



# Sjögren's syndrome with nodular pulmonary amyloidosis

Chang-Wei Wu  & Ying-Chun Chien 

Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan.

## Keywords

Pulmonary amyloidosis, pulmonary nodule, Sjögren's syndrome.

## Correspondence

Ying-Chun Chien, Division of Pulmonary Medicine, Department of Internal Medicine, National Taiwan University Hospital and National Taiwan University College of Medicine, No. 7, Chung-Shan South Road, Taipei 100, Taiwan. E-mail: firstaidg@gmail.com

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## Introduction

Amyloidosis is a disease caused by aggregation of autologous protein and its extracellular deposition as fibrils. It can be locally affecting a single organ or systemically affecting multiple organs, causing function decline, organ failure, or even death if left untreated. Pulmonary amyloidosis is rare and presented as diffuse alveolar-septal, nodular, or tracheobronchial pattern [1]. Most cases are asymptomatic or with only subtle symptoms and are often diagnosed incidentally. Tissue biopsy is the method of choice for diagnosis. Previous literature has reported pulmonary amyloidosis to be associated with mucosa-associated lymphoid tissue (MALT) lymphoma or autoimmune disease, such as rheumatoid arthritis or Sjögren's syndrome [1]. We report a rare case of primary Sjögren's syndrome with nodular pulmonary amyloidosis.

## Case Report

A 65-year-old female non-smoker without known systemic disease presented to our clinic with chronic cough and dyspnoea on exertion for seven years. Symptoms progressed in the past year along with xerostomia, chest tightness, and body weight loss from 52 to 49 kg in three months. Her physical examination was unremarkable. Chest radiography revealed a round-shaped left upper lung

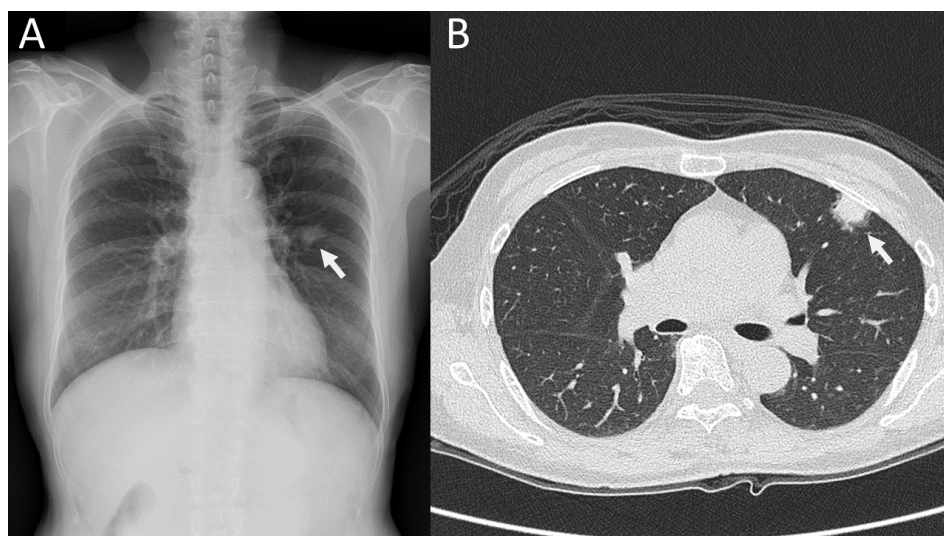
## Abstract

We report a case of Sjögren's syndrome with nodular pulmonary amyloidosis. Amyloidosis is a heterogeneous group of diseases caused by aggregation of autologous protein and its extracellular deposition as fibrils. Most cases of nodular pulmonary amyloidosis are the result of an underlying disorder such as mucosa-associated lymphoid tissue lymphoma, rheumatoid arthritis, or multiple myeloma. Nodular pulmonary amyloidosis with Sjögren's syndrome is very rare. The clinical outcome of patients with nodular pulmonary amyloidosis is good if the underlying disease can be controlled.

