Primary Thoracic Manifestations in Connective Tissue Diseases on High Resolution Computed Tomography: A Prospective Study

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A B S T R A C T

Introduction: The aim of this paper was to evaluate the thoracic manifestations associated with the Connective tissue disorders, with an emphasis on interstitial and airway disease pattern on the High Resolution computed tomography (HRCT) findings.

Material and methods: The present study was conducted for a period of one year. A total of 70 patients with various connective tissue disorders having respiratory complaints were evaluated.

Results: During the study period 70 patients (58 females and 12 males) underwent evaluation. Cough and dyspnea were the most common presenting symptoms. Variety of thoracic abnormalities were detected in 67 (95%) cases. Most common parenchymal abnormalities seen were reticulations (61.4%), ground glass opacification (40%), mosaic attenuation (32.8%) and honeycombing (24.3%). Airway abnormalities seen were bronchiectasis (48.5%), emphysema (12.8%), and ground glass nodules (2.8%).

Conclusion Interstitial lung disease is the most common pulmonary manifestation among patients with connective tissue disorders, and early detection and prompt treatment is expected to improve the outcome.

Keywords: Connective Tissue Disorders, Thoracic Manifestations, Interstitial Lung Disease

INTRODUCTION

Connective tissue disorders (CTDs) or collagen disease are a heterogeneous group of systemic inflammatory diseases of autoimmune origin that affect a wide range of organs and systems. These include rheumatoid arthritis, systemic lupus erythematosus, systemic sclerosis, sjogren’s syndrome, polymyositis/dermatomyositis, mixed connective tissue disorders. These are often associated with a wide range of lung conditions The frequency and way in which the respiratory system is affected depend on each type of collagen disease with a specific entity.¹ ² The most common lung condition in every case is pneumonitis³ which appears in all the histopathological patterns of idiopathic interstitial pneumonitis (IIP).⁴ Since these patients are immunocompromised, infections are one of the most common causes of respiratory disease.⁵ Lastly, drug-related adverse reactions should also be included in the differential diagnosis. Therefore, the diagnosis and clinical management of these patients is complex and should be based on the combination of different diagnostic approaches: clinical symptoms, laboratory and imaging findings. Sensitivity of chest radiography for the detection of interstitial lung disease is very low. Conversely, HRCT provides good sensitivity and specificity and is able to provide a confident diagnosis of interstitial lung disease and fibrosis. In addition, It allows multiplanar reformatted images and has the advantage of being an affordable and non-invasive technique.⁶ ⁷ The aim of this paper is to evaluate the pulmonary manifestations associated with the CTDs on the high-resolution computed tomography (HRCT), which facilitate early diagnosis of these conditions.

MATERIAL AND METHODS

The present study was conducted in the department of radiodiagnosis of the Dayanand Medical College and Hospital, Ludhiana and included assessment of Primary thoracic manifestations in connective tissue diseases on high resolution computed tomography (CT). All patients with connective tissue disorders presenting with respiratory symptoms over a period of one year were included in the study. Consent was obtained from each patient. HRCT or CECT chest (on Somatom definition AS+128 slice CT machine by Siemens Germany Ltd.) was done. All the results were recorded on Microsoft excel sheet. Analysis was done by using SPSS software. Statistical analysis was done using tests of significance.
RESULTS
Study was done for a period of one year to evaluate the thoracic imaging findings in patients with various CTDs (Rheumatoid arthritis (RA), Systemic lupus erythematosus (SLE), Systemic sclerosis, Sjogrens syndrome, Polymyositis, Mixed connective tissue disorder (MCTD)). Total of 70 patients were evaluated.

Out of total 70 patients Thirty nine cases were of RA, eight cases each of SLE and systemic sclerosis, five cases were of sjogrens, fourcases were of polymyositis and three cases were of MCTD. Four cases were autoantibody positive and were placed in others category.

