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## *Case report*

# Pulmonary hypertension in primary Sjögren's syndrome

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SUMMARY The clinical course of a patient with pulmonary hypertension associated with Sjögren's syndrome is reported. The clinical features and outcome of this case are compared with those of two other reported cases in the Spanish and Japanese published work. Thus far, pulmonary hypertension has not been reported with primary Sjögren's syndrome in English publications. These three cases suggest that the development of pulmonary hypertension in primary Sjögren's syndrome is uncommon but should be included as part of the clinical spectrum.

Pulmonary abnormalities in patients with primary Sjögren's syndrome have been well documented. These abnormalities vary in severity from chronic bronchitis, pleurisy, lymphocytic interstitial disease, and interstitial fibrosis to lymphoma. Primary pulmonary hypertension has not been well described in association with primary Sjögren's syndrome in the English published work, though two cases have been reported in Spanish and Japanese publications.[1 2]

This report describes a patient with a diagnosis of primary pulmonary hypertension in whom a diagnosis of Sjögren's syndrome was concomitantly made. These three cases are reviewed and compared with the features of primary pulmonary hypertension.

### Case report

Two years before this presentation the patient, a 42 year old black woman, developed progressive dyspnoea following her last pregnancy. Ten months previously she was diagnosed as having primary pulmonary hypertension after an extensive cardiopulmonary evaluation including echocardiography, radionuclide perfusion lung scanning, pulmonary function testing, and cardiac catheterisation. The results of these tests showed a pulmonary artery pressure of 65/32 mmHg with a pulmonary capillary wedge pressure of 6 mmHg. Echocardiography showed a normal sized left atrium with a markedly dilated right ventricle. Perfusion lung scanning disclosed non-segmental patchy uptake throughout the lungs, suggesting a low probability of major pulmonary embolism. Pulmonary function testing was unremarkable except for a very mild restrictive defect that was felt to be secondary to poor patient effort. Chest *x* ray demonstrated clear lung fields with an enlarged right ventricle and pulmonary arteries.

The patient admitted to a 32 kg weight loss and several syncopal episodes. She denied fever, sweats, rashes, arthralgias, hair loss, mouth ulcers, dry eyes or mouth, or any recent exacerbation of her dyspnoea. Her past medical history included an episode of 'mumps' as an adult. Physical examination showed a thin middle aged chronically ill black woman with a raised jugular venous pressure, left parasternal lift, fixed split S2, S3 gallop, hepatomegaly with hepatojugular reflux, and slight ankle oedema. There was no evidence of salivary or lacrimal gland enlargement.

Routine laboratory values were unremarkable except for mild proteinuria and slightly raised liver transaminases. Clotting studies and Venereal Disease Research Laboratory test were normal, electrocardiographic changes consisted of right axis deviation and right ventricular strain. Arterial blood gases on room air showed pH 7·48, $Paco_2$ 24 mmHg and $Pao_2$ 87 mmHg. Her serology showed a negative fluor-

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escent antinuclear antibody test with $HEp_2$ cell and mouse kidney substrates. Anti-SS-A(Ro) antibodies were the only specific autoantibodies detected. Despite a normal Schirmer's test, staining with rose bengal dye showed punctate and filamentous conjunctival uptake without corneal involvement. A minor salivary gland biopsy showed grade IV inflammatory changes[3] consistent with Sjögren's syndrome.

After several months of unsuccessful therapy with vasodilators and anticoagulants treatment was started with prednisone and azathioprine. Despite four months of this immunosuppressive therapy her pulmonary hypertension worsened and she died in severe right heart failure.

## Discussion

Primary pulmonary hypertension is clinically defined as an increased pulmonary artery pressure with a pulmonary capillary wedge pressure ≤15 mmHg in the absence of any known cause. Secondary forms of pulmonary hypertension can result from a variety of disorders, including recurrent thromboemboli, veno-occlusive disease, congenital heart disorders, and pulmonary parenchymal disease. Primary pulmonary hypertension, therefore, remains a diagnosis of exclusion.

Right heart catheterisation confirmed the presence of an increased pulmonary artery pressure with a normal capillary wedge pressure in this patient. Echocardiography, lung radionuclide perfusion scanning, pulmonary function testing, and chest radiography were performed to search for an underlying cause of the pulmonary hypertension. No primary cause was found.

Pulmonary hypertension is known to be associated with systemic lupus erythematosus, scleroderma, CREST (calcinosis, Raynaud's phenomenon, oesophageal dysmotility, sclerodactyly, telangiectasia), dermatomyositis, and rheumatoid arthritis, often in the absence of pulmonary vasculitis, thrombosis, or parenchymal fibrosis. Although Sjögren's syndrome is a disorder frequently displaying pulmonary manifestations, no case associated with pulmonary hypertension has been reported in the English published work. A review of world publications shows two isolated cases reported in the Spanish and Japanese published work. The patient described here represents the first case reported in English publications. A comparison of the clinical and haemodynamic features of the three cases is given in Table 1.

No underlying cause of the pulmonary hypertension could be found in these three cases, leading the authors to a clinical diagnosis of primary pulmonary

Table 1 *Comparison of patients with Sjögren's syndrome and pulmonary hypertension*

| *Patient No* | *Age at diagnosis of PHT* (years)* | *Sex* | *Duration of sicca symptoms before diagnosis of PHT* | *Raynaud's phenomena* | *PAP* (mmHg)* | *CO* (l/min)* | *RF** | *SS-A(Ro) /SS-B(La)* | *Clinical response to vasodilators, steroids, cytotoxic therapy* | *Clinical outcome after diagnosis of PHT* |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 42 | F | Asymptomatic | Absent | 65/32 | 3·5 | Negative | +/− | Poor | Died 17 months later |
| 2 | 48 | F† | Simultaneous | Unknown | 90/40 | 2·4 | +++ | Unknown | Poor | Died 37 months later |
| 3 | 33 | F‡ | 8 years | Absent | 65/30 | 5·8 | ++ | Unknown | Poor | Alive 8 months later |

*PHT=pulmonary hypertension; PAP=pulmonary artery pressure; CO=cardiac output; RF=rheumatoid factor.
†Ref 1; ‡ref 2.

hypertension. As no biopsy or necropsy material was obtained neither histopathological classification of the pulmonary hypertension nor an evaluation for microthromboses or occult parenchymal disease could be made.

With the exception of the sicca complex, there are few if any significant differences between the clinical aspects of these three cases and those reported in a recent review of primary pulmonary hypertension.[4] All three cases involved women of child bearing age. This is comparable with the age range and female preponderance noted in this cited review. The presenting cardiovascular symptoms, initial laboratory data, and clinical course were also similar. There were no features of any other connective tissue disease present in any of the patients.

The response to vasodilator therapy was poor in the three patients with Sjögren's syndrome, as it often is in primary pulmonary hypertension. Although one patient initially improved haemodynamically, no improvement in the length of survival was noted. In general the poor response to vasodilator therapy in these three patients suggests that reversible vasoconstriction was not the predominant pathogenic mechanism in their disease at that time.

It is difficult to make any correlation between the severities of the sicca symptoms and the degree of the pulmonary hypertension as the extent of the sicca symptoms varied considerably among the three patients.

In conclusion this report presents the first case recorded in the English published work of Sjögren's syndrome associated with primary pulmonary hypertension. The clinical course of the patient was compared with that of two other cases from the Spanish and Japanese published work who also had primary pulmonary hypertension, and no significant differences were noted. Although rare, primary pulmonary hypertension should be considered as part of the spectrum of pulmonary manifestations seen in Sjögren's syndrome.

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