CASE REPORT OLGU SUNUMU

DOI: 10.5336/archlung.2024-105032

Rare Cause of Pulmonary Hypertension: Sjögren's Syndrome

Pulmoner Hipertansiyonun Nadir Bir Nedeni: Sjögren Sendromu

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This study was presented as an oral presentation at ADHAD 5th National Congress, November 23-26, 2023, Muğla, Türkiye.

ABSTRACT Different pathogenic mechanisms for pulmonary arterial hypertension (PAH) in connective tissue diseases have been discussed, and the literature on the prevalence of PAH in these patients is limited and contradictory. The prevalence of PAH due to primary Sjögren's syndrome is also described as rare. While the disease requires immunosuppressive treatment as a primer, specific treatments may be given to patients with PAH. PAH due to primary Sjögren's syndrome may not be diagnosed by routine assessment to determine the underlying cause, so clinicians should carefully assess the possibility of primary Sjögren's syndrome in patients with PAH with special care.

Keywords: Pulmonary arterial hypertension; connective tissue disease; sjögren's syndrome

ÖZET Bağ dokusu hastalıklarında görülen pulmoner arteriyel hipertansiyonda (PAH) farklı patojenik mekanizmalar tartışılmaktadır. Bu hastalarda PAH yaygınlığına ilişkin literatür bilgisi sınırlı ve çelişkilidir. Primer Sjögren sendromuna bağlı PAH prevalansı da nadir olarak tanımlanmaktadır. Hastalık pimer olarak immunsupresif tedavi gerektirirken, PAH gelişen hastalara spesifik tedaviler uygulanabilir. PAH, rutin değerlendirme ile altta yatan nedenin saptanmasıyla teşhis edilemeyebilir. Bu yüzden klinisyenler, PAH'lı hastalarda Primer Sjögren sendromu olasılığını dikkatli bir şekilde değerlendirmelidir.

Anahtar Kelimeler: Pulmoner arteriyel hipertansiyon; bağ dokusu hastalığı; sjögren sendromu

Pulmonary arterial hypertension (PAH) represents a significant and potentially fatal complication in a variety of connective tissue diseases, including, but not limited to, scleroderma (SSc), mixed connective tissue disease, systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and others.[1] It is more prevalent in conditions such as CREST syndrome (limited cutaneous form of systemic sclerosis (lcSSc) (50%), diffuse SSc (4.9%-38%), RA (27.5%), and SLE (3%-5%).[2] The prevalence of PAH due to primary Sjögren syndrome (pSS) has been reported rarely.[3] Since the correct diagnosis of primary SS often requires special attention, it is possible that some patients with PAH due to primary SS may have been misdiagnosed with idiopathic PAH. Our case presented for treatment and follow-up with an endothelin receptor antagonist (masitentan) in a patient thought to have developed secondary to Sjögren syndrome, which is a rare cause of PAH. The patient provided verbal consent for the presentation of the case.

TO CITE THIS ARTICLE:
Pazarlı AC, Karaman K. Rare cause of pulmonary hypertension: Sjögren's syndrome. Turkiye Klinikleri Arch Lung. 2024;23(2):40-3.

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Peer review under responsibility of Turkiye Klinikleri Archives of Lung.

Received: 04 Aug 2024 ***Received in revised form:*** 25 Nov 2024 ***Accepted:*** 02 Dec 2024 ***Available online:*** 29 Jan 2025

CASE REPORT

A female patient, aged 54, with a clinical presentation of Sjögren's syndrome for five years was admitted to our clinic due to an increase in respiratory distress. The patient had been undergoing treatment with an inhaler for asthma for several years, yet her respiratory distress persisted. Pulmonary function tests, carbon monoxide diffusion capacity (DLCO), chest radiographs and high resolution lung tomography were conducted, and the results were within normal limits (Figure 1). An echocardiogram (ECHO) was conducted in 2018 and did not reveal any abnormalities. In a new ECHO, right heart cavity dimensions were found to be within normal limits, with normal left ventricular diameter and systolic function, as well as an estimated systolic pulmonary artery pressure (SPAP) of 40 mmHg (TRV: 3.0 m/sec). A pulmonary computed tomography angiography and ventilation/perfusion imaging were both normal, with a right heart catheterization indicating a mean pulmonary artery pressure, pulmonary artery wedge pressure and pulmonary vascular resistance of 30 mmHg, 10 mmHg and 4 Wu and Co (cardiac output) (Fick): 5.1 Ci (cardiac index) (Fick): 2.5, sv (stroke volume): 60.7 mL, mix venous gradient: sv index, 29.7 mL/m^2, heart rate: 84/min, mix venous PO_2: 74.3 mmHg respectively. The six-minute walk test revealed an initial oxygen saturation of 96%, a final saturation of 89%, and a covered distance of 234 metres. The pro-BNP value was 170 pg/mL, the functional classification was II, and endothelin receptor antagonist treatment (masitentan 10 mg single dose per day) was initiated in accordance with the diagnosis of PAH, which was presumed to have developed secondary to connective tissue disease, in the intermediate-risk category in accordance with comprehensive risk assessment in PAH (three-strata model) as outlined in the 2022 ESC/ERS Pulmonary hypertension diagnosis and treatment guidelines.[4] It is recommended that PAH cases be managed in a pulmonary hypertension center. Since our center has the necessary expertise and infrastructure for the treatment of these patients, their follow-up is carried out in accordance with the established guidelines. The patient's 3th and 6th month follow-up parameters demonstrated improvement, and the year end evaluation revealed a 6 minute walk test of 350 meters without desaturation. The treatment and follow-up of patients whose functional capacity has decreased to I and four-strata risk-assessment score was low, are still ongoing (Table 1). Informed consent was obtained from the participant involved in the study.

