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CASE REPORT

Xerotrachea: The Silent Signal of Sjogren's Syndrome

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Abstract

Sjögren's syndrome (SS) is a progressive autoimmune disease predominantly affecting women, characterized by lymphocyte infiltration in exocrine glands, leading to dryness of mucosal surfaces. Primary SS (pSS) can involve multiple organs, with pulmonary manifestations ranging from dry cough to interstitial lung disease (ILD) and lymphoma. The aim of this study was to explore pulmonary involvement and the management of xerotrachea as an extraglandular manifestation in pSS, as well as the impact of sinusitis on the incidence of rheumatic diseases.

We examined a patient with pSS presenting with persistent dry cough and atypical early onset, without the classic symptoms of xerostomia or xerophthalmia. A differential diagnosis was conducted, ruling out common causes of cough.

Xerotrachea may be an early manifestation of pSS, and it is crucial to differentiate it from other causes of chronic cough. While corticosteroids remain a mainstay of treatment for pulmonary manifestations, there is a need for further studies to optimize diagnosis and management strategies for xerotrachea and other pulmonary complications of SS. early recognition of xerotrachea in primary Sjögren's syndrome is essential, and a multidisciplinary approach should be taken to manage both glandular and extraglandular manifestations.

Keywords: Sjogren's Syndrome; chronic cough; xerotrachea; fatigue; asthma; autoimmune disease; sinusitis.

Introduction

Sjögren's syndrome is a slowly progressive autoimmune disease characterized by lymphocytes infiltrating exocrine glands (e.g., salivary and lacrimal glands), leading to destruction of exocrine epithelial cells and dryness of mucosal [1]. It may occur at any age but mainly affects women at the fourth decade of life; the estimated ratio female:male equal to 9:1. Cardinal symptoms are dry eyes (xerophthalmia) and dry mouth (xerostomia). Extraglandular sites may also be involved (particularly neurological, renal, cutaneous, pulmonary) [2]. Perhaps the least understood part of SS is fatigue/cognitive, possibly features of autonomic neuropathy and/or central nervous system sensitization [3].

SS can be primary(pSS) which means it is not associated with other autoimmune diseases, or secondary SS (sSS) associated different autoimmune diseases (particularly systemic lupus erythematosus [SLE], rheumatoid arthritis [RA], and scleroderma). SS has in general good prognosis but B-cell non-Hodgkin lymphoma (NHL) is a severe complication of pSS, affecting approximately 5% of patients. Mucosa-associated lymphoid tissue (MALT) lymphoma, particularly in the salivary glands, is the most common histological type. However, more aggressive forms, such as diffuse large B-cell lymphomas, can also occur. Independent predictors for NHL development include salivary gland enlargement, lymphadenopathy, Raynaud phenomenon, anti-Ro/SSA and/or anti-La/SSB antibodies, rheumatoid factor positivity, monoclonal gammopathy, and C4 hypocomplementemia [4].

Pulmonary manifestations can be present in 16% to as high as 75% in patients with this percentage detected by systemic imaging and pulmonary function testing [5]. Most commonly presenting with only dry cough [6]. Pulmonary involvement is associated with higher mortality and reduced quality of life [5]. It may include xerotrachea, bronchiolitis, bronchiectasis, asthma, ILD, nonspecific interstitial pneumonitis (NSIP), usual interstitial pneumonia (UIP), lymphoid

interstitial pneumonia (LIP), pulmonary cysts, and bronchus or lung-associated lymphomas [2,7]. According to Matthew Koslow, 36% (8 patients out of 22) presenting with unexplained cough and concomitant dry eyes ruled out to be SS [8].

This study shows that lung involvement in patients with primary Sjögren's syndrome is common and mostly subclinical. Xerotrachea, which can be one of the first manifestations of primary SS, is manifested with cough varying in intensity from a mild foreign body sensation to exhaustive dry cough ending in vomiting. Different diagnosis such as chronic bronchitis, gastroesophageal reflux, posterior drop or asthma are taken into account [9].

