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ORIGINAL ARTICLE

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Lung findings on thoracic high-resolution computed tomography in patients with ankylosing spondylitis. Correlations with disease duration, clinical findings and pulmonary function testing

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Abstract The aim of this study was to identify the spectrum of abnormalities revealed on high-resolution computerized tomography (HRCT) in patients with ankylosing spondylitis (AS), to compare findings with those of plain radiography and pulmonary function testing (PFT), and to look for correlations between lung involvement and AS severity. We prospectively studied 55 consecutive patients with a diagnosis of AS according to the modified New York criteria who attended our department over a period of 2 years. All patients had a detailed rheumatological examination and underwent plain chest radiography, chest HRCT and PFT. HRCT revealed abnormalities in 29 patients (52.7%), whereas plain chest radiography was abnormal in only 2. Abnormalities consisted of interstitial lung disease (ILD) ($n=4$), apical fibrosis ($n=5$), emphysema ($n=5$), bronchiectasis ($n=4$), ground glass attenuation ($n=2$), and non-specific interstitial abnormalities ($n=26$). Only apical fibrosis and bronchiectasis were statistically more frequent with increasing disease duration (significant trend χ^2test, $p=0.0029$ and 0.028, respectively). PFT showed a restrictive process in 19 patients (34.5%). No correlation was noted between HRCT and PFT, nor with AS symptomatic and structural severity parameters. However, there was a statistically significant correlation between PFT and AS symptomatic and structural severity parameters. In conclusion,: this study confirms that the chest HRCT of patients with AS showed a great number of abnormalities undetectable by standard X-rays. The high incidence of lung abnormalities emphasizes the importance of excluding such a diagnosis in patients with AS even without respiratory symptoms.

Keywords Ankylosing spondylitis · High-resolution computerized tomography · Lung

Abbreviations *AF* Apical fibrosis · *AS* Ankylosing spondylitis · *FVC* Forced vital capacity · FEV_1 Forced expiratory volume in 1 s · *HRCT* High-resolution computerized tomography · *ILD* Interstitial lung disease · *PFT* Pulmonary function tests · *VC* Vital capacity

Introduction

Ankylosing spondylitis (AS) is a chronic rheumatic disorder characterized by inflammation of the enthesis (especially of the axial skeleton) and sometimes the joints, which may lead to ankylosis [1]. Extra-articular manifestations may involve in particular the eyes, heart, gut and lungs [2, 3]. The incidence of pleuropulmonary involvement in AS varies from 0 to 30% in the medical literature [4, 5, 6, 7]. The most frequently recognized pleuropulmonary manifestations are upper lobe fibrosis, mycetoma formation and pleural thickening [5, 6, 7, 8, 9, 10]. The advent of high-resolution computerized tomography (HRCT) offered the possibility of examining the entire lung parenchyma and pleura in many conditions with diffuse lung disease using a non-invasive method. Recently, studies using chest CT have highlighted the superiority of this technique in detecting and defining the extent of pulmonary changes in patients

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with many rheumatic diseases, in particular rheumatoid arthritis, systemic sclerosis and AS.

The aims of the study were to identify the spectrum of abnormalities revealed on HRCT in patients with AS and without a history of respiratory symptoms, and to compare our findings with those of plain radiography and pulmonary function testing; to evaluate the distribution of abnormalities with disease duration; and to look for correlations between lung involvement and symptomatic and structural severity parameters of AS.

Patients and methods

Fifty-five consecutive patients with a diagnosis of AS according to the modified New York criteria [11] who attended our department over a period of 2 years were included in the study. Consent was obtained from all patients. All had a prospective rheumatologic assessment conducted by two rheumatologists (AEM and AB) using a structured questionnaire. None of the patients had a history of respiratory symptoms. Clinical assessment included demographic data, age, gender and duration of disease, defined as the time between the date of first symptoms and patient enrolment. An accurate smoking history, and a history of tuberculous infection were recorded. Clinical examination involved auscultation of the chest and measurement of chest expansion at the level of the xiphisternum. Lumbar flexion was measured by Schöber's index. Disease symptom severity was measured by the Bath Ankylosing Spondylitis Metrology Index (BASMI) [12], the Bath Ankylosing Spondylitis Functional Index (BASFI) [13] and the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) [14]. Global evaluation of disease handicap was evaluated by Bath Ankylosing Spondylitis Global Score (BAS-G) [15].

