CASE REPORT

Early amiodarone pulmonary toxicity simulating heart failure

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Introduction

We report a case of very early onset of amiodarone-induced pulmonary toxicity, which appeared 12 days after starting treatment.

Case report

A 68-year-old man was admitted with palpitations and dyspnoea of acute onset. He was a non-smoker and was normotensive. He had no history of angina or myocardial infarction. On examination, he was afebrile and there were no stigmata of infective endocarditis. His pulse was 150 beats per minute and regular, and his blood pressure was 110/70 mmHg. The jugular venous pressure was not raised and there was no ankle oedema. There was no clinical cardiac enlargement or signs of heart failure. At the mitral area there was a loud late ejection systolic murmur. There were a few fine crepitations at the lung bases.

The ECG showed atrial flutter with 2:1 block, with a ventricular rate of 150 beats per minute. The heart axis was normal and there was no left ventricular hypertrophy. The chest X-ray showed mild pulmonary oedema with borderline cardiomegaly. The echocardiogram showed severe mitral regurgitation due to prolapse of P2-P3 scallops of the posterior mitral leaflet. Left ventricular function was normal. The left ventricular diastolic dimension (LVlDd) was 5.6 cm (normal range 4.5–4.8 cm) and left ventricular systolic dimension (LVlSd) was 3.5 cm (2.8–3.0 cm). The left atrium was moderately dilated at 5.5 cm (3.4–4.0 cm). There was mild tricuspid regurgitation, with an estimated pulmonary artery systolic pressure of 33 mmHg + RAP (right atrial pressure). Right ventricular systolic function was normal.

He was treated with furosemide 80 mg once daily, lisinopril 20 mg once daily, bisoprolol 2.5 mg once daily and amiodarone 200 mg three times daily for one week, tapering down to 200 mg twice daily for the second week and then 200 mg once daily.

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Figure 1. Chest X-ray, showing bilateral perihilar interstitial shadowing, bilateral upper lobe shadows and borderline cardiomegaly

He was discharged after nine days with a view to readmission for cardiac catheterisation and mitral valve surgery.

He was re-admitted one week later with progressive dyspnoea on minimal exertion and at rest but without nocturnal dyspnoea. The pulse was 72 beats per minute and the blood pressure was 130/65 mmHg. There were no signs of congestive cardiac failure. In the chest there were no crepitations or added sounds. The ECG showed that he had reverted to sinus rhythm and there were occasional atrial premature beats. The chest X-ray showed bilateral perihilar interstitial shadowing and bilateral upper lobe shadows in addition to borderline cardiomegaly (figure 1). The pulmonary features had increased from the original X-ray. The troponin T was 0.12 µg/L (normal - undetectable); creatine kinase (CK) was 56 IU/L (25–200) and lactic dehydrogenase (LDH) was 54 IU/L (125–255).

Cardiac catheterisation showed severe eccentric mitral regurgitation into a modestly enlarged left atrium. The left ventricle was mildly enlarged with normal contraction. Coronary arteriography showed a severe stenosis in the circumflex (LCx) artery and mild disease at the bifurcation in the mid left anterior descending artery (LAD).

Initially his deterioration was attributed to heart failure but despite increasing the dose of furosemide to 80 mg twice daily the appearances of the chest X-ray failed to improve. The patient

Figure 2. High Resolution Contrast Tomography (HRCT) scans, showing patchy alveolar/interstitial infiltrates with associated fibrosis
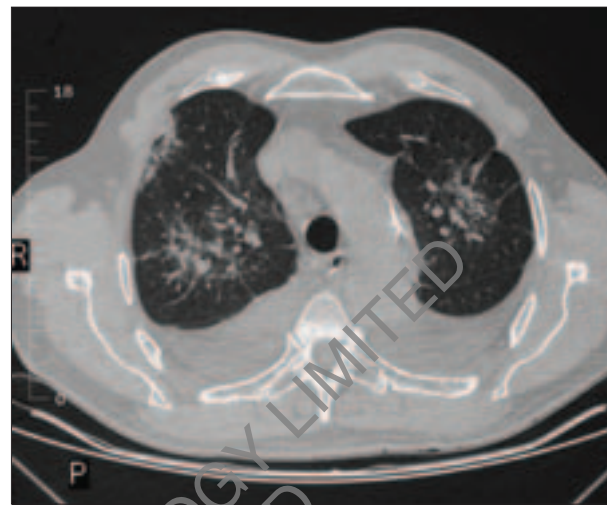
Table 1. Comparison of pulmonary function tests

Predicted value (normal)	Early Aug 2002	Mid Sept 2002
FEV1 L (2.62–3.64)	2.32	3.63
FVC L (3.46–4.68)	3.32	4.89
FEV1/FVC % (68–82)	70	74
TLC L (6.34–7.72)	4.75	8.44
RV/TLC % (35–45)	30	37
KCO (3.08–4.66)	3.88	3.12
TL (23.09–31.39)	18.87	22.2

Key: FEV1 = forced expiratory volume in 1 sec; FVC = forced vital capacity;
TLC = total lung capacity; RV = residual volume; KCO = diffusion coefficient;
TL = carbon monoxide transfer

Figure 3. Chest X-ray after withdrawal of amiodarone, showing almost complete clearing of pulmonary infiltration

remained very breathless. The possibility of amiodarone toxicity was then considered and a High Resolution Contrast Tomography (HRCT) scan was performed. This showed basal atelectasis, patchy alveolar/interstitial infiltrates in both upper lobes associated with fibrosis and patchy infiltrates in lower lobes (figure 2). These features suggested interstitial pneumonitis due to amiodarone.

