

CASE REPORT

Amyloidosis: The Value of Bone Scintigraphy

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ABSTRACT

An 80-year old woman complained of a 1-month history of dry cough. Bronchoscopy and tracheobronchial biopsy revealed tracheobronchial amyloidosis. Computed tomography scan showed narrowing of the trachea with intraluminal nodularity. Whole body and single photon emission computed tomography ^{99m}Tc pyrophosphate scan revealed diffuse uptake in the tracheobronchial tree, liver, and myocardium — with a unique biventricular pattern. Scintigraphy may assist in establishing the diagnosis, as well as in evaluating systemic involvement in amyloidosis.

Key Words: Amyloidosis, Computed tomography, Radionuclide imaging

INTRODUCTION

Tracheobronchial amyloidosis is rare, with fewer than 100 cases reported. Primary tracheobronchial amyloidosis is idiopathic and unrelated to any chronic disease. Patients are usually middle-aged and present with cough, haemoptysis, dyspnoea, and hoarseness. The disease affects males more often than females.¹ Tracheobronchial amyloidosis is not typically associated with systemic amyloidosis, and bronchoscopy is most useful in establishing the diagnosis by biopsy.² A small number of reports in the literature have focused on radiological imaging, principally CT findings. Scintigraphy has proven useful in supporting the diagnosis, as well as in systemic evaluation of amyloidosis, but is still underutilised.

CLINICAL DETAILS

An 80-year-old woman presented with a 1-month history of dry cough. Chest radiography showed right middle lobe consolidation. She had mild diabetes treated with oral hypoglycaemic agents, and no other known chronic medical or cardiac disease. With the exception of a raised neutrophil count, routine blood biochemistry, rheumatology, and myeloma screening tests were all

unremarkable. Bronchoscopy showed obliteration of the right middle lobe bronchus, and narrowing of the trachea with intraluminal nodularity. Tracheomalacia was also noted on expiration during bronchoscopy.

Tracheobronchial biopsy revealed almost complete replacement of subepithelial tissue by deposition of amyloid, demonstrated with Congo red staining. Immunohistochemical staining showed amyloidosis to be of the amyloid light-chain-derived (AL) type. Echocardiography was unremarkable, with satisfactory left ventricular function.

Spiral CT of the thorax (10 mm collimation with 10 mm spacing at pitch 1.5, iopamirol 300 mg 100 mL at



Figure 1. Spiral computed tomography image of the thorax at the level of carina shows tracheobronchial narrowing with intraluminal nodularities (arrow). Right middle lobe consolidation is also seen.

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2 mL/second, delay 45 seconds) showed diffuse tracheobronchial narrowing, with nodularities on the intraluminal surface and right middle lobe consolidation. The diffuse nodularities were compatible with bronchoscopic findings at the site of biopsy. There was no mediastinal or hilar lymphadenopathy, nor other parenchymal lung lesion (Figure 1).

Whole body pyrophosphate (PYP) scan (920 mCi ^{99m}Tc pyrophosphate intravenous injection and imaging at 3 hours) showed diffuse uptake of radiotracer in the liver and heart (Figure 2). Single photon emission CT (SPECT) clearly demonstrated increased radiotracer uptake in the tracheobronchial tree (Figure 3), biventricular myocardial uptake (Figure 4), and diffuse uptake in the liver. There was no uptake of radiotracer in the spleen or gastrointestinal tract.