Pulmonary function tests (PFT)

Pulmonary function tests were performed in all patients prior to HRCT imaging and included measurement of the vital capacity (VC), forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1), and FEV_1/FVC. Observed values were expressed as a percentage of the predicted value compared with individuals of similar sex, age, weight and height. Depending on the results of these tests, the patients were categorized as having obstructive disease ($FEV_1 < 75\%$, $FEV_1/FVC1 < 75\%$, FVC% predicted $< 75\%$, $FEV_1/FVC > 70\%$) or normal ($FEV_1 > 75\%$, FVC% predicted $> 75\%$, $FEV_1/FVC > 70\%$).

Radiological assessment

Each patient had a posteroanterior chest radiography. On the same day spiral CT scans of the thorax were taken using a Siemens Somatom S CT scanner with images windowed to highlight both lungs and mediastinal structures. Nine HRCT slices were obtained on suspended respiration at 2 cm intervals from the lung apices to bases. After a period of X-ray reading training, the abnormalities of the chest radiographs and HRCT were assessed by two observers (CS and AEM) blinded to the clinical data of the patients. Results were based on consensus agreement. The CT scans were evaluated for the presence, distribution and extent of airway and parenchymal abnormalities. Standard CT criteria were used to establish a diagnosis of interstitial lung disease (ILD), bronchiectasis and emphysema. ILD was defined by the presence of characteristic abnormalities (e.g. subpleural opacities, parenchymal bands, thickened interlobular septae, an irregular pleural interface, honeycomb lung) if they were multifocal or diffuse, bilateral and present at multiple levels. All mild and non-specific abnormalities of insufficient severity or extent to be labeled as ILD were recorded. Disease severity was graded semiquantitatively according to a 7-point scale (grade 0, 0%; grade 1, 1– 10% of lung parenchyma involved; grade 2, 10– 20%; grade 3, 20– 30%; grade 4, 30– 40%; grade 5, 40– 50%; and grade 6, $> 50\%$).

Recent (within 6 months) X-rays of the pelvis, lumbar and cervical spine were read by the same observer (AEM). Sacroiliitis and hip involvement were assessed on anteroposterior pelvic X-rays and graded respectively on the New York [16] and Bath Ankylosing Spondylitis Radiological Index for the hips (BASRI-h) scales [17]. Syndesmophytes were assessed on posteroanterior and lateral lumbar spine standard radiography. Syndesmophyte score was obtained after grading on a 0–3 scale (already used in previous studies [18, 19]) with 3 equal to complete bony bridging (bamboo spine), 2 to more than three syndesmophytes bridges, and 1 to incipient syndesmophytes. Lumbar and cervical involvement was measured by the Bath Ankylosing Spondylitis Radiological Index (BASRI) [20, 21].

Erythrocyte sedimentation rate (ESR) was measured by the standard method.

Statistical analysis

The study was conducted in different steps. The first step consisted of the description of the study population. In the second step we measured the prevalence of lung involvement (on plain films and HRCT) and described the distribution of the thoracic HRCT finding in three subgroups depending on disease duration: group 1 < 5 years, group 2 between 5 and 10 years, and group 3 > 10 years, using the trend χ^2test (5 years being the median and 10 years the 4th percentile). In the third step, we described the lung functional tests abnormalities and looked for correlations between HRCT abnormalities, lung function abnormalities and AS symptomatic and structural indexes.

Results

The characteristics of the study population are summarized in Table 1. Plain radiography was abnormal in only two patients. Twenty-nine patients (52.7%) showed abnormalities on HRCT. Table 2 lists the abnormalities detected on HRCT. In all patients with lung abnormalities HRCT findings were classified as subtle, never exceeding grade 3 (mean 1.3 ± 0.4).

