

Amiodarone - induced pulmonary nodules mimicking metastatic lung disease - investigation by somatostatin radio peptide scanning

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Teaching Points

1. Consider Amiodarone as a cause for solitary or multiple pulmonary nodules on chest X-ray.
2. Neospect scanning may be useful in the differentiation of benign (including amiodarone-induced) nodules from malignant lesions seen on chest X-ray.

Keywords

Amiodarone, Pulmonary Nodules, Radio-Peptide Scanning, Somatostatin, Neospect.

Case Report

A 61 year old former paramedic presented to A&E complaining of palpitations. He was found to be in atrial fibrillation, which reverted spontaneously to sinus rhythm. A chest x-ray taken at that time showed multiple pulmonary nodules consistent with metastatic malignancy (Figure 1). In the past he had been treated with amiodarone 200mg daily for 6 years following a previous diagnosis of atrial fibrillation, which had been attributed to alcoholic cardiomyopathy. He had discontinued the drug 8 months earlier, after self-diagnosing hypotension and bradycardia. A previous chest X-ray, taken before starting amiodarone, was normal.



Figure 1. Chest X-ray showing multiple lung nodules

He was an ex-smoker, but denied weight loss, cough, wheeze or shortness of breath. On examination there was no evidence of finger clubbing or cardiac failure. Respiratory examination revealed scattered inspiratory crackles over the lower zones. Abdominal and urogenital examination was normal.

Oxygen saturation was normal with a peak flow of 530 l/min and a mild restrictive defect (FVC 71%, TLC 74% of predicted) on lung function testing. CT scan of the chest and abdomen showed multiple nodules of varying size in both lungs, predominantly in the lower lobes, and measuring up to 2.5cms (Figure 2). These were reported as likely metastases. Bronchoscopy was entirely normal and lavage was negative for malignant cells. Tumour markers were all normal as were electrolytes, liver function and inflammatory markers.

It was considered that these shadows may have been a legacy of previous amiodarone treatment although no chest X-ray had been taken for 6 years. As the patient was reluctant to have a fine needle aspirate unless essential, we elected to do a *Neospect* scan. *Neospect* is a technetium 99m labelled synthetic peptide, which contains somatostatin receptor binding sites (SSTR). It is known that malignant tumours over-express Somatostatin receptors. These can be identified by the radiotracer, which localises in tumours expressing SSTR.

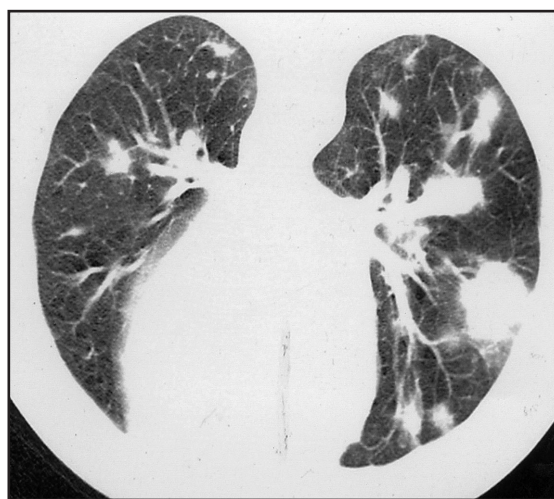


Figure 2. CT appearances of multiple lung nodules

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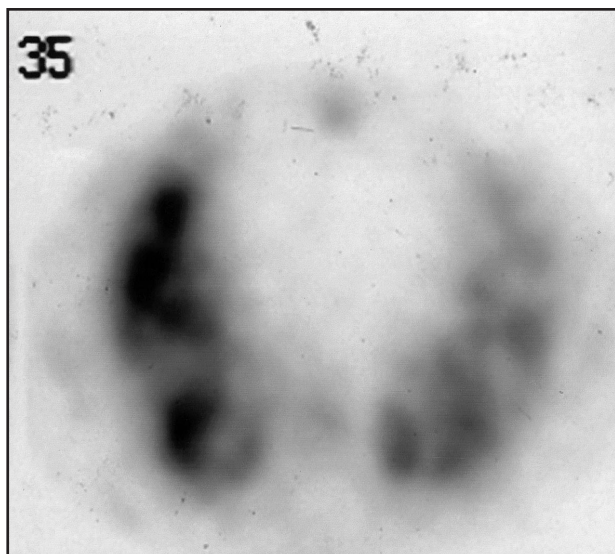


