Strait Circulation Journal
海峽循環學雜誌

Case Report

Pneumonitis, Hepatotoxicity, and Keratopathy under Low-Dose Amiodarone

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Accepted 28 May 2021; Volume: 3; Issue: 2; Pages: 1-3; DOI: 10.6907/SCJ.202104_3(2).0001
Citation: str.circ.j., 2021, 3, 2, 1, 1-3

1. Case report

Amiodarone is an effective anti-arrhythmic drug for both ventricular and supra-ventricular arrhythmia. In the past, low-dose amiodarone was considered safe [1]. However, serial reports have challenged this viewpoint [2] and severe adverse effects could still develop under low-dose amiodarone [3,4]. We report a case with amiodarone-related pneumonitis, hepatotoxicity, and keratopathy under low-dose amiodarone.

A 66-year-old man, who had been a heavy smoker for 40 years, was a patient of coronary artery disease diagnosed in February 2006. Percutaneous occlusive balloon angioplasty and stenting to left anterior descending artery was done at the time of diagnosis. Acute myocardial infarction with ventricular tachycardia occurred in August 2006. Coronary angiography disclosed in-stent restenosis of left anterior descending artery and repeated percutaneous coronary intervention was performed. Amiodarone was prescribed from that time. After average 730 mg per day for 4 weeks, low-dose amiodarone (200 mg/day) was maintained from September 11th 2006. Because of progressive dyspnea from late March 2007, he visited ER on March 31st 2007. He didn't have fever in accompany, but dry cough and blurred vision were noted. The chest radiograph (Fig. 1, Panel A) showed multiple patches in bilateral peripheral lung fields, together with enlarged sizes of heart and pulmonary trunk. Hemogram showed leukocytosis (14130/μL, neutrophil 88%). Biochemistry revealed elevated aminotransferases (AST/ALT 75/93 U/L), without abnormal cardiac enzyme levels. Pulmonary edema and community-acquired pneumonia were suspected initially. Dobutamine infusion (3 μg/kg/min) and bumetanide were prescribed. Cefmetazole was also given empirically. Nevertheless, rapid clinical deterioration was noted with progression of the pulmonary lesions. Hypoxic respiratory failure developed and he was admitted to ICU on April 3rd. Fine crackles were heard over bilateral lung fields on admission. BiPAP and non-rebreathing oxygen mask were used alternatively for maintaining oxygenation. Pulmonary congestion was not favored by the clinical course and Dobutamine was discontinued after admission to ICU. Moxifloxacin was prescribed in replacement of Cefmetazole for suspect of atypical pneumonia. Amiodarone was discontinued after admission to ICU under the suspect of amiodarone pneumonitis. The sputum culture yielded only normal flora. Serologic studies of Chlamydia pneumoniae and Mycoplasma pneumoniae were negative. The lung lesions kept in progression despite moxifloxacin treatment (Fig. 1, panel B). High-resolution computed tomography (HRCT) (Fig. 1, panel C) showed diffuse ground-glass opacities, with subpleural consolidations in left upper lobe and right lower lobe. Amiodarone pneumonitis was suspected and the patient was started on methylprednisolone (120 mg/day) from April 6th with discontinuation of moxifloxacin. The breath sounds improved after methylprednisolone use for 5 days. The oxygenation status also improved and he could tolerated oxygen simple mask. In addition, the levels of serum aminotransferases also normalized (AST/ALT 27/43 U/L). For blurred vision, ophthalmologic examination proved

