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 drugs administered before HRCT 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.

With the exception of dyspnea, no differences were observed comparing patients with or without ILD (Table I). According to radiological classification, we also compared patients with a definite or possible UIP pattern (UIP group), patients with a pattern inconsistent with UIP (non UIP group), and controls.

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 fullfilled 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).

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). Since IPF showed similar associations (particularly with male gender, elderly and smoke), it would be interesting a future speculation on potential pathogenic and therapeutic overlap between the two diseases (6). On the other side, the presence of anti-ENA in UIP pattern could only theoretically suggest partial overlap with connective tissue disease in RA-ILD (7), with possible prognostic and therapeutic implications. Published data have not clarified the association with anti-CCP and rheumatoid factor (8).

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 (). 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.

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

	Total	ILD group	UIP group	Non UIP group	Non ILD group	ILD *vs.* non ILD	UIP *vs.* non UIP	UIP *vs.* non ILD	Non UIP *vs.* non ILD
Number of patients (%)	97	32 (33)	15 (15.5)	17 (17.5)	65 (67)				
Males (%)	38.1	40.6	64.3	17.6	36.9	ns	0.010	0.045	ns
Smoke (%)	39.1	43.8	66.7	23.5	36.7	ns	0.031	0.045	ns
Antinuclear antibodies (%)	48.9	46.7	46.2	47.1	50.0	ns	ns	ns	ns
ENA (%)	11.7	20.0	30.8	11.8	7.8	ns	ns	0.039	ns
anti-CCP (%)	71.4	71.0	69.2	70.6	64.6	ns	ns	ns	ns
Rheumatoid factor (%)	46.9	58.1	64.3	52.9	41.5	ns	ns	ns	ns
Patients over 63 years of age	74.2	87.1	100.0	76.5	67.7	ns	ns	0.008	ns
Dyspnea (%)	35.4	40.0	53.3	32.1	16.7	0.02	ns	0.06	ns
Cough (%)	22.2	21.0	15.4	33.3	23.1	ns	ns	ns	ns
Rheumatoid arthritis diagnosis (years)	54.2 ± 12.6	55.3 ± 12.9	57.1 ± 12.7	53.8 ± 13.3	53.6 ± 12.6	ns	ns	ns	ns
Interstitial lung disease diagnosis (years)	67.2 ± 9.3	69.3 ± 8.2	71.8 ± 6.5	67.1 ± 9.1	66.1 ± 9.7	ns	0.032	0.029	ns
Disease duration (months)	155.1 ± 123.6	165.6 ± 141.9	176.2 ± 157.3	156.8 ± 132.2	150.1 ± 114.6	ns	ns	ns	ns
Previous therapies									
Methotrexate (%)	68.0	59.4	40.0	76.5	72.3	ns	ns	0.031	ns
Leflunomide (%)	33.0	21.9	20.0	23.5	38.5	ns	ns	ns	ns
anti-TNF alpha (%)	38.1	21.9	13.3	29.4	46.2	0.043	ns	0.021	ns
Methotrexate+anti-TNF alpha (%)	28.9	12.5	0.0	23.5	36.9	0.017	ns	0.004	ns

ENA: anti-extractable nuclear antibodies; anti-CCP: anti-cyclic citrullinated peptides antibodies; TNF: tumour necrosis factor; ILD: interstitial lung disease; UIP: usual interstitial pneumonia.

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