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LUNG FINDINGS ON HIGH-RESOLUTION COMPUTED TOMOGRAPHY IN IDIOPATHIC ANKYLOSING SPONDYLITIS—CORRELATION WITH CLINICAL FINDINGS, PULMONARY FUNCTION TESTING AND PLAIN RADIOGRAPHY

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SUMMARY

Previous studies on the association of ankylosing spondylitis and abnormalities of the lung parenchyma have been based largely on plain radiography and pulmonary function testing. This study, although uncontrolled, is the first to use high-resolution computed tomography to examine the entire lung parenchyma in ankylosing spondylitis patients, and to correlate the findings with clinical assessment, plain radiography and pulmonary function testing. The study population comprised 26 patients meeting the New York criteria for idiopathic ankylosing spondylitis who attended the out-patient department at our institution. High-resolution computed tomography examination revealed abnormalities in 19 patients (70%): these included interstitial lung disease ($n = 4$), bronchiectasis ($n = 6$), emphysema ($n = 4$), apical fibrosis ($n = 2$), mycetoma ($n = 1$) and non-specific interstitial lung disease ($n = 12$). Plain radiography was abnormal in only four patients and failed to identify any patient with interstitial lung disease. All patients with interstitial lung disease on high-resolution computed tomography had respiratory symptoms and three of the four had evidence of a restrictive process on pulmonary function testing. This study raises, for the first time, the possible association between interstitial lung disease and ankylosing spondylitis, and highlights the use of high-resolution computed tomography in detecting such disease in ankylosing spondylitis patients.

KEY WORDS: Ankylosing spondylitis, Lung parenchyma abnormalities, High-resolution computed tomography, Interstitial lung disease.

STUDIES of disease affecting the lung parenchyma in ankylosing spondylitis (AS) patients have until now been based on pulmonary function testing [1, 2], plain radiography [3–5], bronchoalveolar lavage (BAL) ± transbronchial biopsy [6–8], and pathological reports [9–16]. The latter have involved small numbers of patients, and have looked at needle biopsy and lobectomy specimens from the lung apex during life or post-mortem examination of the entire lung.

The advent of high-resolution computed tomography (HRCT) in the mid-1980s has allowed physicians to examine the entire lung parenchyma and pleura in many conditions with diffuse lung disease, proving particularly useful in asbestosis [17], sarcoidosis [18], cryptogenic fibrosing alveolitis [19], systemic sclerosis [20] and lymphangitis carcinomatosis. There has been only one previous report [21] which describes the lung findings on HRCT in AS, but this study confined its examination to the lung apex.

In the present study, we examined the lung findings on HRCT in 26 AS patients attending our out-patient department and compared our findings with the previous conventional methods of clinical examination, plain radiography and pulmonary function testing (PFT).

PATIENTS AND METHODS

Patients

Twenty-six patients (19 male, seven female) were recruited consecutively from the rheumatology out-patient service at our institution between February and September 1995. All patients met the New York criteria [22] for AS. No selection was made because of respiratory symptoms or previous radiological findings. All patients gave informed consent following explanation of the study by a physician (IC).

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Methods

Clinical. For each patient, a standardized questionnaire was completed and a physical examination was performed by the same physician (IC). The questionnaire recorded for each patient their disease duration (based on the onset of low back pain), the presence or absence of respiratory symptoms, an accurate smoking history, occupation history, history of tuberculous infection, or radiation therapy for AS. The HLA status (where known) was noted.

Clinical examination involved auscultation of the chest and measurement of the chest expansion at the level of the fourth anterior intercostal space.