Most commonly affected age group was mostly between 51-70 years with mean age of presentation being 56.8+/-13.5 years. Mean age of presentation in RA was 60.6, in SLE was 49.7, in systemic sclerosis was 47, in sjogrens was 57.6, in total no. of patients

<table>
<thead>
<tr>
<th>Connective tissue disorder associated</th>
<th>RA (n=39)</th>
<th>SLE (n=8)</th>
<th>Sjogren (n=5)</th>
<th>SYS Sclerosis (n=8)</th>
<th>Polymyositis (n=3)</th>
<th>MCTD (n=3)</th>
<th>Others (n=4)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough</td>
<td>30 (76.90%)</td>
<td>6 (75.00%)</td>
<td>1 (20.00%)</td>
<td>6 (75.00%)</td>
<td>1 (33.30%)</td>
<td>2 (66.70%)</td>
<td>2 (50.00%)</td>
<td>48</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>35 (89.70%)</td>
<td>8 (100.00%)</td>
<td>5 (100.00%)</td>
<td>8 (100.00%)</td>
<td>3 (100.00%)</td>
<td>3 (75.00%)</td>
<td>3 (75.00%)</td>
<td>65</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>1 (2.60%)</td>
<td>1 (12.50%)</td>
<td>0 (0.00%)</td>
<td>0 (0.00%)</td>
<td>0 (0.00%)</td>
<td>0 (0.00%)</td>
<td>0 (0.00%)</td>
<td>2</td>
</tr>
<tr>
<td>Fever</td>
<td>21 (53.80%)</td>
<td>7 (87.50%)</td>
<td>1 (20.00%)</td>
<td>3 (37.50%)</td>
<td>1 (33.30%)</td>
<td>2 (66.70%)</td>
<td>4 (100.00%)</td>
<td>39</td>
</tr>
</tbody>
</table>

Table-3: Clinical symptoms distribution

<table>
<thead>
<tr>
<th>Connective tissue disorder associated</th>
<th>RA (n=39)</th>
<th>SLE (n=8)</th>
<th>Sjogren (n=5)</th>
<th>SYS Sclerosis (n=8)</th>
<th>Polymyositis (n=3)</th>
<th>MCTD (n=3)</th>
<th>Others (n=4)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reticular</td>
<td>26 (66.70%)</td>
<td>2 (25.00%)</td>
<td>2 (40.00%)</td>
<td>7 (87.50%)</td>
<td>3 (100.00%)</td>
<td>1 (33.30%)</td>
<td>2 (50.00%)</td>
<td>43</td>
</tr>
<tr>
<td>Honeycombing</td>
<td>12 (30.80%)</td>
<td>0 (0.00%)</td>
<td>4 (0.00%)</td>
<td>0 (0.00%)</td>
<td>0 (0.00%)</td>
<td>0 (0.00%)</td>
<td>1 (0.00%)</td>
<td>17</td>
</tr>
<tr>
<td>Ground glass opacity (GGO)</td>
<td>43.60%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>12.50%</td>
<td>100.00%</td>
<td>0.00%</td>
<td>75.00%</td>
<td>40.00%</td>
</tr>
<tr>
<td>Mosaic attenuation</td>
<td>14 (35.90%)</td>
<td>2 (50.00%)</td>
<td>2 (50.00%)</td>
<td>1 (25.00%)</td>
<td>33.30%</td>
<td>33.30%</td>
<td>0.00%</td>
<td>23</td>
</tr>
<tr>
<td>Nodular</td>
<td>8 (20.50%)</td>
<td>2 (50.00%)</td>
<td>2 (50.00%)</td>
<td>25.00%</td>
<td>0.00%</td>
<td>33.30%</td>
<td>25.00%</td>
<td>15</td>
</tr>
<tr>
<td>Consolidation</td>
<td>7 (17.90%)</td>
<td>2 (50.00%)</td>
<td>0 (0.00%)</td>
<td>0.00%</td>
<td>0.00%</td>
<td>33.30%</td>
<td>0.00%</td>
<td>10</td>
</tr>
<tr>
<td>Cysts</td>
<td>6 (15.40%)</td>
<td>0 (0.00%)</td>
<td>1 (20.00%)</td>
<td>12.50%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>25.00%</td>
<td>9</td>
</tr>
</tbody>
</table>

