Organ limited amyloidosis with lymphadenopathy

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Summary: Hilar and mediastinal lymphadenopathy associated with localized pulmonary amyloid is very rare. We describe two cases of this unusual combination, one of endobronchial amyloid with adenopathy and the other of nodular parenchymal amyloid with hilar nodes. In both these cases the nodes contained calcification, and in the nodular parenchymal case in particular, this appearance is highly suggestive of pulmonary amyloid.

Introduction

Amyloid deposition in the respiratory tract may be a manifestation of systemic amyloidosis or part of a localized process. When it is part of generalized amyloidosis the lung involvement is usually sub-clinical and radiological findings in the chest are often incidental or secondary to a complication such as heart failure.

Localized disease is usually easily detected but may be subclinical. It may affect the lung parenchyma or airways and manifests either as nodules, single or multiple, or less commonly as diffuse alveolar septal disease. The airways may also be involved by localized submucosal amyloid infiltration. Lung parenchyma and airways are normally involved independently of each other, but very occasionally both are affected together.¹

Lymph node involvement is occasionally seen with thoracic amyloidosis, usually as the sole radiological finding.^{2,3} Both mediastinal and hilar nodes may be involved, and the enlargement is often massive. Nodal calcification is common² and the pattern of calcification is described as coarse or non-specific, and occasionally eggshell in type.³

Only a few patients have been described in whom amyloid involvement of lung parenchyma or airways has been found in association with mediastinal nodes. We describe two cases of pulmonary amyloid associated with adenopathy.

Case report

Case 1

A woman presented in 1987 at the age of 65 years with a five month history of dry cough. She had no other symptoms and no relevant past history, but had smoked 10–20 cigarettes per day for many years.

Her chest radiograph showed a right hilar mass containing several areas of calcification (Figure 1). Bronchoscopy revealed an area of erythematous, oedematous mucosa adjacent to the orifice of the right upper lobe bronchus. The other airways were normal. Bronchial biopsies taken from this site showed mucosal infiltration with deposits of homogenous material. These deposits showed green bi-refringence under polarized light after staining with Congo Red: findings consistent with a diagnosis of amyloidosis. Indirect immunoperoxidase staining for light chains, prealbumin, amyloid A protein, beta-2-microglobulin and cytokeratin intermediate filaments were all negative. However, amyloid P component was identified in the deposits.

A subsequent computed tomographic (CT) scan demonstrated partially calcified, non-enhancing mediastinal masses. These measured between 1–2 cm and were situated behind the superior vena cava, in the aortopulmonary window (Figure 2) and at the right hilum.

There was no evidence of any underlying systemic disease and in particular no evidence of myelomatosis. She remains well after three years follow-up and her chest radiograph is unchanged.

Case 2

A man presented in 1979 at the age of 35 years, after a routine chest radiograph was found to be abnor-

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Figure 1 Case 1: Chest radiograph demonstrating a right hilar mass containing several areas of calcification.

Figure 2 Case 1: Thoracic CT scan. There are several partially calcified mediastinal masses. These are seen behind the superior vena cava, and in the aortopulmonary window.

mal. He had smoked 20 cigarettes per day for 20 years, but had no relevant past medical history. Clinical examination was normal. The chest radiograph showed 6–8 intrapulmonary nodules. These varied in size from 0.5–3 cm, were well demarcated, non-cavitated and situated in the mid/lower zones bilaterally. One nodule at the right hilum contained nodular calcification. There was, in addition, some pleural shadowing at the right

costophrenic angle (Figure 3). Whole lung tomograms confirmed the presence of discrete intrapulmonary nodules and a partially calcified lymph node at the right hilum (Figure 4).

He was followed up for several years at the referring hospital and remained symptom-free. In 1988 he was referred to St George's Hospital and a percutaneous lung biopsy of one of the pulmonary nodules was performed. Histology showed birefringent material under polarized light after staining with Congo Red, confirming the diagnosis of amyloid deposition.

His current chest radiograph (9 years after the original one) shows that all nodules have increased in size by 1–4 cm. In addition, there are 2–3 new nodules, again in the lower zones. The calcified hilar nodes have increased moderately in size (Figure 5). He remains symptom-free and is on no treatment.

Discussion

Both of our patients had amyloid deposition limited to the respiratory system. Pulmonary amyloid is frequently of light chain (AL amyloid) origin⁴ and associated with a generalized or localized plasma cell dyscrasia. However, there was no evidence of a plasma cell dyscrasia in either of our patients. In addition, immunohistochemical studies in the first patient showed no evidence of light chains in the deposits. The only positive immunohistochemical finding was amyloid P component, which is a nonfibrillar glycoprotein moiety common to all deposits of amyloid.⁵

Pulmonary deposition of reactive systemic (AA) amyloid is rare. Our first case was negative for amyloid A protein, which excludes AA amyloid. Our second patient has followed a benign course over several years with no evidence of any other underlying disease. It would, therefore, seem unlikely that he has reactive systemic (AA) amyloid, although it has not been possible to confirm this immunohistochemically.

