Partial Anomalous Pulmonary Venous Return (PAPVR) in a Patient with Sjogren’s Syndrome

Jennifer Lee, Honk-Ki Min, Keun-Suk Yang, Hee-Chul Nam, Hae-Min Lee, Kyung-Su Park, Sung-Hwan Park, Ho-Youn Kim, Seung-Ki Kwok

Division of Rheumatology, Department of Internal Medicine, School of Medicine, The Catholic University of Korea, Seoul, Korea

Pulmonary hypertension (PH) is a rare manifestation in patients with primary Sjogren’s syndrome (pSS) and it can occur with or without interstitial lung disease (ILD). Patients with PH and ILD who show signs of exacerbation of dyspnea are commonly assessed for pure PH aggravation, ILD progression or pulmonary infection. However, the presence of congenital cardiac anomalies, such as partial anomalous pulmonary vein return (PAPVR), can also be a cause of dyspnea exacerbation. PAPVR is a rare congenital anomaly that involves drainage of 1 to 3 pulmonary veins into the right-sided heart circulation, resulting in a partial left-to-right (L-to-R) shunt. Here we present a case of PAPVR as the cause of PH aggravation in a patient with pSS accompanying PH.

Key Words. PAPVR, Pulmonary hypertension, Sjogren’s syndrome

Introduction

Pulmonary hypertension (PH) is defined as mean pulmonary artery pressure (mPAP) that exceeds 25 mmHg at rest, as measured by right heart catheterization (RHC) (1). PH can occur as an isolated condition or in association with various clinical settings, including connective tissue disease (CTDs) (2). CTD-associated PH is most common in patients with systemic sclerosis (SSc) (3). Chang et al. (4) reported that 37.3% of the patients with SSc had PH. However, PH is a rare manifestation in patients with primary Sjogren’s syndrome (pSS) and the prevalence of PH was reported to be only 3.8% of the pSS patients in a Chinese cohort (5). PH associated with CTD can occur with or without interstitial lung disease (ILD) (6). When patients with PH combined with ILD show signs of dyspnea exacerbation, the possibility of pure PH aggravation or ILD progression, as well as pulmonary infection is commonly assessed. However, there are rare conditions that can contribute to PH aggravation. For instance, partial anomalous pulmonary venous return (PAPVR) which is a congenital anomaly that 1 to 3 pulmonary veins drain into the right-sided circulation results in a partial left-to-right (L-to-R) shunt that leads to pulmonary hypertension (7). We describe a case of PH in a patient with pSS and ILD who had PAPVR as a coexisting condition. To the best of our knowledge, this is the first case of PAPVR as the cause of PH aggravation in a patient with pSS.

Case Report

A 50-year-old woman was admitted to our hospital in May 2011. She complained of dry cough and dyspnea that had persisted during the previous one month. In September 2008, she was diagnosed with ILD (non-specific interstitial pneumonia (NSIP)) by video-assisted thoracoscopic surgery and had been treated with steroid and azathioprine until May 2010. She ini-
tially visited the Rheumatology Clinic with complaints of multiple arthralgia, and sicca symptoms in September 2010. She was diagnosed with Sjogren’s syndrome based on her dry eyes, dry mouth, positive anti-Ro antibody (Ab), impaired excretory function of her salivary glands on the scan, and impaired function of lacrimal glands on Schirmer’s test (less than 5 mm). She didn’t show the symptoms related to other autoimmune disease, such as systemic lupus erythematosus (SLE) or SSc, and there was no evidence of synovitis. On her extractable nuclear antigen profile, other autoantibodies including anti-dsDNA Ab, anti-centromere Ab, anti-ScI70 Ab, anti-RNP were all negative. The lupus anti-coagulant ratio was 0.87 (reference range, <1.3), the serum level of anti-cardiolipin antibody immunoglobulin (Ig) G was 2.1 U/mL (reference range, <10.0), and the serum level of anti-β2GPI was 2.4 U/mL (reference range, <7.0). The serum anti nuclear antibody (ANA) level was 1:1,600 with a speckled pattern, and the levels of rheumatoid factor, anti-CCP were 146.2 IU/mL (reference range, 0~20.0) and 0.72 U/mL (reference range, <7.0), respectively. Based on these findings, the diagnosis of pSS was made. To determine the cause of dyspnea, echocardiography was performed. Echocardiography showed a dilated right ventricle (RV) and a right ventricular systolic pressure (RVSP) of 57 mmHg, suggesting moderate PH. Sjogren’s syndrome-associated PH and ILD were diagnosed and she was treated with 62.5 mg of bosentan, 7.5 mg of prednisolone and 200 mg of aceclofenac. On March 2011, she presented with cough, febrile sensation and dyspnea. Chest x-ray showed increased haziness in the right lower lobe. She was treated with levofloxacin and cefditoren consecutively for one month under the impression of pneumonia. On admission, she complained of cough with whitish sputum, rhinorrhea and exertional dyspnea, despite having been treated with antibiotics for one month. Her blood pressure was 140/90 mmHg. Pulse rate, respiratory rate and body temperature were normal. Coarse breathing sounds with crackles were auscultated in both lower lung fields. The initial laboratory findings revealed a white blood cell (WBC) count of 12,340/μL (neutrophils: 65.2%) (reference range, 4,000~10,000), a hemoglobin level of 12.9 g/dL (reference range, 12.0~16.0), an erythrocyte sedimentation rate (ESR) of 55 mm/h (reference range, 0~20.0), a C-reactive protein (CRP) level of 0.36 mg/dL (reference range, 0.01~0.47) and, a serum AST/ALT level of 57/52 mg/dL (reference range, 14~40/9~45). Arterial blood gas analysis showed a pH of 7.339 (reference range, 7.35~7.45), a pCO2 level of 49.6 mmHg (reference range, 35.0~48.0), a pO2 level of 72.1 mmHg (reference range, 83~108), a bicarbonate level of 26 mEq/L (reference range, 21~28), and an O2 saturation of 93.4% (reference range, 95~99). Other laboratory findings were unremarkable. Plain radiography of the chest showed diffuse reticular opacities in the middle and lower lobes of both lungs, bulging of the pulmonary conus and enlargement of both hilar shadows suggesting ILD and pulmonary arterial dilatation. The computed tomography (CT) scan of the chest showed no evidence of newly developed pneumonia as compared to the previous CT scan. Pulmonary function tests (PFTs) were performed in order to assess the status of the ILD. Forced vital capacity (FVC) was 48% which showed minimal change since last PFTs (FVC: 36%) performed on September, 2009. Echocardiography was done twice before the admission. The second echocardiography revealed a decreased RVSP from 57 mmHg to 41 mmHg after the initiation of bosentan treatment. However, the third echocardiography performed during the admission showed an increased RVSP of 56 mmHg and right ventricular dilatation. In order to clarify the diagnosis and to assess the status of the PH, RHC was planned. RHC revealed a mPAP of 35 mmHg at rest, which confirmed the PH. In addition, a L-to-R shunt without ASD or VSD was incidentally found. A retrospective review of the CT scan showed that the right upper pulmonary vein which drained the right upper lobe (RUL) and right middle lobe (RML), joined not the left atrium (LA) but the superior vena cava (SVC), suggesting PAPVR (Figure 1). The Qp/Qs ratio was 2.45, indicating that surgical treatment was mandatory. However, the patient refused to undergo surgery. Nifedipine was added to her treatment. Her condition improved with medical therapy during her stay in the hospital. She was discharged with bosentan, nifedipine and prednisolone.