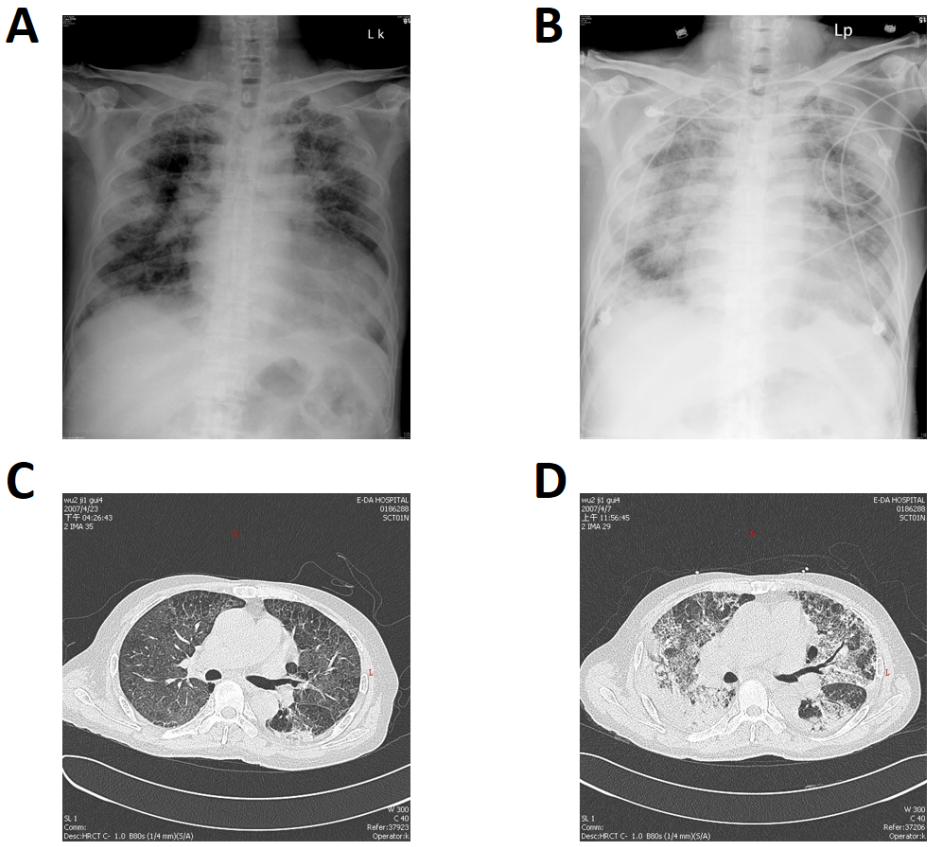

Figure 1. (A) Initial chest x-ray of our patient, which showed multiple patches in bilateral peripheral lung fields. (B) Subsequent chest x-ray at ICU, which showed rapid progression of the pulmonary lesions despite discontinuation of amiodarone and treatment with moxifloxacin. (C) HRCT before corticosteroid treatment, which showed alveolar and interstitial opacities with diffuse distribution in bilateral lung fields. The attenuation of the opacities wasn't significantly increased. (D) Subsequent HRCT after corticosteroid treatment for 18 days, which showed almost complete resolution of the lesions.

amiodarone-related keratopathy, which also improved under methylprednisolone treatment. The dose of corticosteroid was tapered gradually and smoothly from April 16th. Oxygenation was maintained well by nasal prong at that time. Subsequent HRCT (Fig. 1, panel D) showed almost complete resolution of the opacities.

Despite well efficacy as an anti-arrhythmic agent, amiodarone is known for several adverse effects. Amiodarone pulmonary toxicity is the most serious with a mortality rate up to 10% to 23% [5]. Results of pulmonary function test, bronchoalveolar lavage, HRCT, and lung biopsy may establish the presumptive diagnosis, under compatible clinical background. However, high clinical suspicion was still needed for timely diagnosis. In our patient, pneumonitis, hepatotoxicity and keratopathy were caused by low-dose amiodarone. According to previous literatures, amiodarone pneumonitis was suggested by high attenuation opacities on HRCT [6]. Increased attenuation of the liver may be present as well [7]. However, our patient's image didn't show such findings, which might be due to lower accumulation dose. Despite lack of controlled studies, corticosteroid treatment should be considered in patients with advanced disease. Optimal clinical response in our patient suggests that timely corticosteroid treatment in severe amiodarone pneumonitis could be life-saving and accelerates clinical recovery.

In conclusion, no dose of amiodarone could be considered safe without the risk of amiodarone pneumonitis. Long-term amiodarone use and unexplained pulmonary opacities on the images should arouse the suspicion about this diagnosis, because timely corticosteroid treatment might decrease the

mortality. Other adverse effects of amiodarone, such as hepatotoxicity and keratopathy, may also be present and should be surveyed if amiodarone pneumonitis is suspected.

Conflicts of Interest:
The authors declare no conflict of interest.

References

1. Kowey, P.R.; Friehling, T.D.; Marinchak, R.A.; Sulpizi, A.M.; Stohler, J.L. Safety and efficacy of amiodarone: the low-dose perspective. *Chest* **1988**, *93*, 54–59.
2. Vorperian, V.R.; Havighurst, T.C.; Miller, S.; January, C.T. Adverse effects of low dose amiodarone: a meta-analysis. *Journal of the American College of Cardiology* **1997**, *30*, 791–798.
3. Ott, M.C.; Khoor, A.; Leventhal, J.P.; Paterick, T.E.; Burger, C.D. Pulmonary toxicity in patients receiving low-dose amiodarone. *Chest* **2003**, *123*, 646–651.
4. Coban, S.; Köklü, S.; Sencer, H.; Ekiz, F.; Ormeci, N. Low dose amiodarone associated cirrhosis. *Journal of gastroenterology and hepatology* **2007**, *22*, 140–141.
5. Vrobel, T.R.; Miller, P.E.; Mostow, N.D.; Rakita, L. A general overview of amiodarone toxicity: its prevention, detection, and management. *Progress in cardiovascular diseases* **1989**, *31*, 393–426.
6. Vernhet, H.; Bousquet, C.; Durand, G.; Giron, J.; Senac, J. Reversible amiodarone-induced lung disease: HRCT findings. *European radiology* **2001**, *11*, 1697–1703.
7. Hopper, K.; Potok, P. Gastrointestinal case of the day. Hepatic and pulmonary accumulation of amiodarone. *AJR. American journal of roentgenology* **1994**, *162*, 1449–1450.