Of the four patients with ILD, a 66-year-old woman with late-onset AS (5 years' disease duration) had also

Table 1 Characteristics of the study population ($n = 55$)

	Mean ± SD	Range
Age (year)	37.6 ± 11.0	17–67
Sex: n = 50, M/F = 90.9%		
Disease duration (years): mean (SD)	7.5 ± 5.1	0.4–34
Smoking history		
Patients:$n = 20$ (43%)		
Packs/year	5.09 ± 7.3	1–42
Chest expansion (cm)	3.5 ± 1.6	0–8
Schöber (cm)	2.3 ± 1.5	0–6
BASMI	3.2 ± 2.6	0–10
BASFI	38.3 ± 26.1	0–100
BASDAI	36.5 ± 27.5	0–100
BASG	69.0 ± 29.9	0–100
BASRI	5.4 ± 3.2	2–12
ESR	34.0 ± 27.8	2–104

Table 2 Results of chest HRCT in 55 patients with anklosing spondylitis and distribution of the lung abnormalities with disease duration. Results are expressed as number (percentage)

	Total	Disease duration < 5 years ($n = 30$)	Disease duration ≥5 and < 10 years ($n = 14$)	Disease duration ≥10 years ($n = 11$)	p
	n (%)				
Normal	26 (47.2)	11 (36.7)	6 (42.9)	2 (18.2)	NS
Emphysema	5 (9.0)	1 (3.3)	1 (7.1)	2 (18.2)	NS
Upper lobe fibrosis	5 (9.2)	1 (3.3)	1 (7.1)	3 (27.3)	0.029
Bronchiectasis	4 (7.2)	1 (3.3)	–	3 (27.3)	0.028
Interstitial lung disease	4 (7.2)	2 (6.7)	1 (7.1)	1 (9.1)	NS
Ground glass attenuation	2 (3.6)	2 (6.7)	–	–	NS
Non-specific interstitial change	26 (47.2)	14 (46.7)	5 (35.7)	7 (63.6)	NS
Pleural thickening	13 (23.6)	8 (26.7)	3 (21.4)	3 (27.3)	NS
Parenchymal bands	13 (23.6)	6 (20.0)	3 (21.4)	4 (36.4)	NS
Blebs	7 (12.7)	3 (10.0)	2 (14.3)	2 (18.2)	NS
Parenchymal micronodules	7 (12.9)	4 (13.3)	2 (14.3)	1 (9.1)	NS
Subpleural bands	6 (10.9)	1 (3.3)	4 (28.6)	1 (9.1)	NS
Irregular interfaces	4 (7.2)	4 (13.3)	–	–	NS

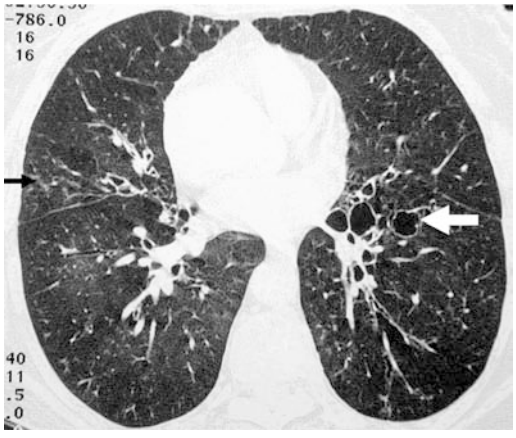

Fig. 1 Chest HRCT of a 66-year-old woman (5 years' disease duration) demonstrating interstitial lung disease with interfaces irregularities, micronodules, parenchymal bands (*black arrow*) and severe bronchiectasis (*white arrow*)

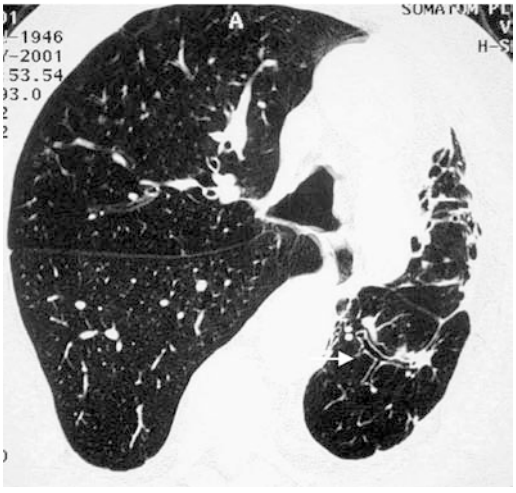

Fig. 2 Chest HRCT of a 53-year-old man (22 years' disease duration) demonstrating interstitial lung disease and left lung fibrosis with traction bronchiectasis (*white arrow*)

severe bronchiectasis (Fig. 1) and restrictive syndrome in PFT. ILD was diagnosed also on plain radiography. The second case was a 67-year-old man with long-standing AS (22 years' disease duration). HRCT showed also left lung fibrosis and traction bronchiectasis (Fig. 2), which was also observed on plain radiography. PFT showed severe restrictive syndrome. The remaining two cases were males of 39 and 43 years old with 4 and 10 years' disease duration, respectively. PFT showed restriction in the first case and normal values in the second.

