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Successful Treatment of Primary Sjögren's Syndrome Associated with Interstitial Lung Disease

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ABSTRACT

We report a rare case of interstitial lung disease as the first clinical manifestation of primary Sjögren's syndrome. A 49-year-old woman was assessed, complaining of dyspnea, dry cough, dry mouth, inflamed right cheek, dry skin, bilateral gastrocnemius pain, multiple peripheral arthralgia, and generalized weakness for the previous 2 months. Serology examination was positive for Sjögren's syndrome antibodies. Thorax CT demonstrated Crazy Paving appearance. Glucocorticoid alone did not improve the respiratory symptoms, hence azathioprine was given. Subsequent dyspnea regression and disease control obtained after 5 months of therapy. This case demonstrated that ILD could be the first clinical manifestation in pSS, and azathioprine could be used as the first line therapy for Sjögren's syndrome-related lung disease.

1. Introduction

Primary Sjögren's syndrome (pSS) is a rare chronic systemic autoimmune disease, affecting 0.1% of the general population.[1] Women are more vulnerable than men with 20:1 ratio.[2] Keratoconjunctivitis sicca and xerostomia are the most common early manifestations for pSS, but non-sicca manifestations, such as interstitial lung disease (ILD), often arise as the initial signs. Furthermore, pulmonary complications are more severe in non-sicca onset patients. Previous cases reported that an average of 10 years is needed to make pSS diagnosis after initial systemic manifestations. Non-sicca manifestations of pSS may be
insidious and can be easily overlooked by the rheumatologists.[3]

We report a case of pSS in a 49-year-old woman, presenting with ILD as the first clinical manifestation, before successfully treated with azathioprine.

Case Report

A 49-year-old woman was consulted to rheumatology division due to persistent exertional dyspnoea for the past 4 months. Furthermore, in the previous 2 weeks she reported dry cough, eating difficulty because of dry mouth, recurrent inflammation in right cheek, dry skin, bilateral gastrocnemius pain, multiple peripheral joint pain especially in the hands, and generalized weakness. Uniquely, there were no ocular

symptoms. She was hospitalized 2 months ago due to severe dyspnoea, the worst arterial blood gas revealed: PaO_2 34 mmHg and $PaCO_2$ 42.4 mmHg, and there were combined restrictive and obstructive lung defects from spirometry. The dyspnea became slightly improved after being discharged, however she continued to have mild dyspnea. During examination, we found sticky oral mucosa, swollen right parotid gland, swelling and tenderness of the hand, and bilateral basal rhonchi on chest auscultation. The other physical examination was unremarkable. We did additional laboratory examination and the results were positive for Antinuclear Antibody along with anti-Ro-52 recombinant, anti-SS-A native and anti-Jo-1. Subsequent chest CT scan showed bilateral predominant patchy ground-glass appearance with superimposed interlobular septal thickening and intralobular lines-Crazy Paving appearance (Figure A). Based on clinical manifestations, serology test, and imaging, she was diagnosed as primary Sjögren's syndrome (pSS) with interstitial lung disease (ILD). Administration of triamcinolone 8 mg PO and azathioprine 50 mg PO once a day, along with other symptomatic therapy was started. For the following 3 months, azathioprine dose was titrated up to 3x50 mg, and the patient's symptoms improved significantly. Follow up CT scan obtained 5 months later showed a reductionof consolidations and pulmonary infiltrates, there was no further disease progression (Figure B). After 4 years of treatment, she remains stable with azathioprine 50 mg once a day.

Figure 1. Posteroanterior Chest X-ray demonstrated extensive patchy reticulonodular opacities in both lungs (arrows).

