Thoracic amyloidomas: Two case reports of an evasive diagnosis

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Lesson
Amyloidosis is a rare differential diagnosis of a mass detected in the chest. Amyloidoma is caused by a local proliferation of clonal B-cells secreting an unstable immunoglobulin light chain which accumulates. FDG-PET scan are useful but not specific. Treatment is generally by local resection for treatment of symptoms.

We report two cases of amyloidomas, which are rare entities characterised by large local amyloid deposits. These can occur in the upper respiratory tract, soft tissues and central nervous system.¹

Case 1
A 64-year-old man presented with an incidental right lung mass on chest X-ray. Mediastinoscopy and lymph node biopsy confirmed amyloid, remaining asymptomatic until four years later, developing exertional dyspnoea matched by significant increase of the mass by chest radiography. Basic laboratory evaluation and immunohistochemistry was unremarkable. Immunoelectrophoresis revealed a faint immunoglobulin G (IgG) kappa band. No mass spectrometry was performed. Colonic biopsy, bone marrow aspires, immunophenotyping and trephine were normal.¹²³I Serum amyloid P-component (SAP) scintigraphy showed abnormal uptake within the mass only. Computerised tomography (CT) revealed mediastinal and hilar lymphadenopathy, with a 9.5 × 6.5 × 10 cm right mediastinal mass containing fat and calcification with a radiological differential diagnosis of a teratoma. F-18 fluorodeoxyglucose (FDG)-Positron Emission Tomography (PET)/CT demonstrated intermediate to high-grade uptake within the soft tissue and low-grade uptake in the fatty component (Figure 1). Cardiac magnetic resonance imaging excluded cardiac involvement. Repeat core biopsy demonstrated fibrovascular tissue with focal amyloid deposition. The patient proceeded to surgical mass de-bulking for diagnosis and symptom relief and histology confirmed evidence of amyloid. The patient’s postoperative course was uneventful; no evidence of recurrence three months following surgery and marked symptomatic improvement, with disappearance of the IgGκ paraprotein following resection, currently planned for local consolidation radiotherapy.

Case 2
A 71-year-old woman was investigated for a one-year history of deteriorating dyspnoea on a background of well-controlled asthma. Other co-morbidities included cutaneous systemic lupus erythematosus, rheumatoid arthritis and Sjogren’s syndrome. High-resolution computerised tomography (HRCT) showed multiple cysts, solid nodules and aggregate masses – the largest (2 × 1.5 cm) in the peripheral left lower lobe with fine-needle aspiration suggestive of amyloid. Serum biochemistry showed a polyclonal elevation of IgG, no detectable monoclonal band and normal serum-free light chains. Immunohistochemistry showed no specific staining for kappa or lambda antibodies. Mass spectrometry was not performed. Echocardiography excluded cardiac involvement and no visceral uptake by¹²³I SAP scintigraphy. Pulmonary function tests demonstrated a restrictive pattern, and a further HRCT raised suspicion of lymphocytic interstitial pneumonitis. FDG-PET/CT demonstrated similar low-grade uptake in all lung nodules (Figure 2). A mini-thoracotomy was performed to obtain tissue from the largest nodule showing evidence of amyloid but too few infiltrating cells were present to confirm clonality.

A low-grade lymphoplasmocytic lymphoma (LPL) was presumed to be driving the pulmonary amyloid, based on the assumption of low-grade B-cell clonal...
disorders that can occur with Sjogren’s syndrome. A trial of R-CVP (Rituximab – Cyclophosphamide, Vincristine, Prednisolone) chemotherapy was commenced for four months resulting in no progression of symptoms and stable lesions.

Discussion

Light chain (primary) amyloidosis (AL amyloidosis) is caused by an underlying plasma cell dyscrasia secreting unstable light chain proteins which misfold, resulting in abnormal insoluble fibrillar deposition of immunoglobulin light chains (κ or λ) in tissues which can lead to organ dysfunction or failure. Amyloidomas are isolated masses of amyloid deposition and only reported to occur in AL amyloidosis. With only 12 cases of solitary thoracic amyloidomas reported in the literature, evidence for treatment is scarce and diagnosis is challenging.

Diagnosis requires evidence of amyloid deposition, immunohistochemistry for typing of amyloid fibrils and evaluation of systemic organ involvement versus localised disease. Demonstration of characteristic apple-green birefringence with Congo red staining under cross-polarised light remains the gold standard for diagnosis. The international consensus guidelines describe methods for diagnosis of organ involvement in AL amyloidosis. Diagnosis of isolated thoracic amyloidomas is by exclusion of amyloidotic involvement of other organs. Traditional imaging techniques and, increasingly, radionuclide imaging can be used to assess the extent of disease and response to treatment.

A chest radiograph may show shadowing or discrete masses with no diagnostic features. CT findings are diverse, ranging from large solitary amyloidomas, multiple nodular pulmonary amyloidosis to more widespread disease, with no pathognomonic features of amyloidosis. Magnetic resonance imaging does not add additional information in most cases but may be a useful test for long-term monitoring to avoid radiation exposure.

Serum amyloid P component is a pentameric non-fibrillar protein component of all amyloid deposits. 123I SAP scintigraphy is used to identify and monitor visceral amyloid deposition in patients with systemic amyloidosis, with an acceptable dose of radiation but with limitation in assessing cardiac amyloidosis. Recent use of Single Positron Emission Computed Tomography allows accurate localisation of large amyloid solitary deposits.

All cases of thoracic amyloidomas described in the literature showed FDG avidity, like the two cases reported here. Review of the literature showed FDG-PET positivity in all cases of localised pulmonary amyloidomas. A small series from the French amyloidosis group showed positive FDG-PET scans in seven of 10 cases of localised AL amyloidosis but interestingly, the two pulmonary cases in the series had no FDG-PET/CT uptake in contrast with the two cases reported here. The reason for FDG avidity in localised amyloidosis, thoracic or otherwise, has not been clearly explained.

Localised thoracic amyloid deposits result from localised clonal proliferation of plasma cells or LPL, with FDG avidity most likely due to the low-grade plasma cell proliferation. However, there is often a local giant cell reaction, as seen in our first case, which may partially account for this activity. The clonality can be difficult to prove due to the scanty infiltrate. In our first case, initial needle biopsies were inconclusive, and LPL was only apparent following resection of the mass. FDG-PET/CT appears to be a very useful supportive investigation in patients with suspected localised amyloidomas, but cannot distinguish between malignant, granulomatous, inflammatory or infectious conditions.
Conclusion

Localised amyloidomas are rare but important as a differential diagnosis for a singular nodule in the thorax. Standard radiographic investigations do not have characteristic features sufficient for accurate diagnosis and histology is needed for definitive diagnosis. Exclusion of systemic involvement is crucial in management of these patients. FDG-PET/CT may prove to be an important modality in locating and monitoring response to therapy for patients with localised amyloidomas but further experience is needed.

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