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Original Research Article

A study of respiratory system involvement in autoimmune connective tissue diseases: a marker of morbidity

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ABSTRACT

Background: The auto-immune connective tissue diseases (AICTD) are polygenic clinical disorders having heterogeneous overlapping clinical features. Certain features like autoimmunity, vascular abnormalities, arthritis/arthralgia and cutaneous manifestations are common to them. Lung involvement can present in AICTDs in form of: pleurisy, acute/ chronic pneumonitis, pulmonary artery hypertension (PAH), shrinking lung syndrome, diffuse alveolar damage, pulmonary embolism (PE), bronchiolitis obliterans organizing pneumonia, pulmonary infections, cardiogenic pulmonary edema, etc. High-resolution computed tomography (HRCT) plays an important role in identifying patients with respiratory involvement. Pulmonary function tests are a sensitive tool detecting interstitial lung disease.

Methods: The present study was an observational study carried out on 170 patients of AICTD in department of Dermatology, Venereology and Leprosy at a tertiary care centre during a period of 2 years from October 2017 to August 2019. Detailed history, examination and relevant investigations like chest X-ray, pulmonary function test (PFT), HRCT thorax were done as indicated.

Results: The overall incidence of respiratory involvement was 56.7% with maximum involvement in systemic sclerosis cases (82.8% of cases). 45.7% of patients of systemic lupus erythematosus had respiratory involvement, most common being pleural effusion in 11.5%. Impaired PFT's were seen in 82.8% cases of systemic sclerosis (SSc) and all cases of UCTD. Interstitial lung disease was seen in 34.7% and 25% cases of SSc and DM respectively. PAH was found in 15.2% cases of SSc and 9.8% cases of mixed connective tissue diseases.

Conclusions: AICTD are multisystem disorders in which pulmonary involvement can be an important cause of morbidity to the patient and early detection is necessary for prevention of long-term respiratory complications.

Keywords: Auto-immune connective tissue diseases, High-resolution computed tomography, Pulmonary function

INTRODUCTION

The auto-immune connective tissue diseases (AI-CTDs) are a group of polygenic clinical disorders often having heterogeneous and overlapping clinical features. It includes a spectrum of diseases like systemic lupus erythematosus (SLE), systemic sclerosis (SSc), dermatomyositis-polymyositis (DM), Sjogren's syndrome, mixed connective tissue diseases (MCTD), undifferentiated connective tissue diseases (UCTD), overlap syndrome and rheumatoid arthritis to name a few. Certain features are common to them viz. autoimmunity, vascular abnormalities, arthritis/arthralgia and cutaneous manifestations. But the hallmark of these disorders is production of circulating auto antibodies.

The pleuro-pulmonary manifestations are common in patients with connective tissue disorders. All elements of the respiratory system are affected, either separately or in combination. This includes the respiratory muscles, the pleura and the lung parenchyma- the small airways, the interstitium and pulmonary vessels.[1]

Some of the common pulmonary features observed in SLE were pleurisy (most common), acute/ chronic lupus pneumonitis (HRCT: ground glass infiltrates), pulmonary hypertension (PAH), shrinking lung syndrome (respiratory muscle weakness-diaphragm).[2] The incidence of interstitial lung disease (ILD) is reported to be as high as 80% in patients of scleroderma, 75% in patients of rheumatoid arthritis and 5-97% in polymyositis.[3]

Objectives

The present study was carried out as an attempt to gauge the overall auto-immune connective tissue diseases (AICTDs) and to delineate the pulmonary manifestations among the patients.

METHODS

The present study was an observational study carried out on 170 patients of AICTD in department of Dermatology, Venereology and Leprosy at P. D. U. Government Medical College and Hospital, Rajkot, Gujarat for a period of 2 years from October 2017 to August 2019. All patients diagnosed with AICTD according to various clinical and immunological criteria were included in the study and patients not willing to participate in the study were excluded.

After informed consent, a detailed history regarding the onset, duration and progression of the mucocutaneous lesions, systemic manifestations and precipitating factors were noted. Cases of systemic lupus erythematosus were diagnosed according to systemic lupus international collaborating clinics (SLICC) criteria.[4] MCTD patients were diagnosed according to Alarcon Segovia criteria.[5] All cases were subjected to routine investigations, which include complete blood count (CBC) with erythrocyte sedimentation rate, routine biochemistry panel (fasting and post prandial blood sugar, liver function test, renal function test), urine routine and microscopic examination, serum proteins, X-ray chest, ultrasonography abdomen and pelvis, electrocardiogram, rheumatoid factor, and special investigations like: ANA and ENA profile, X-rays of symptomatic joints, 24 hours urinary albumin and creatinine, serum creatine kinase levels, echocardiography, high resolution computed tomography (HRCT) thorax, barium swallow and meal and pulmonary function test. Microsoft excel 2016 and Epi Info version 7.2.3.1 were used to analyse the data.