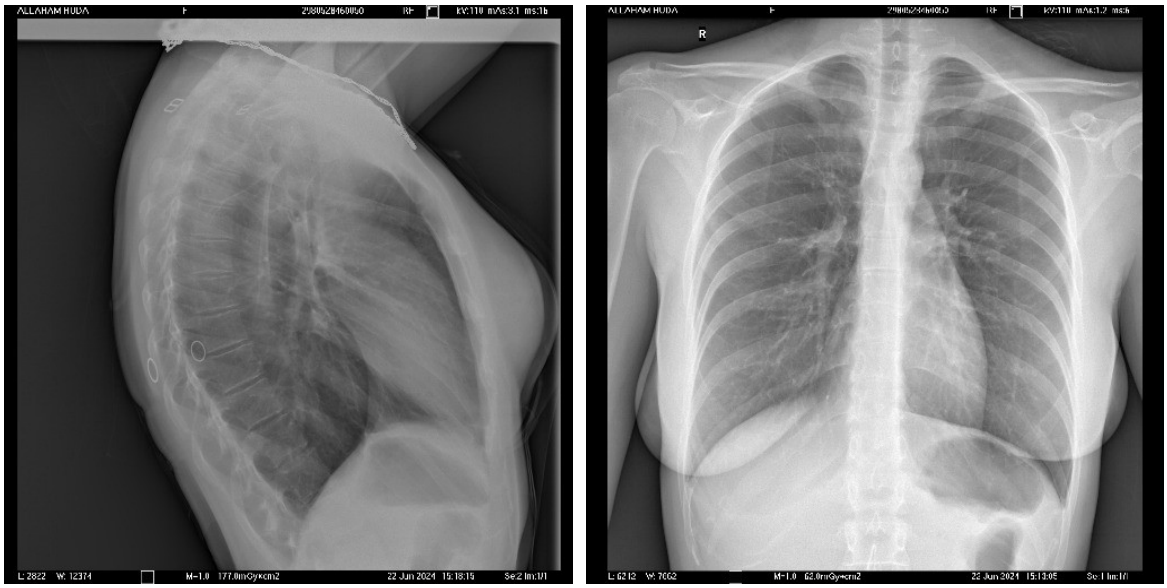
Case Presentation

A 26-year-old woman, with no significant medical history, presented in June 2024 at the emergency room with dry cough, chronic fatigue and recurrent sinusitis. Her symptoms began 4 months ago following an episode of acute upper respiratory tract infection (AURTI). She is a non-smoker and denies any professional exposure to respiratory toxins. The patient was infected with SARS-CoV-2 in November 2020, presenting with dry cough symptoms, and has been vaccinated three times with the Pfizer vaccine. The patient reports that since being infected with COVID, she has experienced a dry cough following any upper respiratory tract infection (URTI), with the cough lasting approximately 3 weeks. Regarding the current manifestation, the patient describes the cough as irritating, dry, and worsening at night, waking her from sleep and accompanied by vomiting. It is unrelated to food intake, and she denies any sensation of reflux or regurgitation. There is no significant family medical history.

On clinical examination, the patient was febrile (38.5°C), had dry skin (xerosis) and no signs of glandular or lymph node swelling. The frontal and ethmoidal sinus points were tender to palpation, with the most recent episode of sinusitis occurring one week ago, for which the patient was treated with Amoxiclav. Pulmonary examination revealed no abnormal findings, with no rales present.

Blood tests were within normal range, without any inflammatory syndrome.

A chest radiography was performed which shows a nodular formation with diffuse contour in the right hilum (Figure 1).



(a) (b)

Figure 1. *The pulmonary X-ray showing a nodular formation with diffuse contour in the right hilum.*

An ENT consultation was requested, which considered the diagnosis of acute sinusitis and recommended antibiotic treatment with Ceftriaxone, along with the recommendation to perform chest CT and sinus CT after the course of antibiotics.

The CT was performed in July 2024 after completing the course of recommended antibiotics. The sinus CT describes minimal mucosal thickening in a localized area of the left maxillary sinus and a dextroconvex septal deviation of approximately 3.5 mm, with no notable inflammatory changes in the paranasal sinuses or bilateral mastoid cells (Figure 2).

