Cavitary pulmonary lesions secondary to amyloidosis in a patient with Sjögren’s syndrome, diagnosed in a population where tuberculosis is endemic

Background: Sjögren’s syndrome (SS) is an autoimmune disorder that affects the lacrimal and salivary glands, and is a rare cause of pulmonary symptoms. The most common form of pulmonary involvement is interstitial lung disease. Very rarely SS can cause secondary amyloidosis which can present with cavitary pulmonary nodules, easily mistaken for pulmonary tuberculosis, especially in populations where tuberculosis is endemic. An awareness of the various forms of lung involvement in SS patients, and considering amyloidosis as a differential early on could save medical resources and prevent a lengthy disease course. The estimated prevalence of TB in urban Sri Lanka was 13.9% in 2013. The estimated annual burden of newly infected or re-infected TB cases of 400/100,000 was nearly 3-fold that of the global average burden. Our patient is a 58-year-old Sri Lankan female working in Doha, Qatar, who presented with recurrent attacks of Hemoptysis and cavitary lung lesions.

Introduction

Sjögren’s syndrome (SS) is a disorder that manifests as diminished exocrine gland function due to immune-mediated inflammation directed against the exocrine glands. Most commonly involved are the salivary and lacrimal glands [1,2], presenting with a combination of xerostomia and keratoconjunctivitis sicca as the only manifestations in around 30% of patients. SS can also present with extra-glandular involvement, most commonly affecting the skin, joints, muscles, thyroid gland, gastrointestinal tract, lungs and heart [3]. The disease has a primary form that occurs in isolation, and a secondary form that complicates other rheumatic illnesses, most commonly rheumatoid arthritis. Current criteria for diagnosis and classification rely on the American College of Rheumatology’s criteria, set in 2012 [4]. Commonly observed serologic markers are antinuclear antibodies (ANA) in around 74% of cases, anti-Ro/SSA antibodies in 40%, rheumatoid factor (RF) in 38%, antismooth muscle antibodies in 35%, and anti-La/SSB antibodies in 26% of patients diagnosed with SS [5]. The most common form of pulmonary involvement in SS is interstitial lung disease, that is often asymptomatic [6]. Several mechanisms were proposed to explain pulmonary involvement in SS. One theory describes the proposed role of high endothelial venules in channeling lymphocytes and various proteins to extranodal sites such as the lacrimal and salivary glands, as well as the lung and gastrointestinal tract; a process that is being recognized as an important part of management in such cases [7].

The proposed definition of SS by the American College of Rheumatology (ACR) set in 2012 requires two or more of the following findings to present to make a diagnosis:

- Ocular staining score of more than or equal 3, while the patient is not concurrently using lubricant eye drops.
- Positive serum rheumatoid factor and an ANA titer ≥ 1:320, or positive serum anti-SSA and/or anti-SSB antibodies.
- The presence of focal lymphocytic sialadenitis, with a focus score of ≥ 1 focus/4 mm² in a labial salivary gland biopsy [8].

Case report

A 58 year-old Sri Lankan female, who is a
known case of Sjögren’s syndrome manifesting as xerostomia and keratoconjunctivitis sicca, presented with recurrent episodes of self-rermittent hemoptysis and dyspnea on exertion. She has no history of smoking, nor any significant family history of malignant, cardiopulmonary or hematological disease. She denied any incidence of fever, shortness of breath, weight loss, night sweats, or chest pain, had no history of recent travel, respiratory tract infections or exposure to sick contacts, and did not complain of any other significant cardiopulmonary symptoms. The first time she had an episode of hemoptysis was 2 years after initially being diagnosed with Sjögren’s syndrome.

On examination she was afebrile, with vital signs within normal limits, and had equal air entry in both lungs, with no wheezes, rubs, rales or basal lung crepitations. Heart sounds were normal, and the abdomen was lax and non-tender, with no hepatosplenomegaly. On examining her lymph nodes, she had no significant cervical, supraclavicular, apical or inguinal lymph node enlargement, and no masses could be elicited on breast examination. Cranial nerves II to XII were grossly intact and she had no motor or sensory deficits.

Laboratory work-up was normal, showing no anemia or leukocytosis, and was only significant for an elevated ESR of 37, an ANA titer of 1:160, and a positive SSA (Ro 52 & 60) and SSB (La). Rheumatoid factor and anti-smooth muscle antibodies were negative, as well as sputum cultures for mycobacteria on three separate sets. Three sputum smears were negative for acid-fast bacilli (AFB) on microscopic examination. Bronchoscopic examination was done and was unremarkable, with bronchoalveolar lavage from multiple lung segments coming out negative for any bacterial, mycobacterial or fungal pathogens. Chest X-ray and chest CT scans were also performed, showing multiple cavitary nodules bilaterally and in all lung lobes (Figure 1a-c).