Apical fibrosis (AF) was present in five patients. The upper lobe changes were all unilateral and right-sided. Five had emphysema, which in 2 cases was accompanying AF. Four had bronchiectasis. Whereas two of these were in primary form, the others were in the form of traction bronchiectasis at the right upper lobe (accompanying AF). Two patients had ground glass attenuation, limited to the lower lobe of the left lung in the first case (Fig. 3) and to the lower lobe of the right

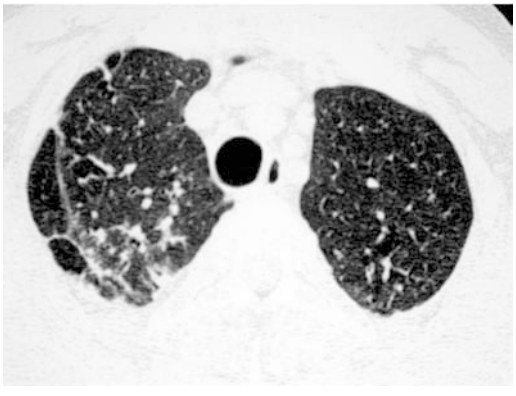

Fig. 3 Chest HRCT of a 40-year-old man (16 years' disease duration) demonstrating apical fibrosis, parenchymal bands and subpleural emphysema

lung in the second. Twenty-six patients (46.2%) had mild non-specific interstitial abnormalities of insufficient severity or extent to be labeled as ILD. The distribution of parenchymal changes, depending on disease duration, showed no significant statistical differences for the majority of the abnormalities. Only AF and bronchiectasis were statistically more frequent with increasing disease duration (significant trend χ^2test, $p = 0.0029$ and 0.028, respectively).

PFT showed a restrictive process in 19 patients (34.5%), but only two had an obstructive process. No correlation was noted between HRCT severity index and PFT variables, nor with AS symptomatic and structural severity parameters. However, there was a statistically significant correlation between PFT parameters and AS symptomatic and structural severity parameters (Table 3).

Comparison between smokers and non-smokers did not show any significant statistical difference in HRCT lung abnormalities distribution or severity, or in PFT results (data not shown).

Discussion

The association of pleuropulmonary manifestations and AS was first reported by Dunham and Kautz [22] in 1941 and Hamilton [23] in 1949. Rosenow et al. [24], in a retrospective study based on plain radiography analysis of 2080 patients, reported an incidence of 1.2%. Recently, studies using chest HRCT have highlighted the superiority of this technique in detecting and defining the extent of pulmonary changes [25, 26, 27].

Our study revealed a great percentage of defined as well as mild and non-specific interstitial abnormalities on HRCT undetectable on plain radiography in a series of patients with AS and without a history of respiratory symptoms. Among these lung abnormalities, only two seemed to be more prevalent with increasing disease duration: apical fibrosis and bronchiectasis. Only two patients had evidence of ground glass shadowing, which is associated with active alveolitis. This is usually considered a feature of early and potentially reversible disease. As previously described, the overall correlation of pulmonary function with radiographic appearance was poor.

Smoking is recognized as carrying an adverse prognosis in patients with pulmonary fibrosis, independent of its aaetiology, by increasing the rate of decline in pulmonary function. However, in our study no differences were shown between smokers and non-smokers, neither in HRCT lung abnormalities nor in PFT.

