Letters to the Editors

Radiologic classification of usual interstitial pneumonia in rheumatoid arthritis-related interstitial lung disease: correlations with clinical, serological and demographic features of disease

Sirs,

Interstitial lung disease (ILD) is a relevant extra-articular manifestation of rheumatoid arthritis (RA) and usual interstitial pneumonia (UIP) is considered the most frequent histopathological pattern of RA-ILD (1); high-resolution computed tomography (HRCT) is crucial for the evaluation of ILD patterns without recourse to lung biopsy (2). In 2011, the ATS/ERS/JRS/ALAT statement for diagnosis and management of idiopathic pulmonary fibrosis (IPF) provided consensus guidelines to identify a definite, possible or inconsistent with UIP pattern on HRCT, based on radiological features (3); previous studies suggest that the above classification should also be appropriate for RA-ILD (4).

We retrospectively identified 97 unselected RA patients, classified according to 2010 ACR/EULAR classification criteria (5), referred to our Rheumatology Unit from October 2004 to March 2013, with at least one chest HRCT, regardless of its indication. Demographic, clinical, serological data, and radiographic pulmonary fibrosis patterns were collected for all patients (Table I). RA-ILD diagnosis was conventionally identified with HRCT.

A thoracic radiologist experienced in interstitial lung disease scored all HRCT images, classifying them as definite, possible or inconsistent with UIP (3).

Among 97 RA patients, 32 showed RA-ILD (15 with definite or possible UIP pattern and 17 with an inconsistent with UIP pattern), while the 65 patients without ILD were used as control group.

The occurrence of dyspnea increased according to the number of significantly associated features (namely, male gender, smoking habit, presence of ENA, and age over 63). In fact, patients with UIP pattern showed the co-presence of 3 or 4 factors in 61% of cases, compared with no cases in non UIP group and 13.6% in the control group (p=0.039).

Anti-Jo1 and anti-SSA were the prevalent specificities of ENA, without differences between the groups (only 1 patient fulfilled also criteria for Sjögren’s syndrome).

All patients with UIP pattern were over 63 years of age at the time of HRCT, and they were more frequently males and smokers (Table I).

No differences were observed comparing anti-CCP, rheumatoid factor, and ANA positivity, while ENA were more frequent in the UIP group, compared to the controls (p=0.039). Anti-Jo1 and anti-SSA were the prevalent specificities of ENA, without differences between the groups (only 1 patient fulfilled also criteria for Sjögren’s syndrome).

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Since IPF showed similar associations in non UIP group and 13.6% in the control group (p<0.001 and p=0.001, respectively). The occurrence of UIP pattern increased according to the number of significantly associated features (namely, male gender, smoking habit, presence of ENA, and age over 63). In fact, patients with UIP pattern showed the co-presence of 3 or 4 factors in 61% of cases, compared with no cases in non UIP group and 13.6% in the control group (p<0.001 and p=0.001, respectively).

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Table I. Comparison of clinical, serological and demographic features of rheumatoid arthritis patients with and without interstitial lung disease.

