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A case report on Sjögren Syndrome: it's more than just autoimmune epithelitis

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ABSTRACT

Background. Primary Sjögren's syndrome (pSS) is an autoimmune epithelitis associated with various pulmonary manifestations, including PAH (pulmonary arterial hypertension), a severe complication often found in collagen tissue disorders.

Case presentation. A 26-year-old female having chest pain and exertional dyspnea diagnosed with severe PAH associated with pSS is presented in this case study. Clinical, laboratory, and imaging findings supported the diagnosis, and treatment involved immunosuppressive therapy and standard PAH medications.

Discussion and conclusion. The report highlights the complexities of diagnosing and treating PAH associated with pSS, emphasizing the importance of early intervention for improved long-term outcomes. The prognosis for PAH in connective tissue diseases, encompassing pSS, remains challenging, underscoring the need for accurate diagnosis and timely management with immunosuppressants and PAH-specific therapies.

Keywords: PAH, Sjögren syndrome, epithelitis, autoimmune disorders, connective tissue disorder

INTRODUCTION

One type of autoimmune epithelitis is primary Sjögren's syndrome (pSS). One significant and serious consequence that arises from numerous collagen tissue abnormalities is pulmonary arterial hypertension (PAH) [1]. To identify it at the asymptomatic stage, early diagnostic techniques are needed.

A range of interstitial lung complaints, airway complaints, pleurisy, amyloidosis, carcinoma, granulomatous complaints, diaphragmatic myopathy, pulmonary vasculitis, as well as mock-carcinoma are examples of pulmonary instantiations in primary Sjögren's pattern's patients. While primary Sjögren's pattern can coexist with pulmonary hypertension (PH), other connective tissue disorders are more frequently linked to other CTD (connective tissue diseases) [2,3].

CASE PRESENTATION

A 26 year old female presented having chest pain on exertion for 1 week and breathlessness on exertion grade 2 MMRC, insidious in onset, progressive in nature. No history of dry mouth, enlargement of the parotids. She denied using additional medications or anorexicants. She also lacked any family history of any kind. Heart rate, blood pressure, and breathing rate were 105/min, 120/80mmHg, 24/min correspondingly. A grade 2/6 systolic murmur in left low parasternal area and a more acute P2 than A2 were found during the cardiovascular examination.

Laboratory exam showed thrombocytopenia – 72,000, leucopenia -3,900cells/cumm, Erythrocyte sedimentation rate of 75. Autoantibody tests revealed that anti-nuclear antibodies along with anti-Ro{SSA} antibodies as well as antibodies to La {SSB} were positive, on the other hand, negative results were obtained for double stranded DNA, ANCA (anti-neutro-