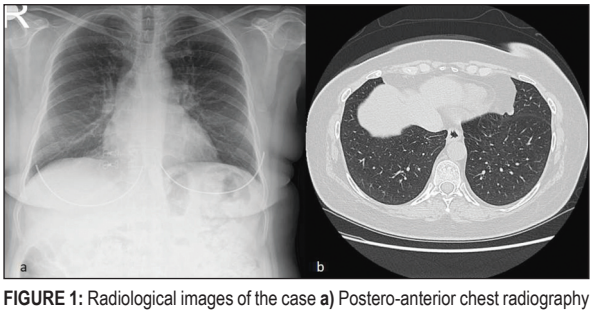

FIGURE 1: Radiological images of the case **a)** Postero-anterior chest radiography **b)** High resolution lung tomography.

TABLE 1: Diagnosis, treatment and follow-up results of the case.

	Moment of diagnosis	3rd month	12th month
ECHO TRV (m/sec)	3.0	3.0	2.8
ECHO sPAP (mmHg)	40	35	24
Pro-BNP (picog/mL)	170	85	72
6MWT (metres)	234	255	350
WHO-FS	II	I-II	I
RHC mPAP (mmHg)	30	-	-

ECHO: Echocardiography; TRV: Tricuspid regurgitation velocity; sPAP: Systolic pulmonary artery pressure; Pro-BNP: pro-B-type natriuretic peptide; 6MWT: Six-minute walking test; WHO-FS: World Health Organisation Functional classification; RHC: Right heart catheterization; mPAP: Mean pulmonary artery pressure.

DISCUSSION

Primary Sjögren's syndrome (pSS) represents a systematic autoimmune disorder that affects exocrine glands, such as the salivary and lacrimal glands. PAH is a rare complication of pSS, although recent studies using echocardiography suggest that a significant proportion of pSS patients may develop PAH. However, the prevalence of PAH in patients with primary SS remains uncertain.[5] Some suggest that etiological factors may include endothelial damage, immune complex deposition, necrotizing vasculitis, and imbalances in the synthesis and metabolism of endothelial vasoactive molecules.[6] A total of 47 patients who met the criteria for pSS according to the American-European Study Group diagnostic criteria were

included in the study conducted by Kobak et al. Of the patients included in the study, 23.4% exhibited PAH on doppler echocardiography, defined as a SPAP value exceeding 30 mmHg.[3] In a prospective study by Sato et al., one patient was diagnosed with PAH associated with pSS during the initial evaluation of 40 patients diagnosed with PAH. Furthermore, five out of 25 patients initially diagnosed with idiopathic PAH were found to have PAH associated with pSS. It was observed that patients diagnosed with PAH exhibited symptoms indicative of pSS during the course of their disease. Three of the five patients exhibited findings suggestive of pSS, which suggests that they may have been misdiagnosed during the initial evaluation. However, the other two patients diagnosed with pSS did not exhibit pSS findings.[7] A study conducted in Taiwan utilised a national database in order to assess the cumulative incidence of PAH amongst patients diagnosed with SSc, SLE, pSS, polymyositis/dermatomyositis (PM/DM), and RA over the period 2002 to 2013. Additionally, the study evaluated the probability of survival following the diagnosis of PAH in these patient groups. A total of 38 (0.22%) of 17,316 patients with pSS were diagnosed with PAH. Among all connective tissue diseases (CTD), SLE is the most prevalent, affecting 57% of patients. SSc is the second most prevalent CTD, affecting 30% of patients, while pSS is the third most prevalent CTD, affecting 9% of patients. RA affects 3% of patients, while PM/DM affects 1%.[8] In another study, 108,657 patients with systemic autoimmune rheumatic diseases were enrolled (24,512 with SLE, 53,803 with RA, 2,456 with SSc, 1,551 with DM, 1061 with PM, and 25,265 with pSS). Severe PAH was detected in 479 patients, of which 94 had pSS (19.6% of the pSS group) (0.08% of all patients, 0.37% of the pSS group).[9]

In conclusion, pSS is a challenging condition to diagnose due to its heterogeneous nature. Consequently, a significant proportion of patients with pSS-related PAH may be misdiagnosed with idiopathic PAH, which in turn results in their inability to receive immunosuppressive treatment. Standard PAH therapies, including endothelin receptor antagonists, type 5 phosphodiesterase inhibitors, and epoprostenol, may be effective in the treatment of pSS-related PAH. Nevertheless, it is important to note that treatment failure may occur, either in the short or long term, and therefore requires close monitoring.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Ahmet Cemal Pazarlı, Kayıhan Karman;* ***Design:*** *Ahmet Cemal Pazarlı, Kayıhan Karman;* ***Control/Supervision:*** *Ahmet Cemal Pazarlı, Kayıhan Karman;* ***Data Collection and/or Processing:*** *Ahmet Cemal Pazarlı;* ***Analysis and/or Interpretation:*** *Ahmet Cemal Pazarlı;* ***Literature Review:*** *Ahmet Cemal Pazarlı;* ***Writing the Article:*** *Ahmet Cemal Pazarlı;* ***Critical Review:*** *Ahmet Cemal Pazarlı;* ***References and Fundings:*** *Ahmet Cemal Pazarlı;* ***Materials:*** *Ahmet Cemal Pazarlı, Kayıhan Karman.*

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