Amiodarone is a classic example of a cardiovascular drug that causes pulmonary toxicity. Amiodarone-induced pulmonary toxicity (APT) occurs in approximately 5%-10% of patients, usually within months of starting therapy. The risk of APT is increased if the daily maintenance dose is greater than 400 mg and if the patient is elderly. Mortality due to APT is as high as 20%-30%. Since the first manifestation may be an abnormal finding on the chest radiograph, it may be necessary to perform chest radiography every three months for the first year after the initiation of amiodarone therapy. It is imperative that the history of amiodarone administration should be available and that the radiologist become aware of this entity. They are quite common but seldom reported in Taiwan, thus we report a case of amiodarone induced pneumonitis in our institution.

Key words: Amiodarone, Chest radiography, Interstitial pneumonitis

Drug-induced lung disease is a major source of iatrogenic injury [1]. Amiodarone is a classic example of a cardiovascular drug that causes pulmonary toxicity [1-4]. It is widely used to suppress ventricular and supraventricular tachyarrhythmias [1]. Amiodarone-induced pulmonary toxicity (APT) occurs in approximately 5%-10% of patients, usually within months of starting therapy [2]. Though amiodarone induced pneumonitis are common. Early diagnosis is important. Thus we present a case of amiodarone induced pneumonitis in our institution.

CASE REPORT

A 74-year-old man was sent to emergency room of our institution because of dyspnea for more than ten days. He had been well until two weeks before the day of admission. He had difficulty in walking more than 100 meters or climbing steps more than one floor. He denied fever, productive cough but had some whitish sputum when he waked up. The early morning of the day of admission, progressive dyspnea was noted. His families rushed him to our institution.

On arrival, the patient was awake and oriented. The pulse was 89 beats per minute and the blood pressure was 140/90 mmHg. The respiratory rate was 22 breaths per minute. There were rhonchi over the right lung and the results of the physical examination were otherwise normal.

The patient had history of pulmonary tuberculosic (TB) under medical medical control. Symptomatic paroxysmal supraventricular tachycardia was also noted. Thus radiofrequency current application was performed 2 years ago. He had regular clinical follow up with amiodarone control thereafter. He had had smoke about one pack per day and had quit smoking for more than ten years.

A chest plain film (Fig. 1) revealed bilateral peripheral patches. Under impression of TB, he was admitted to our chest ward. On the second day of admission, the following chest computed tomography (CT) (Fig. 2) showed patchy fibrosis of
Amiodarone induced pneumonitis

bilateral lungs and interstitial pneumonitis. Thus amiodarone induced pneumonitis was diagnosed. We stopped amiodarone and began corticosteroid therapy. The patient was discharged 14 days uneventfully. In his regular clinical follow up 3 months after admission, the chest plain film (Fig. 3) revealed improvement of previous peripheral patches.

**DISCUSSION**

Drug-induced lung disease is a major source of iatrogenic injury. Awareness of drug-induced pulmonary disease is increasing such that a review published in 1972 identified only 19 drugs with the potential to cause pulmonary disease, recently at least 150 agents were recognized [1]. Amiodarone is a classic example of a cardiovascular drug that

**Figure 1.** Chest plain film revealed patchy infiltrations in the bilateral peripheral lungs.

**Figure 2.** a. and b. Chest CT without contrast, lung window revealed bilateral interstitial patches and ground grass appearance of involved lung parenchyma, compatible with interstitial pneumonitis. c. and d. Soft tissue window revealed high attenuated infiltrates in the left basal lung. Computer aid measuring of the HU ranged 38-188 within the square area.
Amiodarone induced pneumonitis

causes pulmonary toxicity. It is widely used to suppress ventricular and supraventricular tachyarrhythmias [1-4].

Amiodarone hydrochloride is a benzofuran derivative that resembles thyroxine chemically [3-6]. It was originally used for the treatment of angina before its antiarrhythmic properties were recognized. Amiodarone has multiple effects on the cardiac conduction system, including an increase in the atrium-His bundle interval, ventricular refractory period, and spontaneous sinus cycle length. Side effects of amiodarone have included asymptomatic cornea microdeposits, nausea, hyperthyroidism and hypothyroidism, gray-blue skin discoloration, muscle weakness, peripheral neuropathy, and bradycardia [3]. The most significant complication of the drug, however, is pulmonary toxicity [4]. APT occurs in approximately 5%-10% of patients, usually within months of starting therapy [2]. Mortality due to APT is as high as 20%-30% [5].

Amiodarone can cause different patterns of pulmonary toxicity, including chronic interstitial pneumonitis, bronchiolitis obliterans, acute respiratory distress syndrome, and solitary lung mass [1]. The risk of APT is increased if the daily maintenance dose is greater than 400 mg and if the patient is elderly [2, 4]. Suspected mechanisms of APT include immunologic disorders, direct toxicity to the lung cells, and effects of free radicals [1].

