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CASES OF INTERSTITIAL LUNG DISEASE IN WOMEN WITH SYSTEMIC SCLEROSIS AND OTHER CONNECTIVE TISSUE DISORDERS

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ABSTRACT

Background: Interstitial lung disease (ILD) can be a complication of Systemic Sclerosis (SSc), and other Connective Tissue Disorders (CTDs), and often has a poor prognosis. The cases described here show the association between ILD and SSc/CTDs in two Saudi female patients. Of interest, our first case of a younger patient with SSc, had a more severe form of ILD, whilst the older patient with Mixed Connective Tissue Disorder (MCTD) had a milder case of ILD. In a study looking at ILD in rheumatologic disorders, it was noted that ILD appeared more severe when the patient presented with predominantly SSc symptoms, which is also our observation in this case series. The diagnosis, management and future therapies of ILD are discussed. **Design:** This case series shows the association between ILD and SSc/MCTDs in two Saudi female patients. The study describes ILD associated with SSc of an advanced nature and the association between ILD and MCTD of a milder severity. **Significance:** Knowledge about ILD is essential for doctors caring for patients with SSc and MCTDs. The cases remind us to initiate an early evaluation and management of respiratory symptoms in SSc/MCTDs.

KEYWORDS: Interstitial lung disease, Systemic sclerosis, Mixed connective tissue disorder, Family Medicine, Pulmonology, Rheumatology.

INTRODUCTION

Systemic Sclerosis (SSc) is a multisystem disease with a severe underlying inflammatory process and extreme fibrosis. "Lung involvement is a frequent complication and a leading cause of morbidity and mortality in this syndrome"[1]."Interstitial lung disease (ILD) affects about 40% of patients with SSc".[2] It is associated with tissue fibrosis in the lungs and possibly other organs like the heart and kidneys.[3] As for CTDs, the underlying process is one of fibrotic nonspecific interstitial pneumonia.[4] The development of ILD in patients with SSc and CTDs may be slow and progressive.[1]

In one study looking at SSc, 40 per cent of patients had a restrictive ventilatory defect, either alone or combined with pulmonary arterial hypertension.[5] Anti-SCL-70 antibodies are associated with diffuse cutaneous involvement, increased rate of pulmonary fibrosis and higher mortality.[6] Mixed connective tissue disease (MCTD) can be a combination of the clinical features of progressive systemic sclerosis, systemic lupus erythematosus, rheumatoid arthritis, polymyositis/ dermatomyositis, with a high anti-snRNP antibody titre. When SSc manifestations are present, MCTD-ILD seems to be more commonly associated with pulmonary hypertension and progressive ILD.[6] The poor outcome and prognosis for ILD in systemic sclerosis has led to an active search for early diagnosis as well as new treatment strategies.[7] Investigation of lung involvement in rheumatic diseases requires skills, to pick up both early clinical features and serologic conversion.[4] Recent developments in diagnostic methods and treatment approaches represent an important step towards better knowledge and management of ILD in systemic sclerosis.[7] Cyclophosphamide (CYC), which has been used for twenty years, was investigated in two randomized studies and these did not demonstrate a significant benefit in lung function. Studies have reported mycophenolate mofetil (MMF), azathioprine (AZA) and rituximab as alternatives to cyclophosphamide.[8] Recent research into the pathogenesis of SSc-ILD has led to a renewed interest in looking at targeted therapies in SSc-ILD.[9] Severe lung

fibrosis commonly seen in MCTD with predominantly SSc features, has an impact on pulmonary function and is associated with high mortality.[10] Effective therapies for CTD-ILD have yet to be developed. To date, the aim of immunosuppressive therapy is to prevent the progression of the disease.[11] There has been great progress in the identification of effector cells and proinflammatory mediators and more understanding of the pathways involved in the pathogenesis of MCTD-ILD.[12]

CASES

Case 1: The first case is a 24-year-old Saudi female patient known to have asthma since childhood, presented with shortness of breath, productive cough and wheezing. She was on Budesonide and Salbutamol inhalers but her symptoms were not controlled. She attributed the deterioration in control to recent sand storms and since acquiring H1N1 infection one year before this presentation. She noted that her fingers turned blue, when exposed to cold and then from red to white after reheating. She also mentioned that she had gastric reflux and hair fall. These symptoms started after a recent pregnancy. On examination, her peak flow rate was 180 liters/minute, temperature 36.9, pulse 88 and regular and oxygen saturation 99%. Chest examination revealed diffuse rhonchi bilaterally. There were no signs of skin or joint abnormalities.

