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Correlation of ultrasound B-lines with high-resolution computed tomography in antisynthetase syndrome

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ABSTRACT

Objective. *Interstitial lung disease is a common finding in patients with the antisynthetase syndrome. High-resolution computed tomography is the reference test for diagnosis and follow-up of this condition, but it involves considerable radiation exposure. Our aim was to describe chest ultrasound features and its correlation with high-resolution computed tomography findings in a series of patients with the antisynthetase syndrome.*

Methods. *The study included patients from our antisynthetase syndrome cohort with varying degrees of interstitial lung disease, consulting in our outpatient clinic over a 1-year period. Chest high-resolution computed tomography and chest sonography were prospectively performed within a 1-week period. High-resolution computed tomography Warrick score was calculated and chest sonography findings (B-lines) at several sonographic points along the anterior and posterior intercostal spaces were semi-quantitatively analyzed. Rho Spearman statistics were applied for possible correlations.*

Results. *Twenty-one consecutive patients were studied. A median of 59 thoracic points was studied per patient (IQR 6); 44.1% (95% CI 29.9–60.7) of them showed at least one B-line. A correlation coefficient of 0.135 (p=0.5) was found between the percentage of ultrasound points with B-lines and the Warrick ´s score. Only the number of bronchopulmonary segments showing ground glass findings was associated with the percentage of sonographic points with B-lines (Rho=0.5, p=0.02).*

Conclusion. *A good correlation between the percentage of sonographic points with B-lines and high-resolution computed tomography ground glass opacities was observed in patients with the antisynthetase syndrome.*

Introduction

In 1984, Hochberg *et al.* (1) described a clinical syndrome characterised by arthritis and myositis associated with interstitial lung disease (ILD). Autoantibodies directed against the aminoacyl-transferRNA synthetases, a group of cytoplasmic enzymes that catalyse binding of an amino acid to its cognate tRNA, were associated with this condition, which is known as antisynthetase syndrome.

Pulmonary function testing and chest computed tomography (CT) studies are generally used to evaluate ILD over time. The oncogenic potential associated with ionising radiation received during medical testing is a well-recognised concern, particularly in relation to CT (2). Alternative imaging methods that do not involve ionising radiation such as chest ultrasound (US) study have emerged over recent years to monitor patients with ILD, as is the case of scleroderma-related ILD (3-5).

Hyperechoic, wedge-shaped, linear images perpendicular to the pleural surface (B lines) are US findings resulting from thickening of the interlobular subpleural septa. This feature is an indication of interstitial lung involvement of any aetiology, such as fluid accumulation (pulmonary oedema) or, as in antisynthetase syndrome, pulmonary alveolitis/fibrosis (6).

Our objective in this study was to analyse whether the presence of B lines detected by chest US was related with chest CT findings in the evaluation of antisynthetase-associated ILD in a cohort of patients from a single centre.

Patients and methods

Patient population

This study includes patients from our antisynthetase syndrome cohort with varying degrees of ILD, who consecutively consulted in our specialised outpatient clinic in Barcelona (Spain) from January to December 2011. The diagnosis of dermatomyositis/polymyositis (DM/PM) was established on the criteria of Bohan and Peter (7); all patients with myositis met the criteria for probable or definite DM/PM. Interstitial lung disease was diagnosed according to the ATS criteria (8). Independent operators who were not aware of the results of the other tests or the patients' clinical characteristics performed all tests. The principal investigator collected the data as the tests were performed. The hospital ethics committee approved the study protocol [PR (AG) 186/2011] and patients gave informed consent for the tests carried out.