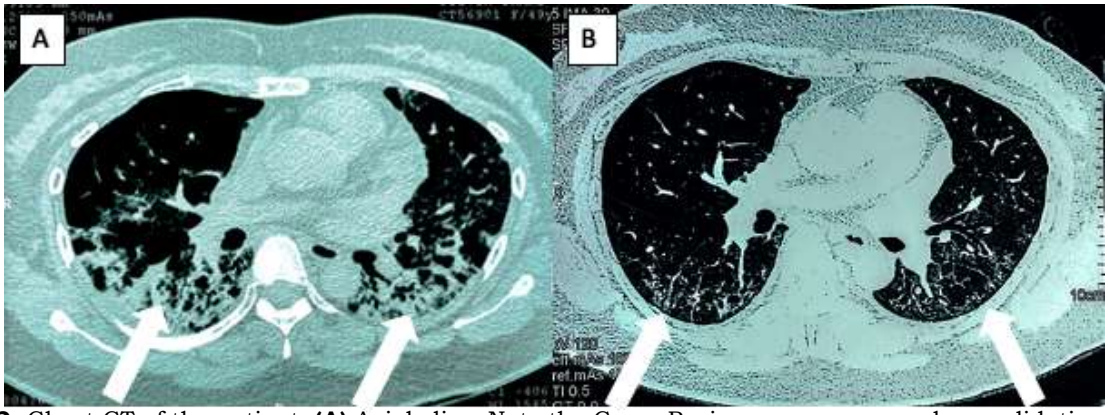

Figure 2. Chest CT of the patient. **(A)** Axial slice. Note the Crazy Paving appearance and consolidation areas in bilateral lung lobes (arrows). **(B)** Axial slice. Follow up chest CT, note the lung improvement after 5 months of azathioprine (arrows).

4.Discussion

Sjögren's syndrome (SS) is an autoimmune disease with many presentations, from exocrine glands to multi-organ involvement. SS may occur as a single disease entity (pSS) or in combination with other autoimmune diseases (secondary SS). [1] In 2014, a systematic review released by the European League Against Rheumatism – Sjögren's Syndrome (EULAR-SS) Task Force reported that 16% patients with pSS had pulmonary involvement, with the mean age of 58.4 years. Among them, women are more vulnerable than men with 6:1 ratio.[4]

Pulmonary manifestations are not the classical or sicca form of pSS, but recent study reported 49% of pSS-ILD patients presented with non-sicca symptoms as the chief complaint. Moreover, non-sicca onset pSS associated with more severe pulmonary complications, but delayed diagnosis was more common in this group.[3] Several studies described ILD prior to pSS diagnosis.[5-7] Our report is consistent with those previous studies, which also explained that ILD in pSS is always insidious and gradually increases. [3, 8, 9]

The most common pulmonary manifestations in pSS are dyspnea, cough, rhonchi, and chest pain. Ground-glass appearance or interstitial changes is found in almost 50% of cases.[4] There are several histologic patterns from ILD which can be associated with pSS, such as usual interstitial pneumonia, nonspecific interstitial pneumonia (NSIP), cryptogenic organizing pneumonia, diffuse alveolar damage, lymphocytic interstitial pneumonia and apical fibrosis. Ito et al in 2005 reported NSIP as the most common ILD histologic finding in pSS patient, mostly characterized by bilateral, symmetric lower pulmonary lobes abnormalities. [1, 5] In our patient, based on clinical appearance and imaging results, we believe NSIP is the histologic type for the ILD, although we did not do lung biopsy.

Systemic treatment is mandatory in pSS patients with systemic symptoms, it should be adjusted based on involved organs and disease severity. Due to lack of comprehensive data from controlled studies, the management of extraglandular manifestations are based on multiple case reports, studies and expert analysis, combined with understanding from other autoimmune diseases. For pSS patients whose pulmonary symptoms are prominent, the combination of glucocorticoids and azathioprine are drugs of choice along with other symptomatic therapy. Hence, azathioprine can be used as the first line therapy for Sjögren's syndrome-related lung disease. Other cytotoxic drugs like rituximab is confined for refractory cases of pSS.[10]

Fortunately, despite of prior severe respiratory failure and delayed diagnosis, our patient was fully recovered after the initiation of azathioprine along with other supporting drugs.

Conclusion

ILD can arise as the non-sicca initial manifestations of pSS. Since pulmonary complications in non-sicca pSS is associated with more severe complications, early detection and treatment are necessary in this patients category. Non-sicca onset pSS is still a challenge for clinicians to diagnose.

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