Management and Outcome: A chest x-ray and laboratory tests were organized and she was prescribed Prednisolone 50mgs daily for 5 days along with an antibiotic (Azithromycin) and advised to use Symbicort inhaler (budesonide/formoterol) after the oral steroid treatment. One week after treatment, her symptoms had improved and her peak flow rate was 270 liters/minute. Her Chest X-ray showed chronic interstitial infiltrates and a CT Chest was organized. Her tuberculin test was positive, so it was recommended by the radiologist to out rule TB. Sputum for acid fast bacilli was negative and the Quantiferon test was non-reactive. Computed tomography (CT) of the chest was organised which showed bilateral diffuse reticular and nodular opacities consistent with fibrosis. The anti-nuclear antibody was positive (1 in 160) with a positive Anti-SCL 70 (22.6). Her pulmonary function test showed a reduced FVC and FEV1 with a FEV1/FVC of 85.49 consistent with a restrictive lung pattern. This patient was diagnosed with systemic scleroderma and interstitial lung disease and referred to the Rheumatology department. The patient was managed by the Rheumatology and Pulmonology services. She was commenced on Azathioprine 100mgs daily, Nifedipine 30mgs daily and Omeprazole 20mgs daily. Nine months after her initial presentation, her CT Chest changes were stable.

Case 2: The second case is a 69-year-old female patient who presented to the Family Medicine Department at our Hospital in February 2012 with cough and shortness of breath. She also reported pain in her knees and wrists for over 10 years, associated with early morning stiffness lasting 30-60 minutes and she had Raynauds symptoms. She had a history of allergic rhinitis and osteoporosis. Medications included Symbicort, Flixonase nasal spray, Loratidine, Calcium, Vitamin D and Alendronate. On clinical examination, her BP was 101/64, Pulse 103 and regular, O2 saturation 96%. Chest examination revealed crepitations to the midzones bilaterally.

Management and Outcome Chest X-ray showed fibrocystic changes bilaterally, more in the lower zones with minimal cardiomegaly. CT Chest showed bilateral fibrocystic changes noted mainly in the lower zones with cystic changes in the lung peripheries. Pulmonary function tests showed mild restrictive pulmonary disease with a FEV1 of 1.24 (73% of predicted), FVC of 1.28(61.5% of predicted), FEV1/FVC of 97.3% and TLC of 58.1. Anti-nuclear antibody was positive, speckled pattern with a titre of 1:2560. Anti-RNP (1,864.8 u/ml) and Anti-smith antibodies (71.2 u/ml) were positive as was the rheumatoid factor (87.8). Anti-ds-DNA, Anti-Ro, Anti- La, Anti-SCL, and Anti-Jo were all negative. The patient was seen by Rheumatology and Pulmonology departments and diagnosed with interstitial lung disease secondary to MCTD. The MCTD was non-active and she was commenced on hydroxychloroquine 200mgs daily. When she was reviewed in June 2013, she was stable with no signs of progression.

CONCLUSION

SSc-ILD was diagnosed in the first patient when she presented with an exacerbation of her asthma. It is important to take a careful history and perform imaging in patients with worsening asthma control, to check for other pathology (**see Appendix 1, images 1a and 1b**). In the second case, the patient also presented with predominantly respiratory symptoms and after investigations including imaging **(see Appendix 2, images 2a and 2b**), was diagnosed with ILD secondary to MCTD. Pulmonary symptoms may be the first manifestations of rheumatologic disease, as in these cases. It is important to make an early diagnosis and this is made possible by computed tomography (CT). CT will determine the severity of ILD, along with pulmonary function tests. Our patient with SSc had more severe pulmonary disease than our patient with MCTD but fortunately, both patients have remained stable on treatment.

Appendix 1

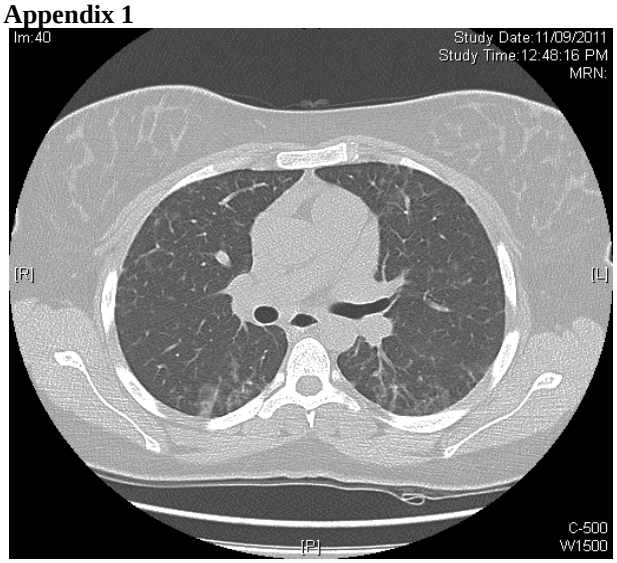

Image 1a: High resolution CT Chest Sept 2011 showing bilateral fibrosis mainly lower lobes.