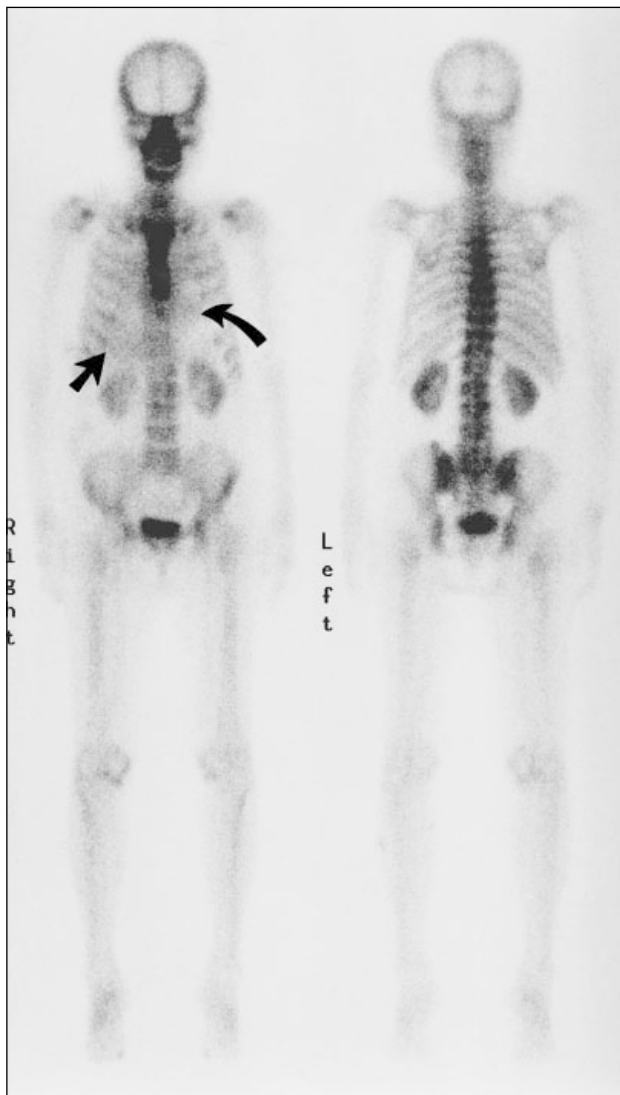


Figure 2. Whole body pyrophosphate scan shows abnormal uptake in the heart (curved arrow) and liver (straight arrow).

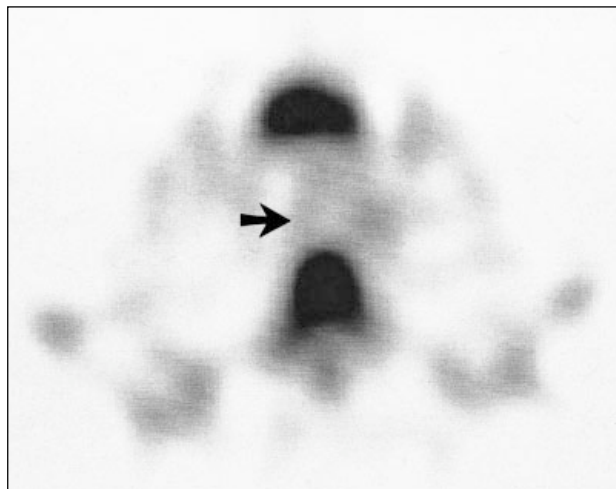


Figure 3. Pyrophosphate axial single photon emission computed tomography image of the thorax below the aortic arch shows tracheobronchial uptake (arrow). The nodular uptake in the left hilar region lateral to the tracheobronchial uptake is due to blood pooling activity in the aorta.

The right middle lobe consolidation later progressed into a lung abscess. Sputum culture yielded *Staphylococcus aureus*. The patient's symptoms were relieved by a course of intravenous antibiotics (cloxacillin and gentamicin). She was subsequently discharged with regular follow-up. Although scintigraphy showed liver and myocardial uptake, the patient declined to obtain histological proof of liver or gastrointestinal involvement. The case was classified as systemic amyloidosis with histologically proven tracheobronchial involvement.