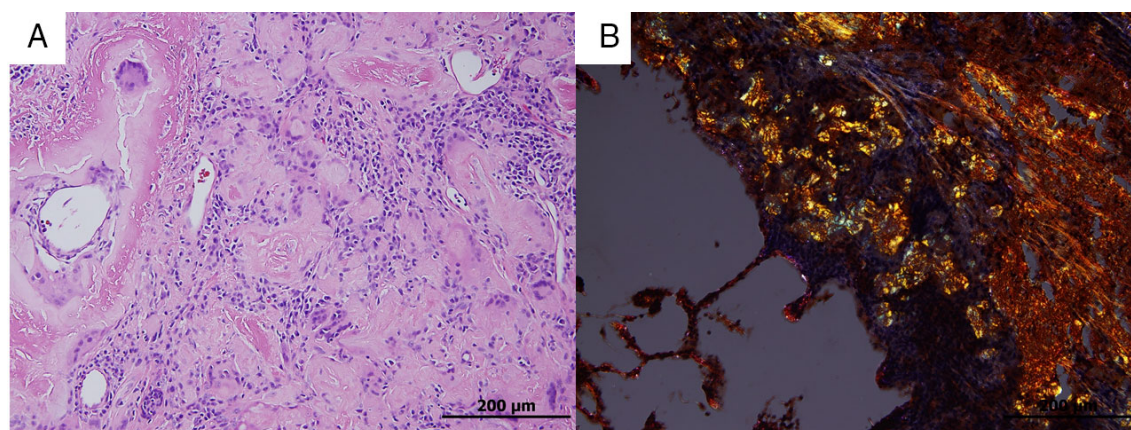
subpleural lesion with a clear margin. Computed tomography (CT) showed similar findings as in the chest radiography, with the size of the single subpleural nodular consolidation over the left upper lung, measuring 23 × 13 mm (Fig. 1).

Core needle biopsy via CT guidance revealed fibrinofibrous and hyalinized contents only. Subsequently, excisional biopsy using video-assisted thoracoscopy revealed accumulations of amorphous eosinophilic material that is sharply demarcated from the surrounding lung. The eosinophilic amorphous substance shows focal apple green birefringent in Congo red stain. Aggregates of plasma cells and lymphocytes are noted and foreign body giant cells are occasionally seen engulfing the amyloid (Fig. 2). Mediastinal lymph nodes showed no malignant cells or granuloma. The diagnosis of pulmonary amyloidosis was made.

Further evaluation was initiated for aetiology and disease extensity of pulmonary nodular amyloidosis. Electrocardiography, echocardiography, cardiac magnetic resonance image, and abdomen fat biopsy showed no evidence of systemic involvement of amyloidosis. The result of serum immunofixation electrophoresis and urine analysis excluded multiple myeloma or monoclonal gammopathy of undetermined significance. Bone marrow examination was not performed due to low evidence of plasma cell



**Figure 1.** (A) The chest X-ray film showed a left upper lung solitary pulmonary nodule with no cavitation or calcification. (B) Computed tomography identified a subpleural pulmonary nodule at the left upper lobe, measuring 23 × 13 mm.



**Figure 2.** Histopathological examination of the nodule. (A) Dense accumulations of amorphous eosinophilic material were sharply demarcated from the surrounding lung in haematoxylin and eosin stain (100×). (B) The eosinophilic amorphous substance showed focal apple green birefringent in Congo red stain (400×).

dyscrasia or lymphoma. Autoimmune profiles were as follows: antinuclear antibody (ANA) 1:2560 with a speckled nuclear pattern, anti-Sjögren's syndrome-related antigen A (anti-SSA)  $\geq 240$  U/mL, anti-Sjögren's syndrome-related antigen B (anti-SSB)  $\geq 320$  U/mL, and negative rheumatoid factor ( $< 9.50$  IU/mL). Technetium-99m sialoscintigraphy reported excretory dysfunction of bilateral salivary glands. The diagnosis of primary Sjögren's syndrome was made [2]. The final diagnosis was primary Sjögren's syndrome with nodular pulmonary amyloidosis. Hydroxychloroquine and pilocarpine were prescribed with symptom improvement. There was no recurrence of pulmonary amyloidosis at the latest clinical follow-up.

