

A Reason of Delayed Weaning in Critical Care: Amiodarone Pulmonary Toxicity

Yoğun Bakımda Gecikmiş Weaning Nedeni Olarak Amiodaron Pulmoner Toksisitesi

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ABSTRACT

Amiodarone is a frequently used antiarrhythmic drug in critical care which was used to treat especially ventricular arrhythmias. But it must known that secondary to its chemical properties, drug tends to accumulate in tissues and it presents as cardiac, ophthalmic, pulmonary and neurological side effects. Amiodarone pulmonary toxicity (APT) is one of the life-threatening side effects of the drug which may present as respiratory failure. And thorax computed tomography scans demonstrate the pathology with pneumonitis, ground glass opacities and fibrosis. Dispnea and cough are common clinical presentations. But an intubated and mechanically ventilated patient's respiratory failure secondary to APT may reflect as only delayed weaning as in our case. Most importantly, rapid diagnosis and early treatment are the most important factors that reduce the mortality of patients.

Key words: amiodarone; pulmonary toxicity; critical care

ÖZET

Amiodaron yoğun bakımda sıkça kullanılan bir antiaritmiktir ve özellikle ventriküler aritmilerin tedavisinde kullanılır. Ama bilinmelidir ki kimyasal yapısından dolayı ilaç dokularda birikebilir ve kardiyak, oftalmik, pulmoner ve nörolojik yan etkiler oluşturabilir. Amiodaron pulmoner toksisitesi (APT) ilacın hayati tehdit eden yan etkilerinden biridir ve solunum yetmezliği şeklinde karşımıza çıkabilir. Hastalık toraks bilgisayarlı tomografisinde pnömonitis, buzlu cam opasiteleri, fibrosis bulgularını verir. Dispne ve öksürük en sık görülen belirtilerdir. Ancak tıpkı bizim olgumuzda olduğu gibi, entübe ve mekanik ventilasyon uygulanan bir hastada APT'nin yarattığı solunum yetmezliği karşımıza sadece gecikmiş ventilatörden ayrılma olarak çıkabilir. En önemlisi hızlı tanı ve erken başlanan tedavi hastaların mortalitesini azaltan en önemli faktörlerdir.

Anahtar kelimeler: amiodaron; pulmoner toksisite; yoğun bakım

Introduction

Amiodarone is one of the most prescribed antiarrhythmic drug by clinicians. The popularity of the drug comes from its efficacy and extend indications in terms of different types of arrhythmias. But amiodarone has relations with dangerous side effects like amiodarone pulmonary toxicity (APT). The prevalence is estimated to be about 5%. The risk of APT occurrence increased by drug dose and therapy duration. Clinical manifestations of APT are; decreased lung capacity, cough, weight loss^{1,2}. But in critical care these manifestations may be masked and clinician must be aware of APT, whether the patient used high dose of amiodarone. In this case report we present a delayed weaning according to APT with its clinical presentation, diagnosis and successful therapy.

Case

65-year-old female patient with hypertension, diabetes and chronic obstructive pulmonary disease, obesity (BMI >35 kg/m²) referred to the hospital with respiratory failure. Acute coronary syndrome was detected and percutan coronary angiography was performed. During the procedure two clogged coronary arteries opened successfully. Secondary to unstable haemodynamic measurements patient transferred to our critical care service. After the physical and laboratory examination, atrial fibrillation, significant respiratory failure secondary to pulmonary edema and pneumonia, impaired renal functions secondary to contrast induced nephropathy were detected additionally to the acute coronary syndrome. Patients glasgow coma scale was 14 at the application to the critical care. Secondary to respiratory failure supportive non-invasive mechanical ventilation started. Hemodialysis was performed for deep metabolic acidosis secondary

