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Case Report

Primary Sjögren's Syndrome Associated Lymphoid Interstitial Pneumonia: The Enemy In Shadows

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ABSTRACT

LIP is characterized by the interstitial infiltration of lung tissue, especially the interalveolar septum by polyclonal lymphocytes, plasma cells and histiocytes. This clinical entity is known for its association with primary Sjögren's syndrome (pSS). In this case presentation, we aim to provide an overview of the diagnosis and treatment processes with a clinical example of this rarely encountered condition. A 69-year-old female patient was referred to our rheumatology department with complaints of cough, shortness of breath, widespread joint pain and bilateral widespread cystic lesions and ground-glass opacities in her thoracic CT scan. The patient had no comorbidities other than a history of metastatic renal cell carcinoma, for which she underwent a left pneumonectomy five years ago. Serological tests revealed ANA > 1:320 and SS-A (Ro) positivity. Salivary gland biopsy showed lymphocytic sialadenitis. Due to the irregular, widespread peribronchial distribution of the cystic lesions seen on the thoracic CT, pSS-associated LIP was considered. Bronchoalveolar lavage (BAL) fluid was rich in lymphocytes but did not provide diagnostic information. In light of these results, the patient was started on treatment with methylprednisolone at a dose of 0.5 mg/kg/day and hydroxychloroquine. Azathioprine was added after tapering steroid and methylprednisolone stopped at 6 months. 4-9% of pSS patients are confronting LIP and 30% of underlying medical conditions in LIP is pSS. It should be noted that rare but potentially life-threatening lung involvements like LIP can develop in Sjögren's cases, and, as in our case, it may even be the initial presentation. Current results are indicating improvement with glucocorticoid+DMARD treatment, but randomized controlled studies are strongly needed.

Keywords: Sjögren, LIP, interstital, lung

INTRODUCTION

Lymphoid interstitial pneumonia (LIP) is a rare type of interstitial lung disease that develops as a result of immune dysregulation and is often associated with rheumatological diseases. LIP is characterized by the interstitial infiltration of lung tissue, especially interalveolar septum, by polyclonal lymphocytes, plasma cells, and histiocytes. This clinical entity is known for its association with primary Sjögren's syndrome (pSS). In this case presentation, we aim to provide an overview of the diagnosis and treatment processes with a clinical example of this rarely encountered condition.

CASE

A 69-year-old female patient was referred to our rheumatology department with complaints of cough, shortness of breath, widespread joint pain, bilateral widespread cystic lesions and ground-glass opacities in her thoracic computed tomography (CT) scan (**Figure 1**). The patient had no comorbidities other than a history of metastatic renal cell carcinoma, for which she underwent a left pneumonectomy five years ago. No chemotherapy or radiotherapy was administered and there was no relapse after five years.

The patient's systemic rheumatological evaluation showed no signs of arthritis, morning stiffness, back pain, Raynaud's phenomenon, photosensitivity, fever, abdominal pain, diarrhea, oral ulcers, genital ulcers, psoriatic rash or erythema nodosum. She also had no history of uveitis, thrombosis or abortions but