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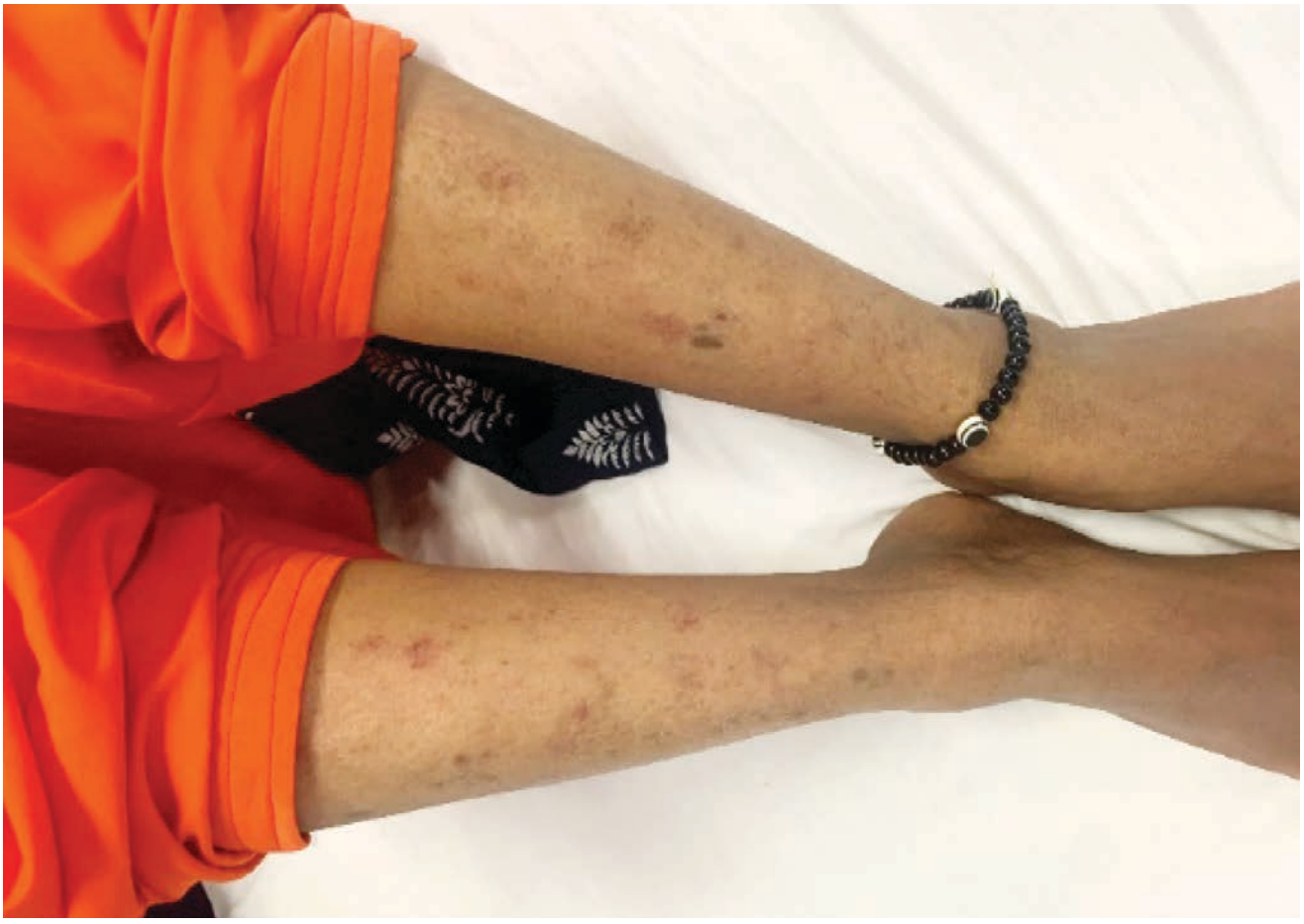

FIGURE 1. Section showing stratified squamous epithelum, with underlying salivary gland with lymphocytic infiltration [4]

phil cytoplasmic antibodies), Sm, Jo-1 (histidyl-tRNA synthetase) RNP (ribonucleoprotein), topoisomerase-I (Scl-70). Lupus anticoagulant was detected while antibodies to cardiolipin and antiphospholipid antibody were negative. All of the serum complement protein levels were slightly reduced { c3-1.08g/l, normal 0.83-1.93g/l; C4 0.113g/l, normal 0.15-0.57g/l}. Hepatitis B virus antigen along with antibodies, anti-hepatitis C antibodies, as well as anti-human immunodeficiency virus antibodies, had been all negative.

The results of the pulmonary function test showed a normal CO diffusion capacity and ventilatory pattern. A slightly enlarged right ventricle and grossly normal lung fields were seen on the chest X-ray. The electrocardiogram presented tall, peak P waves in lead II, III, as well as aVF that is indicative of right atrial hypertrophy. According to transthoracic echocardiography, there was mild circumferential pericardial effusion, ef-59%, severe tricuspid regurgitation, right ventricle, RV dysfunction, grossly dilated right atrium, in addition to main pulmonary artery. There had been also no regional wall motion wall abnormality. After a lower lip biopsy with a Focus score of 1.24 and a negative Schrimers test, a minor salivary gland biopsy indicated localized lymphocytic sialadenitis.