Table-4: Parenchymal abnormalities on HRCT in various CTDs
polymyositis was 55.3, and in MCTD was 52 years. Mean age of presentation in females was 55.9 years and in males was 60.75 years. (Table 2)

In our study 82 percent of the cases were females indicating the female predelection of connective tissue disorders. Most common presenting symptom was dyspnea. Cough

<table>
<thead>
<tr>
<th>Airway abnormality</th>
<th>Connective tissue disorder associated</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RA (n=39)</td>
</tr>
<tr>
<td>BE</td>
<td>26 66.7%</td>
</tr>
<tr>
<td>Emphysema</td>
<td>7 17.9%</td>
</tr>
<tr>
<td>Ground glass nodules (GGN)</td>
<td>2 5.1%</td>
</tr>
</tbody>
</table>

Table-5: Airway abnormalities on HRCT in various CTDs

<table>
<thead>
<tr>
<th>Lobes affected</th>
<th>Right upper lobe (RUL)</th>
<th>Right middle lobe (RML)</th>
<th>Right lower lobe (RLL)</th>
<th>Left upper lobe (LUL)</th>
<th>Left lower lobe (LLL)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA</td>
<td>23 59.0%</td>
<td>24 61.5%</td>
<td>32 82.1%</td>
<td>19 48.7%</td>
<td>33 84.6%</td>
<td>39</td>
</tr>
<tr>
<td>SLE</td>
<td>2 25.0%</td>
<td>3 37.5%</td>
<td>4 50.0%</td>
<td>3 37.5%</td>
<td>4 50.0%</td>
<td>8</td>
</tr>
<tr>
<td>Sjogren</td>
<td>4 80.0%</td>
<td>4 80.0%</td>
<td>4 80.0%</td>
<td>3 60.0%</td>
<td>3 60.0%</td>
<td>5</td>
</tr>
<tr>
<td>SYS sclerosis</td>
<td>6 75.0%</td>
<td>6 75.0%</td>
<td>6 75.0%</td>
<td>7 85.7%</td>
<td>6 75.0%</td>
<td>8</td>
</tr>
<tr>
<td>Polymyositis</td>
<td>2 66.7%</td>
<td>3 100.0%</td>
<td>2 66.7%</td>
<td>2 66.7%</td>
<td>2 66.7%</td>
<td>3</td>
</tr>
<tr>
<td>MCTD</td>
<td>3 100.0%</td>
<td>3 100.0%</td>
<td>3 100.0%</td>
<td>3 100.0%</td>
<td>2 66.7%</td>
<td>3</td>
</tr>
<tr>
<td>Others</td>
<td>3 75.0%</td>
<td>3 75.0%</td>
<td>3 100.0%</td>
<td>3 100.0%</td>
<td>4 100.0%</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>43 61.4%</td>
<td>46 65.7%</td>
<td>54 77.1%</td>
<td>40 77.1%</td>
<td>54 77.1%</td>
<td>70</td>
</tr>
</tbody>
</table>

Table-6: Affection of different lung zones in different diseases

<table>
<thead>
<tr>
<th>Distribution</th>
<th>RA (n=39)</th>
<th>SLE (n=8)</th>
<th>Sjogren (n=5)</th>
<th>SYS Sclerosis (n=8)</th>
<th>Polymyositis (n=3)</th>
<th>MCTD (n=3)</th>
<th>Others (n=4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apicobasal gradient</td>
<td>22 56.4%</td>
<td>0 0.0%</td>
<td>0 0.0%</td>
<td>4 50.0%</td>
<td>0 0.0%</td>
<td>0 0.0%</td>
<td>0 0.0%</td>
</tr>
<tr>
<td>Subpleural sparing</td>
<td>4 10.3%</td>
<td>2 25.0%</td>
<td>1 20.0%</td>
<td>0 0.0%</td>
<td>1 33.3%</td>
<td>0 0.0%</td>
<td>0 0.0%</td>
</tr>
<tr>
<td>Subpleural/Peripheral</td>
<td>10 25.6%</td>
<td>0 0.0%</td>
<td>0 0.0%</td>
<td>4 50.0%</td>
<td>1 33.3%</td>
<td>0 0.0%</td>
<td>1 25.0%</td>
</tr>
<tr>
<td>Subpleural/PB</td>
<td>2 5.1%</td>
<td>0 0.0%</td>
<td>0 0.0%</td>
<td>1 12.5%</td>
<td>0 0.0%</td>
<td>1 33.3%</td>
<td>0 0.0%</td>
</tr>
</tbody>
</table>