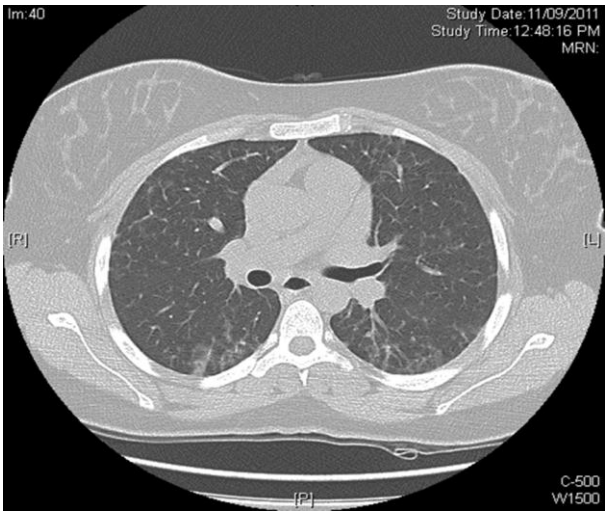

Image 1b: High resolution CT Chest June 2012 showing unchanged lung fibrosis.

Appendix 2

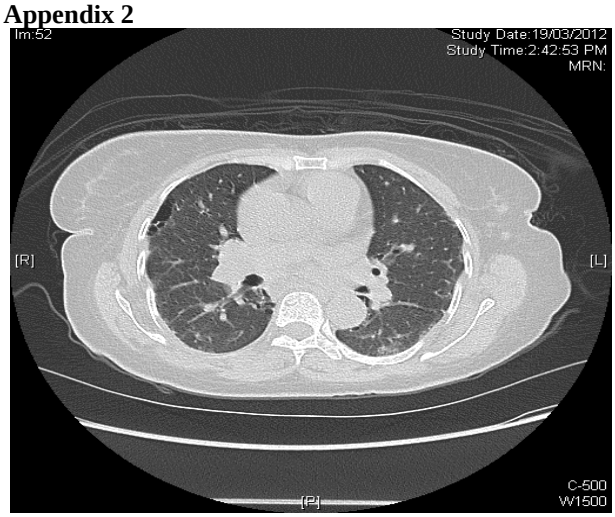

Image 2a: High resolution CT Chest, March 2012 showing bilateral fibrocystic changes lower lobes and cysts in the peripheries.

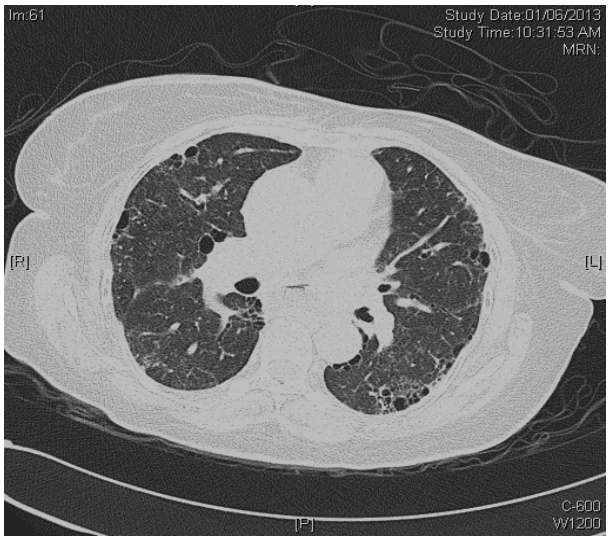

Image 2b: High resolution CT Chest June 2013 showing stable lung fibrotic changes.

