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HIGH-RESOLUTION COMPUTED TOMOGRAPHY IN HYPERSENSITIVITY PNEUMONITIS - CORRELATION WITH PULMONARY FUNCTION

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Abstract: In 20 patients with chronic form of hypersensitivity pneumonitis (HP) pulmonary function tests (FEV_1, FVC, DCO) and high resolution computed tomography (HRCT) scans were obtained. Extent of pathological changes, i.e. nodularity, lines, honeycombing but not ground-glass estimated by HRCT and expressed as a score correlated significantly with lung function abnormalities.

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INTRODUCTION

Hypersensitivity Pneumonitis (HP) is an interstitial lung disease caused by an immune response to a variety of inhaled organic antigens. The commonest examples are farmer's and bird fancier's disease, although many other agents and modes of exposure are now recognized [1]. The clinical presentation may by mainly categorized as acute and chronic forms. The diagnosis of HP requires a correlation of exposure history, laboratory data (serum precipitins), pulmonary function tests showing a restrictive defect with decreased diffusion capacity, radiological findings, bronchoalveolar lavage data, and in some cases, histological data [1, 2, 15]. The use of chest radiographs has been an important diagnostic procedure in HP patients. More recently, high resolution computed tomography (HRCT) - more sensitive and more specific than chest X-ray - has become a very useful tool in the differential diagnosis and monitoring of HP patients [2, 3, 10]. HRCT features in acute and chronic HP are well documented [3, 4, 5, 7, 11, 13] and in the main the various HRCT patterns correlate with known pathologic components of the disease [2, 5, 8]. However, opinions about relationships between HRCT abnormalities and functional impairment in different forms of disease may be sometimes conflicting. The aim of our study is to correlate the HRCT main abnormalities (i.e. nodular, septal, ground-glass and honeycombing patterns) seen in the chronic form of HP with pulmonary function test results.

MATERIAL AND METHODS

The studied group consisted of 20 patients with HP (9 females and 11 males) aged 28–68 years (mean 44 years) diagnosed and followed-up in the Department of Pneumonology at the Silesian Medical Academy in Zabrze).

The diagnosis of HP was confirmed in all patients with a combination of main diagnostic criteria: evidence of specific antigen exposure, dyspnea on exertion, inspiratory crackles, lymphocyte alveolitis in BAL (bronchoalveolar lavage) [7, 14] and supportive findings, i.e. infiltrates on chest radiographs and HRCT, positive serum precipitins in all patients (serum-precipitating IgG antibodies against the offending antigens, i.e. Saccharopoly-

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spora rectivirgula or pigeons' feathers), decreased diffusion capacity according to previously described criteria [6, 15]. According to described criteria, in 14 patients farmer's lung and in 6 bird fancier's lung were finally recognized. All patients were non-smokers and had chronic disease. Sixteen of them were previously treated with glucocorticosteroids. Mean duration of the disease was 26 ± 13 month.

Pulmonary function tests comprising flow-volume spirometry (FVC-forced vital capacity, FEV_1 - forced expiratory volume in 1 sec.) and diffusion capacity for carbon monoxide (DCO) were performed within 1 week of HRCT examination using Transfer screen -2 (Jaeger, Germany). Methodology details of spirometry and diffusion capacity measurements were described by Quanjer [12]. Obtained values were expressed as a percent of the prediction, according to Quanjer [12].

High resolution computed tomography scans were obtained using Somatom ARC (Siemens, Germany), as described previously by Remy-Jardin *et al.* [13] and Ziora *et al.* [16]. Patients underwent scanning in supine position and the study consisted of scans with a 2 mm thickness obtained at 10 mm intervals from the lung apices to diaphragm at the suspended end-inspiratory volume with 1 second scanning time. All images were obtained at window levels appropriate for evaluation of lung parenchyma (window width 1600 HU (Hounsfied units) and window height -600 HU. CT scans were interpreted independently by radiology and pulmonology specialist in random order without knowledge of the clinical and functional status of patients.

