toxicities. Lung involvement is the most serious, with amiodarone-induced pulmonary toxicity (AIPT) occurring in 5 to 10% of patients. AIPT is, on occasion, fatal. Amiodarone can damage lung parenchyma both through an indirect immune reaction and through direct cytotoxic damage. It is believed that the different pathways of injury contribute to the variability in time until onset of symptoms, ranging from 2 to 30 weeks, with nearly two thirds of the patients presenting in a subacute manner, and the remainder presenting more acutely. Although AIPT develops more commonly in patients treated with high doses (> 400 mg/d), it is not uncommon for pulmonary toxicity to develop at low doses (200 mg/d), and after only a short duration of treatment.1,2

It is believed that older patients and those with preexisting lung disease are at greater risk of pulmonary toxicity.1

The presenting signs and symptoms are often nonspecific, including cough, exertional dyspnea, low-grade fevers, pleuritis, and weight loss. Leukocytosis and an elevated erythrocyte sedimentation rate can be present, but these studies may instead be normal. Pulmonary function tests reveal a restrictive pattern and decreased diffusion capacity in the majority of cases.2–4 In patients with preexisting cardiopulmonary disease, the symptoms are often initially falsely attributed to worsening heart failure, pneumonia, or malignancy, and the imaging findings are often variable and confusing.

The radiographic manifestations of AIPT are protean, reflective of its cytotoxic and immune mechanisms of injury. Most commonly, AIPT presents as nonspecific interstitial pneumonia (NSIP) with expansion of the pulmonary interstitium by mononuclear inflammatory cells, mild interstitial fibrosis, and hyperplasia of type II pneumocytes. In these patients, symptom onset is usually within months of treatment initiation. At high-resolution chest CT, bilateral lung disease is characterized by scattered regions of ground-glass opacity and interlobular septal thickening with minimal architectural distortion. This can progress to basal predominant fibrosis with honeycombing and traction bronchiectasis in its later stages. Less commonly, AIPT can manifest as bronchiolitis obliterans organizing pneumonia (BOOP) or cryptogenic organizing pneumonia. This results in more patchy interstitial inflammation and loose fibrotic plugs that occlude terminal bronchioles, alveolar ducts, and alveoli on histopathologic specimens. BOOP in isolation is rare, and it more commonly occurs concomitantly with NSIP. Although patients with BOOP often present with similar nonspecific signs and symptoms of progressive dyspnea, dry nonproductive cough, and fever as those patients with NSIP, a CT scan can demonstrate more nodular areas of peripheral consolidation and bronchial wall thickening or dilation. Subpleural nodular opacities may also occur. The radiographic abnormalities typically resolve after stopping amiodarone, but on occasion steroid therapy may be required.

AIPT can rarely manifest as more focal peripheral opacities that are mass-like. These are usually high in attenuation because of the incorporation of iodine-rich amiodarone into the type II pneumocytes. In fact, high attenuation is noted not only in the lungs but also in the liver and spleen because of the incorporation of metabolites into the reticuloendothelial system. Amiodarone can result in inflammation of the pleura with subsequent exudative effusions or thickening, although these typically do not occur in isolation. AIPT presenting as an isolated pulmonary mass in association with cutaneous vasculitis has also been reported,5 with complete resolution of the mass and of the skin abnormalities following cessation of drug therapy.

Just as there is no correlation between the development of AIPT and the duration of therapy or total cumulative dose, the time to resolution of symptoms and radiographic abnormalities is also variable, often taking months. This is secondary to the long half-life of amiodarone metabolites. Radiographic abnormalities generally resolve after cessation of the drug. There have been reports of regression of radiographic abnormalities after initiation of steroids despite continuation of amiodarone. Similarly, there have been reports of recurrence of radiographic abnormalities with reinitiation of amiodarone or cessation of steroid therapy.

The typical differential diagnosis of a mass or masses generally centers on neoplasm, particularly in a smoker. In patients receiving amiodarone therapy,
the drug may instead be the responsible agent. Resolution of abnormality with cessation of drug therapy is the key to radiologic diagnosis.

REFERENCES
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