If we except our preliminary results reported earlier [3], only three studies of thoracic CT in AS have been published in the literature [28, 29, 30, 31], and ours is the largest ever reported, including 55 patients with AS and without respiratory symptoms. Table 3 compares the results of these studies. Casserly and Fenlon [28, 29] studied 26 patients with AS using HRCT and noted pulmonary abnormalities in 19 (70%). In this study, plain radiographs revealed abnormalities in only four patients. In contrast to our study, all patients with interstitial lung disease had respiratory symptoms. Another study conducted by Turetschek et al. [30] revealed that 15 of 21 patients (71%) had abnormalities on thin-section CT. Recently, Senocak et al., using thoracic HRCT [31], found abnormalities in 17/20 patients with AS. These changes began in the early stages of the disease and increased with disease duration. In our series we found no linear relation between the HRCT abnormalities and the disease duration, except for apical fibrosis and bronchiectasis, which were statistically related in a linear way with the disease duration.

Lung involvement in AS is usually asymptomatic. Classically, pulmonary manifestations consist chiefly of abnormalities of the thoracic cage (e.g. chest wall restriction) and the lung parenchyma (e.g. upper lobe fibrosis). Fusion of the costovertebral joints caused by inflammation and ankylosis of the thoracic spine can give rise to restrictive ventilatory impairment. In addition, anterior chest wall involvement is common in patients with AS [32]. Indeed, as it is classically described [33], we found that pulmonary function is not related to parenchymal lesions but correlates with symptomatic and structural severity parameters of AS.

Pathological examination of the lung in AS comes from small numbers of postmortem reports. In 1962, Zorab [34] reported the entire lung to be essentially normal at autopsy in eight AS patients. Cohen et al. [35] reported focal interstitial edema and inflammation with transbronchial and peribronchial distribution in the lower lobes in an individual patient with AS which was distinct from that of the upper lobes. The results of

Table 3 Correlations between pulmonary function tests and ankylosing spondylitis symptomatic and structural severity indexes and HRCT index

	Disease duration	Thoracic expansion	C7–wall	Schober	BASMI	BASFI	BASDAI	LS syndesmophytes score	BASRI	ESR	HRCT index
VC	–0.20	0.16	–0.04	0.49[a]	–0.54[a]	–0.28[a]	–0.29[a]	–0.34[a]	–0.43[a]	–0.17	0.04
FVC	–0.24	0.15	–0.01	0.45[a]	–0.50[a]	–0.28[a]	–0.30[a]	–0.32[a]	–0.39[a]	–0.15	0.00
FEV1	–0.25	0.20	–0.04	0.42[a]	–0.48[a]	–0.26	–0.22	–0.32[a]	–0.38[a]	–0.14	0.05
FEV1/VC	–0.12	0.09	–0.05	–0.05	0.09	0.01	0.09	0.01	0.07	0.07	–0.02

[a]Marked correlations are significant at $p < 0.05$

HRCT have been shown to correlate closely with those of open lung biopsy in systemic sclerosis [36].

The HRCT findings in our study, as in the previous studies, would favor an inflammatory process rather than a mechanical etiology for the interstitial disease found in AS patients.

Twenty-six patients (46.2%) in our study had non-specific interstitial abnormalities, as had 11 patients (42%) in Casserly et al.'s study, which implied HRCT evidence of interstitial change that was of insufficient severity or extent to be labeled as ILD. The significance of such changes is unknown and must await a prospective longitudinal study to determine their natural history.

Finally, in clinical practice HRCT may be useful to identify a suspicious abnormality in chest X-rays, especially if anti-TNF therapy is planned. As previous tuberculosis may be reactivated in patients given TNF blockers, clinicians must be aware of the HRCT abnormalities observed in AS, which must not be confounded with tuberculosis lesions.

In summary, it appears that HRCT offers an accurate and safe method of assessment of lung disease in patients with AS and without respiratory symptoms. Our study, which included the greatest number of patients in the literature, showed a great number of abnormalities that can be easily overlooked on plain radiograms classically used to evaluate these kinds of patients. As in the other series reported in the literature with CT, these changes are predominantly interstitial. Including our results, the most common findings were non-specific interstitial abnormalities (pleural thickening, followed by varying rates of subpleural and parenchymal band formations, and bronchial wall thickening). Although most of the changes we observed were not severe enough to be categorized as ILD, it is clear that there is an ongoing lung interstitial inflammation in AS. The high incidence of ILD emphasizes the importance of excluding this diagnosis in patients with AS even without respiratory symptoms.

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