Tracheobronchial amyloidosis with hilar lymphadenopathy associated with a serum monoclonal immunoglobulin

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ABSTRACT: We report a case of amyloidosis, restricted to the lower respiratory tract, with prominent tracheobronchial involvement and bilateral hilar lymphadenopathy, associated with a monoclonal serum protein of the immunoglobulin G (IgG) lambda type. The careful search for an extrathoracic site of involvement was negative. This particular association has not been reported previously.

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Tracheobronchial amyloidosis is a frequent presenting type of amyloidosis restricted to the lower respiratory tract [1]. Although amyloid deposits are of the AL-type (i.e. of immunoglobulin origin), a monoclonal serum immunoglobulin has not, to our knowledge, been observed in the course of this disease.

We report a case of severe thoracic amyloidosis, with prominent tracheobronchial involvement, associated with a monoclonal serum protein of the immunoglobulin (IgG) lambda type.

Case report

A 42 year old Italian man was admitted to hospital because of increasing dyspnoea. He had smoked heavily until the age of 41 yrs (cumulative dose 50 pack-years), but had no previous disease.

The patient had a dry cough, with intermittent haemoptysis, and had an increasing exertional dyspnoea for 3 years before admission. Fibreoptic bronchoscopy had been performed in another hospital six months previously. The diagnosis of tracheobronchial amyloidosis was suggested, and confirmed by the histological examination of the tracheobronchial biopsies and specimens obtained by open lung biopsy. Prednisone therapy was started five months before admission (25 mg-day⁻¹), without any improvement of symptoms.

On admission, the patient was dyspnoeic at rest, with stridor. Cardiac examination was normal. There was neither splenic nor hepatic enlargement, and no adenomegaly was found. Blood tests disclosed a blood leukocytosis (10.75x10⁹/l) with 84% neutrophils; lymphopenia (1.01x10⁹/l), erythrocyte sedimentation rate of 50 mm·h⁻¹, and normal values of hepatic, renal and coagulation tests. Proteinuria was absent. Mild hypogammaglobulinaemia (7.6 g·l⁻¹, normal range 8–12 g·l⁻¹), with decreased total IgG (6.6 g·l⁻¹, normal range 8–15 g·l⁻¹), and normal immunoglobulin A (IgA) (4.3 g·l⁻¹) and immunoglobulin M (IgM) (1.5 g·l⁻¹) values were observed. A monoclonal IgG lambda component was detected by serum immunoelectrophoresis. Urine immuno-electrophoresis was negative. An iliac bone marrow biopsy was normal. Arterial blood gases, taken while breathing room air, showed hypoxaemia (arterial oxygen tension (Pao₂) 10 kPa), and hypercapnia (arterial carbon dioxide tension (Paco₂) 6.3 kPa). Chest radiography showed bilateral hilar lymphadenopathy and an ill-defined opacity of the right lower lobe. The pleura and the heart appeared normal. Lung function tests showed slightly decreased lung volumes (total lung capacity 81% pred, vital capacity 86% pred, residual volume 71% pred) and severe airways obstruction: forced expiratory volume in one second/forced vital capacity (FEV₁/FVC) 31% (actual value), airway resistance 1.380% pred. Transfer factor corrected for alveolar volume was normal.

Chest computed tomography (fig. 1) showed a marked thickening of the tracheal and bronchial wall, with linear calcifications and partial obstruction of the bronchial lumen, bilateral hilar calcified lymphadenopathy, and an opacity of the right lower lobe, with partial loss of volume that was interpreted as an atelectasis distal to the bronchial obstruction.

Fibreoptic bronchoscopy showed a diffuse infiltrative process of the trachea and proximal bronchi, which uniformly reduced the bronchial lumen. Tracheal and bronchial biopsy specimens showed amyloid deposits with focal calcifications. This was confirmed by Congo red staining,
Clinical and radiological presentation was that of localized tracheobronchial amyloidosis. Indeed, symptoms due to tracheobronchial amyloid deposits were prominent, with severe airways obstruction, and partial atelectasis of the right lower lobe. Severe airflow obstruction, mimicking bronchial asthma, has been reported previously in tracheobronchial amyloidosis [6]. This presentation is strikingly different from lung involvement in systemic amyloidosis, where the symptoms attributable to the tracheobronchial deposits are rarely observed, although infiltration of the tracheobronchial structures is frequent in autopsy studies. Moreover, extrathoracic involvement is usually evident in systemic amyloidosis [7].

Intrathoracic amyloid lymphadenopathy is an uncommon finding. In a recent review of the literature, Naschitz et al. [8] could find only 11 cases. However, the association of tracheobronchial amyloidosis with hilar or mediastinal masses has been reported previously [9]. Furthermore, amyloid deposits in the wall of pulmonary vessels, as observed here and in the case reported by Arwood et al. [10], are seldom reported in tracheobronchial amyloidosis, since the diagnosis is usually made by fiberoptic bronchoscopy, and an open lung biopsy is not required. However, deposits in the small submucosal bronchial vessels, as observed in this case, are found in as much as 70% of patients [11].

We could not find any report of tracheobronchial amyloidosis associated with a monoclonal protein, although the presence of serum or urine monoclonal proteins (homogeneous immunoglobulins as in this case, or Bence Jones proteins, or both) could be demonstrated in the majority of patients with so-called primary systemic amyloidosis [2], and in some patients with nodular parenchymal pulmonary localized amyloidosis [11]. In fact, it has been suggested that in tracheobronchial amyloidosis or nodular parenchymal amyloidosis, amyloid may be produced locally, whereas, in primary amyloidosis the amyloidosis follows the deposition of circulating amyloidogenic proteins [5].

The presence of a monoclonal protein in serum of a patient with amyloidosis suggests the existence of amyloid fibrils derived from the circulating protein, especially when the serum monoclonal immunoglobulin is of the lambda type (the most frequent type observed in "primary" or "myeloma-related" amyloidosis), as in our patient [2]. However, this is not always the rule, since in some cases of amyloid localized to the tenosynovium at the carpal tunnel, the monoclonal circulating protein is unrelated to the amyloid deposit [12]. In our patient, immunohistochemical typing of deposits confirmed the AL-type amyloid, although the strong labelling of the deposits with both kappa and lambda light chain antibodies did not allow us to further characterize the similarity of the deposits and the circulating monoclonal protein. A similar discrepancy has been observed in renal amyloidosis of the AL-type [4].

**Discussion**

In this patient, amyloidosis, strictly restricted to the lower respiratory tract, was diagnosed on histopathological findings and after an extensive negative search for an extrathoracic site of involvement. Massive amyloid deposits were detected in the tracheobronchial tree, extending from central to peripheral airways. Small deposits were observed in some pulmonary arterial walls. Bilateral, hilar, calcified lymphadenopathy was probably caused by the disease, although we did not obtain an histological proof. Osseous metaplasia, associated with amyloid deposits, is frequent and a relationship between tracheobronchial amyloidosis and tracheobronchopathia osteoplastica has been suggested [5]. As expected, amyloid deposits were of the AL-type, as indicated by the lack of fixation of anti-AA serum and strong fixation of light chains antiserum on the deposits. The singularity of this case resulted from the presence of a monoclonal serum protein (IgG lambda type).

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References