Table-7: Distribution of abnormalities in lung in various CTDs

<table>
<thead>
<tr>
<th>Connective tissue disorder associated</th>
<th>M</th>
<th>F</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA(39)</td>
<td>5</td>
<td>18</td>
<td>23</td>
</tr>
<tr>
<td>SLE(8)</td>
<td>0</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Sjogren(5)</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>SYS sclerosis(8)</td>
<td>0</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Polymyositis(3)</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>MCTD(3)</td>
<td>0</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Others(4)</td>
<td>0</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Total(70)</td>
<td>7</td>
<td>35</td>
<td>42</td>
</tr>
</tbody>
</table>

Table-8: Number of patients having CTD related Interstitial lung disease (ILD)
and fever was the second most common symptom. Few patients of RA and SLE also presented with hemoptysis.

Connective tissue disorders affect the different compartments of lung in characteristic pattern. Various radiological patterns were noted affecting the lung parenchyma, airway and the pleura (Table-4, Figure-1).

## Parenchymal abnormalities

### Rheumatoid arthritis

Reticulations were the most common parenchymal abnormality in RA accounting for 68 percent of cases followed by GGO which was present in over 44 percent of cases. Mosaic attenuation was present in 36 percent of cases. Honeycombing was present in 31 percent of cases. Nodules, consolidation, cysts were present in 20.5, 17.9, 15.4 percent of cases respectively.

### SLE

GGO was the most common parenchymal abnormality present in SLE accounting for 50 percent of cases. Reticulations, mosaic attenuation, nodules and consolidation were present in 25 percent of cases each. Honeycombing and cyst formation were not seen.

### Sjogren’s syndrome

Mosaic attenuation was most common finding in sjogrens presenting in 60 percent of cases. Reticulations were present in 40 percent of cases. Nodules and cysts were present in 20 percent of cases each.

### Systemic sclerosis

Reticulations (87.5%) were most common finding in systemic sclerosis. Honeycombing was present in 50 percent of cases. Mosaic attenuation and nodules were found in 25 percent of cases each. GGO and cysts were found in 12.5 percent of cases each.

### Polymyositis

Reticulations and GGO were present in all the cases with mosaic attenuation seen in one of the case.

### MCTD

Out of the three cases reticulations and mosaic attenuation was found in one of the case. One of the case had consolidation.
and the other had nodules.

**Airway abnormality**

**RA**

Bronchiectasis was most common abnormality and was found in almost 67 percent of cases. Emphysema was found in 18 percent and GGN in 5 percent of cases.

**SLE**

Emphysema was present in one of the case. No other airway abnormality was detected in patients of SLE.

**Sjogrens**

Bronchiectasis was seen in two cases. No other airway abnormality was detected.

**Systemic sclerosis**

Bronchiectasis was found in three cases. No other airway abnormality was detected.

**Polymyositis**

No airway abnormality was detected.

**MCTD**

Bronchiectasis was present in two cases.

**Others**

One case was found to have bronchiectasis and one was found to have emphysema.

**Other abnormalities in various CTDs**

Pulmonary hypertension detected in two cases of sjogrens, one case each of SLE, systemic sclerosis, polymyositis and others and in Four cases of RA.

Pericardial effusion was seen in two cases of SLE and one case each of sjogrens, systemic sclerosis and MCTD.

