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Amiodarone induced pulmonary toxicity: An unusual response to steroids

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Summary

Background:

Amiodarone, class III anti-arrhythmic was originally introduced to treat angina pectoris, was later approved by FDA in 1985 for the treatment of ventricular arrhythmias. Despite its anti-arrhythmic properties, amiodarone is associated with side effects such as thyroid dysfunction, corneal deposits, bluish skin discoloration, neuropathy and pulmonary toxicity. Amiodarone induced pulmonary toxicity (AIPT) is one of the most serious side effect thus limiting its use.

Case Report:

We encountered a 66 year old male with early onset AIPT who presented with dyspnea and chest imaging revealed extensive ground-glass opacities throughout lung parenchyma with rapid resolution of these opacities in a week following treatment with corticosteroids.

Conclusions:

There have been few case reports of AIPT with complete resolution of ground glass opacities on treatment with corticosteroids, but none demonstrated a rapid response to corticosteroids. Health care providers should withdraw amiodarone at the earliest suspicion (as illustrated in our case); any delay can potentially be fatal. This case highlights the fact that AIPT is a reversible phenomenon, provided its early recognition and treatment before fibrosis sets in. This case also highlights the need to include AIPT in the differential diagnosis in any patient on amiodarone who presents with shortness of breath.

key words:

amiodarone • interstitial lung disease • lung toxicity

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BACKGROUND

Amiodarone is a commonly used anti-arrhythmic agent for the treatment of ventricular arrhythmias. Amiodarone induced pulmonary toxicity (AIPT) is one of the most serious side effect thus limiting its use [1]. In this report we describe a case of 66 year old white male who was on amiodarone for >6 months presented with dyspnea with extensive ground-glass opacities throughout lung parenchyma on chest imaging. Because of its vague clinical presentation, AIPT is always a diagnosis of exclusion. Treatment involves immediate discontinuation of amiodarone and administration of corticosteroids for the prompt recovery and to prevent lung fibrosis.

CASE REPORT

A 66-year old man was admitted to the hospital with chief complaint of dyspnea. The patient has a past medical history of coronary artery disease with coronary artery bypass grafting, congestive heart failure (CHF) with AICD placement, ventricular tachycardia, diabetes mellitus, renal insufficiency, and obstructive sleep apnea on CPAP, 40 pack – year smoking history quit - more than a decade ago. The temperature was 98 F, pulse 96/min, respiratory rate of 18/min and blood pressure 148/96 mmHg, 90% saturation

on room air and 99 percent on 2L nasal cannula. There was no lymphadenopathy or jugular venous distension. Air entry was bilaterally symmetrical with bilateral crackles in upper-middle lung fields anteriorly. Abdominal examination was unremarkable and there was bilateral pedal edema (+1). An electrocardiogram at the time of admission showed sinus rhythm at 66 beats per minutes, normal PR and QTc interval and atrial sensed ventricular paced rhythm (Figure 1). Echocardiography was done which reported as left ventricular cavity size normal with ejection fraction of 45% and no significant change from the previous echocardiogram.

At the time of admission, white count was 11,200, blood urea nitrogen 31, creatinine 2.04 and brain natriuretic peptide was 577. Two sets cardiac enzymes 6 hours apart were – troponin I 0.09 and 0.06, CK-MB fraction 2.1 and 1.9. Urinalysis was unremarkable. Given the patient's history of congestive heart failure and smoking, dyspnea was initially attributed secondary to CHF exacerbation. Blood cultures were drawn and empiric antibiotics and ipratropium/albuterol were added to patient's home medications (aspirin, carvedilol, rosuvastatin, furosemide, insulin, prasugrel, paroxetine, amiodarone, folic acid and ferrous sulphate). A chest radiograph showed pulmonary venous congestion bilaterally and bilateral airspace opacities (Figure 2) not evident an year ago

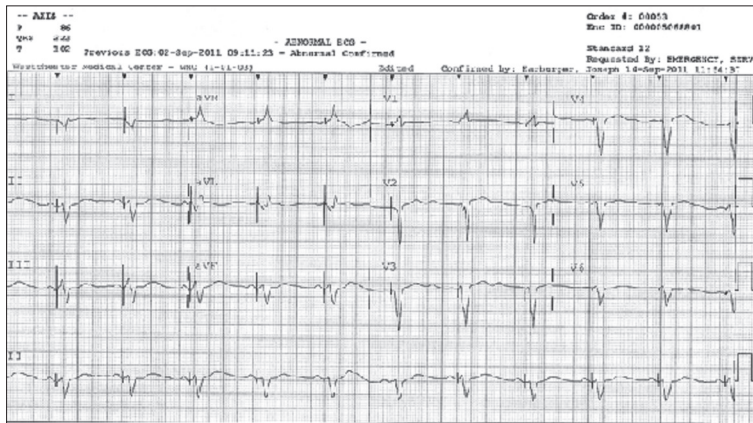


Figure 1. EKG at the time of admission showing atrial sensed ventricular paced rhythm.