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>ILD group</th>
<th>UIP group</th>
<th>Non UIP group</th>
<th>Non ILD group</th>
<th>ILD vs. non ILD</th>
<th>UIP vs. non UIP</th>
<th>UIP vs. non ILD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients (%)</td>
<td>97</td>
<td>32 (33)</td>
<td>15 (15.5)</td>
<td>17 (17.5)</td>
<td>65 (67)</td>
<td>ns</td>
<td>0.010</td>
<td>0.045</td>
</tr>
<tr>
<td>Males (%)</td>
<td>38.1</td>
<td>40.6</td>
<td>64.3</td>
<td>17.6</td>
<td>36.9</td>
<td>ns</td>
<td>0.010</td>
<td>0.045</td>
</tr>
<tr>
<td>Smoke (%)</td>
<td>39.1</td>
<td>43.8</td>
<td>66.7</td>
<td>23.5</td>
<td>36.7</td>
<td>ns</td>
<td>0.031</td>
<td>0.045</td>
</tr>
<tr>
<td>Antinuclear antibodies (%)</td>
<td>48.9</td>
<td>46.7</td>
<td>46.2</td>
<td>47.1</td>
<td>50.0</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
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<tr>
<td>ENA (%)</td>
<td>11.7</td>
<td>20.0</td>
<td>30.8</td>
<td>11.8</td>
<td>7.8</td>
<td>ns</td>
<td>0.039</td>
<td>ns</td>
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<tr>
<td>anti-CCP (%)</td>
<td>71.4</td>
<td>71.0</td>
<td>69.2</td>
<td>70.6</td>
<td>64.6</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
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<tr>
<td>Rheumatoid factor (%)</td>
<td>46.9</td>
<td>58.1</td>
<td>64.3</td>
<td>52.9</td>
<td>41.5</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
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<tr>
<td>Patients over 63 years of age</td>
<td>74.2</td>
<td>87.1</td>
<td>100.0</td>
<td>76.5</td>
<td>67.7</td>
<td>ns</td>
<td>ns</td>
<td>0.008</td>
</tr>
<tr>
<td>Dyspnea (%)</td>
<td>35.4</td>
<td>40.0</td>
<td>53.3</td>
<td>32.1</td>
<td>16.7</td>
<td>0.02</td>
<td>ns</td>
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<tr>
<td>Cough (%)</td>
<td>22.2</td>
<td>21.0</td>
<td>15.4</td>
<td>33.3</td>
<td>23.3</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
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<tr>
<td>Rheumatoid arthritis diagnosis (years)</td>
<td>54.2 ± 12.6</td>
<td>55.3 ± 12.9</td>
<td>57.1 ± 12.7</td>
<td>53.8 ± 13.3</td>
<td>53.6 ± 12.6</td>
<td>ns</td>
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<tr>
<td>Disease duration (months)</td>
<td>155.1 ± 123.6</td>
<td>165.6 ± 141.9</td>
<td>176.2 ± 157.3</td>
<td>156.8 ± 132.2</td>
<td>150.1 ± 114.6</td>
<td>ns</td>
<td>ns</td>
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<tr>
<td>Previous therapies</td>
<td>Methotrexate (%)</td>
<td>68.0</td>
<td>59.4</td>
<td>40.0</td>
<td>76.5</td>
<td>72.3</td>
<td>ns</td>
<td>ns</td>
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<tr>
<td></td>
<td>Leflunomide (%)</td>
<td>33.0</td>
<td>21.9</td>
<td>20.0</td>
<td>23.5</td>
<td>38.5</td>
<td>ns</td>
<td>ns</td>
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<tr>
<td></td>
<td>Methotrexate-SAC (%)</td>
<td>38.1</td>
<td>21.9</td>
<td>13.3</td>
<td>29.4</td>
<td>46.2</td>
<td>0.043</td>
<td>ns</td>
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<tr>
<td></td>
<td>Methotrexate-SAC-TNF alpha (%)</td>
<td>28.9</td>
<td>12.5</td>
<td>0.0</td>
<td>23.5</td>
<td>36.9</td>
<td>0.017</td>
<td>ns</td>
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</table>


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References
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The link between RA-ILD and drugs is still uncertain. The poor quality of published data and the lack of randomised controlled trials contribute to confounding information in clinical practice (1, 8, 9).

HRCT could improve diagnosis and classification of ILD in RA patients, reserving lung biopsy only for selected cases (1). Moreover, at present, definition and classification of RA-ILD are still under debate, and the use of classifications based on radiological findings could improve the identification of more homogeneous groups of patients with different lung involvement. Interestingly, our study highlights the peculiarities of UIP pattern, showing different clinical associations from the ones of the whole ILD group.

Since ILD can significantly affect survival (10), a careful follow-up for ILD is mandatory in all RA patients and a multidisciplinary approach, including rheumatologist, pulmonologist, radiologist and pathologist, should guarantee the most appropriate management.

Letters to the Editors
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References