## Discussion

A case of nodular pulmonary amyloidosis associated with Sjögren's syndrome was demonstrated. Nodular pulmonary amyloidosis could be a localized disease, a presentation of systemic amyloidosis, or secondary to other systemic diseases. MALT lymphoma is the most common cause followed by plasma cell dyscrasia and autoimmune diseases such as rheumatoid arthritis and seronegative spondyloarthropathy. Sjögren's syndrome associated with nodular pulmonary amyloidosis is rare.

CT and magnetic resonance image have poor ability to differentiate amyloidosis from other diseases; hence, the differential diagnosis of secondary amyloidosis relies on a

thorough evaluation including symptoms, image study, electrophoresis, autoimmune profile, and biopsy. A combination of symptoms, signs, and autoimmune profiles can lead to the diagnosis of rheumatic diseases and other autoimmune diseases according to their diagnostic criteria. Serum and urine immunofixation electrophoresis along with bone marrow biopsy can detect multiple myeloma and monoclonal gammopathy. Infections such as tuberculosis can be detected with culture and polymerase chain reaction via bronchial washing or biopsy specimen. Biopsy of the nodule remains to be the only method for the diagnosis of MALT lymphoma and other neoplasms.

For the management of localized nodular amyloidosis, observation may be sufficient due to its slow-growing nature and conservative surgical resection is considered in those with large size or symptomatic disease with a very good long-term prognosis. Systemic treatment with immunosuppressant or chemotherapy is reserved for systemic amyloidosis or secondary amyloidosis.

Amyloidosis in association with primary Sjögren's syndrome was reported sporadically in previous literature [3,4]. It is suggested that Sjögren's syndrome, as a lymphoproliferative disease, may cause lymphocytes and plasma cells infiltration in specific organs, inducing local production of immunoglobulin light chains which deposit as amyloid fibrils [4]. The median age at which pulmonary amyloidosis is diagnosed in primary Sjögren's syndrome is 59 years, with a male : female ratio 1:27, which is higher compared to Sjögren's syndrome or amyloidosis alone. 72.7% of the patients developed symptoms, with cough and dyspnoea being the most commonly reported, each accounting for about 27%. The other symptoms included dyspnoea, fatigue, and chest pain. Pulmonary nodules with or without surrounding cysts or bullae is the most common radiographic presentation. An alveolar-septal pattern is also reported in some cases, with most of them associated with systemic amyloidosis [3]. Lymphoma combining with pulmonary amyloidosis was seen in 9% (3 of 33) in reviewing publication cases with primary Sjögren's syndrome [3].

Amyloidosis and Sjögren's syndrome share similar symptoms and both involve the salivary and lacrimal glands, making it difficult to differentiate between the two

diseases merely by the clinical information. Prior diagnosis of amyloidosis would exclude the diagnosis of primary Sjögren's syndrome according to the latest American College of Rheumatology/European League Against Rheumatism classification criteria due to possible amyloidosis mimicry [5]. Tissue biopsy combined with the exclusion of systemic amyloidosis involvement is the only method to differentiate Sjögren's syndrome, amyloidosis, or concurrent disease.

Pulmonary amyloidosis is a rare disease entity that requires a complete evaluation for the possible underlying systemic disease. We reported a case of primary Sjögren's syndrome with localized amyloidosis based on a thorough evaluation confirming no organs other than the lung were involved.

### Disclosure Statement

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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