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Organising pneumonia due to dronedarone

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ABSTRACT Organising pneumonia is one of the responses of the lung to injury and can mimic bacterial pneumonia but importantly it does not respond to antibiotic therapy. We present the case of a 67-year-old male who was diagnosed with organising pneumonia secondary to dronedarone. Drug reactions are a common cause and early identification of the culprit is mandatory to prevent further morbidity and ensure a favourable outcome. On chest radiography there may be fleeting peripheral consolidation, while computed tomography can show a range of stereotyped patterns including perilobular consolidation. Bronchoscopic biopsy may not always be possible but response to steroids is often rapid following removal of the culprit drug. Dronedarone should be included in the list of possible drugs and the Pneumotox database remains a useful resource for the clinician when acute drug-related pneumotoxicity is suspected.

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CASE REPORT

A previously well 67-year-old retired building engineer presented with a seven week history of breathlessness. He had never smoked and had no other occupational factors for lung disease. Past medical history included exercise-induced atrial fibrillation treated recently with dronedarone on cardiological advice due to previous beta-blocker intolerance. He was taking no other medications.

Two weeks after commencing dronedarone he developed increasing breathlessness, dry cough and fever. Chest radiography demonstrated significant right middle and upper zone consolidation (Figure 1). He was treated for community acquired pneumonia but symptoms progressed over seven weeks. Physical examination revealed pronounced right-sided crackles. Investigations confirmed hypoxaemia with PaO_2 6.7KPa on 2 l of oxygen with saturations of 92%, an elevated C-reactive protein of 163 mg/l and elevated white cell count of 12.5 x 10^9/l (neutrophilia with normal eosinophil count). Computed tomography scanning of the chest showed that the previous extensive consolidation in the right lung had significantly improved leaving widespread ground-glass change. However, new consolidation had developed on the left and there were several areas of localised perilobular consolidation (Figure 2). This flitting consolidation and its perilobular distribution were highly suggestive of organising pneumonia. Extensive infective (bacterial, viral and fungal) and autoimmune screens were negative.

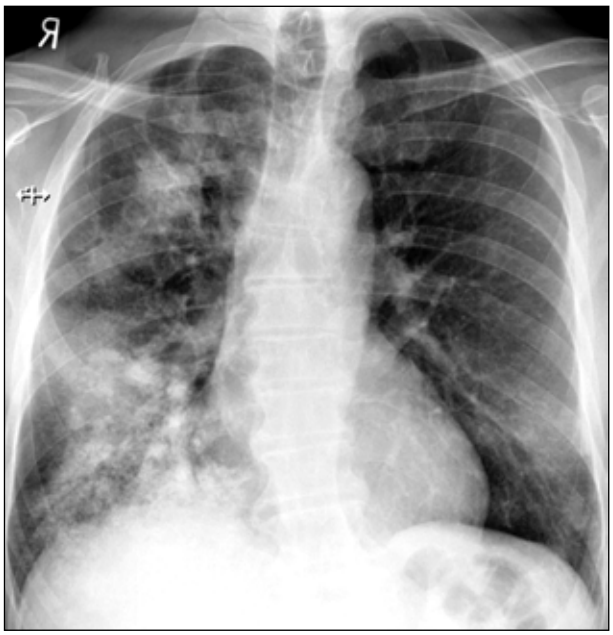

FIGURE 1 Chest radiograph demonstrating right middle zone opacification and right upper zone infiltrates

The patient's dronedarone was stopped but he developed sudden refractory hypoxic respiratory failure (PaO_2 8.9kPa on 15 l/min oxygen therapy) precluding bronchoalveolar lavage with transbronchial biopsy. Daily methylprednisolone was administered for three days given the high clinical suspicion of organising pneumonia. This produced rapid clinical and radiological improvement. After three days the patient did not require supplemental oxygen and he was discharged on a tapering course of oral prednisolone. On outpatient