In contrast to the nodular formation described in the chest X-ray, the chest CT states the absence of pulmonary parenchymal consolidation with an inflammatory-infectious character and describes only scattered random bilateral pulmonary micronodules, nonspecific, recommending monitoring (Figure 3).

The patient undergoes a pulmonology evaluation, where spirometry is conducted with normal results and a negative bronchodilation test, effectively ruling out bronchial asthma (Figure 4).

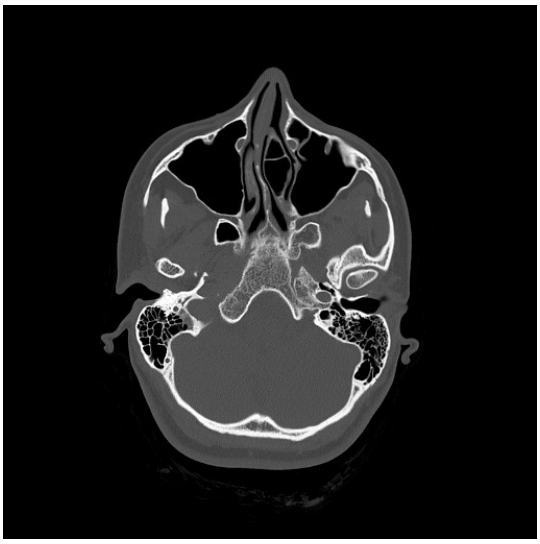


Figure 2. *Sinus CT showing a dextroconcav septal deviation of approximately 3.5mm.*

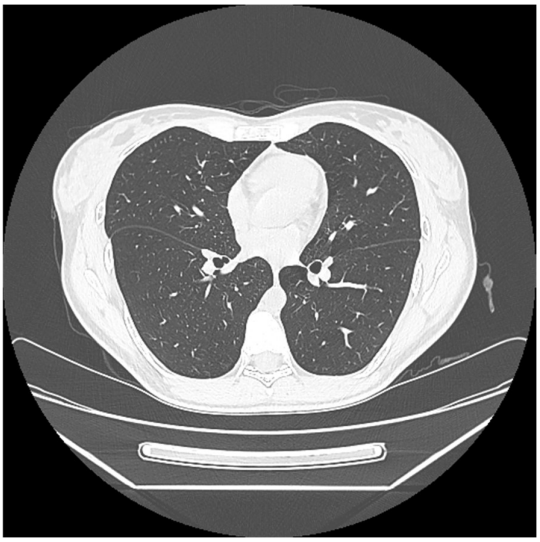


Figure 3. *Native chest CT without parenchymal involvement.*

Considering the persistence of symptoms and the exclusion of pulmonology/ENT causes, the patient is referred for evaluation in the rheumatology department. She was afebrile, with pronounced fatigue, more accentuated, hemodynamically stable, without cutaneous lesions but with xerosis, no xerostomia/xerophthalmia, no arthralgia, non-tender sinus points on palpation, and a persistent dry cough, worsening.