DISCUSSION

In a study looking at ILD in CTDs, it was noted that the ILD appeared more severe, when the patient presented with predominantly SSc symptoms.[3] "Thus the management of patients with SSc-ILD is of paramount importance".[13]

It is essential to take a careful history and perform imaging in patients with worsening asthma control, to check for other pathology. Pulmonary symptoms may be the first manifestations of CTDs. It is crucial to make an early diagnosis and this is made possible by computed tomography (CT), especially high resolution CT (HRCT). "ILD is present on HRCT in 55% of patients with SSc on initial evaluation but the prevalence is higher (96%) among patients with abnormal pulmonary function test (PFT) results".[14]

Early treatment is important in achieving a better prognosis. Current treatment options however for ILD-SSc are limited. There seems to be no difference in efficacy between MMF and CYC, but MMF appears safer and better tolerated.[14] Corticosteroids are often used in SSc patients, predominantly in combination with other immunosuppressive treatments since monotherapy with corticosteroids is generally not effective.[15] As for biological immunotherapies, Rutuximab (RTX) is another treatment option in patients who do not tolerate CYC or who have a contraindication for it.[15] RTX may also be tried after CYC instead of starting maintenance with MMF or AZA, particularly if the patient fails to respond to CYC. Haematopoietic stem cell transplantation (HSCT) and lung transplantation are high intensity treatment considerations in ILD-SSc.[16] The management of patients with CTD-ILD remains suboptimal.[13] Therapies for MCTD-ILD include corticosteroids, CYC, hydroxychloroquine, MTX and different types of vasodilators.[17]

This study highlights the association between ILD and SSc/CTDs and sheds light on the diagnosis and management of SSc-ILD and CTD-ILD, as well as the prognosis. The generalist doctor has an important role in the early recognition of respiratory symptoms in SSc and CTDs.

REFERENCES

1. Hassoun, P.M., Lung involvement in systemic sclerosis. La Presse Médicale, 2011; 40(1): e25-e39.
2. Steen, V.D. and Medsger, T.A., Changes in causes of death in systemic sclerosis, 1972–2002. Annals of the rheumatic diseases, 2007; 66(7): 940-944.
3. King TE Jr. Clinical advances in the diagnosis and therapy of interstitial lung diseases. Am J respire Crit Care Med., 2005; 172-268.
4. Papiris, S.A., Manali, E.D., Kolilekas, L., Kagouridis, K., Maniati, M., Borie, R., Pradere, P., Crestani, B. and Bouros, D., Investigation of lung involvement in connective tissue disorders. Respiration, 2015; 90(1): 2-24.
5. Tan A, Denton CP, Mikhailidis DP, Seifahan AM. Recent advances in the diagnosis and treatment of interstitial lung disease in systemic sclerosis (scleroderma): a review. Clin Exp Rheumatol, Mar-Apr, 2011; 29(2,65): 566-74.
6. Chang B, Wigley FM, White B, Wise RA. Scleroderma patients with combined pulmonary hypertension and interstitial lung disease. J Rheumatol, 2003; 30: 2398.
7. Colin G et al. Clinical study of interstitial lung disease in mixed connective tissue disease. Rev Mal Respire, Mar, 2010; 27(3): 238-46.
8. Cepeda EJ, Reveille JD. Autoantibodies in systemic sclerosis and fibrosing syndromes: clinical indications and relevance. Curr Opin Rheumatol, Nov, 2004; 16(6): 723-32.
9. Bussone G, Maithon L. Interstitial lung disease in systemic sclerosis. Autoimmune Rev., Mar, 2011; 10(5): 248-55.
10. Khanna D et al. Systemic sclerosis-associated interstitial lung disease-proposed recommendation for future randomized controlled trials. Clin Exp Rheumatol, Mar-Apr, 2010; 28(2,58): S55-62.
11. Gunnarsson R et al. Prevalence and severity of interstitial lung disease in mixed connective tissue disease: a nationwide, cross-sectional study. Ann Rheum Dis., Dec, 2012; 71(12): 1966-72.
12. Wells AU, Denton CP. Interstitial lung disease in connective tissue disease--mechanisms and management. Nature reviews. Rheumatology, Dec 1, 2014; 10(12): 728.
13. Castelion F, Varga J. Interstitial lung disease in connective tissue diseases: evolving concepts of pathogenesis and management. Arthritis Research and Therapy, 2010; 12: 213.
14. Silver KC, Silver RM. Management of systemic-sclerosis-associated interstitial lung disease. Rheumatic Disease Clinics,. Aug 1, 2015; 41(3): 439-57.
15. Volkmann ER, Tashkin DP. Treatment of Systemic Sclerosis–related Interstitial Lung Disease: A Review of Existing and Emerging Therapies. Annals of the American Thoracic Society, Nov, 2016; 13(11): 2045-56.
16. Cappelli, S., Randone, S.B., Camiciottoli, G., De Paulis, A., Guiducci, S. and Matucci-Cerinic, M., Interstitial lung disease in systemic sclerosis: where do we stand?. European Respiratory Review, 2015; 24(137): 411-419.
17. Koo, S.M. and Uh, S.T., Treatment of connective tissue disease-associated interstitial lung disease: the pulmonologist's point of view. The Korean journal of internal medicine, 2017; 32(4): 600.