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to renal impairment. Antibiotic therapy for pneumonia and other recommended drugs (acetylsalicylic acid 1x100 mg/day, clopidogrel 1x75 mg/day, metoprolol 1x50 mg/day) by cardiologists were started. At the 4th day of the critical care cardiac arrest occurred secondary to malignant ventricular arrhythmias. Three times cardioversion was performed with successful resuscitation. Patient started to receive per oral amiodarone (2x200 mg/day) therapy. At the 7th day of the critical care malignant arrhythmias reappeared and cardioversion was performed again. The amiodarone dose concluded insufficient and it increased to 3x200 mg/per day. From the fourth day of the process patients was still intubated and mechanically ventilated. Hemodialysis therapy was still continue every two days. Cardiac rithm of the patient stabilized. After a few days pneumonia was deteriorated, volume load on lungs depleted and weaning planned. Intermittent chest x-rays showed new patchy infiltrates. Patient was searched in terms of new pneumonia or pleural edema, pulmonary thromboemboli, but all markers of these diseases were negative. But patient could not wean. Clinicians concluded APT secondary to patchy infiltrations in chest x-ray, respiratory failure without any other reasons and high dose amiodarone medication and thorax computed tomography was performed. Bilateral ground glass opacities, significant parahiler opacities, bronchovascular irregularities, pleural and paranchimal fibrosis, small pleural effusions were detected (Figure 1). All these clinical and radiologic findings inclined clinicians to the APT. After the diagnosis, amiodarone was stopped and 50 mg/day methylprednisolone was started. Patient's respiratory functions started to improve 5 days after the steroid therapy and patient weaned at the 9th day of the APT diagnosis. After weaning, improvement of the patient got faster. She mobilized better, oral intake increased, did not need supportive oxygen therapy and she was discharged from critical care to the ward at the 3rd day of the extubation.

Discussion

The main indication of amiodarone is suppression of ventricular arrhythmias. Additionally amiodarone can maintain sinus rhythm in patients with atrial arrhythmias^{3,4}. So it is a world wide used antiarrhythmic drug with its toxic side effects. Amiodarone is an iodine containing product. In addition, inhibition of thyroxine deiodination to triiodothyroxine may contribute to its antiarrhythmic efficacy. An important property of amiodarone is its high lipid solubility¹. These properties cause the accumulation of the drug to the tissues like