Pleural effusion was present mostly in patients with SLE (50%). One patient of sjogren syndrome (SSJ) also presented with pleural effusion.

LAP was found in nine cases RA, two cases of systemic sclerosis and one case of sjogrens.

Table 6 shows the affection of different zones of lung in
CTDs. It is evident that lower lobe predilection was seen in RA and SLE.

Apico-basal gradient was seen in 22 cases (56.4%) of RA and four cases (50%) of systemic sclerosis. Subpleural sparing was seen in four cases (10.3%) of RA, two cases of SLE, and twocase each of sjogrens and polymyositis. Peripheral/subpleural distribution was seen in 10 cases (25.6%) of RA, four cases (50%) of systemic sclerosis, one case of polymyositis and one case in others category. Peribronchovascular and subpleural distribution was found in two cases of RA, one case of systemic sclerosis and one case of MCTD (table-7).

ILD was diagnosed in 23 cases of RA out of a total of 39, two cases of SLE (8 three cases of sjogren (5), six cases of systemic sclerosis (8), all cases of polymyositis, two cases of MCTD (3) and three in other autoantibody positive cases polymyositis, two cases of MCTD (3) and three in other autoantibody positive cases of polymyositis, two cases of MCTD (3) and three in other autoantibody positive cases. (table-8)

In rheumatoid arthritis UIP pattern was found in 11(28.2%) cases same as that NSIP. One case was diagnosed as COP. In SLE one case was diagnosed as NSIP and one case as DAD. In sjogren’s syndrome one case was diagnosed as NSIP and one case as LIP. In systemic sclerosis four cases were diagnosed as UIP and one case as COP. In polymyositis two were of NSIP and one case of DAD. One case of MCTD was diagnosed as COP. Out of the four autoantibody positive cases one case was diagnosed as UIP, one as COP and one as LIP (Table 9).

DISCUSSION

Involvement of the respiratory system is common in the collagen vascular diseases and results in significant morbidity and mortality. Lung injury from collagen vascular disease can affect each portion of the lung, commonly; more than one compartment. Although there is some overlap, each collagen vascular disease is associated with a characteristic pattern of pulmonary involvement. The lung disease in these cases may precede the clinical presentation of the collagen disease, sometimes by more than five years.

High-resolution computed tomography (HRCT) is the method of choice for assessment of pulmonary abnormalities in collagen vascular diseases, offering the best correlation with histological findings, disease severity, prognosis, evaluation of disease progression, and differential diagnosis. It plays an important role in early detection and characterization of interstitial lung disease. However, it has some limitations. In many cases, HRCT appearance is nonspecific and may or may not be related to an underlying CTD. Thus, radiologic findings should never be interpreted without knowledge of the clinical picture.

In this study, Out of the 70 patients, 67(95%) showed a variety of parenchymal, pleural, and mediastinal abnormalities on HRCT. Three patients had a normal study. This is consistent with Webb (2001) who reported sensitivity level of 94% with MDCT.

Majority of the patients in our study (55%) had RA while SLE and systemic sclerosis contributed to 11% of the cases. consistent with Gaude et al (2009) having RA (61%) and SLE (16.4%) and Verma et al (2013) having RA (48.6%) and SLE (21.2%).

Majority of the patients in our study were females (82%) similar to Verma et al (2013) with females (71.9%) and Gaude et al (2009) with females (64%).

Mean age of presentation in RA was 60.6, in SLE was 49.7, in systemic sclerosis was 47, in sjogren was 57.6, in polymyositis was 55.3, and in MCTD was 52 years. Similar results were noted by Verma et al (2013) who found majority of patients to be in fifth decade of life. Gaude et al (2009) reported 85% of their patients with connective tissue disorders having age more than 40 years. The mean age of presentation as noted by Bilgici et al (2004) was 53.6 years and by Perez et al (1997) was 57.8 years.

Cough and dyspnea were the commonest respiratory symptoms with similar observation was made by both Gaude et al (2009) and Verma et al (2013).