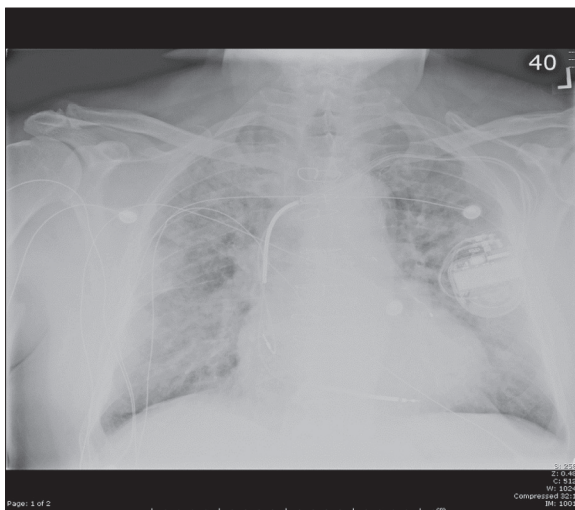


Figure 2. Chest X-Ray at time of admission – pulmonary venous congestion bilaterally and bilateral airspace opacities.

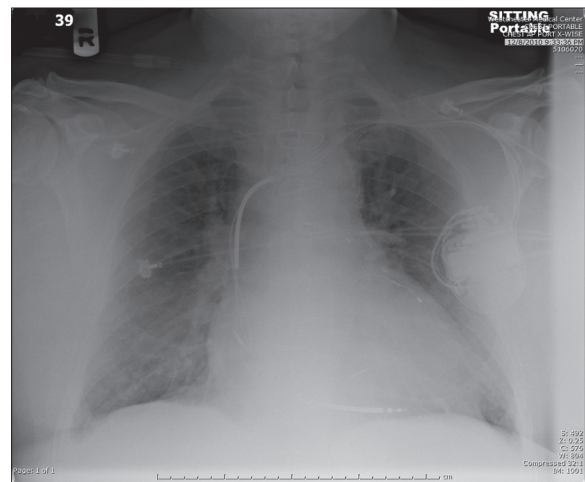


Figure 3. December, 2010 – Prominence of cardiac silhouette with prominence of pulmonary vasculature.

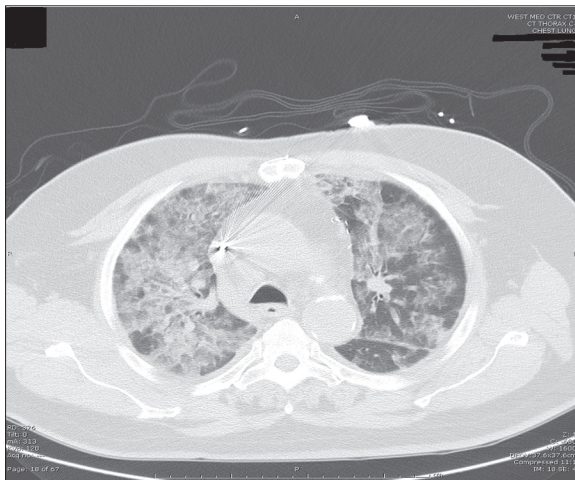


Figure 4. Chest CT scan without contrast showing extensive ground-glass opacities throughout lung parenchyma.

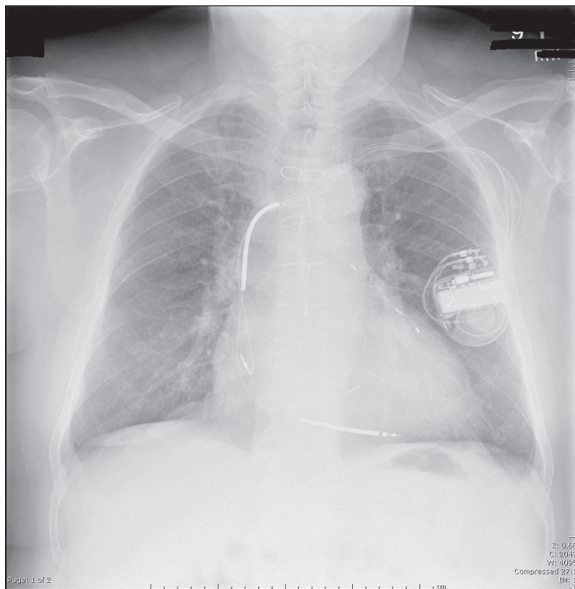


Figure 5. Follow up Chest X-Ray obtained 6 days after corticosteroid treatment showing near complete resolution of patchy airspace opacities bilaterally.

