CASE REPORT

An unexpected diagnosis in a dyspnoeic patient with primary Sjogren syndrome

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rajani_ali@hotmail.com**SUMMARY**

We describe a case of a 50-year-old lady with newly diagnosed primary Sjogren syndrome who presented with severe pulmonary artery hypertension and pericardial effusion. She was managed by immunosuppressive agents and a combination of standard therapy for pulmonary hypertension. Our patient had a clinically significant involvement of cardiopulmonary system that is atypical of this disease. Prompt recognition and management of this condition are extremely crucial as untreated cases carry a grave prognosis. However, the ideal treatment strategy is yet to be defined for this condition.

BACKGROUND

Sjogren syndrome (SS) is a rheumatological condition that is not uncommonly encountered in the clinic. Pulmonary artery hypertension is one of the rare manifestations of this disease, which is a significant cause of morbidity and mortality in such cases. It is therefore vital for a physician to be aware of the possibility of such coexisting conditions and to include it in the differential diagnosis of fatigue in patients with SS.

CASE PRESENTATION

A 50-year-old lady presented with 3 months history of fatigue, exertional dyspnoea and palpitations. Her symptoms and exertion capacity as defined by the New York Heart Association (NYHA) was functional class III. However, there was no associated chest pain, fever, rash or joint pain. Upon further prompting, she also admitted to have been experiencing ocular irritation for the past few months. Her medical history was unremarkable for any cardiac, neurological, endocrine or rheumatological illness. There was no history of seizures or head injury. There was no history of any autoimmune illness in her family. There was no history of use of any anticholinergic medication.

On examination, her vital signs were stable. She had palpable bilateral axillary lymph nodes. Respiratory examination was normal; however, the heart sounds appeared muffled on auscultation. Neurological examination revealed the presence of symmetric sensory neuropathy in the lower extremities. All other systemic examination was normal.

INVESTIGATIONS

The results of her laboratory investigations were: white blood cell count $12.1 \times 10^3/\mu\text{l}$, haemoglobin 15.2 g/dl , platelet $265 \times 10^3/\mu\text{l}$, erythrocyte sedimentation rate 55 mm/h , C reactive protein

125 mg/l and procalcitonin 0.59 ng/ml . Thyroid function test, renal function test and urine/stool tests were all normal. Besides an elevated gamma-glutamyl transpeptidase of 802 U/l , other liver function tests were also normal. Cardiac enzymes were negative and pro-brain natriuretic peptide (pro-BNP) level was 1239 pg/ml . T-spot test was non-reactive. Her HbA1c value was 6.2% .

ECG showed normal sinus rhythm with low QRS voltage and the chest x-ray showed enlarged cardiac silhouette (figure 1). Subsequently, ECG was performed which revealed the presence of a large pericardial effusion with severe pulmonary artery hypertension (figure 2). The right ventricular systolic pressure (RVSP) was 105 mm Hg .

High-resolution chest CT scan did not show any signs of pulmonary pathology. There was no evidence of pleural effusion or mediastinal lymphadenopathy. CT scan of the abdomen and pelvis was also normal.

A diagnostic pericardiocentesis aspirated a straw-coloured fluid. The pericardial fluid was found to be exudative in nature (by Light's criteria) with a protein level of 5.3 gm/dl . Cytology was negative for malignant cells. The pericardial fluid culture was negative for acid fast bacilli.

Right heart catheterisation done and it revealed the following: right atrial pressure of 21 mm Hg , right ventricle pressure of $68/25 \text{ mm Hg}$, pulmonary artery pressure of $68/30/44 \text{ mm Hg}$ and pulmonary capillary wedge pressure of 10 mm Hg .

Subsequently, the patient was screened for autoimmune markers, which showed positive result for rheumatoid factor, antinuclear factor, Ro(SSA) and La(SSB). However, it was negative for antiphospholipid antibodies (lupus anticoagulant, anticardiolipin antibodies), antidouble-stranded DNA, antiribosomal P protein antibodies, anticentromere antibody, anti-scleroderma 70 kD extractable immunoreactive fragment (SCL70) and ribonucleoprotein.

On the basis of autoimmune profile, she underwent salivary gland scintigraphy which showed reduced tracer uptake in both parotid and submandibular glands (figure 3). She was also referred to the ophthalmologist for assessment of the ocular involvement. Schirmer test was found to be positive.

All the above clinical findings were suggestive of primary Sjogren syndrome (PSS) complicated by severe pulmonary artery hypertension and pericardial effusion.

DIFFERENTIAL DIAGNOSIS

- Systemic lupus erythematosus
- Tuberculosis pericarditis

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Figure 1 Chest x-ray showed enlarged cardiac silhouette.

- ▶ Sarcoidosis
- ▶ Malignancy
- ▶ Primary pulmonary hypertension

TREATMENT

She was started on systemic steroids, sildenafil, calcium and vitamin D. She was also prescribed ocular lubricants for ocular dryness.

During her 2-week stay in the hospital, she had three episodes of fainting. There were no arrhythmias recorded during those episodes. She was referred to the neurologist for further assessment. Brain MRI was normal and CT angiography of carotids did not show any stenosis. However, the EEG showed epileptiform activity and, consequently, she was started on carbamazepine. There was no further recurrence.