A thoracoscopic lung biopsy was obtained, and a sample from a right lower lobe lung nodule showed amorphous eosinophilic deposition, as well as apple-green birefringence under polarized light with Congo red staining; consistent with a diagnosis of pulmonary amyloidosis (Figure 2a and b).

Anecdotal reports of the benefit of colchicine in the management of AA amyloid due to Behçet’s syndrome and inflammatory bowel disease, along with a relatively benign adverse-reaction profile in patients with normal kidney and liver function lead us to consider a trial of twice-daily colchicine 0.6 mg. Upon confirmation of the diagnosis, our patient received colchicine therapy and started showing signs of improvement. Her dyspnea gradually improved and her hemoptysis decreased in quantity and frequency until it completely resolved. On further outpatient follow up the patient continued to improve symptomatically and had no further episodes of hemoptysis. Her pulmonary nodules remained stable in size on follow-up imaging [9-11].

**Discussion**

Only a few cases of pulmonary amyloidosis in SS
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Case Report

have been reported so far. A 41-year-old woman with diffuse septal AL amyloidosis related to SS in the absence of systemic amyloidosis was described by Rajagopala et al. [12], as well as a 40-year-old female pulmonary nodular amyloidosis presenting 15 years after being diagnosed with SS in 2015 [13]. There is, therefore, no sufficient data to recommend a particular treatment plan for such patients so far.

The work-up for SS-related interstitial lung disease is generally similar to the approach to ILD in the general population. Chest radiographs are usually recommended as a starting point, with high resolution chest CT scans and complete pulmonary function tests added in case of high clinical suspicion of ILD based on history, physical examination and/or chest x-ray findings. In case of abnormal findings on these tests, bronchoscopic examination with or without biopsies or a bronchoalveolar lavage can be pursued.

Patients with primary Sjögren’s syndrome (pSS) also have an increased of pulmonary infections due to decreased airway secretions, most pertinent to our case is pulmonary tuberculosis (TB), which is endemic in Sri Lanka, and presents with similar symptoms of cough and hemoptysis, as well as similar pulmonary radiologic findings of cavitary lesions on CT scans of the chest. In a population-based study by Chang et al. the risk of TB infection in patients with pSS was 1.58 times that of the control cohort. The risk could also be related to age ≥ 60 years and chronic corticosteroid use [11].

Aside from its exocrine gland manifestations, SS can affect a plethora of extraglandular sites, including: the joints, skin, muscles, kidneys, heart, lungs and gastrointestinal tract. Respiratory complications of the disorder include xerotrachea, or airway mucosal dryness as a result of diminished secretions, in addition to various forms of interstitial lung disease (ILDs) and non-Hodgkin lymphomas.

The onset of SS-associated lung disease is typically 5 to 10 years from the onset of SS, although this may vary and the lung symptoms could even sometimes precede the typical manifestations of SS and precede the diagnosis. Lung involvement has a higher prevalence in females, with a median age of onset of 60 years of age [9]. The severity of the respiratory symptoms varies greatly, and can present anywhere on a spectrum from mild dyspnea on exertion or cough, all the way to respiratory insufficiency. Milder symptoms, however, are much more common [10].

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Other differential diagnoses for a SS patient presenting with mild to moderate cough and/or dyspnea include xerotrachea, pulmonary vascular diseases such as pulmonary arterial hypertension and pulmonary embolism, malignancies with lung involvement, non-Hodgkin lymphomas, and pulmonary sarcoidosis.

Figure 2. (a,b) Thoracoscopic lung biopsy of the right lower lobe cavitary lesion showing amorphous eosinophilic deposition, as well as Apple-green birefringence under polarized light with Congo red staining.
There is no standardized treatment proven to be effective for AA amyloidosis to the date of this writing. The mainstay of treatment of AA amyloidosis is controlling the cause of the underlying inflammation in an attempt to suppress the synthesis of serum amyloid A protein. Other than colchicine, some of the treatment modalities that have been attempted include dimethylsulfoxide (DMSO) in amyloidosis complicating Crohn’s disease [15] and cyclophosphamide in AA amyloidosis complicating rheumatoid arthritis [16,17].

**Conclusion**

The case presents an unusual picture of pulmonary nodular amyloidosis complicating Sjögren’s syndrome presenting with dyspnea and hemoptysis, with a rare cavity appearance on radiologic imaging. The overall picture immediately raised suspicions for pulmonary tuberculosis, especially given the substantial burden of pulmonary TB in the patient’s country of origin. Testing for TB was negative, and a proper diagnosis was eventually with a bronchoscopic lung biopsy. Our patient’s symptoms responded well to colchicine and her pulmonary nodules stabilized.

**Learning point**

It is important to recognize the potential of SS to cause pulmonary lesions that can sometimes mimic other more common causes of lung disease such as infections and neoplasms. Bearing in mind the general framework of interstitial lung disease in Sjögren’s syndrome patients would aid at the arrival at such diagnoses in an efficient manner, saving time and resources, as well as saving patients the unnecessary emotional turmoil and stigma of a tuberculosis diagnosis.

**References**