Recurrent Interstitial Pneumonitis and Pulmonary Hemorrhage Secondary to Amiodarone Toxicity

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Introduction

Amiodarone is a commonly used drug for the treatment of cardiac arrhythmias. It has a broad range of toxicity including photosensitivity, blue-gray discoloration of the skin, thyroid dysfunction, corneal deposits, abnormal liver function tests, and bone marrow suppression.[1] Pulmonary toxicity is the most serious adverse effect of amiodarone. Treatment of amiodarone-induced pulmonary toxicity includes discontinuation of the drug and initiation of glucocorticoid therapy in the majority of symptomatic patients. This case of recurrent amiodarone toxicity was manifested by acute interstitial pneumonitis and diffuse alveolar hemorrhage after a rapid taper of glucocorticoids.

Case Report

A 60-year-old male patient with no previous lung disease was admitted to the hospital with dyspnea and hypoxemia of 85% on room air. On physical examination, he had bilateral late inspiratory rales involving two-thirds of the chest. His chest x-ray showed diffuse bilateral pulmonary infiltrates (see Figure 1).

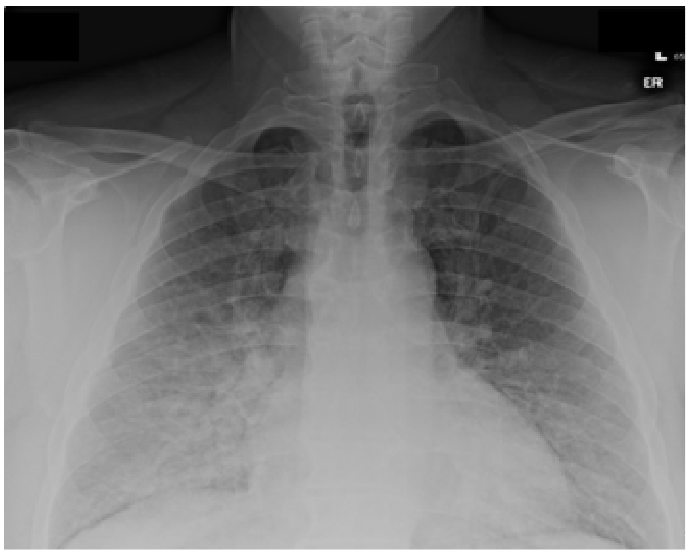

Figure 1. PA chest x-ray showing diffuse interstitial infiltrates especially at the bases.

The patient had no history of occupational pulmonary exposure or history of rheumatologic disorder or joint pain. He was diagnosed with atrial fibrillation nine months prior to presentation and was started on amiodarone 200 mg daily at that time.

After admission, his laboratory workup revealed normal blood counts and electrolytes. His brain natriuretic peptide (BNP) level was 150 pg per milliliter. A 2-D echocardiogram showed normal ejection fraction. There was no clinical or radiologic improvement after empiric antibiotics and treatment with diuretics.

A high resolution computed tomography of the chest was performed and showed bilateral ground glass opacities associated with small bilateral effusions (see Figure 2). Amiodarone-induced hypersensitivity pneumonitis was suspected. Subsequently, amiodarone was stopped and treatment with glucocorticoids initiated.

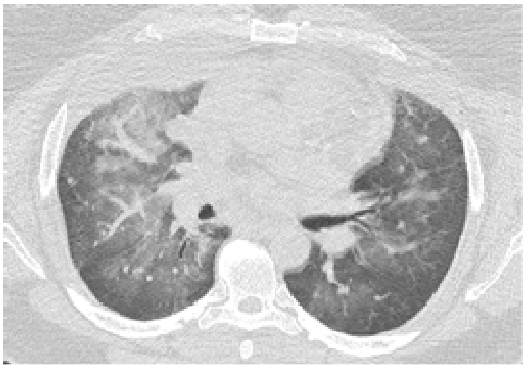

Figure 2. High resolution CT scan of the lung demonstrating bilateral ground glass appearance more prominent in the right middle lobe.

There was a significant clinical and radiologic improvement (see Figure 3) on a follow-up visit one month later. The glucocorticoids were tapered over two weeks, then stopped.

One week after stopping glucosteroids, the patient complained of shortness of breath on minimal activity, rapidly worsening to occur also at rest. He also complained of a dry cough that progressed over the next few days to mild hemoptysis. He again was hypoxic with bilateral rales on physical examination and his chest x-ray revealed bilateral infiltrates.

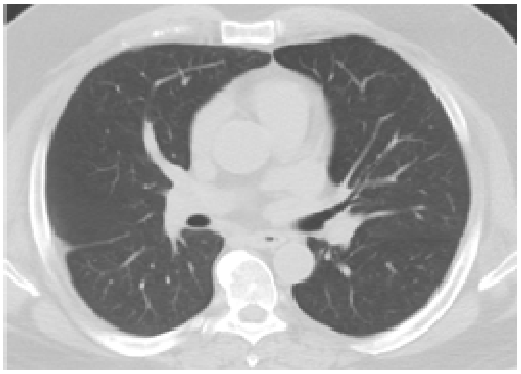

Figure 3. High resolution CT scan after steroid treatment showing almost complete resolution of the infiltrates.