Each of the following HRCT signs was separately coded as present or absent: a) parenchymal micronodules (nodules) were defined as rounded lesions less than 7 mm in diameter, b) ground glass attenuation (ground glass) defined as an area of increased attenuation, c) linear attenuation (lines) appeared as septal lines (thickened interlobular septa), or as polygonal lines and as nonseptal lines, d) honeycombing, defined as areas of cystic spaces with thickened walls. Traction bronchiectases, distortion of lung architecture, air trapping or emphysema were also taken into consideration but for these pathological abnormalities no correlations with lung function parameters were performed. To determine the distribution of parenchymal abnormalities, each lung was divided into three zones: the upper zones - superior to the level tracheal carina, the middle zones - between the level of the carina and the level of inferior pulmonary veins, and the lower zones-inferior of the level of the inferior pulmonary veins [13]. Intensity of parenchymal nodules, lines, ground-glass and honeycombing was determined with the scoring system according to Remy-Jardin et al [13]. Scoring was done for each zone, for left and right lung separately (six regions per subject). A gradation of 0-3 was given for each zone. For each descriptor a score 0 represented no anomaly, score 1 - involvement of <25% of examined zone, score 2 - involvement 25-50% and score 3 > 50% [13]. Therefore the maximal, hypothetical score was 18. An additionally summarized score for all the above mentioned four patterns was calculated in the same way.

Statistical analysis was performed with Statistica 6.0. Data were expressed as mean ± standard deviation. Non-parametric tests (Mann-Whitney U test, Spearman's) were applied for calculation and p value <0.05 was assumed as statistically significant.

RESULTS

In all but one patient the restrictive spirometric disturbances (FVC and FEV_1 below the lower limit and $FEV_1/FVC \geq 75\%$), and in all patients a diminished diffusion capacity (DCO) was observed. No significant increase of FEV_1 (i.e. 12% of predicted) was observed after 2 puffs of Salbutamol MDI (Polfa). The mean percentages of predicted values of the pulmonary function test results are presented in Table 1.

In the examined group the most frequent HRCT pattern was a micronodular pattern (n = 20 i.e.100%) without any zonal predominance, followed by a honeycomb pattern seen in 16 (80%), mainly in the middle and lower lung zones, linear pattern (randomly distributed), seen in 14 (70%) and ground-glass pattern, also randomly distributed and observed in 11 (55%) subjects. In 13 (65%) patients, all 4 categories of HRCT abnormalities, mentioned above,

Table 1. Mean values of lung function parameters and mean HRCT-score values in examined patients with HP.

Parameter	Mean ±SD
FEV_1 (% of predicted)	63.8±18.6
FVC (% of predicted)	62.9±20.3
DCO (% of predicted)	42.3±25.9
Score for:	
nodules	5.29±2.6
lines	3.18±2.2
ground-glass	3.01±2.4
honeycombing	3.71±2.7
summarized score	5.29±2.6

Table 2. Correlation coefficients between HRCT-score pattern and pulmonary function parameters.

	nodules	lines	Ground-glass	honeycombing	Summarized score
FEV_1					
r	-0.80	-0.89	-0.11	-0.72	-0.89
p	0.03	0.008	0.81	0.006	0.008
FVC					
r	-0.83	-0.85	-0.14	-0.76	-0.85
p	0.0019	0.016	0.077	0.046	0.002
DCO					
r	-0.76	-0.87	0.19	-0.62	-0.87
p	0.048	0.012	0.69	0.14	0.012

occurred concurrently. In 9 patients the parenchymal small areas of low attenuation suspected on emphysema and air trapping were also present.

The highest mean HRCT score (5.29) was stated for the nodular pattern, and the lowest (3.0) for the ground-glass pattern (Tab. 1). Mean value of summarized score for all 4 examined patterns was exactly the same as that achieved for nodules.

Both nodular and reticular pattern correlated negatively and strongly with FVC, FEV_1, DCO ($p < 0.05$) (Tab. 2). The scores for honeycombing pattern correlated significantly and negatively only with FVC ($r = -0.76$ $p < 0.05$). No relationship between ground-glass pattern and pulmonary function was noticed (Tab. 2). The relationship between summarized score and lung function was exactly the same as for the mean nodular score (Tab. 2).