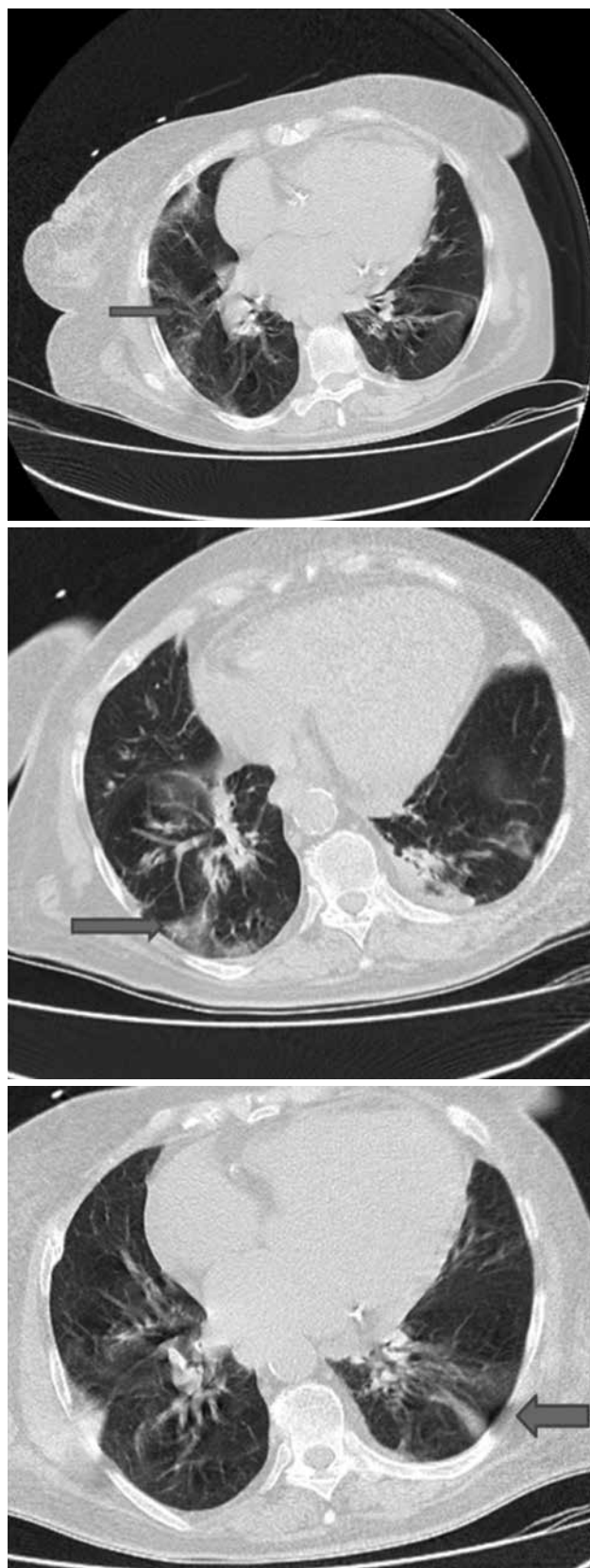


Figure 1. Bilateral ground glass opacities, significant parahilar opacities, bronchovascular irregularities, pleural and paranchimal fibrosis, small pleural effusions were seen in thorax CT of the patient.

fat, liver, spleen and lungs. The most serious one is pulmonary toxicity. Pulmonary toxicity risk correlates by plasma amiodarone concentration. Although toxicity may occur in any time or dose of the therapy but more than the dose of 400 mg/day or therapy of more than two months caused highest risks of pulmonary toxicity, a lower dose, commonly 200 mg daily, for more than two years⁵. Male gender and pre-existing lung disease are potential risk factors of the toxicity. Additionally it was concluded that supplemental oxygen therapy, thoracic or non-thoracic surgery and mechanical ventilation may potentiate the toxicity⁶⁻⁸. Even our patient was female the supportive moderate oxygen therapy and mechanical ventilation might potentiate APT. The risk of developing amiodarone-induced pulmonary toxicity may increase with age and an abnormal chest xray or poor pulmonary reserve before treatment with amiodarone⁹.

APT pathophysiology consist of direct cytotoxic T cell damage or indirect immunologic damage.⁹ Secondary to these mechanisms, finding cytotoxic T cells with bronchoalveolar lavage (BAL) is an one of diagnosis method. Accumulated concentrations of amiodarone derivative in specific lung compartments, such as the type II pneumocyte, further exaggerate this effect¹⁰.

The most common clinical manifestation is interstitial pneumonitis with a subacute onset¹. Shortness of breath, nonproductive cough, malaise, chest pain are the common clinical presentations.⁶ But these findings may not be clarified in an intubated critical care patient. As our case report delayed weaning process may be the only presentation. With this aspect, the patient's weaning delayed, the dose of oxygen concentration could nor decreased and newer patchy infiltrates occurred in chest x-ray. And the other reasons of this presentation like infectious pneumonia etc were excluded with BAL culture and other infection markers. Especially clinicians must be suspicious of APT in terms of respiratory impairments whether a critical care patient received high doses of amiodarone (our patient received 600 mg per day) with respiratory supportive therapy.

There are no symptoms for the diagnosis of APT. New infiltrates on chest x-ray, reduced diffusion capacity in the DLCO, restrictive or mixt type pulmonary function test results, evidence of the immune response with BAL are the diagnostic methods of APT. Interstitial, alveolar or mixt infiltrates, ground glass opacities, pleural thickening, pulmonary fibrosis are the signs of the APT^{10,11}. In our case, bilateral ground glass opacifications, pleuroparanchimal fibrosis were detected as mentioned in previous literature.

After APT diagnosis, cessation of the drug and systemic corticosteroid therapy were recommended. It must known that amiodarone has long elimination half life and the clinical improvements may be delayed. Recurrences have been described up to 8 months after amiodarone withdrawal. Amiodarone induced fibrosis is irreversible and respondent to treatment with corticosteroid drugs¹¹. In our patient significant clinical improvements were recorded on the 10th day of the drug cessation. Prednisone therapy is recommended in doses of 40–60 mg/day orally¹. We used 50 mg/day methylprednisolone after the diagnosis and patients may weaned secondary to pulmonary resolution.

The prognosis of APT is usually positive. Mortality in amiodarone pneumonitis ranges between 21% and 33% of patients who are treated in hospital¹¹.

There are numerous reports about APT but less of them from critical care. Intensive care givers must be aware of APT because being intubated and mechanically ventilated and other frequent critical care disorders like pneumonia, pulmonary thromboemboli may mask the diagnosis. It was known that prompt diagnosis, early cessation of amiodarone and steroids increase the survival rate as happens in our case.

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