Amiodarone-induced Pulmonary Toxicity

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ABSTRACT

A 76-year-old woman presented with dyspnea caused by pulmonary thromboembolism and chronic obstructive pulmonary disease (COPD). During management for COPD, the patient experienced ventricular tachycardia, which was controlled by the administration of amiodarone. Six weeks after amiodarone administration, she visited the hospital due to aggravation of the dyspnea. A chest computed tomography scan indicated increased haziness in both lung fields. The haziness observed in the lung fields and dyspnea improved several weeks after discontinuation of amiodarone treatment and initiation of glucocorticoid treatment.

Key words: amiodarone

Introduction

Amiodarone is very frequently used as an antiarrhythmic agent owing to its wide indication and various antiarrhythmic mechanisms. However, physicians should be extremely cautious of the toxicities associated with it, such as thyroid or pulmonary changes. Although most toxic reactions are reversible, they develop very quickly and aggressively, and therefore, their prompt detection and management is mandatory. Here, we report a case of amiodarone-induced pulmonary toxicity and briefly review amiodarone–related toxicities.

Case

A 76-year-old woman visited our hospital for dyspnea 2 years ago for the first time. She had hypertension on medication and mild chronic obstructive pulmonary disease (COPD). Echocardiography revealed normal left ventricular systolic function without any valvular diseases. A chest computed tomography (CT) scan revealed a large thrombus in both pulmonary arteries. Anticoagulation with warfarin was initiated for the treatment of acute pulmonary thromboembolism.
(PTE). Although PTE improved with anticoagulation therapy, the patient was admitted to the pulmonology department several times because of exacerbation of the COPD. During the management of COPD, the patient developed sustained ventricular tachycardia (VT) without hemodynamic collapse, and therefore, amiodarone treatment was initiated.

Following treatment with amiodarone (200 mg, twice a day), no VT was recorded on the electrocardiogram. However, 6 weeks later, she visited the outpatient clinic before her appointment because of severe dyspnea. There were crackles in both lung fields and the posterior–anterior view of the chest and high resolution CT (HRCT) showed increased opacities in both lungs (Figure 1). Arterial blood gas analysis showed hypoxemia. Thereafter, amiodarone treatment was discontinued and steroid therapy was initiated. Several days later, the oxygen requirement decreased rapidly and the haziness in both lung fields also improved. After 3 months, the haziness in the lung fields disappeared completely.

**Discussion**

Amiodarone is very widely used for the treatment of atrial and ventricular tachyarrhythmia. It has multiple effects on electrical myocardial activation, primarily by blocking potassium, sodium, and calcium channels, as well as the adrenergic receptors. It can also be used to control atrial fibrillation in patients with heart failure.

However, several toxicities associated with amiodarone have also been widely reported. Pulmonary toxicity, a major cause of death, is an amiodarone–related toxicity. Thyroid dysfunction has been reported in up to 20% of the cases in which high doses of amiodarone were administered and approximately 3–4% of the cases in which low doses of amiodarone were administered. Cardiac toxicities, such as sinus bradycardia and QT prolongation; hepatotoxicity; ocular changes, such as corneal microdeposits and optic neuropathy; and skin reactions are other common complications that are noted in clinical settings.

![Figure 1. Increased opacities in both lung fields as shown on a chest radiograph (Left) and a high resolution computed tomography scan (Right).](image-url)
The incidence of pulmonary toxicity is approximately 5%. The onset time often ranges from several months to several years after initiation of amiodarone treatment, and varies among cases. The cumulative dose rather than the serum level is major determinant of toxicity. It is known that a maintenance dose of <305 mg/day does not cause pulmonary toxicity. However, our patient was on a maintenance dose as low as 200 mg/day.

Pulmonary manifestations of amiodarone-induced pulmonary toxicity include chronic interstitial pneumonitis, organizing pneumonia, acute respiratory distress syndrome, and even a solitary pulmonary mass–like lesion of fibrosis. Chronic interstitial pneumonitis is the most common pulmonary manifestation. It clinically presents as nonproductive cough and dyspnea. Weight loss and fever can also be observed in certain cases. Pulmonary toxicity is more common in elderly patients, patients with preexisting lung diseases, and those receiving amiodarone treatment for 6 to 12 months. The other risk factors include history of cardiothoracic surgery, the use of high oxygen mixture, and co-existing respiratory infection.

In the present case, posterior–anterior view of the chest and pulmonary HRCT revealed diffuse or localized interstitial or alveolar opacities. Although bronchoalveolar lavage and lung biopsy could be helpful in such cases, their results are variable without pathognomonic findings.

Amiodarone-induced pulmonary toxicity is rarely fatal and mostly reversible. Discontinuation of amiodarone treatment is the first–line treatment. Because of the fatty accumulation and long half–life of amiodarone, pulmonary manifestation can persist even after discontinuation of amiodarone treatment.

Therefore, glucocorticoid treatment is commonly used for symptomatic amiodarone–induced pulmonary toxicity. The common glucocorticoid dose at treatment initiation is 40 to 60 mg of prednisone per day. It can be tapered over a period of 2 to 6 months. As described above, because of the prolonged systemic effect of amiodarone, pulmonary symptoms can recur after steroid withdrawal. Glucocorticoid treatment at a reduced dose can be continued to control the symptoms. Amiodarone should be avoided in patients with a previous history of amiodarone–induced pulmonary toxicities.

References