![Figure 1. Chest CT shows the upper right pulmonary vein draining into the superior vena cava.](image-url)
Discussion

Sjögren’s syndrome is a systemic autoimmune disease that mainly affects exocrine glands and it causes dryness of the mouth and the eyes (8). The spectrum of disease extends from organ specific autoimmune exocrinopathy to systemic involvement with various extraglandular manifestations. In a cohort of 400 patients with pSS, articular involvement was the most common extraglandular manifestation (9). Pulmonary manifestations were reported to occur in 9% of the patients and these mainly consisted of ILD and small airway disease. PH is a rare manifestation of pSS and it can occur with or without ILD (10). The diagnosis of PH in a patient with ILD depends on a high index of suspicion. Although RHC is the standard diagnostic procedure for diagnosing PH, its invasiveness often makes physicians reluctant to perform this procedure. Therefore, measuring the RVSP on echocardiography is a commonly used alternative method in estimating mPAP. Echocardiography is a noninvasive, valuable tool to screen for PH, and its sensitivity and specificity for predicting PH is 0.79 to 1.0 and 0.6 to 0.98, respectively (11). RHC was not initially performed in our patient for these reasons. This case emphasizes that RHC is required not only for making a definite diagnosis but also for ruling out any possible comorbidities. Moreover, as PH is far less frequent in pSS than in other connective tissue diseases such as SSc, RHC should be performed especially in patients with suspected Sjögren’s syndrome-associated PH to rule out other conditions. The management of PH with ILD includes the treatment of PH itself, and the underlying ILD (6). Standard PH treatment (e.g. vasomodulating agent) is a major component of various treatment options. Some reports have advocated that corticosteroids with or without immunosuppressants used to treat ILD also has a beneficial effect on PH (12). Generally, patients with PH and associated ILD are known to have a worse prognosis (2,13). When a patient with PH and ILD shows signs of worsening dyspnea, pure PH deterioration, ILD progression and pulmonary infection are commonly assessed. The CT findings and PFTs ruled out ILD progression and pulmonary infection in our patient. RHC was performed to accurately assess the state of PH which led to the incidental discovery of a congenital cardiac anomaly-PAPVR. PAPVR is a rare cardiac anomaly that involves drainage of 1 to 3 pulmonary veins into the right heart circulation and this results in a partial, functional L-to-R shunt (7). PAPVR more frequently involves a right side anomaly. PAPVR is usually diagnosed using echocardiography with color flow mapping. Multidetector computed tomography has recently been adopted as a diagnostic tool to find PAPVR (7), and it played a crucial role in finding PAPVR in our patient. Our patient underwent echocardiography three times and this failed to reveal PAPVR which was partly because our patient had a right upper pulmonary vein PAPVR without an ASD. Surgical correction is recommended for both symptomatic patients and asymptomatic patients with a Qp/Qs greater than 1.5 (14). Although surgery could not be performed due to the patient’s refusal, surgical correction of PAPVR would have alleviated the PH in our patient.

Summary

In summary, this is a case of PH accompanying pSS that was aggravated by coexisting PAPVR. We recommend that the possibility of coexisting congenital cardiac anomaly should be considered as a cause of worsening dyspnea in a patient with PH as well as other conditions such as infection or pure PH progression. To the best of our knowledge, this is the first reported case of PAPVR as the cause of PH aggravation in a patient with pSS with accompanying PH and ILD.

References


