Tracheobronchial Amyloidosis in a Patient with Sjögren’s Syndrome

Takeshi Saraya¹, Hiroki Nunokawa¹, Masachika Fujiwara², Kosuke Ohkuma¹, Naoki Tsujimoto¹, Yayoi Tsukahara³, Haruyuki Ishii¹, Hajime Goto¹ and Hajime Takizawa¹

Abstract

A 65-year-old woman was referred to our respiratory department because of incidentally detected endobronchial deposits. She had been diagnosed with Sjögren’s syndrome 12 years earlier. Bronchoscopy showed protrusion of the reddened, shiny or edematous mucosa at the orifice of the lower lobe bronchus, suggesting a submucosal tumor. Based on the pathological findings of the transbronchial biopsied specimens, the patient was diagnosed with non-classified type tracheobronchial amyloidosis associated with Sjögren’s syndrome, which was negative for both λ and κ chains, transthyretin and amyloid A. She has remained in good health without a relapse of the tumor.

Key words: tracheobronchial amyloidosis, Sjögren’s syndrome


Introduction

Tracheobronchial amyloidosis (TBA) is much less common than systemic amyloidosis (1), which represents 0.5% of all symptomatic tracheobronchial lesions (2, 3). TBA associated with Sjögren’s syndrome has rarely been reported. We herein describe an extremely rare case of TBA associated with Sjögren’s syndrome along with a review of the literature on respiratory amyloidosis in patients with Sjögren’s syndrome.

Case Report

A 65-year-old woman was referred to our respiratory department because of tracheal stenosis due to endobronchial deposits, which were detected by chance in the otorhinolaryngology outpatient department. She had a 20-year history of Sjögren’s syndrome, but had not been treated for this condition. She denied having any respiratory symptoms. However, she experienced persistent hearing loss in her left ear for one year, which was pathologically diagnosed as a plasmacytoma located near the left pharyngeal opening of the auditory tube. On initial examination, she appeared to be in good health, and her vital signs were normal. A physical examination showed xerostomia, ankyloglossia, Raynaud’s phenomenon and purpura affecting both lower legs. No digital ulcers, periungal erythema or dermal sclerosis were observed. Serum laboratory examinations showed mild anemia (Hb 10.5 g/dL), hypergammaglobulinemia (IgG 1,837 mg/dL), presence of autoantibodies such as anti-SSA/Ro (18,000 U/mL), anti-La/SSB antibodies (19.4 U/mL), an elevated antinuclear antibody titer of 1,280 and an elevated rheumatoid factor of 484; neither M-protein nor Bence-Jones protein were observed. The result of a chewing gum test was 8 mL in 10 minutes, and the patient had a score >1 focus/4 mm² for focal lymphocytic sialadenitis. These results satisfied two of the three American College of Rheumatology classification criteria for Sjögren’s syndrome (4). Serum tumor markers were negative. Thoracic computed tomography showed the endobronchial lesion as large as 10 mm (Fig. 1A, B) at the bifurcation of the left lower lobe bronchus, which corresponded to the protrusion of the reddened, shiny or edematous mucosa at the orifice of the lower lobe bronchus (Fig. 1C, D, arrow).

Based on the suspicion of the presence of a bronchial tu
mor or a metastatic tumor from other organs, a transbronchial biopsy was performed, and the tumor was found to be very firm. On hematoxylin and eosin staining, biopsied specimens from the orifice of the left lower lobe bronchus showed an amorphous acidophilic salmon pink material in the connective tissues beneath the epithelial layer (Fig. 2A), which tested positive during direct fast scarlet staining (Fig. 2B). This suggested bronchial amyloidosis. However, the specimens were immunohistochemically negative for both λ (Fig. 2C) and κ chains (Fig. 2D), transthyretin (Fig. 2E) and amyloid A (Fig. 2F). The patient was therefore diagnosed with non-classified type TBA associated with Sjögren’s syndrome. The large part of the endobronchial tumor was successfully removed during a transbronchial biopsy. She has since remained in good health without a relapse of the tumor.