(December 2010, Figure 3). Duplex ultrasound lower extremities showed no evidence of thrombosis in femoral and popliteal deep venous system. AICD was interrogated – AICD was working fine with good battery life and no arrhythmias were detected. No recent shocks delivered with last shock delivered in December, 2010.

On second hospital day patient's dyspnea improved but was tachypneic at rest. Blood pressure was 154/64 mmHg, pulse 66/min, temperature 98 F and oxygen saturation 96% on 2L nasal cannula. CT scan chest demonstrated extensive groundglass opacities throughout lung parenchyma with normal appearing lung parenchyma between these ground-glass opacities (Figure 4). Patient refused broncho-alveolar lavage. Blood cultures were negative so far. Based on the physical examination and investigations, clinical diagnosis of AIPT was made. Amiodarone, assumed causative agent for

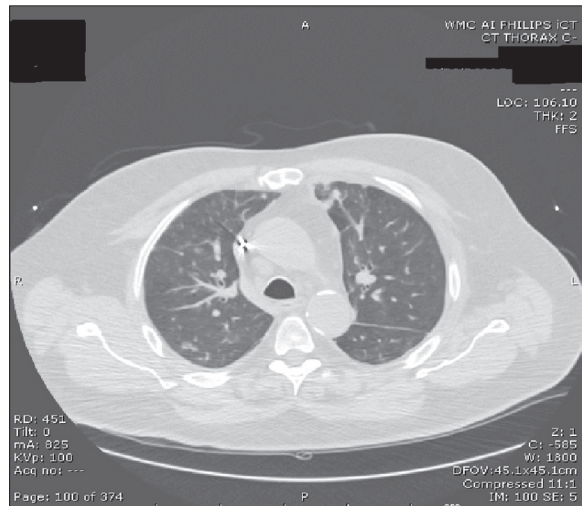


Figure 6. Chest CT scan obtained 1 month later as an outpatient demonstrates marked improvement of bilateral ground-glass opacities compatible with resolving amiodarone toxicity.

the pulmonary manifestation was discontinued and a trial of corticosteroids was initiated. Repeat chest x-ray on day 7 of hospitalization showed near complete resolution of previously described ground glass opacity bilaterally (Figure 5). There was a significant improvement in patient's symptoms. The patient was discharged on oral prednisone with slow taper. Chest CT scan done as an outpatient a month later showed marked improvement in bilateral ground-glass opacity compatible with amiodarone toxicity (Figure 6).

DISCUSSION

Amiodarone induced pulmonary toxicity (AIPT) is the most serious and one of the major cause for discontinuation of amiodarone [2–4]. Ernawati et al. demonstrated that the duration of amiodarone therapy was a significant risk factor for AIPT with increased risk after 1 month of therapy and being highest in the patients who were on amiodarone for 6–12 months [2]. Total cumulative dose of amiodarone is considered an independent risk factor in addition to the duration of therapy for amiodarone toxicity. Yamada et al. in a trial confirmed a cumulative increase in the incidence of AIPT from 4.2% to 7.8% and 10.6% with 1 year, 3 years and 5 years use of amiodarone respectively [5]. The possible explanation for the increased toxicity (although not demonstrated in our case) could be due to its long half life [6] and lipophilic moiety due to which amiodarone concentrates in the organs with high lipid content such as liver, lung, adipose tissue and thyroid [7].

There are no precise diagnostic criteria for AIPT and monitoring guidelines have not been implemented universally [8]. AIPT is mainly a diagnosis of exclusion of other clinical conditions including but not limited to heart failure, pneumonia, pulmonary fibrosis (secondary to tuberculosis, systemic lupus erythematosus, rheumatoid arthritis) and medications (bleomycin, cyclophosphamide, methotrexate) [5,9].

If the clinical suspicion of AIPT is high, amiodarone should be discontinued. And corticosteroids should be started in

attempt to accelerate recovery and to prevent lung fibrosis as illustrated in this case. Interestingly, there have been case reports of AIPT [10,11] with complete resolution of ground glass opacities on treatment with corticosteroids, but none demonstrated a rapid response to corticosteroids as rapid as ours.

CONCLUSIONS

Health care providers should withdraw amiodarone at the earliest suspicion; any delay can potentially be fatal [12]. This case also highlights the fact that AIPT is a reversible phenomenon, provided its early recognition and treatment before fibrosis sets in. Clinicians should always include amiodarone induced pulmonary toxicity in the differential diagnosis in any patient on amiodarone who presents with shortness of breath.

Acknowledgement

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