Pulmonary function tests. Pulmonary function testing included measurement of the forced expiratory volume in 1 s (FEV1), forced vital capacity (FVC), FEV1/FVC, and the diffusion capacity (DLCO) using the single breath technique and correcting for lung volume and haemoglobin levels. Observed values were expressed as a percentage of the predicted value compared with individuals of similar sex, age, weight and height. The following categories were defined:

Normal:

FEV1 > 75%, FVC > 75%, FEV1/FVC > 75%, DLCO > 75%

Restrictive with normal diffusing capacity:
FEV1 < 75%, FVC < 75%, FEV1/FVC > 75%, DLCO > 75%
Restrictive with impaired diffusing capacity:
FEV1 < 75%, FVC < 75%, FEV1/FVC > 75%, DLCO < 75%
Obstructive:
FEV1 < 75%, FEV1/FVC < 75%, DLCO > 75%
Isolated impairment diffusing capacity:
FEV1 > 75%, FVC > 75%, FEV1/FVC > 75%, DLCO < 75%

Chest radiographs and high-resolution computed tomography. Each patient had a postero-anterior and lateral CXR (high kVp technique). On the same day, spiral computerized tomography of the thorax was performed using a Siemens Somatom S CT scanner with images windowed to highlight both lung and mediastinal structures. Nine HRCT slices were obtained through the lung: six supine, performed with the patient supine on suspended respiration at ~ 2 cm intervals from the lung apices to bases; three prone, obtained with the patient in a prone position to reduce the effects of increased flow to the dependent parts of the lungs. The results of the chest radiographs and HRCT were assessed independently by two radiologists who were unaware of the clinical details of the patient. Standard CT criteria were used to establish a diagnosis of interstitial lung disease (ILD), bronchiectasis and emphysema [23]. The degree of lung involvement was subjectively graded as mild, moderate or severe (grade 1, 2 and 3) based on the extent and severity of the abnormalities observed.

RESULTS

The results of the questionnaire and physical examination are outlined in Table I. Table II lists the numbers of patients in each of the five categories of pulmonary function (outlined in Patients and methods) on the basis of dynamic spirometery and measurement of diffusion capacity. Table III lists the abnormalities detected on HRCT and plain radiography. Sixteen patients with normal chest radiographs had abnormal HRCT. Plain radiography failed to identify interstitial disease in any of the four cases in whom such disease was seen on HRCT. Non-specific interstitial change refers to cases in which there was some HRCT evidence of interstitial change but of insufficient severity or extent to be labelled as such.

Table IV divides the 26 cases into three categories based on HRCT appearance: ILD; non-specific interstitial change; other. Each category can be compared in terms of their clinical characteristics and results obtained on PFT and plain radiography.

TABLE I
Results of questionnaire and physical examination

Total 26 patients (male $n = 19$; female $n = 7$)	Mean	S.D.	Range
Age (yr)	44.8	12.4	25–68
Disease duration (yr)	18.5	12.6	1.5–48
Smoking history (pack-years)	12	12.5	0–50
Never smokers $n = 3$			
Ex-smokers $n = 9$			
Current smokers $n = 14$			
Chest expansion (cm)	2.5	1.3	0.5–4.5
Symptoms (total 6)			
Cough $n = 1$			
Cough and SOB* $n = 3$			
SOB $n = 1$			
Cough and haemoptysis $n = 1$			
Previous radiotherapy (total = 2)			
HLA B27 status (where known) (total 20)			
Positive $n = 20$			
Negative $n = 0$			
History of tuberculosis exposure (total = 0)			
Abnormal lung auscultation (total = 2)			
Creps left base $n = 1$			
Bibasal creps $n = 1$			

*SOB, shortness of breath.

TABLE II
Results of PFTs

Normal	16
Restrictive with normal DLCO	5
Restrictive with reduced DLCO	1
Isolated reduction DLCO	1
Obstructive	3

DISCUSSION

Involvement of the lung parenchyma is an uncommon yet well-recognized extra-articular manifestation of AS [24–27]. The association was first prompted by Hamilton in 1949 [28] and subsequently by Campbell and McDonald in 1965 [10]. They reported two and six cases, respectively, of apical fibrobullous disease in association with AS. Rosenow *et al*. [4], in a retrospective study of 2080 patients, reported the incidence of such change at 1.2%, which to date remains the most accurate estimate in view of the large study population. These studies were based almost entirely on plain radiography with occasional pathological confirmation. Since then, isolated cases of pulmonary effusions [4], localized pulmonary amyloidosis [29], severe pleural disease [4], cor pulmonale,