RESULTS

In the present study of 170 cases of AICTDs, there were 50% cases of LE, 26.87% of scleroderma, 14.37% of mixed connective tissue disease, 2.5% of dermatomyositis, 2.5% of undifferentiated connective

Table 1: Overall pattern of AICTDs.

AICTDs		% of total patients
LE	Total	50
	SLE	22.5
	SCLE	1.87
	NLE	0.62
	DLE	17.50
	DDLE	7.50
Scleroderma	Total	26.87
	Systemic sclerosis	13.12
	Morphea	13.75
Dermatomyositis		2.5
MCTD		14.37
UCTD		2.5
Overlap syndrome		1.87
Primary Sjogren's syndrome		1.25
Cutaneous manifestations in RA		0.62

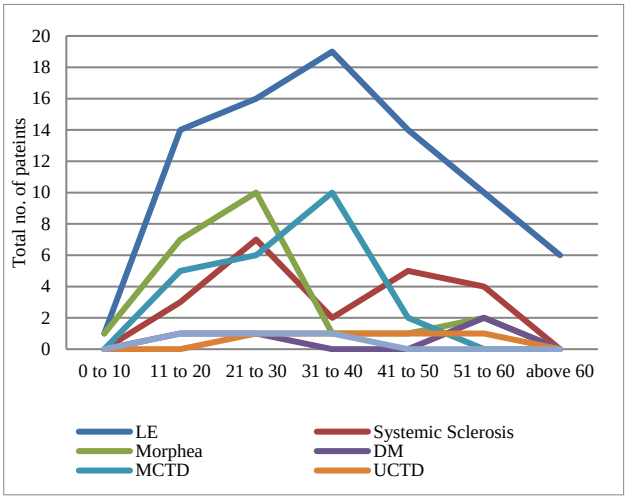

Figure 1: Age distribution of various AICTDs.

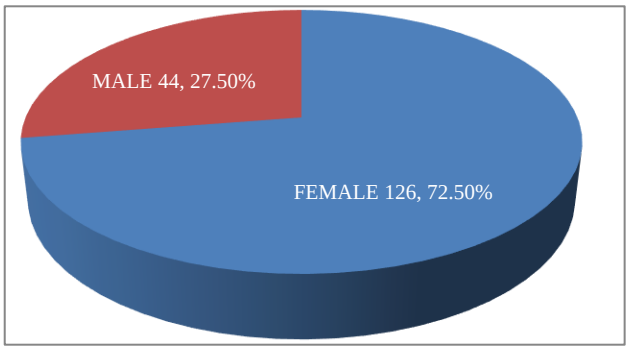

Figure 2: Sex distribution of various AICTDs.

Table 2: Various symptoms pertaining to respiratory system in various AITCDs.

Disease	Patients having respiratory involvement (%)	Dyspnoea (%)	Recurrent cough (%)	Pleuritic chest pain (%)
LE	45.7	62.5	25.6	12.5
SSc	82.8	82.8	21.5	0
DM	25	50	0	25
MCTD	35.5	75.6	12.5	6.25
UCTD	50	100	25	0
Overlap syndrome	66.66	66.66	33.33	0

Table 3: Various investigations and radiological findings in AICTDs.

Disease	Patients having respiratory involvement (%)	Impaired pulmonary function test (%)	Pleural effusion (%)	ILD (%)	Consolidation (%)	Bronchiectasis (%)
LE	45.7	8.4	11.5	0	5.8	0
SSc	82.8	82.8	14.9	34.7	0	24.3
DM	25	50	0	25	0	0
MCTD	35.5	50.4	24.8	0	0	24.8
UCTD	50	100	25	0	0	0
Overlap syndrome	66.66	33.33	33.33	0	0	0

Tissue disease and 1.87% of overlap syndrome, 1.25% of primary Sjogren's syndrome, 0.62% of cutaneous manifestations in rheumatoid arthritis (Table 1). The highest incidence (26.25%) cases of AICTDs was found in the age group of 21-30 years followed by 21.87% cases in age group of 31- 40 years, with least incidence present below 10 years (1.25%) (Figure 1). Overall M: F ratio is 1:2.63 with female predominance (Figure 2).