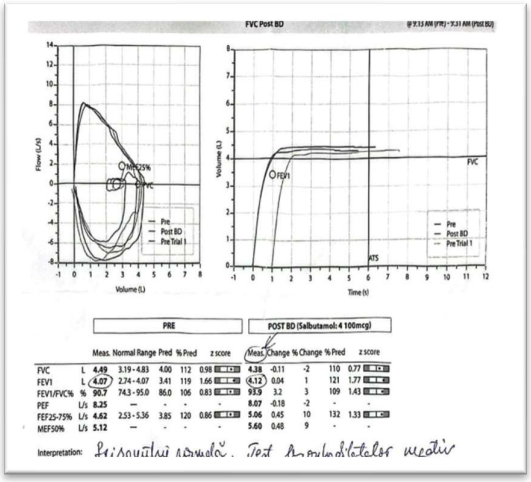
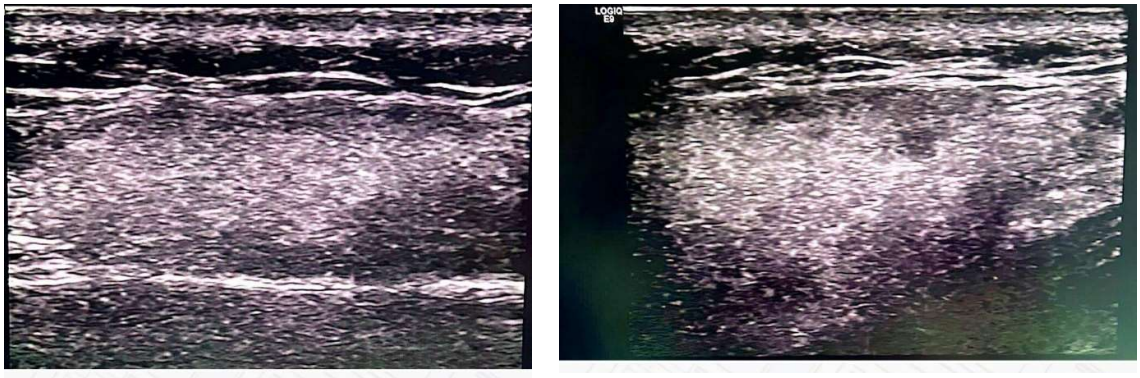


Figure 4. *Spirometry within normal range and negative bronchodilation test.*

The tests showed a normal complete blood count, with no biological inflammatory syndrome; however, specific tests revealed a rheumatoid factor of 140 IU/ml (normal range: 0-15 IU/ml), complement C4 consumption (C4 = 6.4 mg/dl; N = 10-40 mg/dl), elevated IgG (IgG = 1660 mg/dl; N = 700-1600 mg/dl), positive ANA x7 N with high anti-Ro antibody titer (anti-dsDNA, anticentromere antibodies negative), and normal electrophoresis with immunofixation. Urinalysis showing no hematuria or proteinuria.

Given the immunological results, attention turned toward SS. Considering that the patient did not present the typical manifestations of SS (denies xerostomia/ xeropthalmia, does not have glandular swelling), further evidence was needed to confirm this diagnosis suspicion.

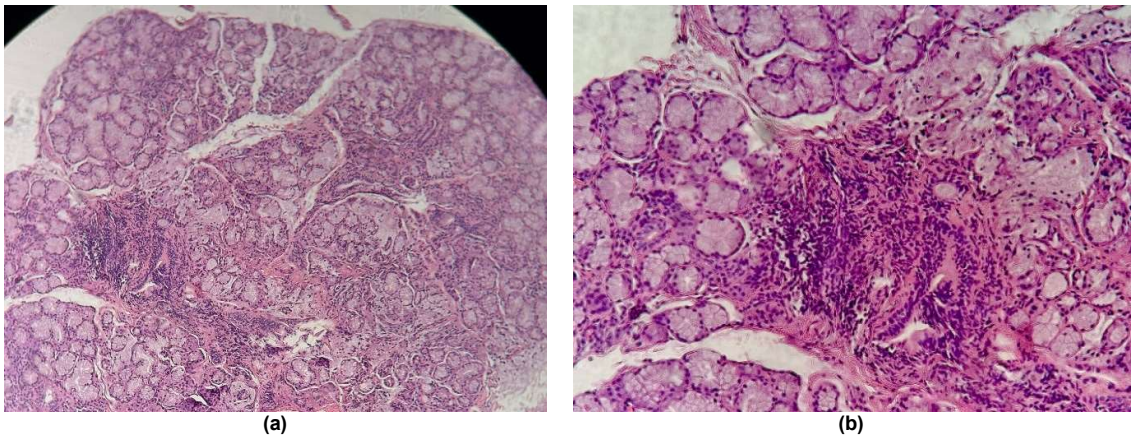
Schirmer test was negative. The ultrasound of the parotid (Figure 5a) and submandibular glands (Figure 5b) is within normal limits, with no signs of enlargement, masses, cysts, or abnormal structural changes. The glandular parenchyma appears homogenous and well-defined, with normal echogenicity and no evidence of inflammation or pathology.