DISCUSSION

Amyloidosis is generally classified according to the biochemical nature of the fibril-forming protein, but

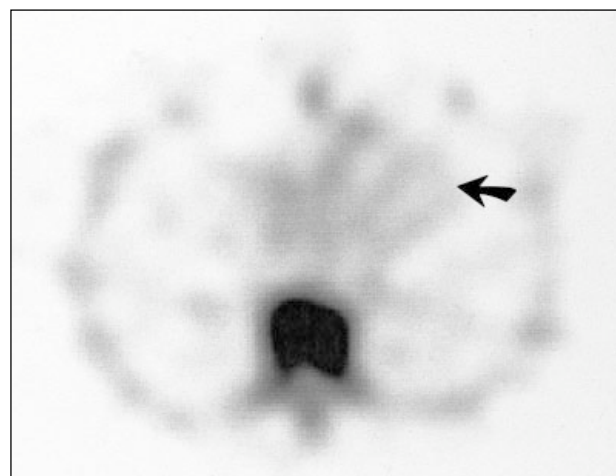


Figure 4. Pyrophosphate axial single photon emission computed tomography image of lower thorax shows biventricular uptake pattern of myocardium (arrow).

such classification is complicated as there are over 10 types of amyloid proteins. Clinical classification divides amyloidosis into systemic amyloidosis and localised or organ-limited amyloidosis.

Amyloidosis in the respiratory tract can be further divided into tracheobronchial, nodular, and diffuse parenchymal patterns.³ The tracheobronchial type is the most common, and consists of diffuse intraluminal nodularities of the tracheobronchial tree, resulting in narrowing of airways and obstructive pneumonitis on CT. Differential diagnosis includes endobronchial tuberculosis, sarcoidosis, Wegener's granulomatosis, relapsing polychondritis, and tracheobronchopathia osteochondroplastica. The nodular type shows diffuse nodular calcified lesions in the lungs and differential diagnosis includes metastatic calcification and granulomatous diseases. The diffuse parenchymal type is the least common, and is similar to other interstitial lung diseases.

Scintigraphy has been shown to be useful for assessment of systemic amyloidosis. The most sensitive and specific method is purified serum amyloid protein (SAP) scintigraphy.⁴ The SAP has affinity for all types of amyloid fibrils, but no uptake occurs in control or healthy subjects. SAP scintigraphy can be used for diagnosing, locating, and monitoring the extent of systemic amyloidosis. However, supply of SAP remains restricted, and it is not available in Hong Kong. Another common form of scintigraphy is bone scanning, using either PYP or diphosphonates.

The mechanism of PYP uptake is not completely understood, but is postulated to be related to the high calcium content in the non-fibrillar protein of the amyloid P-component.⁵ Although uptake in major airways, liver, spleen, gastrointestinal tract, and uterus have been reported in amyloidosis, they are not specific enough to make the diagnosis without pathological proof. In cases of cardiac involvement, a biventricular uptake pattern on the PYP scan is said to be unique for cardiac amyloidosis, after exclusion of extensive subendocardial infarct and myocarditis.⁶ Nevertheless, the main role of scintigraphy is to evaluate the extent of systemic involvement in amyloidosis, and to reduce the risk of bleeding from biopsy. It is also helpful to monitor disease progress and treatment response.⁷

Recently, the MRI features of tracheobronchial amyloidosis were described by Yamamoto.⁸ Submucosal

areas of the tracheobronchial tree which were involved in amyloidosis showed iso-intensity on T1-weighted imaging and low signal intensity on T2-weighted imaging, relative to skeletal muscle. Slight enhancement was observed in the enhanced T1-weighted image. These findings were observed in both submucosal areas with and without calcification seen on CT, and were thought to be due to the orientation of the amyloid fibrils in a repeating b-pleated fibrillar sheet configuration.

Treatment of tracheobronchial amyloidosis includes palliative procedures such as forceps debulking through rigid bronchoscopy, laser resection, or dilatation and stenting to relieve airway obstruction.⁹ Chemotherapy and external radiation treatment have also been used, but the condition tends to recur. The clinical significance in searching for systemic versus localised amyloidosis is that the systemic form carries a poor prognosis with a limited life expectancy, whereas the localised form is usually self-limiting.

In summary, we report a case of histologically proven tracheobronchial amyloidosis with systemic involvement (heart and liver), and illustrate how ^{99m}Tc PYP scan demonstrates the extent of systemic involvement of amyloidosis without the need for biopsy.

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