DISCUSSION

The different patterns of HRCT in chronic HP include not only fibrotic changes (i.e. reticular opacities or honeycombing) but also centrilobular nodules, ground-glass opacifications, air-space consolidation, mosaic perfusion, air-trapping or mixed opacities [2, 3, 5, 10, 11, 13]. The present study confirms these observations and support the opinion that the extent of all parenchymal pathological changes, revealed by HRCT, contribute to lung function impairment [5, 10, 13].

Poorly defined small nodular opacities with centrilobular distribution are seen mainly in the subacute form of disease, recognized by some authors [5, 9, 13], and also in chronic forms of HP [5, 9, 13]. Histologically, nodules correspond to the presence of poorly marginated granulomas and active alveolitis around the central area of the lobule [2, 5, 10]. On HRCT these centrilobular nodules are often associated with larger areas of ground-glass.

Interestingly, unlike other authors [5, 13] we have found a relatively strong correlation between nodules and examined spirometric and diffusion parameters, which suggests that the presence of intraluminal granulation tissue in bronchioles and adjacent alveoli may impair the ventilatory and diffusion capacity in HP patients. However, nodules seen in examined patients coexisted with other HRCT abnormalities, i.e. lines, honeycomb and ground-glass, which may additionally influence lung function impairment. It should be underlined that the score system applied in this study, as in other studies [4, 5, 13], helped us to estimate only pathologically changed areas of lung parenchyma below 25%, equal to 25–50% and above 50% of it's surface. Hence, the summarized score for all superimposed patterns may be not only hypothetically but practically equal to the score for each of the other patterns.

The lack of correlation between the extent of ground-glass opacification and the relevant lung function abnormalities may reflect the complex and variable derangement of conducting airways and gas exchange surface that occurs in HP. Another factor that may obscure the functional contribution of ground-glass pattern are difficulties in identification and recognition of this abnormality. Additionally, we found the relatively low extensiveness (expressed as ground-glass score) of this pattern in the studied group with chronic HP. In the study by Hansell *et al.* [5] ground glass opacification and reticulation (lines pattern) correlated independently with restrictive lung function. We found excellent negative correlations between fibrotic changes (lines score) and FVC, FEV_1 and DCO.

In the chronic form of HP, fibrotic changes include irregular linear opacities, honeycombing and traction bronchiectases. These findings are rather nonspecific and overlap those for other chronic lung diseases, such as advanced sarcoidosis, usual interstitial pneumonia, or collagen vascular disease [3]. However, in HP fibrotic changes predominate in mid-lung zones with relative sparing of apices and bases and need not be subpleural [3, 10, 11].

Honeycombing, usually considered the main feature of chronic forms of HP [2, 3, 5, 13], was identified in all the presented patients with chronic farmer's lung or bird breeder's lung. Remy-Jardin *et al.* [13] found this abnormality without any zonal predominance in only 50% of examined patients with chronic bird breeder's lung. The concurrent presence of ground-glass attenuation or micronodules on CT scans obtained in patients with honeycombing strongly suggests eventual acute or subacute changes superimposed on chronic disease [5, 13]. Our results seem to support this opinion.

In patients with HP, both in acute and chronic stages, the coexisting emphysematous changes and air trapping due to bronchiolitis are often revealed by HRCT, which may explain eventual obstructive spirometric disturbances coexisting with restriction and diminished diffusion [4, 5, 9]. In our studied group, there predominated restrictive and diffusion lung function abnormalities and were characterized for chronic HP [1, 6]. However, unfortunately, body-pletysmography was not performed in all our examined patients; therefore the results of body-pletysmography measurements were not included in this study. Nevertheless, HRCT findings in our study also confirm previous observations [4, 5, 13] that emphysema must be considered as a integral part of the chronic form of HP. Eventual emphysematous areas should be differentiated with caution from patchy areas of air trapping on expiratory views reported with a variable frequency in chronic HP [10]. On expiration, HRCT scans air trapping appears as areas that fail to increase in attenuation, as expected in a normal lung. On inspiration, HRCT views areas of decreased attenuation adjacent to areas of high attenuation and may indicate mosaic perfusion due to shunting of blood away from poorly ventialated regions of the lung [11]. We, like others [5, 13], have included only inspiratory HRCT scans for scoring mainly fibrotic and nodular changes, without a complicated score system for small areas of emphysematous patterns.

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