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Amiodarone-Induced Lung Toxicity: An underrecognized and fatal presentation

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Abstract
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Keywords
Amiodarone-induced Pulmonary Toxicity, Amiodarone Induced Pneumonitis, Diagnostic Dilemma

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Amiodarone-induced Lung Toxicity: An Underrecognized and Fatal Presentation

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Abstract

Amiodarone, a widely utilized antiarrhythmic drug, poses a significant risk of amiodarone-induced lung toxicity (ALT) in up to 10% of patients and can be fatal. This report presents the diagnostic challenges associated with ALT, given its non-specific clinical and radiological presentation. Clinicians should maintain a high index of suspicion for potential ALT, especially in patients with progressive respiratory failure despite optimization of other potential causes such as CHF. The mainstay of treatment is discontinuing amiodarone and initiating steroids. However, outcomes can remain unpredictable, emphasizing the need for heightened awareness and regular monitoring of patients on amiodarone therapy.

Keywords: Amiodarone-induced pulmonary toxicity, Amiodarone induced pneumonitis, Diagnostic dilemma

1. Introduction

Amiodarone is a widely used antiarrhythmic agent known for its effectiveness in managing both atrial and ventricular tachyarrhythmias. While it has therapeutic benefits in rhythm control, its administration is not without risks. Among the spectrum of side effects, amiodarone-induced lung toxicity (ALT) remains one of the most concerning complications due to its potential for significant morbidity and mortality. ALT encompass a spectrum of diseases that affect the lungs, with interstitial pneumonitis being the most common. Recognizing this side effect is crucial, especially given its insidious presentation that can easily be misconstrued as other common clinical entities. In this report, we present a case of an elderly male who, after a series of intricate clinical developments, was suspected of having ALT. Through this lens, we aim to show the challenges in diagnosis and emphasize the importance of maintaining a high index of suspicion in patients on amiodarone therapy presenting with respiratory symptoms.
intake and overdiuresis. Consequently, volume resuscitation with 1 L of normal saline was administered. Home diuretics were withheld, and amiodarone 200 mg daily, Rivaroxaban 20 mg daily, as well as metoprolol succinate 50 mg daily, were resumed.

Two days later, the patient developed hypoxemic respiratory failure, initially requiring a 2-liter nasal cannula and progressing to 10 L towards the evening, along with atrial fibrillation with rapid ventricular response 120 bpm. A repeat CXR showed bilateral airspace disease concerning for pulmonary edema (Fig. 1b). This was initially thought to be in the setting of congestive heart failure (CHF) exacerbation, for which diuresis with furosemide 40 mg BID was initiated, as well as BiPAP. Antibiotics, including Vancomycin, piperacillin/tazobactam, and doxycycline, were also initiated due to the rapid deterioration of his respiratory status.

Upon careful chart review, it was observed that the patient had been inconsistently taking amiodarone 200 mg daily, which was prescribed 6 months prior to admission. The patient was not adherent with the medication due to increasing shortness of breath, vision problems, recurrent falls, and mild transaminitis. The exact duration of the patient's amiodarone intake was unclear, but based on the chart, it appeared to be around 4–5 months. Further testing with transthoracic echocardiography (TTE) showed an ejection fraction of 55% with mild mitral regurgitation. Right heart catheterization revealed mildly elevated filling pressures, with a right atrial pressure of 12 mmHg, right ventricular pressure of 44/12 mmHg, pulmonary artery pressure of 47/19 mmHg, wedge pressure of 13 mmHg, and preserved cardiac output/index. This suggested that the patient's deterioration in respiratory status was less likely to be from heart failure exacerbation.

Fig. 1. A. CXR on day 1 showing clear lung fields and elevated hemidiaphragm. B. CXR on day 3 showing bilateral infiltrates. C. CXR on day 7 showing bilateral ground glass opacities.