Various abnormalities on HRCT affecting the parenchyma (reticulations, GGO, honeycombing, nodules, cysts), airway (bronchiectasis, GGN, emphysema), pleura (effusion) and mediastinum (PAH, pericardial effusion, lymphadenopathy (LAP)) were evaluated.

Reticulations in the form of inter and intralobular septal thickening were found in almost 67% of cases of RA. Same seen by J.Biederer et al (2003) (75%) and Bilgici et al (65%). GGO was noted in 43% of cases consistent with J.Biedere et al (2003) (37.5%). Honeycombing which is defined as thin walled cysts sharing walls arranged in layers in subpleural location was found in 30.8% of cases of RA similar to verma et al 2013 (31%).

Lynch et al (2009) found honeycombing in 10% of cases. Mosaic attenuation with areas of air trapping on expiratory film was found in 35.9% of cases. Similar to Perez et al 1998 (32%) and Cortet et al 1997 (25%). Nodules were seen 20.5% of cases in RA. Consistent with B.Crestani 2005 (20%). Similarly Cortet et al 1997 reported 28% of parenchymal nodules in RA. Consolidation was noted in 18% cases of RA.

Bronchiectasis was seen in 66.7% of cases in RA which was much higher than the study done by Rockall et al., (2001) and Cortet et al 1997 who reported bronchiectasis in 30% of cases. The colonization of these bronchiectases by different microorganisms is the cause of repeated respiratory infections, which is very important to take into account in these patients who receive immunosuppressive treatment for their underlying disease.

Emphysema in RA patients was seen in the current study in 17.9% of cases. Similar to Zrour et al 2005 (13.3%) and Tanaka et al., (2004). The distribution of abnormalities was found predominantly in peripheral location with lower lobes predominance.

The prevalence of PAH in RA can only be grossly estimated by echocardiographic data, and according to several studies, it ranges from 0.8% to 21–27.5. In our study PAH was found in 10.3% cases of RA. Mediastinal lymphadenopathy was noted in 23% cases. Out of total 39 cases of RA, 23 (59%) cases were found to have CTD related ILD. Both UIP (Fig 1) and NSIP (Fig 2)
pattern was observed in 28.2% of cases with COP in 2.6% of cases. Similar to verma et al 2013 and Ysamatmarfa et al 2013.

The most common pulmonary manifestation of SLE is unilateral or bilateral pleural effusion (Fig 3) frequently associated with pericardial effusion. In this study pleural effusion associated with pleural thickening was found in 50% of cases same as Fekih et al. (2011) with pleural abnormalities seen in 50% cases. In our study reticulations, mosaic attenuation, nodules, and cysts were seen in 40%, mosaic attenuation in 60%, nodules and cysts in 20% of cases. Interstitial lung disease associated with polymyositis and dermatomyositis has a wide spectrum of histopathologic features, on the basis of which four major disease patterns can be identified: cryptogenic organizing pneumonia, UIP, NSIP, and diffuse alveolar damage. The most common pattern is NSIP and cryptogenic organizing pneumonia.

In our study 66.7% cases had NSIP pattern on HRCT. Mixed connective tissue disease, a condition in which manifestations of systemic lupus erythematosus, rheumatoid arthritis, progressive systemic sclerosis, and polymyositis or dermatomyositis are combined, was described by Sharp et al in 1972. Thoracic involvement in mixed connective tissue disease occurs with a frequency ranging from 20% to 85%. In our study almost (fig 7) 33% of cases presented with parenchymal abnormalities like reticulations, mosaic attenuation, nodules, and consolidation. Pattern of COP was identified in one of the patient.

**CONCLUSION**

From this study it is evident that thoracic organs are frequent targets of immune-mediated injury in CTDs. Any thoracic compartment (parenchyma, airway, pleura and mediastinum) can be affected; however, the most important manifestation is interstitial lung disease. HRCT is the diagnostic modality for early detection which can help in prompt treatment for better prognosis.

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Primary Thoracic Manifestations in Connective Tissue Diseases


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