TABLE III
Results of HRCT and plain radiography

HRCT		CXR	
Normal	7	Normal	23
Abnormal	19	Abnormal	4
Non-specific interstitial change $n = 12$		Septal lines $n = 1$	
Interstitial lung disease $n = 4$			
Grade 1 $n = 3$			
Grade 2 $n = 1$			
Bronchiectasis $n = 6$		Bronchiectasis $n = 1$	
Basal $n = 2$			
Apical $n = 4$			
Mycetoma $n = 1$			
Upper lobe fibrosis $n = 2$		Upper lobe fibrosis $n = 2$	
Emphysema $n = 4$			
Paraseptal $n = 3$			
Panacinar $n = 1$			

TABLE IV
Clinical characteristics, PFTs and CXR findings in the three patient subgroups as defined by the findings on HRCT

	ILD* $n = 4$	NSIA† $n = 11$	Other $n = 11$
Male/female	3/1	8/3	8/3
Age (yr)	42	48	42.6
Disease duration (yr)			
Average	14.8	21.7	16.5
Range	1.25–25	5–44	4–48
Symptomatic	4	2	0
Smoking (pack-years)	10.8	13	11.4
Chest expansion (cm)	2.1	2.2	3.2
Abnormal examination	0	2	0
Radiotherapy TX	0	1	1
PFTs			
Normal	0	7	9
Restrictive/reduced DLCO	1	0	0
Restrictive/normal DLCO	2	3	0
Isolated reduction DLCO	0	1	0
Obstructive	1	0	2
CXR			
Normal	2	9	11
Abnormal	2	2	0

*ILD, interstitial lung disease.
†NSIA, non-specific interstitial change.

tracheobronchomegaly [30], and bronchiolitis obliterans and organizing pneumonia [31] have been reported in AS patients. However, the major interest of most reports of lung disease in AS remains that of apical fibrobullous disease and super-infection of these cavities with fungal (usually *Aspergillus*) [4, 9, 12] and mycobacterial (usually non-tuberculous) [32, 33] organisms.

HRCT allowed us to examine the entire lung parenchyma in a sizeable population of AS patients by a method that has proven its superior sensitivity to plain radiography [34], and had the advantage over pathological studies of allowing 'sampling' of the entire lung parenchyma in a large number of patients. The abnormalities detected by HRCT are listed in Table III. The most interesting of these was the hitherto unreported finding of ILD in 4/26 patients (16%), all of whom had respiratory symptoms, but normal clinical examination and no evidence of interstitial disease on plain radiography. All four patients had abnormal results on pulmonary function testing.

Of the four patients with ILD, two had long-standing disease (>20 yr) with apical fibrobullous disease, one of which was complicated by a mycetoma (Fig. 1). In both of these cases, the FEV1/FVC ratio remained normal or increased in association with a decrease in both FEV1 and FVC. However, the DLCO was reduced in only one of these cases despite the interstitial change on HRCT. The HRCT appearance suggested fibrosing alveolitis characterized by subpleural band opacities, non-dependent areas of attenuation, thickened interlobular septae, parenchymal bands and honeycomb lung (Fig. 2).

The remaining two cases with ILD had disease of 1 and 13 yr duration, respectively, with no associated apical disease. Surprisingly, the PFT results in one of the latter two cases (a smoker with a 15 pack-year history) revealed a mild obstructive picture with a normal DLCO despite having a similar HRCT appearance outlined above suggesting fibrosing alveolitis. In the final case with ILD, the HRCT showed ground-glass opacification and pulmonary micronodules (Fig. 3) in addition to subpleural band opacities, thickened interlobular septae and parenchymal bands. This ground-glass appearance has been found to correlate with an active fibrosing alveolitis and an inflammatory cell infiltrate on histology in conditions like cryptogenic fibrosing alveolitis [35]. Interestingly, this patient was female, in whom lung parenchymal involvement in AS is felt to be rare [4]. Furthermore, BAL [6–8] studies to date have failed to show convincing evidence for a subclinical alveolitis in idiopathic or secondary AS, which may, however, be due to the small numbers of patients involved in such studies and limitations in sampling. The PFT findings in this woman were of restriction with a reduced FEV1, FVC and VC, but again despite evidence of interstitial disease on HRCT, the DLCO was normal.