Discussion

The first report of an amyloid localized to the lower respiratory tract was by Lesser in 1877 (5), followed by sporadic reports of respiratory amyloids. Primary pulmonary amyloidosis was radiologically classified by Fraser et al. (6) into three groups: tracheobronchial form, nodular parenchymal form and diffuse interstitial form. The present case was classified as the tracheobronchial form using Fraser’s criteria. TBA is much less common than systemic amyloidosis (1), which represents 0.5% of all symptomatic tracheobronchial lesions (2, 3). However, the frequency of TBA in patients with Sjögren’s syndrome is unknown. TBA can simulate carcinoma, including metastasis from other organs, diffuse lung fibrosis, pulmonary edema, bronchiectasis, tuberculosis and other cardiothoracic diseases. On bronchoscopy, the submucosal amyloid can be seen as ridges and stenoses that are shiny or pale owing to stretching of the overlying surface epithelium (5), as in the present case.

To characterize the patients with respiratory amyloidosis occurring in Sjögren’s syndrome, we reviewed the relevant literature on Japanese patients (Table) (7-17). There were a total of 13 cases, ranging in age from 42 to 79 years (median: 61 years), and the male to female ratio was 1:12. The proportion of TBA among the patients in our review was small (n=3, 23.1%), indicating that it is an extremely rare disease presentation (Table). The present case had no clinical symptoms at the time of diagnosis, but TBA can cause atelectasis, bloody phlegm and pneumonia with wheezing.
Figure 2. On Hematoxylin and Eosin staining, the biopsied specimens from the endobronchial deposit show an amorphous acidophilic salmon pink material in the connective tissues beneath the epithelial layer (A), which is immunohistochemically positive during direct fast scarlet staining (B), but immunohistochemically negative for λ (C) and κ chains (D), transthyretin (E) and amyloid A (F).

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<th>Age</th>
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and a chronic cough (18). In our review, among those in the TBA group, two of the three patients (66.7%) suffered from dyspnea, while six of 10 patients (60%) from the parenchymal form group had a cough or hoarseness. Although the frequency of symptoms in both groups was comparable, hoarseness or stridor may be present if the larynx is affected (16).

Amyloid precursors often have genetic mutations and undergo conformational changes. Antibodies produced against the wild-type protein may be less reactive against the mutant form, which seems particularly problematic for AL (19, 20). Therefore, the type of amyloidosis (AA or AL) could not be determined in the present case, but our review demonstrated that TBA with Sjögren’s syndrome could be present as not only the AA type (n=3) but also the AL type (n=6), and only one-third of the patients had an antecedent diagnosis of Sjögren’s syndrome. The characteristic feature of TBA associated with Sjögren’s syndrome remains unclear. Therefore, further accumulation of such cases will be needed. TBA tends to progress slowly but is relentless with rare spontaneous remissions. Consequently, our patient needs careful follow-up. A palliative surgery including the use of an expandable metal stent or Nd-YAG laser should be considered for TBA cases with severe tracheal stenosis. Additionally, physicians should consider that primary Sjögren’s syndrome is a high risk for low-grade B cell non-Hodgkin lymphoma.

Regarding the patient’s medical history of pharyngeal plasmacytoma, no definite evidence of amyloidosis was found during a pathological analysis, and no solid evidence showing a direct correlation between plasmacytoma and Sjögren’s syndrome has been reported. Amyloidosis can generate a plasmacytoma possibly through pathogenetic mechanisms involving local immunoglobulin production by chronic local antigenic stimulation or local abnormally functioning plasma cells. Interestingly, McAlpine et al. (21) reported that local amyloidosis deposition in an area such as the oropharyngeal region, posterior part of the tongue, nasal or oral cavity and tracheobronchial regions seldom presents as a manifestation of systemic amyloidosis.

The present case showed that TBA is an extremely rare phenomenon of Sjögren’s syndrome and can present without clinical symptoms. Additionally, both types of amyloidosis (AL and AA) can be involved.

The authors state that they have no Conflict of Interest (COI).

References