Dyspnea on exertion is the most common clinical manifestation of APT. This may be accompanied by muscle weakness, anorexia, and weight loss. Low-grade fever may be present but is not a prominent feature. Some of the patients had pleuritic pain. The radiographic findings may be associated with abnormal pulmonary function tests, for example: a restrictive pattern on spirometry, severe impairment of gas transfer with hypoxemia, and markedly diminished diffusion capacity [4].

Since the first manifestation may be an abnormal finding on the chest radiograph, it may be necessary to perform chest radiography every three months for the first year after the initiation of amiodarone therapy. It is imperative that the history of amiodarone administration should be available and that the radiologist become aware of this entity [6].

Conventional radiographic findings in patients with APT have been described by several authors. Most reported cases show areas of consolidation, infiltrates, or interstitial disease, which are entirely nonspecific and easily confused with pulmonary abnormalities caused by congestive heart failure, pneumonia, and pulmonary infarction [5].

Peripheral areas of consolidation, predominantly in the upper lobes and resembling chronic eosinophilic pneumonia or tuberculosis, and diffuse interstitial disease are seen [4]. Chronic interstitial pneumonitis is characterized by insidious onset of nonproductive cough, dyspnea, weight loss, and diffuse interstitial and patchy alveolar infiltrates on chest plain film. Organizing pneumonia is characterized by nonproductive cough, pleuritic chest pain, fever, dyspnea, and patchy, alveolar opacities on chest radiographs. It is seen in approximately 25% of cases of APT [1].

A carefully obtained history that included medications is essential to suspect a drug-induced reaction. APT is a diagnosis of exclusion. The clinical presentation can be similar to pneumonia, congestive heart failure or pulmonary embolism. Several tests may be helpful. It is important to emphasize, however, that none of these tests is specific or pathognomonic for APT and not reliable to make the diagnosis [1].

These tests are used primarily to exclude other causes of the patient’s presentation rather than to confirm APT. A positive gallium scan is seen in almost all patients with amiodarone pneumonitis and can help differentiate it from pulmonary embolism and congestive heart failure. A positive gallium scan,
Amiodarone induced pneumonitis

however, can also reflect pneumonia or other diseases causing infection or inflammation in the lungs, and thus cannot be relied upon exclusively to make the diagnosis [1].

Because amiodarone contains about 37% iodine by weight, CT of the lung without contrast may be helpful in diagnosis [1]. Nonspecific interstitial pneumonitis is the most common manifestation of APT [2]. The most common CT abnormality is ground-glass attenuation. The ground-glass attenuation is usually bilateral and symmetric with a tendency to subpleural and basal predominance [7]. Other findings include consolidation and irregular reticular lines that can be superimposed on a background of ground-glass attenuation. Pleural inflammation is an accompanying feature and can manifest as pleural effusion.

A distinctive feature of APT is the occurrence of focal, homogeneous pulmonary opacities. These opacities are typically peripheral in location and of high attenuation at CT due to incorporation of amiodarone into the type II pneumocytes. The combinations of high-attenuation abnormalities within the lung, liver, or spleen are characteristic of APT [2].

Parenchymal-pleural lesions demonstrate uniform high attenuation values in some patients may be seen, while in others, focal areas within a larger consolidation show high CT attenuation [5]. Nonspecific infiltrates consisting of increased interstitial markings, patchy, mixed alveolar and interstitial disease, or a conglomerate mass.

Only a limited number of disease processes are known to produce high-attenuation pleural-parenchymal abnormalities at CT. Metastatic pulmonary calcifications occurring as the result of hyperparathyroidism from renal failure or from the infusion of large amounts of calcium salts in children with congenital heart disease have been reported to cause high-attenuation consolidations at CT [5]. Infiltrates caused by APT may enhance even though contrast was not given. This enhancement, however, is not pathognomonic for APT either.

A bronchoscopy with bronchoalveolar lavage may be helpful in excluding infection. Histologically, an accumulation of foamy macrophages in the alveolar spaces, type II cell hyperplasia, and fibrosis are seen in APT. These changes, however, are also seen in patients receiving amiodarone without toxicity and cannot be used solely to make the diagnosis [1].

Primary treatments for APT are the cessation of drug use and the administration of corticosteroids, prednisone 40 to 60 mg/day and tapered over 2 to 6 months, can be life-saving in severe cases [1]. The radiographic abnormalities may be completely reversible [4].

CONCLUSION

For early diagnosis of amiodarone induced pneumonitis, it may be necessary to perform chest radiography every three months after the initiation of amiodarone therapy.

REFERENCE

Amiodarone引發之肺間質炎：病例報告

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Amiodarone為一種具有肺毒性的心臟血管用藥，在治療數月內有5到10百分比的人會發生肺毒性。在每日服用400毫克以上及老年人有較高的肺毒性風險。而肺毒性的最初表現可以是胸腔X光片異常，因此治療後有必要每三個月用胸腔X光片加以追蹤。無庸置疑地放射科醫師要清楚amiodarone的藥物史才會聯想到肺毒性。

關鍵詞：胺碘酮；胸部放射檢查；間質性肺炎