Fig. 2. CT scan on day 7 showing bilateral ground glass opacities and interlobular sepal thickening.
Despite adequate swan-guided diuresis, the patient remained hypoxic with repeat CXR and CT scan showing worsening ground-glass opacities and underlying interlobular septal thickening (Figs. 1c and 2). Subsequently, he was intubated on day 7. Respiratory cultures and tests for Beta-D glucan and pneumocystis jiroveci PCR were unrevealing. Broad spectrum antibiotics were initiated with poor response. Bronchoscopy showed minimal airway inflammation, and bronchoalveolar lavage (BAL) ruled out alveolar proteinosis or alveolar hemorrhage. Autoimmune panel was negative. Thyroid profile was concerning for thyroiditis, with low TSH, elevated T4, and low T3 levels.

Amiodarone was discontinued and the patient was started on IV methylprednisolone at a dose of 400 mg. Nevertheless, subsequent cases have documented side effects of acute amiodarone toxicity typically appear several months after treatment initiation and are seldom reported in the early stages of treatment. Risk factors contributing to ALT encompass preexisting lung conditions, advanced age, treatment duration, and the dosage of amiodarone. It's worth noting that our patient was started on a daily dose of 200 mg of Amiodarone intermittently for 6 months. This raises the index of suspicion for the development of such a condition, even with lower doses and durations than those reported in the literature. The patient's prior non-compliance with amiodarone, attributed to symptoms like shortness of breath and vision problems, may have served as early indicators of amiodarone toxicity that should have been addressed promptly. The drastic decline in the respiratory status of the patient after volume resuscitation remains enigmatic. Factors such as advanced age and an elevated hemidiaphragm, suggesting a restrictive pulmonary pathology, served as predisposing factors for ALT. Although fluid overload, as indicated by RHC, was not significant, it may have also played a role, especially considering his underlying HFrEF.

Diagnosing ALT can be challenging, given the non-specific clinical and radiological features. In our case, several potential causes of the patient's presentation were considered and ruled out, including congestive heart failure, infectious etiologies, and autoimmune disorders. The diagnosis of ALT is often a diagnosis of exclusion. Important diagnostic criteria include exposure to amiodarone, consistent clinical and radiological findings, and the exclusion of alternative diagnoses. Unfortunately, baseline pulmonary function testing was not available, and diffusing capacity of carbon monoxide was not performed, which is usually reported to be reduced in patients with ALT.

Our patient's clinical presentation was complex, after ruling out other causes, his rapidly deteriorating respiratory status coupled with the CT findings of ground-glass opacities, interlobular septal thickening, and hypoxemia, fits the profile of amiodarone-induced pneumonitis (AIP), one of the more severe and aggressive manifestations of ALT. Symptoms may include cough, dyspnea, pleuritic chest pain, and fever. Radiological findings are diverse, but diffuse alveolar damage or organizing pneumonia are the most frequent patterns. Additionally, the patient's thyroid profile suggestive of thyroiditis correlate with other well-documented side effects of acute amiodarone toxicity favoring the diagnosis of ALT.

Once ALT is suspected, amiodarone should be discontinued. Corticosteroids, as initiated in our case, are the mainstay of treatment for severe cases, especially when AIP is suspected. Prednisone at a dosage of 40–60 mg per day is typically recommended. Once a clinical response is evident, glucocorticoid therapy should be gradually tapered over a period of 2–6 months. In the event of symptom recurrence, the glucocorticoid dose is returned to the last effective dose, and further tapering should proceed more slowly over a span of 12 months. While...
corticosteroids can lead to clinical improvement in many cases, it’s important to note that some patients, especially those with delayed diagnosis or severe initial presentations, may have a poor prognosis, as observed in this case.13

4. Conclusion

Amiodarone is effective in rhythm control but carries a risk of lung toxicity. This case displays the importance of clinical vigilance in monitoring patients on amiodarone therapy. Providers should maintain a high index of suspicion for ALT in patients presenting with new or worsening respiratory symptoms while on amiodarone, and early discontinuation of the drug may improve outcomes.

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Conflicts of interest

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References