After considering her laboratory, clinical, imaging, cardiologic, as well as the Revised International Classification Criteria for Sjögren's Syndrome by the American-European Consensus Group, she had been finally examined with severe PH linked to pSS. She had been started on cyclophosphamide pulse therapy, ENDOBLOC-T (Ambrisentan 5mg - endothelin receptor antagonist and Tadalafil 20mg), 200mg hydroxychloroquine twice a day and corticosteroids. Her dyspnea has significantly improved, in addition, she is currently receiving follow-up therapy at an outpatient facility.

DISCUSSION

Sjögren's syndrome is a chronic inflammatory autoimmune disorder defined by lymphocyte infiltration in the exocrine glands in addition to extraglandular regions. Dry mouth and eyes are one of its symptoms [6,7]. The disease predominantly impacts women in their forties as well as fifties, with a female to male ratio of nine to one. It is most frequently secondary to rheumatoid arthritis, but it can also be primary to another CTD [8]. The illness can present with a range of clinical symptoms, including exocrinopathy (ocular or else salivary involvement, such as keratoconjunctivitis sicca), less frequent

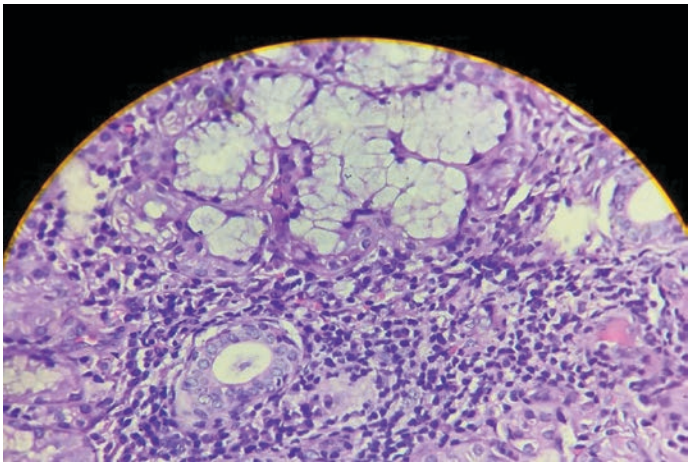

FIGURE 2. Leucocytoclastic lesions seen in bilateral lower limbs [5]

gastrointestinal or respiratory tract involvement, as well as systemic extraglandular symptoms (for example Raynaud's phenomenon, lymphoma, lung, kidney involvement, or else arthritis). pSS can cause pulmonary symptoms such as airway disease, various forms of lymphoma, diffuse interstitial lung disease, pseudolymphoma, Plueral effusion, and others [9,10]. Scleroderma, its restricted cutaneous variation, calcinosis, Raynaud phenomenon, esophageal dysmotility, sclerodactyly, telengiectasis (CREST) syndrome, SLE (systemic lupus erythematosus), as well as MCTD(mixed connective tissue disease) are the prevalent CTDs that are linked to PH [11-14].

Primary Sjögren's disease is hypothesized to have PH as a result of vasculitis with protracted vasospasm and structural vascular remodeling, which ultimately results in the irreversible thrombotic blockage of pulmonary arterioles. The exact PH's pathophysiology is not known. As per Launay et al., Raynaud phenomenon, interstitial lung disease, and cutaneous vasculitis had been more frequent in pSS individuals with PAH (pulmonary arterial hypertension) than in those without PAH. They were also more likely to have positive rheumatoid factors, hypergammaglobulinemia, and autoantibodies against nuclear, Ro/SSA, and RNP. These findings suggest that autoimmunity, B-cell activation, as well as systemic vasculopathy, contribute to pathophysiology of PAH linked to main Sjögren's syndrome, hence corroborating the notion that immunosuppressants are essential for treating PAH in pSS [15].