The pathogenesis of this interstitial change can only be speculated upon at this stage. Clues from pathological studies are few as histological examination of the lung in AS comes predominantly from the lung apex where the usual histology is that of a prominent interstitial fibrosis with hyaline and elastic

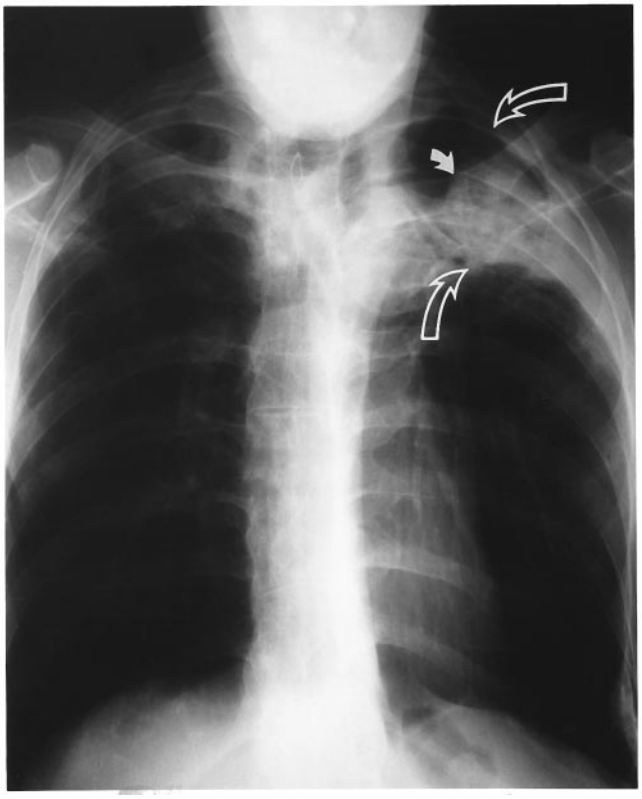

FIG. 1.—Frontal chest radiograph of a 49-yr-old male demonstrates left apical fibrosis with a 6 cm cavity (large curved arrows). Within the cavity there is a mycetoma (small curved arrow).