The overall incidence of respiratory involvement in this study was 56.7% with maximum involvement in SSc cases (82.8% of cases) followed by overlap syndrome (66.66% of cases). In SLE, dyspnoea (62.5%) was the most common symptom followed by recurrent cough (25.6%) and pleuritic chest pain (12.5%). In SSc, Breathlessness on exertion was the most common feature in all the cases with pulmonary involvement (100%) followed by recurrent dry cough in 21.05% cases. Most patients of MCTD had complaints of breathlessness on exertion (75.6%) followed by recurrent cough (12.5%), pleuritic chest pain (6.25%). 6.25% of cases with MCTD were diagnosed with pulmonary TB. Respiratory system was involved in 66.66% cases of overlap syndrome, with breathlessness on exertion being the commonest symptom (Table 2).

Impaired PFT was found in 82.8% cases of SSc and all cases of UCTD. ILD was found in 34.7% and 25% cases of SSc and DM respectively. Pleural Effusion was present in 33.33% cases of Overlap syndrome and 25% cases of UCTD. Consolidation was observed in 5.8% cases of SLE. PAH was found in 15.2% cases of SSc and 9.8% cases of MCTD (Table 3).

DISCUSSION

The incidence of respiratory involvement in this study was maximum in SSc cases (82.8% of cases) compared to 64.3% in study by Arakkal et al.[6] In present study, Breathlessness on exertion was the most common feature in all the cases of SSc with pulmonary involvement (100%) followed by recurrent dry cough in 21.05% cases compared to dyspnea (64.3%), cough (32%) which were reported in patients of systemic sclerosis in the study done by Arakkal et al.[6]

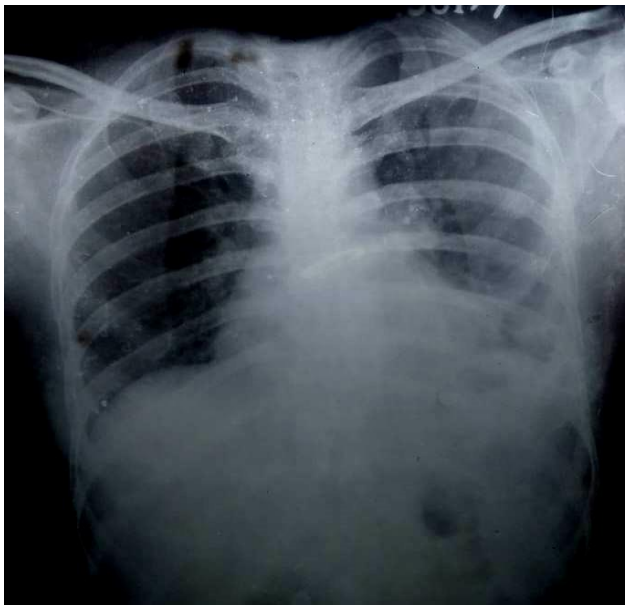

Figure 3: Pleural effusion in SLEq.

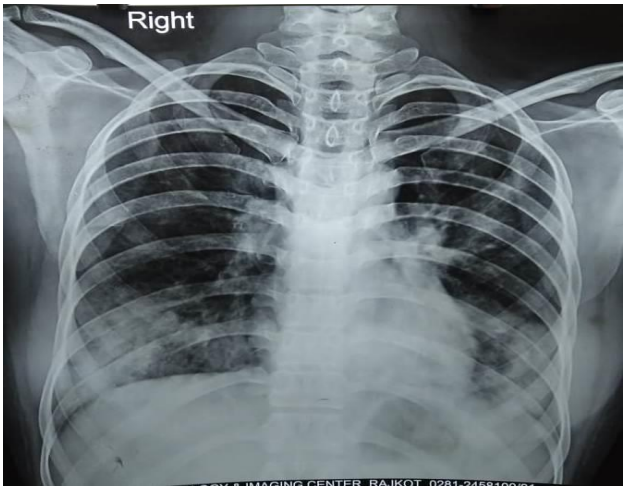

Figure 4: Chest X-ray of ILD in a patient of systemic sclerosis.