Because there aren't many cumulative instances, there isn't a perfect treatment plan for PAH linked to primary Sjögren's disease. However, as PAH is the primary cause of CTD-PH and because PAH linked with CTD-PAH (connective tissue disease) as well as idiopathic PAH share pathogenic pathways and similarities in histology, idiopathic PAH treatment may also be suitable to CTD-PAH. If hypoxemia is present, oxygen should be given in addition to the possibility of using diuretic medication to lower the right ventricular preload. Long-term anticoagulants have been linked to better survival in idiopathic PAH; however, their effectiveness in treating people with PAH from other causes, such as CTDs, has not been established [13]. The right heart's afterload should be decreased by using efficient pulmonary vasodilators. When doing the right cardiac catheterization, responders to the short-acting vasodilator challenge test should be treated with calcium channel blockers. It is well known, nonetheless, that fewer than 10% of individuals with idiopathic PAH benefit from this medication6. Moreover, compared to individuals with idiopathic PAH, a larger number of CTD-PAH patients do not react to calcium-channel blockers. Numerous medications that target the PAH pathway have been produced. Strong vasodilators for example Treprostinil, Iloprost, and Epoprostenol are examples of prostacyclin analogues that may be employed. Endothelin receptor antagonists, like Bosentan along with Ambrisentan, may also be utilized since PAH raises endothelin, which has strong vasoconstrictive effects. The third therapy targets the "nitric oxide pathway. Phosphodiesterase-5 inhibitors, for example, Vardenafil as well as Sildenafil, block cyclic guanosine monophosphate, the second messenger in nitric oxide-induced pulmonary vasodilation. Since immunological or inflammatory pathways are significant in the origins or development of PAH, especially in the CTD-PAH", corticosteroids and/or other immunosuppressants would be utilized in addition to these traditional PAH medications. According to certain research, pulse steroid therapy for PAH linked to MCTD is beneficial since it improves dyspnea functional class as well as hemodynamic parameters. Additionally, it had been demonstrated, cyclophosphamide intermittent palpitation remedy was salutary for mild to moderate PAH linked to SLE [7]. While randomized controlled studies on PAH linked to other CTDs were not yet available, The PAH associated with pSS treatment protocol was proposed by Launay et al. They suggested that individuals with NYHA class I/II dyspnea should be treated with original immunosuppressive medication (cyclophosphamide or azathioprine); patients with NYHA class III/IV dyspnea should be subjected to standard PAH medication (phosphodiseterase-5 impediments, endothelin receptor antagonists, or else prostanoids) [7,15].

CONCLUSION

The long-term prognosis for cases of "CTD-PAH is recognized to be worse than that of idiopathic PAH. Furthermore", data gathered indicated that the sur-

vival rates were also low in cases of PAH linked to primary Sjögren's pattern. In cases when PAH has been associated with primary Sjögren's pattern, correct diagnosis and prompt, efficient treatment with immunosuppressants as well as standard PAH remedy are therefore crucial.

Ethical approval

The participant provided their informed consent before their involvement in the research. The Saveetha Medical College and Hospital Institutional Ethics Committee gave its approval to the protocol, which allowed the study to be performed in compliance with the Declaration of Helsinki.

Authors' contributions

Conceptualization, D.S. and P.K.; methodology, D.S.; software, D.S. and K.G.; validation, D.S., A.S. and M.K.; formal analysis, D.S.; investigation, D.S..; resources, D.S..; data curation, D.S..; writing—original draft preparation, D.S.,P.K..; writing—review and editing, D.S.,K.G..; visualization, D.S., A.S.; supervision, P.K.; project administration, D.S.