Figure 3. Neospect scan showing diffuse uptake by the lung but no intense uptake in the nodules themselves

The *Neospect* scan undertaken on our patient showed a diffuse increase in tracer uptake throughout the lungs, sparing the upper lobes (Figure 3). This uptake was greater than would be expected in normal lung tissue, suggesting increased SSTR receptors due to pneumonitis. Although uptake was noted in the nodules there was no focus of intense uptake to suggest malignancy.

A decision to observe with a repeat CT scan in 3 months was taken. This follow up scan showed clearing of the nodules with 'ground glass' change remaining at the sites of previous nodules. At 5 months the chest X-ray was entirely normal and the patient was discharged.

Discussion

Amiodarone treatment for tachyarrhythmia is effective but long-term treatment can lead to lung disease in 5-7% of patients.^{1,2} The respiratory effects are commonly indolent, with febrile illness and malaise mimicking acute infection.³ The chest X-ray may show a diffuse interstitial shadowing often confused with pulmonary oedema, pneumonitis or even diffuse fibrosis.⁴ Isolated reports of solitary pulmonary nodules exist.^{5,6} A cumulative dose effect giving toxicity is considered the cause. Total doses as low as 12g can cause changes but generally 226g or more are required. Toxicity is often seen after 6-60 months of treatment. Drug withdrawal is reported to resolve the chest X-ray findings in 2-6 months.

Lipoma
Fibroma
TB granuloma
Sarcoid
Neurofibroma
Hamartoma
Rheumatoid nodule
Aspergilloma
Pulmonary infarction
Amyloidosis
Lymphangioleiomyomatosis
Leiomyoma

Table 1. Recognised causes of benign pulmonary nodules

Benign lung nodules may arise from a variety of causes (Table 1). Patients with multiple lung nodules due to amiodarone are not easily distinguishable from those with multiple metastases.^{7,8} Such a finding will usually lead to extensive tests to find the primary tumour. If amiodarone is a possible cause of nodules, avoidance of invasive tests such as bronchoscopy and fine needle aspirate would be desirable.

In vitro⁹ and in vivo studies have shown show the affinity of *Neospect* for a range of malignant tumours including small cell and non small cell lung cancer, moderate to poorly differentiated adenocarcinoma, neuroendocrine tumours, breast and intestinal adenocarcinoma, melanoma and pheochromocytoma. Metastases of these tumours also show affinity. Multicentre trials (Phase II/III) have evaluated *Neospect* in 115 solitary pulmonary nodules, demonstrating sensitivity of a 97% and specificity of 73%¹⁰ for the diagnosis of malignancy.

In the case described, the lack of respiratory symptoms and mild restrictive defect without weight loss or other systemic features led to scepticism regarding the initial diagnosis of malignancy. The cessation of amiodarone 8 months before presentation is unusual, although the findings may have been more florid if a chest X-ray had been taken when the drug was first stopped.

Although *Neospect* scanning is not a substitute for biopsy, a positive scan would have led us to advise our patients to reconsider consenting to biopsy to obtain a tissue diagnosis. The combination of a low clinical suspicion of malignancy and negative scan enabled us to adopt a 'wait and watch' policy, which led to complete resolution. Clinicians should consider *Neospect* in the evaluation of pulmonary nodules thought to be induced by amiodarone before undertaking more invasive tests.

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References

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