Figure 2 The apical four chamber view of the transthoracic echocardiogram showing moderate-to-severe pericardial effusion.

The follow-up echocardiogram after 3 months showed moderate pericardial effusion and RVSP of 80 mm Hg. She had an NYHA functional status of class II. Cardiac BNP levels had decreased to 851.4 pg/ml. At this time, she was commenced on azathioprine, hydroxychloroquine, ambrisentan (endothelin-receptor antagonist), anticoagulant and spironolactone. Steroids and sildenafil were also continued.

After using systemic steroids for a period of 5 months, she had developed diabetes and had to be put on insulin and metformin. Her HbA1c level had risen from 6.2% to 12.8% over this time period. Islet cell antibodies, Glutamate decarboxylase antibodies (GAD 65) and insulin antibodies to human insulin (IgG) were all negative at that time.

OUTCOME AND FOLLOW-UP

At a 6-month follow-up visit, she had an NYHA functional status of class I. ECG was performed which showed a mild pericardial effusion and with an RVSP of 58 mm Hg.

DISCUSSION

SS is a fairly common chronic, autoimmune disease that is characterised by lymphocytic infiltration of the exocrine glands.¹ It is classified into PSS and secondary SS. The latter term is used for the same condition when it occurs in association with other connective tissue diseases. Its prevalence is estimated to be about 0.2% in the adult population.²

SS involves multiple organ systems and follows a variable course of illness. The classification criterion for SS was updated in 2002 by the American–European Consensus group.³ This criterion was fulfilled in our patient as she exhibited the presence of ocular symptoms, a positive shirmer's test, reduced salivary gland uptake in salivary scintigraphy and a positive serological test for Ro (SSA) and La (SSB).

Our case describes a patient with newly diagnosed PSS, who presented with the uncommon cardiac, pulmonary and neurological complications of this disease.

Neurological complications of PSS is predominantly composed of involvement of the peripheral nervous system,⁴ among which sensory neuropathy is the most commonly cited symptom.⁵ Central nervous system involvement manifests by seizures, multiple sclerosis-like syndrome, optic neuropathy, myelopathies, etc.⁶

Connective tissue disorders are known risk factors for causing pulmonary artery hypertension (PAH).^{7–8} However, clinically significant PAH is a rare manifestation of PSS.⁹ Nevertheless, there is increasing interest in identifying the spectrum of cardiac involvement of this disease. Cases of PAH can present with subtle non-specific complaints, like our case that presented with fatigue and dyspnoea. By the time the classic symptoms of PAH are seen, it is often too late because morphological and structural changes have already occurred in the pulmonary vasculature.⁹

There are several case reports that have discussed the occurrence of PAH in PSS.^{10–14} Launay *et al*¹² have reviewed nine newly diagnosed cases with the former diagnosis in their study. The patient population consisted predominantly of female patients with a mean age of 50 years. Majority of cases were severely symptomatic at the time of presentation with an NYHA functional class of III or IV. The mean pulmonary artery pressure was reported as 44 ± 11 mm Hg (range, 24–60 mm Hg). Selected patients were initially treated by immunosuppressive agents alone, but eventually all of them required standard PAH therapy.¹²

Figure 3 Salivary scintigraphy showing delayed uptake of tracer.

Vassiliou *et al*¹⁵ have performed a study about the echocardiographic findings in 107 patients with PSS, where they showed that clinically silent pericardial effusion was found in 8.4% (9/107) of patients. On the other hand, 22.4% (24/107) of PSS cases had signs PAH.¹⁵ In another study involving patients with PSS, Lin *et al*¹⁶ have found the prevalence of pericardial effusion to be 14.8% (52/352) of which 41 had a small amount of effusion and the remaining 11 had a moderate or large amount of effusion fluid.

Some factors that influence the outcome in such cases include NYHA functional class,¹⁷ haemodynamics¹⁷ and cardiac pro-BNP levels.¹⁸ PAH can lead to the development of pericardial effusion¹⁹ and its presence is a marker of adverse outcome in cases of PAH.²⁰

Various studies have identified the presence of PAH as a poor prognostic marker for patient survival in cases of PSS.^{12 16}

The management of patients with PAH in the presence of connective tissue diseases is complex. Only a small fraction of patients respond to immune suppression^{10 21 22} and calcium channel blockers.^{8 23} The role of oral anticoagulants in such cases is also controversial.⁸ Thus, the main therapeutic agents include prostacyclin therapy, endothelin-receptor antagonist and nitric oxide pathway-targeted therapy.^{24 25} Such agents may be prescribed individually or in combinations. Combination therapy is currently emerging as a novel treatment modality; however, its precise role in such cases is still under investigation.²⁴

Learning points

- Cases of primary Sjogren syndrome can present with extraglandular manifestations.
- Take a detailed history and perform a meticulous clinical examination in patients with pulmonary artery hypertension (PAH) in order to look for secondary causes.
- Combination therapy is an emerging treatment modality in cases of PAH.
- Patients with PAH secondary to connective tissue diseases should ideally be managed by a multidisciplinary approach, involving a rheumatologist, a cardiologist, an ophthalmologist and a dentist.

Competing interests None.

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