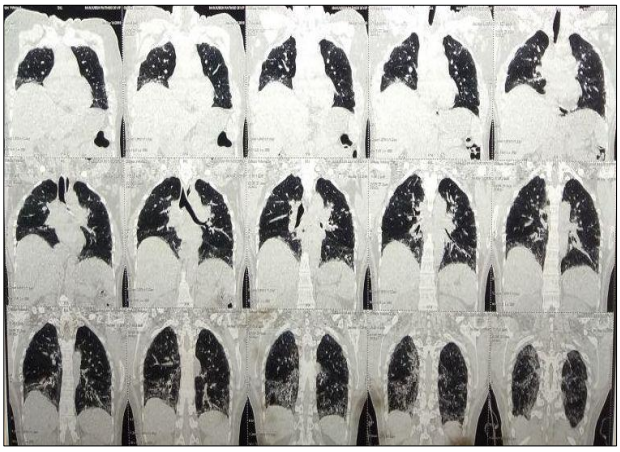

Figure 5: HRCT of thorax of changes of ILD in a patient of dermatomyositis.

Interstitial lung disease and pulmonary arterial hypertension was observed in 75% and 25% respectively in study done by Arakkal et al compared to the present study in which the incidence of ILD was seen in 34.7% and PAH in 15.2% patients of SSc.

The most frequently found feature was findings of consolidation in 5.8% patients of SLE against pleural effusion in 33% in study by Yeison et al.[7]

The autoimmune connective tissue diseases include various disorders like systemic lupus erythematosus, systemic sclerosis, dermatomyositis- polymyositis, mixed connective tissue disease, undifferentiated connective tissue disease, overlap syndrome, etc. The essence of AICTDs lies in their protean manifestations and the challenge to the clinicians lies in recognizing relevant patterns within these mosaics of features. The frequency and type of lung involvement in connective tissue disorders varies based on the underlying disease. Of all the connective tissue disorders, systemic sclerosis is most likely to affect the lungs. AICTD can affect the chest wall, pleura, vasculature, airways, and parenchyma8. Pulmonary fibrosis, also known as interstitial lung disease (ILD), which results in progressive scarring of the lungs is most likely to affect patients of systemic sclerosis. A definitive diagnosis of AICTD-ILD is difficult due to variations in pathological presentation and clinical findings. AICTD-ILD is defined as ILD within the setting of well-defined AICTD which involves cases of AICTD that affect the lung parenchyma and present with respiratory symptoms.[9,10] ILD occurs in over two thirds of systemic sclerosis patients.[11] The most serious pulmonary complication of the connective tissue disorders is the involvement of the blood vessels in the lungs, which causes decreased oxygen uptake and pulmonary arterial hypertension (elevated blood pressure in the arteries of the lungs). This occurs in 10 to 15 percent of patients with systemic sclerosis and in up to 5 percent of patients with the other AICTDs.[11] In systemic lupus erythematosus, lung involvement leads to pleurisy (most common), acute/ chronic lupus pneumonitis (HRCT: ground glass infiltrates), pulmonary hypertension (PAH), shrinking lung syndrome (respiratory muscle weakness- diaphragm), diffuse alveolar damage, pulmonary embolism (PE), bronchiolitis obliterans organizing pneumonia (BOOP), pulmonary infections (mycobacterial, nocardial infection, pneumocystis jiroveci pneumonia infections), cardiogenic pulmonary oedema, pleural effusion (Figure 3), etc. Lung infections are common in connective tissue disorders. This association may be related to the immunologic abnormalities accompanying the primary disease, aspiration of stomach or mouth contents into the lungs, or, most importantly, the effects of immunosuppressive agents used to treat these diseases. Recently, the advent of powerful new immunosuppressive agents (tumour necrosis factor blockers) has placed renewed focus on the risks associated with immunosuppressant therapy. These agents may also increase the rates of tuberculosis and other serious infections.[12] In systemic sclerosis, respiratory system involvement leads to chronic dry cough, dyspnoea, interstitial fibrosis (Figure 4, chest X-ray showing ground glass appearance, Figure 5, HRCT thorax showing honey-comb pattern of ILD) pulmonary artery hypertension, alveolitis, frequent infections. In SSc, pulmonary function test shows restrictive pattern with low vital capacity. In dermatomyositis, it can present as diffuse interstitial pneumonitis/ fibrosis (cause of mortality and morbidity), aspiration pneumonia, respiratory failure due to respiratory muscle weakness leading to hypoventilation. Pulmonary function tests and chest X-ray are sensitive tools for detecting interstitial lung disease. High-resolution computed tomography plays an important role in identifying patients with respiratory involvement. The proposed therapies for treatment of ILD associated with AICTD includes immunosuppressive agents like corticosteroids, azathioprine, cyclophosphamide, mycophenolate mofetil, endothelin receptor antagonists like bosentan and ambrisentan, PDE5 inhibitors like Sildenafil, Tadalafil etc.

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