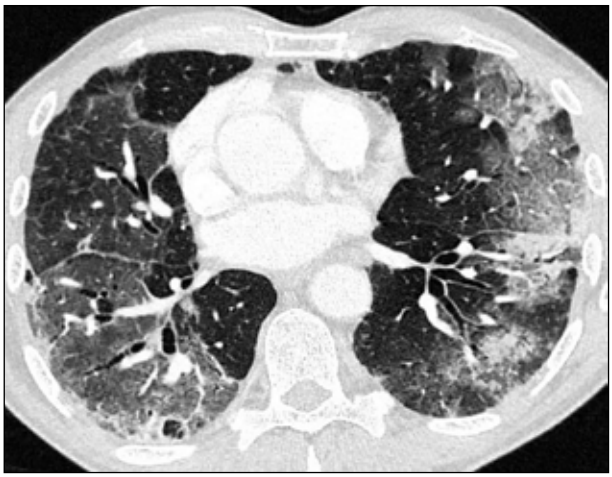

FIGURE 2 Computed tomography of the thorax (lung windows) demonstrating perilobular consolidation

review two weeks later he had significantly improved with near complete resolution of chest radiographic changes. He remains well, and is no longer taking systemic steroid treatment or dronedarone.

DISCUSSION

Organising pneumonia is a form of diffuse interstitial lung disease characterised by intraluminal plugs of inflammatory debris predominantly within small airways, alveolar ducts and adjacent alveoli and mild interstitial inflammation in the surrounding lung. It is usually a secondary phenomenon but is occasionally cryptogenic. Lung biopsy may be required for definitive diagnosis but transbronchial biopsy can sometimes confirm the diagnosis and a lymphocytic broncho-alveolar lavage may provide supportive evidence. Causes of organising pneumonia include: drug reactions, connective tissue disease, hypersensitivity pneumonitis and lymphoma.[1] Dronedarone is approved for use in the UK and North America for non-permanent atrial fibrillation.[2,3] Although we were unable to obtain histological confirmation, the clinical presentation (failure to respond to antibiotics and fleeting radiological changes), rapid response to steroids, negative microbiological screen and withdrawal of the putative drug in timing are highly suggestive of organising pneumonia.

In the absence of other associated pathologies or medications, we hypothesise that dronedarone was the stimulus for organising pneumonia here. Given the well-known pneumotoxicity of amiodarone in the same drug class, dronedarone may also have similar toxicity. This is supported by a study demonstrating that at equimolar concentrations dronedarone had greater alveolar macrophage toxicity than amiodarone.[4] There have been three case reports of organising pneumonia with dronedarone implicated as a contributing factor,[5,6] with a fatality in one of the three cases despite removal of the causative agent and administration of pulsed methylprednisolone in all cases. There has also been one reported case of diffuse alveolar damage attributed to dronedarone again treated with methylprednisolone with a successful outcome.[7] In addition to our case this implies that, while rare, reactions may be severe, prolonged and require corticosteroid treatment. It is already listed on the Pneumotox database as a causative factor in subacute pneumonitis, organising pneumonia (two reports) and left ventricular dysfunction.[8] When organising pneumonia is suspected, medication history must be reviewed carefully and we suggest dronedarone should be included in the list of potential culprits.

LEARNING POINTS FOR CLINICIANS

Organising pneumonia remains an important differential of unexplained fleeting chest radiograph infiltrates especially in patients treated for presumed infective pneumonia but not responding to antibiotics. It is important to review the drug history carefully, in particular any new drugs that might be implicated. Dronedarone should be added to the list of potential culprits. Early recognition is important to avoid the offending drug and response to the correct treatment is often rapid. Computed tomography findings may provide sufficient evidence to initiate treatment in the absence of other explanations when biopsy is not possible. Pneumotox remains a useful resource for the clinician when suspecting drug related causes of pneumotoxicity.

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