(a) (b)

Figure 5(a). *Ultrasound of parotid glands.* **Figure 5(b).** *Ultrasound of submandibular glands, both with normal echogenicity and no evidence of inflammation or pathology.*

Therefore, a biopsy of the minor salivary glands (gold standard) is performed, which shows >1 focus. Consequently, a diagnosis of Sjögren's syndrome with xerostomia-type involvement is established (Figure 6).



(a) (b)

Figure 6. *Salivary gland tissue showing nodular lymphocytic aggregates, consisting of >50 cells (H&E stain 10x objective vs 20x objective).*

The patient receives treatment with hydroxychloroquine, initially at a dose of 400 mg, and methylprednisolone at an initial dose of 16 mg. The patient reports improvement in fatigue and cough one month after starting treatment. The progression during treatment was favorable without adverse reactions. The hydroxychloroquine dose was reduced to 200 mg (based on body weight), but the patient reports the onset of arthralgia, which is why the dose is maintained at 300 mg/day. In January 2025, complete discontinuation of corticosteroids is considered appropriate (after 6 months of treatment).

Two weeks after discontinuing treatment, the dry, bothersome cough reappears, accompanied by vomiting, which occurs throughout the day and limits the patient's ability to live normally. The patient denies other symptoms. Influenza and COVID tests are negative. Biologically: normal blood count, no complement consumption, ANA 5.5 IU/mL, RF 65 mg/dL, normal immunogram, anti-RO antibodies>200. Urine summary: microscopic hematuria, leukocyturia, and trace proteinuria (patient is menstruating). Urine culture is negative. Pulsed therapy is initiated with Solu-Medrol 250 mg/day for 3 days, with remarkable improvement. The patient is then switched to Methylprednisolone 8 mg.

The chest X-ray shows minimal thickening of the pulmonary interstitial tissue in the right interclavicular-hilar region (Figure 7).

A high-resolution CT was performed which excludes interstitial involvement in the context of a systemic disease (Figure 8).

The patient remains advised to continue treatment with methylprednisolone 8 mg, with gradual dose reduction, and hydroxychloroquine. In parallel with the attempt to reduce corticosteroids, non-pharmacological measures are being followed, including nebulization with saline solution, hydration, the use of bronchodilators, and inhaled corticosteroids, with further reevaluation to follow.

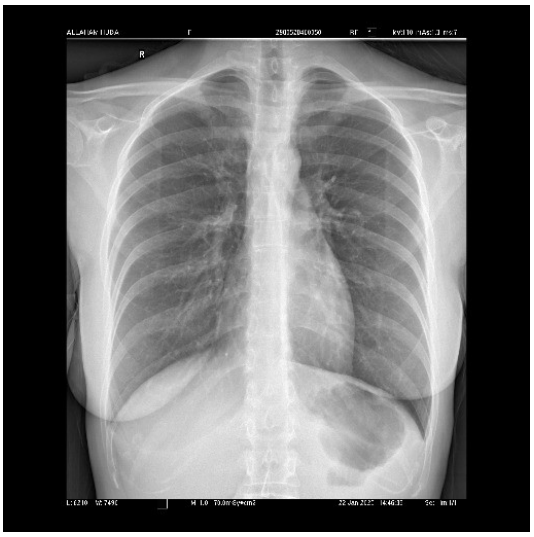


Figure 7. *Pulmonary X-Ray describing minimal thickening of the pulmonary interstitial tissue in the right interclavicular-hilar region.*