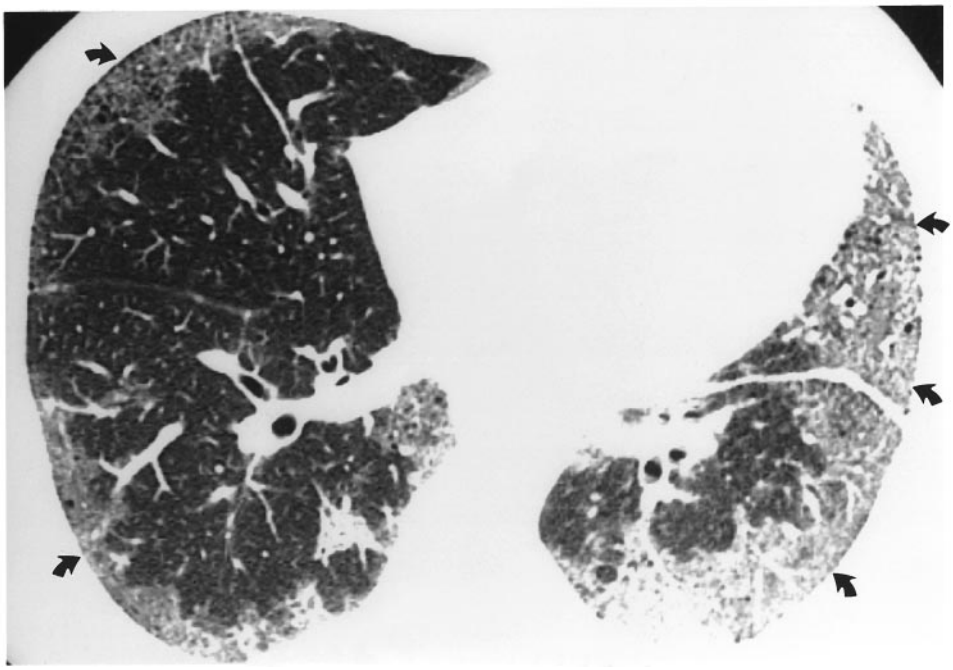

FIG. 2.—Supine HRCT of a 49-yr-old male (same patient as Fig. 1) demonstrating bilateral basal interstitial lung disease (Grade 2) with honeycomb lung (arrows).

degeneration of collagen [15]. A chronic inflammatory cell infiltrate has been reported [10], but was not noted by Jessamine [15] in four needle biopsies or two upper lobectomy specimens. Ferdoutsis *et al*. [36] reported the transbronchial biopsy findings from the lung apex of a 35-yr-old asymptomatic woman as showing a patchy pneumonia with round cell and fibroblastic infiltration. Pathological examination of the remainder of the lung in AS comes from small numbers of post-mortem reports. In 1962 Zorab [11] reported the entire lung to be essentially normal at autopsy in eight AS patients. Cohen *et al*. [13] reported focal interstitial oedema and inflammation with a transbronchial and peribronchial distribution in the lower lobes in an individual patient with AS which was distinct from the upper lobes.

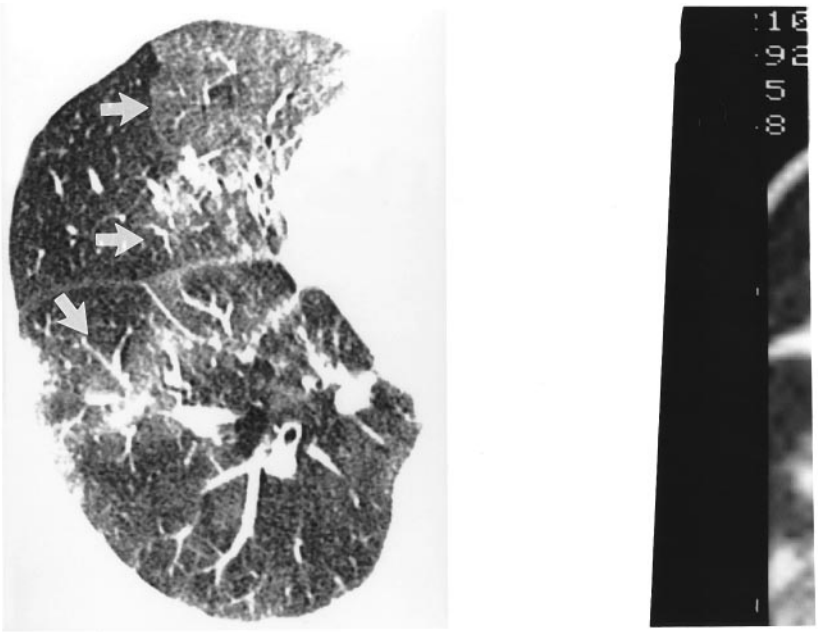

FIG. 3.—Supine HRCT of a 29-yr-old female demonstrates a well-demarcated area of ground-glass opacification in the medial portion of the right upper lobe and more diffusely in the right lower lobe (arrows). This is on a background of thickened interlobular septae, parenchymal bands and subpleural band opacities.