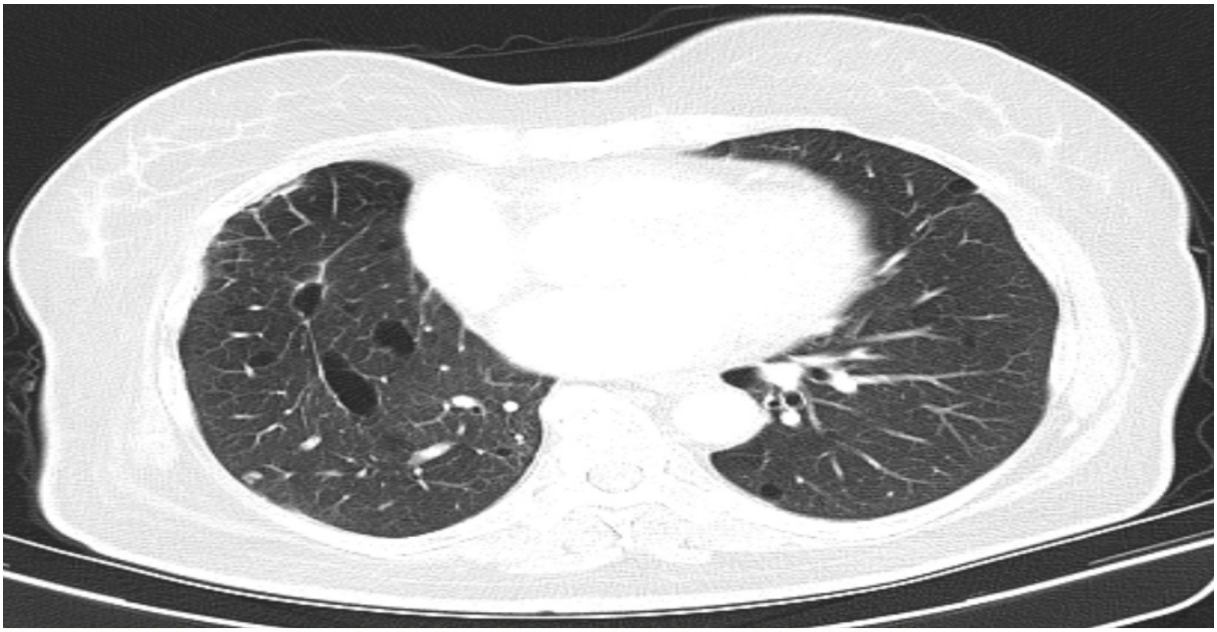

Figure 1. Thin-walled peribronchovascular cysts and ground-glass opacities in CT

complained of severe dryness of mouth not accompanied by dry eyes.

Serological tests revealed ANA > 1:320 and SS-A (Ro) positivity. Schirmer scores were 5 mm for both eyes and salivary gland biopsy showed lymphocytic sialadenitis with focus score 3. Viral panels for hepatitis B/C and HIV were negative and serum protein electrophoresis result was normal. Regarding these findings, pSS diagnose was established according to 2016 ACR-EULAR classification criteria. Due to the irregular, widespread peribronchial distribution of the cystic lesions seen on the thoracic CT, pSS-associated LIP was considered and a lung tissue biopsy was planned. However, due to the patient's history of pneumonectomy and the reduced capacity of the remaining lung, the biopsy could not be obtained. Bronchoalveolar lavage (BAL) fluid was rich in lymphocytes but did not provide diagnostic information.

In light of these results, the patient was started on treatment with methylprednisolone at a dose of 0.5 mg/kg/day and hydroxychloroquine. After 6 weeks of treatment, the patient reported significant improvement in clinical symptoms and the steroid dose was tapered while azathioprine was added to the treatment. Methylprednisolone was stopped after 6 months. Although absence of radiological improvement, the patient experienced amelioration in shortness of breath and complete resolution of cough. She is still under azathioprine and hydroxychloroquine treatment.

DISCUSSION

LIP is characterized by the interstitial infiltration of lung tissue, especially interalveolar septum, by benign polyclonal, mostly mature B or T-cell lymphocytes, plasma cells, and histiocytes. This infiltration can be diffuse or focal and may contain germinal centers, non-caseating granulomas, and multinucleated giant cells (1).

4-9% of pSS patients are confronting LIP and 30% of underlying medical conditions in LIP is pSS (2). It has also been reported in viral infections like HIV, Epstein-Barr virus, chronic active hepatitis or autoimmune conditions such as autoimmune thyroiditis, autoimmune hemolytic anemia, primary biliary cirrhosis, myasthenia gravis. Other rheumatological diseases like systemic lupus erythematosus or juvenile rheumatoid arthritis have also been associated with LIP (5).

The most common clinical symptoms are cough (71%) and dyspnea (61%), but weight loss and fever may also accompany. Due to its slow progression, median time-to-diagnosis was reported as 19 months (3). On thoracic CT scans, thin-walled peribronchovascular cysts associated with ground-glass opacities are observed in up to 80% of LIP cases (4).

Although BAL is crucial for the diagnosis of many interstitial lung diseases, its findings are non-specific for LIP. Therefore, tissue biopsy is mostly mandatory. Video-assisted thoracoscopic surgery or thoracotomy is recommended because transbronchial fine needle aspiration biopsy may not reveal the characteristics of tissue involvement (3).

Regarding treatment, there are no controlled trials in the literature and current guidelines are also not recommend a standardized approach for treatment (5,6). However, data from the literature indicate that the most commonly preferred approach is the addition of glucocorticoids to

disease-modifying antirheumatic drugs (DMARDs) such as hydroxychloroquine, cyclophosphamide, cyclosporine, colchicine and azathioprine. In the study with 15 LIP patients (3), treatment response was evaluated in five out of eight Sjögren's cases. Clinical improvement was observed in three while stable clinical condition was maintained in two. The median overall survival was 11.5 years and three Sjögren's patients were still alive at the end of the follow-up. Although not observed in this study, 5% of LIP patients are under risk of developing lymphoma in the following years (7).

CONCLUSION

It should be noted that rare but potentially life-threatening lung involvements like LIP can develop in Sjögren's cases, and, as in our case, it may even be the initial presentation. Although pneumonectomy history of our case prevented the biopsy, in suitable cases it is critically important for differential diagnose. Current results are indicating improvement with glucocorticoid+DMARDs treatment, but randomized controlled studies are strongly needed.

DECLARATIONS

Ethics Committee Approval Number: Not necessary.
Informed Consent: Informed consent was obtained from patient.
Referee Evaluation Process: Externally peer-reviewed.
Conflict of Interest Statement: Author declares no conflict of interest.

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