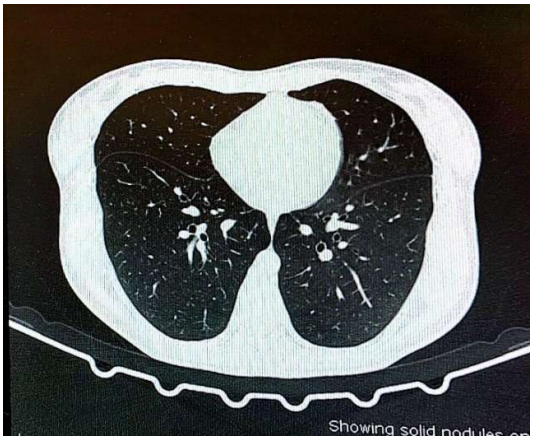


Figure 8. *Normal aspect of chest HRCT*

Discussions

The case presented an atypical manifestation of Sjögren's syndrome, notably without the common symptoms of xerostomia or xerophthalmia, as well as an unusually early age of onset. Concerning the patient's persistent dry cough, various differential diagnoses were considered, systematically ruling out the most frequent causes of dry cough, including postnasal drip, gastroesophageal reflux, and bronchial asthma [10]. Since the disease was with a moderate activity disease (scor ESSDAI 6), immunologically active (low C4 complement fraction, elevated rheumatoid factor, hypergammaglobulinemia, and increased levels of autoantibodies Ro52), and after excluding more common causes of dry cough, as well as the favorable response to corticosteroid therapy, xerotrachea was considered as a possible diagnosis.

Although no specific criteria exist for xerotrachea, recommendations for management of chronic cough are based on experience from similar airway conditions in SS which may indicate follicular or constrictive bronchiolitis with variable inflammation types (neutrophilic, lymphocytic, eosinophilic, fibroblast). The recommendations include inhaled corticosteroids despite an increased risk of candidiasis. Empirical use of bronchodilators and humidification is advised for chronic cough, alongside a trial of secretagogues or guaifenesin [11].

The immunological improvement observed in our patient can be due to Hydroxychloroquine [12]. This should not lead us to dismiss the involvement of Sjögren's disease in the cough recurrence. A study has shown that there is no significant correlation between clinical and laboratory findings and pulmonary manifestations, except in the case of ILD, where a higher prevalence of monoclonal gammopathy was observed, though it remains unclear whether this represents a significant correlation or a random association [13].

Not least, considering that the patient is of reproductive age, it is important to mention that Sjögren's syndrome (SS) can become active during pregnancy and the postpartum period. A specific obstetric complication is neonatal lupus, where cardiac involvement, particularly atrioventricular block, can be severe and sometimes irreversible, correlating with elevated anti-Ro antibody levels [14]. Women with SS have a higher risk of spontaneous abortion, low birth weight, and preterm delivery [15].

Conclusions

Xerotrachea can be one of the first manifestations of primary SS, considered to be extraglandular, that must be differentiated from the cough caused by interstitial involvement in SS as the management would be different [8].

Corticosteroids are the main treatment for follicular bronchiolitis, LIP, and BOOP. For UIP and NSIP, low-dose corticosteroids with azathioprine are usually recommended [16]. On the other hand, authors suggest that the “use of systemic therapy for dryness, chronic pain, or fatigue is not warranted.” High dose of CS and/or second line therapy should be considered for refractory or rapidly progressive cases [2]. There is no clear recommendation regarding treatment of xerotrachea. However, saline nebulization, bronchodilators and humidification, alongside a trial of secretagogues or guaifenesin are recommended though its efficacy is uncertain [11,16].

Parallel to the myriads of symptoms and manifestations associated with SS, it was found that a history of sinusitis was linked to a higher incidence of rheumatic diseases, including Sjögren's, particularly 5-10 years prior to disease onset, with the strongest associations in non-smokers [17].

It is also important to note that it is crucial to manage the patient holistically, considering not only the objective manifestations but also symptoms of fatigue, depression, and chronic pain that contribute to the decreased quality of life in a significant proportion of patients [3].

There is a need for further studies regarding the

diagnosis and treatment of xerotrachea, as well as the risk of progression to other forms of pulmonary involvement.

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Conflicts of Interest: The authors declare no conflicts of interest related to the research, authorship, or publication of this article.

Patient Consent for Publication: Written informed consent for publication of the clinical details and any accompanying images was obtained from the patient. The identity of the patient has been kept anonymous in accordance with ethical standards.

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