Bronchoscopy was performed and transbronchial biopsies were obtained from the right lower lobe. The pathology examination showed interstitial fibrosis with no evidence of vasculitis or neoplasm (see Figures 4 and 5).

Bronchoalveolar lavage in the right middle lobe yielded a progressively bloodier return. Cytology of the fluid was negative for malignant cells and revealed numerous lipid-laden macrophages (index of 70%), characteristic of amiodarone toxicity. A significant number of hemosiderin-laden macrophages (index of 41%) were present, confirming the diagnosis of alveolar hemorrhage.

The patient was started on intravenous glucocorticoids. He significantly improved and was discharged home on prednisone 60 mg daily with plans to follow-up for several months. A follow-up examination after two weeks revealed clinical and radiologic amelioration.

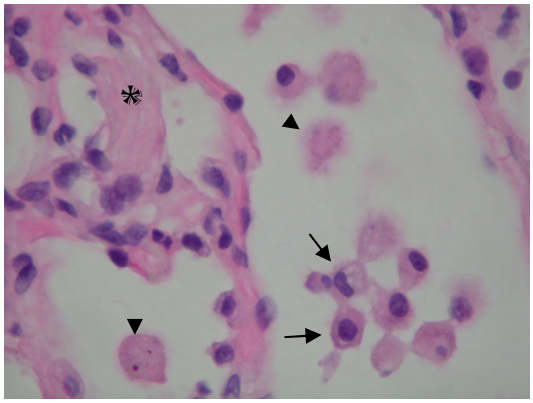

Figure 4. Transbronchial biopsy showing fibrosis (asterisk), lipid-laden macrophages (black arrows), and hemosiderin-laden macrophages (arrowheads).

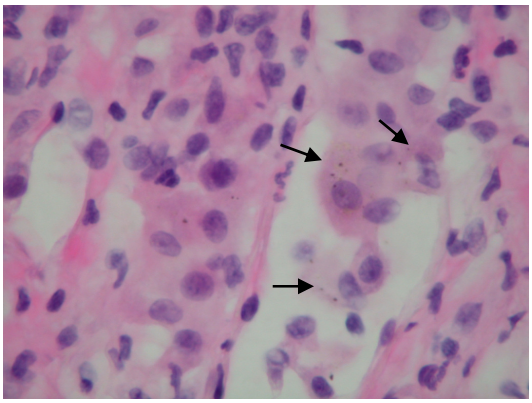

Figure 5. Transbronchial biopsy with hematoxylin and eosin stain. The arrows indicate macrophages with hemosiderin granules.

Discussion

Pulmonary toxicity secondary to amiodarone use occurs in 5-15% of patients.[2] Pulmonary manifestations range from mild to severe and even fatal disease such as ARDS. The most common presentation is interstitial pneumonitis accounting for one-third of patients.[3]

Interstitial pneumonitis usually is recognized after two or more months of therapy, especially in patients in whom the dose of amiodarone exceeds 400 mg per day. Cytology from bronchoalveolar lavage is characterized by mononuclear cells predominance and foamy alveolar macrophages. Type II cell hyperplasia and pulmonary fibrosis have been reported. Other manifestations include organizing pneumonia,[4] eosinophilic pneumonia, and lung nodules.[5]

Alveolar hemorrhage is a rare complication of amiodarone pulmonary toxicity. Only a few cases were reported in a large study of 171 patients.[4] Two other cases of alveolar hemorrhage secondary to amiodarone use also were reported.[6]

Amiodarone is a highly lipophilic drug that avidly binds to adipose tissues, resulting in a large distribution volume and a prolonged half-life reaching 180 days.[7] Given the high accumulation in adipose tissue, pulmonary toxicity may progress despite drug discontinuation. Treatment includes stopping the offending drug with initiation of glucocorticoid therapy in severe cases. Prednisone at 40 to 60 mg daily is recommended with slow tapering, as tolerated, over two to six months. Despite the slow tapering, cases of recurrent pulmonary intoxication may occur.[8]

In our case, the rapid tapering of prednisone may have been responsible for the acute recurrence of a more severe form of interstitial pneumonitis with evidence of diffuse alveolar hemorrhage. The patient's elevated body mass index suggested a high volume of distribution of amiodarone which might explain the severity of the recurrent disease. This case emphasizes the importance of slow tapering of glucocorticoids following amiodarone-induced lung injury.

References

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Keywords: interstitial lung disease, hemorrhage, amiodarone, drug toxicity, case report