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REFERENCES

1. Wang J, Li M, Wang Q, Zhang X, Qian J, Zhao J, et al. Pulmonary arterial hypertension associated with primary Sjogren's syndrome: a multi-centre cohort study from China. *Eur Clin Respir J.* 2020:1902157. doi: 10.1183/13993003.02157-2019.
2. Ribeirinho-Soares P, Sousa E, Silva I, Cunha F, Almeida J. Pulmonary Arterial Hypertension Associated With Primary Sjögren's Syndrome: An Unusual Association. *Eur J Case Rep Intern Med.* 2022 Nov 10;9(11):003606. doi: 10.12890/2022_003606.
3. Benza RL, Miller DP, Barst RJ, Badesch DB, Frost AE, McGoon MD. An evaluation of long-term survival from time of diagnosis in pulmonary arterial hypertension from the REVEAL Registry. *Chest*. 2012 Aug;142(2):448-456. doi: 10.1378/chest.11-1460.
4. Liao R, Yang HT, Li H, Liu LX, Li K, Li JJ, et al. Recent Advances of Salivary Gland Biopsy in Sjögren's Syndrome. *Front Med* (Lausanne). 2022 Jan 10;8:792593. doi: 10.3389/fmed.2021.792593.
5. Tsai TC, Chen CY, Lin WT, Lee WJ, Chen HC. Sjogren's syndrome complicated with IgA nephropathy and leukocytoclastic vasculitis. *Ren Fail.* 2008;30(7):755-8. doi: 10.1080/08860220802213054.
6. Kokosi M, Riemer EC, Highland KB. Pulmonary involvement in Sjögren syndrome. *Clin Chest Med.* 2010 Sep;31(3):489-500. doi: 10.1016/j.ccm.2010.05.007.
7. Hwang JA, Yang TH, Lee JY, Koo DW, Choi IS, Cho SY, Kim MS. Severe Pulmonary Hypertension in Primary Sjögren's Syndrome. *Korean Circ J.* 2013 Jul;43(7):504-7. doi: 10.4070/kcj.2013.43.7.504.
8. Ungerer RG, Tashkin DP, Furst D, Clements PJ, Gong H Jr, Bein M, Smith JW, Roberts N, Cabeen W. Prevalence and clinical correlates of pulmonary arterial hypertension in progressive systemic sclerosis. *Am J Med.* 1983 Jul;75(1):65-74. doi: 10.1016/0002-9343(83)91169-5.
9. Ma D, Lu H, Qu Y, Wang S, Ying Y, Xiao W. Primary Sjögren's syndrome accompanied by pleural effusion: a case report and literature review. *Int J Clin Exp Pathol.* 2015 Nov 1;8(11):15322-7.
10. Ohnishi H, Yabe H, Fujiyama R, Tomioka H, Tada K, Sakurai T, Sakamoto H, Iwasaki H, Hashimoto K. [Sjögren's syndrome with malignant lymphoma, interstitial pneumonia, and pulmonary hypertension]. *Nihon Kokyuki Gakkai Zasshi.* 2000 Mar;38(3):190-4. Japanese.
11. Salerni R, Rodnan GP, Leon DF, Shaver JA. Pulmonary hypertension in the CREST syndrome variant of progressive systemic sclerosis (scleroderma). *Ann Intern Med.* 1977 Apr;86(4):394-9. doi: 10.7326/0003-4819-86-4-394.
12. Sanchez O, Humbert M, Sitbon O, Nunes H, Garcia G, Simonneau G. [Pulmonary hypertension associated with connective tissue diseases]. *Rev Med Interne.* 2002;23:41–54.
13. Wiener-Kronish JP, Solinger AM, Warnock ML, Churg A, Ordonez N, Golden JA. Severe pulmonary involvement in mixed connective tissue disease. *Am Rev Respir Dis.* 1981 Oct;124(4):499-503. doi: 10.1164/arrd.1981.124.4.499.
14. Kim KH, Jeong MH, Kim W, et al. A case of systemic lupus erythematosus with severe pulmonary hypertension and pericarditis. *Korean Circ J*. 2000;30:605–610.
15. Launay D, Hachulla E, Hatron PY, Jais X, Simonneau G, Humbert M. Pulmonary arterial hypertension: a rare complication of primary Sjögren syndrome: report of 9 new cases and review of the literature. Medicine (Baltimore). 2007 Sep;86(5):299-315. doi: 10.1097/MD.0b013e3181579781.