Reversible amiodarone-induced lung disease: HRCT findings

Introduction

Amiodarone is a unique anti-arrhythmic agent originally developed as a vasodilator. It is highly effective in controlling ventricular and supra-ventricular arrhythmias. Unfortunately, many adverse effects are related to the use of this drug, especially lung toxicity. Since the first report 12 years ago, of CT patterns in cases of amiodarone-induced lung disease, very few studies have been carried out concerning CT findings [1, 2, 3, 4, 5]. Kulhan et al. have established the value of CT using standard techniques that provide a means of identifying patients with significant pulmonary accumulation of amiodarone [6]. High-resolution computed tomography (HRCT) is well established in noninvasively evaluating the thin structural details of the normal and pathological pulmonary parenchyma [7].

The aim of our study was to describe HRCT patterns in a large number of symptomatic patients considered as having a reversible amiodarone-induced lung disease. With regard to the possible differential diagnosis, our second goal was to emphasize the semiological value of these findings.

Abstract

The aim of this study was to describe thoracic high-resolution computed tomography (HRCT) findings of reversible amiodarone-induced lung disease (AILD). The thoracic HRCT of 20 symptomatic patients who were considered as having reversible AILD by the medical staff of our institution were retrospectively reviewed. The patient-selection criteria used were the development of new respiratory symptoms while receiving amiodarone, the exclusion of other respiratory and cardiac diseases, and the decrease of both respiratory symptoms and radiological abnormalities after cessation of amiodarone and corticotherapy. The CT data recorded were those usually sought infiltrative lung diseases. The radiological findings using chest film (n = 20) and HRCT (n = 4) follow-up was noted. All patients had ground-glass opacities, associated with consolidations (n = 4), thin intralobular reticulations (n = 5), or both (n = 11), with a subpleural (n = 18) or central (n = 2) location. Eight patients had high-density areas and 13 had pleural thickening (n = 13). Bronchial abnormalities included dilation (n = 16) and wall thickening (n = 19). After therapeutic management, the radiological follow-up showed complete (n = 17) or incomplete (n = 3) improvement. Ground-glass opacities associated with thin intralobular reticulations and/or subpleural consolidations and bronchial abnormalities are common HRCT findings in reversible AILD.

Keywords

High-resolution CT · Lungs · Infiltrative lung diseases · Drug effects · Amiodarone
**Materials and methods**

**Patients**

For the past 10 years, in our institution, approximately 100 patients with clinically suspected AILD were eligible to undergo thoracic HRCT. The thoracic HRCT of 20 patients, who were considered by the medico-radiological staff of our institution as having a reversible amiodarone-induced disease, were retrospectively reviewed. The patient population included 13 men and 7 women (age range 59–75 years, mean age 65 years).

Three criteria were needed for the patients to be included in the study. The first criterion was the development of new respiratory symptoms while receiving amiodarone. The second criterion was the exclusion of other respiratory diseases especially infection, infarction, and cardiac failure. The last criterion was the decrease of respiratory symptoms and radiological abnormalities after cessation of amiodarone and corticotherapy. The amiodarone treatment (oral presentation) was taken for a period ranging from 3 months to 3 years in 7 cases and for more than 3 years in 13 cases at the time of the CT evaluation. Eight patients received 200 mg/day 5 days a week and 12 patients received 100 mg/day 5 days a week. Clinical symptoms at the time of CT evaluation included shortness of breath (n = 20), coughing (n = 8), chest pain (n = 8), and fever (n = 3). All patients had a normal pulmonary parenchyma at chest radiographs and no history of respiratory disease prior to starting treatment with amiodarone.

One patient with previously known rheumatoid arthritis but without history of respiratory disease treated with methotrexate and without clinical and biological signs of active rheumatoid arthritis was included in the study. None of the 20 patients were smokers at the time of the examination. The paraclinical tests used to exclude other diagnoses depended on clinical presentation. All patients underwent cardiac echocardiography and a cardiac catheterism was performed in 7 patients, in order to exclude cardiac failure. Bronchial fiber-optic examination and bronchioalveolar lavage were performed in 7 patients, serodiagnoses of usual respiratory infections, and serum level of precipitins were obtained in 5 patients in order to exclude pulmonary infection or eosinophilic pneumonia and hypersensitivity pneumonitis. Spiral CT with injection of contrast media was performed in 4 patients to exclude pulmonary embolism.

All patients underwent chest film at the time of diagnosis and during the follow-up period.

All patients had an initial HRCT and 4 patients had HRCT during the follow-up period. In addition, 3 patients with a high clinical suspicion of irreversible AILD were studied. These 3 patients presented with new shortness of breath and cough while receiving amiodarone, 200 mg/day 5 days a week for 1 year in 1 case and 100 mg/day 5 days a week for 2 years in 2 cases. Another respiratory or cardiac disease was excluded in all of them. No clinical nor radiological (HRCT) improvement was obtained after cessation of amiodarone and corticotherapy. These patients were not included in the study because no histological proof of amiodarone toxicity was available.

**Techniques**

High-resolution CT scans were obtained with a Prospeed (General Electric, Milwaukee, Wis.) by using 1-mm-thick sections obtained at 10-mm intervals from the apexes to the bases. Technical parameters were as follows: 120 kV; 200 mA; high-spatial-frequency algorithm and field of view (FOV), which was adapted to the width of each patient after performing the scout view. The scan images were photographed with a wide window setting (–400 HU, 2000 HU) and a mediastinal window setting (40 HU, 400 HU).

Using the technique previously described by Rémy-Jardin et al., spiral CT with contrast media was performed in cases of large pulmonary arteries found in HRCT [8].

**Expiratory CT**

Six patients had three expiratory scans with 1-mm collimation obtained at the level of the aortic arch, the carina, and the inferior pulmonary veins.

**Data**

**Chest film data**

Chest film data recorded at the initial chest film examination and during the follow-up examination were presence of alveolar opacities and/or interstitial opacities.

**HRCT data**

Pleuroparenchymal abnormalities searched for were the presence, profusion, and location of parenchymal consolidation, ground-glass opacities, reticulations, honeycombing, micronodules, and nodules. The presence of a “crazy-paving” pattern, defined by the association of ground-glass opacities and reticulations [9], was also noted. The presence of focal high-density parenchymal lesions with a CT attenuation superior to 82 HU [6] was sought. Concerning pleural abnormalities, pleural thickening were noted.

The search for bronchial abnormalities included bronchial dilatation when the bronchial diameter was 1.5 times larger than the corresponding pulmonary artery or absence of normal tapering of bronchi and bronchial wall thickening.

**Expiratory CT**

The presence of air trapping, defined as the lack of physiological increase of the lung density during expiration, was sought.

**Imaging follow-up**

Concerning radiological follow-up, in case of abnormalities (n = 1) or difficulty in assessing the normality of the parenchyma (n = 3) with chest film examination, HRCT was performed. The presence or regression of the HRCT data was noted. The HRCT images were reviewed separately by two thoracic radiologists and decisions were reached by consensus. Correlations between HRCT findings and the duration of the amiodarone therapy or clinical symptoms were sought.

**Results**

**Chest film findings**

Alveolar opacities were present in 4 cases, interstitial opacities in 5 cases, and both alveolar and interstitial...