Amyloid deposition in an airway occurs submucosally and may be focal or diffuse, the latter being more common.⁴ When diffuse it may involve the trachea, mainstem, lobar and proximal segmental bronchi, together or in part. Focal involvement gives rise to endobronchial masses that are radiologically indistinguishable from bronchial neoplasms.⁴ In either type of lesion, the chest radiograph may be normal⁶ or show obstructive features, particularly collapse, seen in over 50% of patients.⁷

Hilar and mediastinal lymphadenopathy associated with endobronchial amyloid as illustrated in our first case, is a very rare event. Of the 57 patients with tracheobronchial submucosal amyloid de-

Figure 3 Case 2: Chest radiograph (1979) demonstrating bilateral intrapulmonary nodules in the mid and lower zones. The nodule at the right hilum contains nodular calcification.

Figure 4 Case 2: Whole lung tomograms demonstrating a partially calcified lymph node at the right hilum.

scribed in the literature⁸⁻¹⁰ only four previous cases with hilar or mediastinal nodes have been described. In 1952, Noring and Paaby documented a 39 year old male with a long history of recurrent pneumonias, whose chest radiograph at presentation showed a right pleural effusion and a lymph node at the right hilum. Later bronchoscopic examination found amyloid tissue in the middle of the trachea extending down both main bronchi. No further mention of the right hilar node was made

Figure 5 Case 2: Chest radiograph (1988). The intrapulmonary nodules have increased in size by between 1–3 cm. There are also 2–3 new nodules in the lower zones. The calcified hilar lymph nodes are more prominent.

and no calcification was described within it. In 1953 Schmidt *et al.* described a 35 year old man with haemoptysis who was thought to have bronchiectasis but thoracotomy revealed induration and distortion at the right hilum and a palpable, hard mass. The pneumonectomy specimen showed infiltrating amyloid tissue about the bronchi, right pulmonary artery and inferior pulmonary vein. Calcification was found in this mass, although nodes taken from the hilum did not contain amyloid.

A further case report,⁹ described a 34 year old man with haemoptysis who was found to have amyloid deposition in both main bronchi on bronchoscopy, with a comment in the summary that probably calcified hilar nodes were noted too. The fourth case, described in 1968 by McGurk, was a 52 year old woman with stridor and haemoptysis whose chest radiograph showed prominence of the right hilar shadow. Bronchoscopy revealed amyloid tissue almost completely obstructing both main bronchi. No further mention of the aetiology of the right hilar prominence was made.

In Case 1 airway involvement appears localized and it seems possible that amyloid infiltration has spread directly from lymph nodes. The nodes themselves were never biopsied as it was not considered justifiable on clinical grounds. Adenopathy was stable, quite marked, and in part, contained peripheral calcification. This pattern and behaviour would be very atypical for tuberculous involvement in an adult white, and the patient had not visited areas endemic for relevant fungal infec-

tion. Sarcoidosis remains a remote but unlikely possibility in view of negative bronchial biopsies.

In the nodular parenchymal form of localized respiratory amyloidosis the nodules are discrete, often subpleural and calcification or ossification within them is common. They may be single or multiple and vary in size and shape with no lobar predilection.¹¹ The nodules tend to behave in an indolent manner, growing slowly or remaining stable over several years.¹

Our second case illustrates the unusual combination of adenopathy with nodular parenchymal disease. As in the first case, biopsy material from the node is not available. In the context it seems highly unlikely that a large node, containing central calcification which has enlarged slowly over the years, *pari passu* with the lung nodules could be due to anything other than amyloidosis. In a recent literature review⁴ there were only 55 reports of parenchymal nodular amyloidosis, and of these only 3 cases had mediastinal adenopathy.¹²⁻¹⁴

In 1964 Brown described the case of a 45 year old female with a history of cough and weight loss.¹² The chest radiograph showed widespread mottling throughout both lung fields and enlargement of both hilar shadows. Subsequent open lung biopsy confirmed the diagnosis of amyloidosis. Thompson

*et al.*¹³ described a 59 year old Greek man with dull chest pain whose chest radiograph showed a confluent shadow in the right hilum and right upper zone, suggestive of carcinoma with nodal metastases. Biopsy specimens obtained at bronchoscopy showed amyloid. Pathological examination of the resected mass and lymph nodes confirmed an amyloid tumour affecting peripheral lung tissue associated with infiltration of the draining hilar nodes. Laden *et al.*¹⁴ reported the remaining example of this unusual combination in an 86 year old woman who presented with weakness and weight loss. Her chest radiograph showed multiple, ill-defined pulmonary nodules and at post-mortem amyloid involvement of the parenchyma and hilar lymph nodes was found.

Hilar and mediastinal lymphadenopathy associated with localized pulmonary amyloid is very rare and we have described two cases of this unusual combination i.e. endobronchial amyloid with adenopathy, and nodular parenchymal amyloid with hilar nodes. In both our cases the nodes contained calcification, and in the nodular parenchymal case in particular, this appearance is very suggestive of amyloid involvement and allows a specific diagnosis prior to biopsy.¹⁵

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