Pulmonary function tests showed a moderate reduction of the total lung capacity to 67% of the predicted value along with decreased FEV1 and FVC (table 1). The tests suggested a restrictive pattern with moderate intrapulmonary restriction compatible with amiodarone toxicity, which was then withdrawn.

The dose of furosemide was reduced from 160 mg (80 twice daily) to 120 mg daily. After a week his symptoms began to improve. The chest X-ray after three weeks showed almost complete clearing of the lung infiltration (figure 3). Lung function tests improved and by six weeks they had returned to normal (table 1).

Mitral valve repair, coronary artery bypass graft surgery (CABG) with saphenous venous graft (SVG) to the left circumflex (LCx) and pulmonary vein radiofrequency ablation were per-

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Key messages

- Amiodarone does carry significant risks of toxicity
- Pulmonary toxicity can be particularly difficult to diagnose in cardiac patients
- It is usually reversible on withdrawal of the drug

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formed. Atrial flutter, which had recurred pre-operatively, was corrected to sinus rhythm at surgery using radiofrequency ablation.

Discussion

Amiodarone is an effective antiarrhythmic drug for the treatment of both supraventricular and ventricular arrhythmias. It does, however, carry significant risks of toxicity, especially to the thyroid and lungs. Less common side effects are hepatic, neurological, ophthalmic, photosensitivity and drug interactions including warfarin and digoxin.

Pulmonary toxicity can be difficult to diagnose. The symptoms may be mild and may develop slowly. In cardiac patients radiological changes may be mistaken for those of heart failure. The commonest radiological manifestation of amiodarone toxicity is mild diffuse shadowing in the lung fields. Nonetheless, more extensive shadowing with a diffuse alveolar fibrosis and cavitating masses may occur. Bronchiolitis obliterans leading to pneumonia (sometimes fatal), pleural effusions and adult respiratory distress syndrome have all been described[1] Pulmonary toxicity is usually reversible after withdrawal of the drug. Corticosteroid therapy can be helpful and supportive pulmonary treatment may also be required. The incidence of pulmonary toxicity is relatively low, at 1% per annum,[2,3] of treatment.

Pulmonary toxicity can be particularly confusing in cardiac patients. In our patient worsening heart failure was the initial explanation for the pulmonary changes on the chest X-ray. Only when the patient failed to respond to increasing anti-failure treatment was the possibility of amiodarone toxicity considered. The prompt improvement after withdrawal of amiodarone supported the diagnosis of amiodarone toxicity.

Amiodarone toxicity developed very rapidly with this patient, within two weeks of starting treatment, at a cumulative dose of approximately 7 g. Review of the literature has shown only one report of pulmonary toxicity occurring within two weeks of initiation of treatment.[4] Darmanta and colleagues reported a case of toxicity that began after three weeks of therapy and ended in death.[5]

Conclusion

This case is noteworthy for two reasons. First, amiodarone pulmonary toxicity occurred very soon, within two weeks of initiating treatment. Second, the chest X-ray mimicked the radiological changes of cardiac failure, illustrating the difficulty in distinguishing amiodarone-induced pulmonary toxicity from shadowing due to cardiogenic pulmonary oedema.

Conflict of interest

None declared.

References

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BOOK REVIEWS

The endothelin system in cardiopulmonary disease

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For copies, contact www.actelion.com

Astonishing progress has been made over the past few years in understanding the pathophysiology of the endothelin (ET) system and its role as a new therapeutic target for cardiopulmonary diseases. In the context of this rapidly evolving field, this new book appears. Its particular strength lies in the many chapters written collaboratively by clinicians and researchers. For this reason alone, the book is an exceptional resource for cardiologists and pulmonologists, particularly for those with special interests in pulmonary hypertension and heart failure.

This book is well illustrated and comprehensively referenced. It contains three major sections: the pathophysiology of endothelin; the role of the endothelin system in cardiopulmonary disease; and new therapeutic approaches. The extremely well written and comprehensive chapters reveal a clear view of the pathophysiology of the endothelin system and the role of endothelin receptor antagonists in the management of pulmonary hypertension, the cardiovascular manifestations of HIV and heart failure. Each chapter has one or more tables that refer to points made in the text.

The book begins with a comprehensive review of the role of ETA and ETB receptors in the pathogenesis of vascular diseases such as pulmonary hypertension. The book then proceeds to the numerous