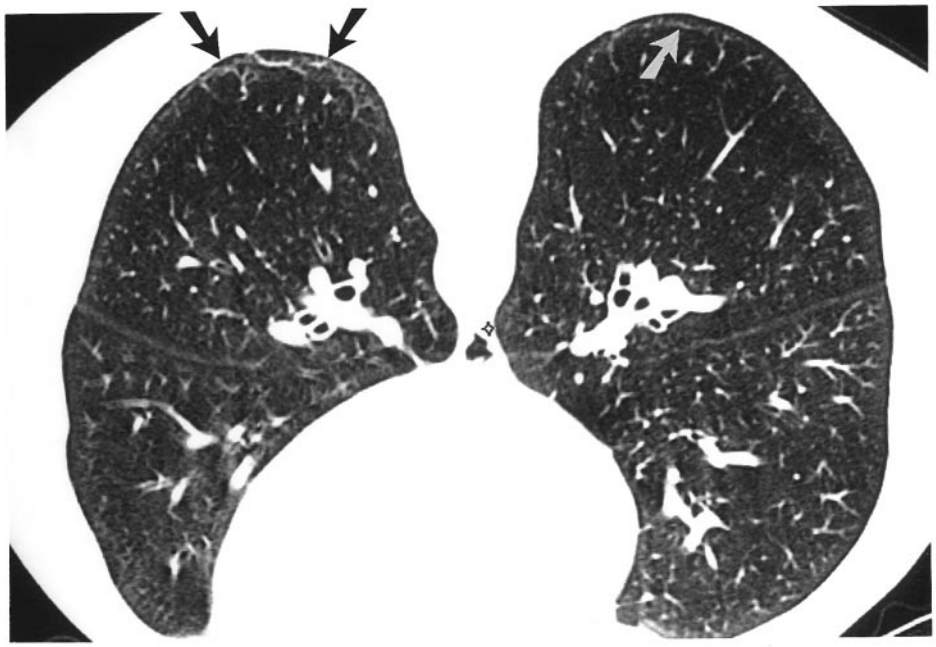

FIG. 4.—Prone HRCT of a 42-yr-old male demonstrates non-specific subpleural band opacities bilaterally (arrows). Lung parenchyma is otherwise normal.

The HRCT findings in this study would favour an inflammatory rather than a mechanical aetiology for the interstitial disease found in our four AS patients. Perhaps our case with a 'ground-glass' appearance on HRCT represents the early stage in the evolution toward interstitial fibrosis. It should also be noted that this interstitial process occurred in the absence of apical disease in two cases. This, together with the distinct HRCT appearance between disease in the lung apex and interstitial disease in the bases and mid-zones, suggests that the aetiology of these pathologies may indeed be distinct.

Eleven patients had non-specific interstitial change, which implied HRCT evidence of interstitial change that was of insufficient severity or extent to be labelled as ILD (Fig. 4). This patient group did not differ significantly from those with ILD in terms of age, disease duration or smoking history. Only two, however, were symptomatic and four had abnormal PFTs (three restrictive and one with an isolated reduction in DLCO). The significance of such change on HRCT is unknown. A prospective study of these patients to determine the natural history of this change would be of obvious interest.

Of the remaining 11 patients with no evidence of ILD or non-specific interstitial change on HRCT, none was symptomatic and only two had abnormal PFTs, both of which were obstructive. Three of these 11 patients had an abnormality on HRCT: two with bronchiectasis and one with paraseptal emphysema (grade 1).

The other principal abnormality picked up on HRCT was bronchiectasis, which was found in six cases, two of which were secondary to apical fibrosis. Pleural thickening was found only in association with apical fibrosis, supporting the previous opinion that non-apical fibrosis is an incidental finding in AS patients.

In conclusion, this study reports for the first time the correlation of the HRCT findings of the entire lung parenchyma in AS with the previous conventional parameters of clinical examination, pulmonary function testing and plain radiography. It raises the possibility of a primary association between AS and ILD. In addition, it highlights the inability of clinical examination or conventional radiology to pick up such disease and the insensitivity of pulmonary function testing to detect interstitial change in AS. HRCT offers a very useful non-invasive tool for the detection of ILD and the investigation of AS patients with respiratory symptoms. We accept that a major limitation of the study was the absence of a control group and further accept that the population examined in this study probably represents individuals with disease of greater severity than a random group of AS patients, but feel that this report should prompt the examination of further populations of AS patients for evidence of ILD and efforts to correlate HRCT findings with histological examination of the lung parenchyma.

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