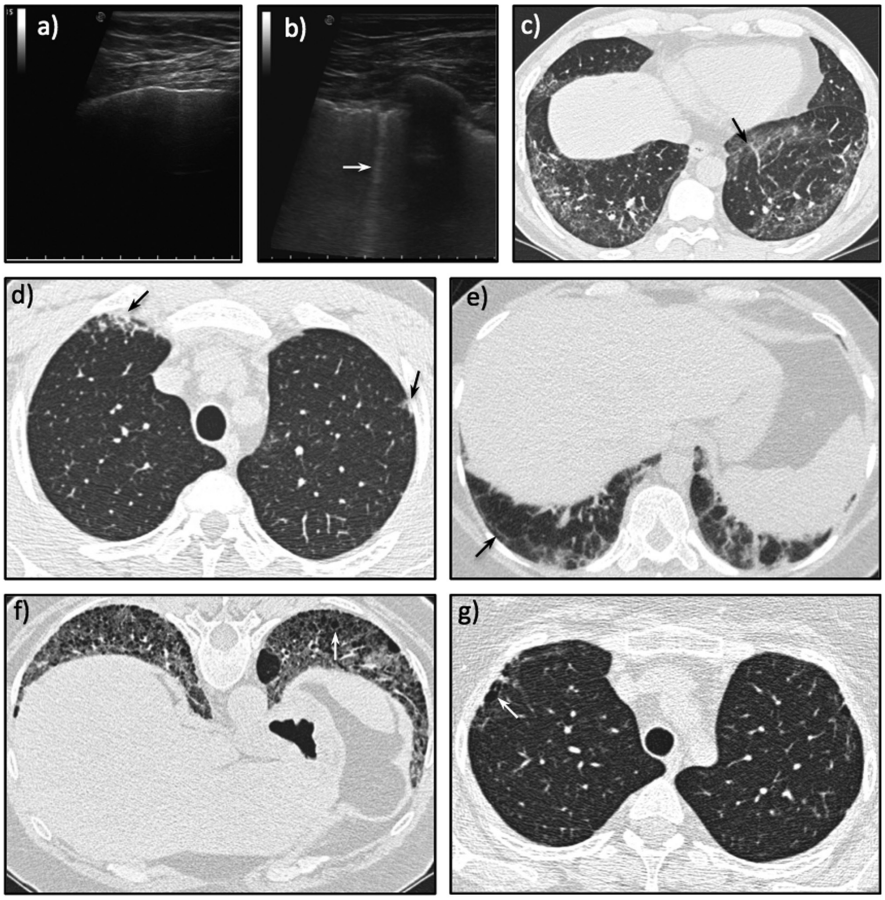

Fig. 1. Images showing: **a**) Normal sonographic point. **b**) Sonographic point with one B-line (white arrow). **c**) Ground glass appearance (black arrow). **d**) Irregular pleural margins (black arrows). **e**) Septal/subpleural lines (black arrow). **f**) Honeycombing (white arrow). **g**) Subpleural cysts (white arrow).

High-resolution chest CT

High-resolution computed tomography examinations of the chest were performed on a spiral CT scanner (Philips Brilliance 64) with 64 detector rows and 0.75 s rotation time. All patients underwent a preliminary A-P scout view. Subsequently, 25 to 35 slices were acquired at the end of inspiration, in apnoea, from the lung apex to the base, either in supine or in prone decubitus position. The acquisition parameters were as follows: sequential mode, 1-mm collimation and 10-mm interval, 150 mA average tube current (depending on the patient's build), and 120 kV tube voltage. A bone plus reconstruction with lung window was used. No intravenous contrast material was administered. The duration of CT acquisition was 20 to 30 s, matrix was 512-512 and absorbed dose was in the range 5 to 7 mSv. Pulmonary involvement was quantified through the Warrick score (Fig. 1 c-g) (9).

Chest sonography

Commercially available US equipment was used (MyLabTwice, Esaote, Genoa) with a linear probe (LA 527 with a 5-cm-length, 5 MHz transducer) (10). US examination was performed with patients in supine position to record the anterior sonographic points (up to 28), and in sitting position for the posterior ones (up to 44). The 72 sonographic points corresponded to the anatomical distribution defined by Gargani (3). We excluded sonographic points with scarce lung parenchyma or absence of pleural interface, where B-lines cannot be detected. B-lines were defined as discrete laser-like vertical hyperechoic reverberation artifacts that arise from the pleural line, extend to the bottom of the screen without fading, and move synchronously with lung sliding (Fig. 1 a-b) (6).

Statistical analysis

It was a convenience sample; all patients fulfilling inclusion criteria during the study period were invited to participate. Continuous variables are expressed as median, first and third quartiles (Q1-Q3). Percentages are expressed with the 95% confidence interval (95% CI), when appropriate. A positive sonographic point was defined as a point with any number of B-lines (making unnecessary to set a maximum of B-lines, seeking to increase the reproducibility of the study). To properly describe the results on B-lines and to adjust the results to the patient´s lung size (thus avoiding to underscore patients with small lungs due to ILD), we calculated the percentage of positive sonographic points by dividing the number of positive sonographic points by the number of sonographic points studied per patient. The correlation between the percentage of positive sonographic points and the HRCT scan findings was calculated using Spearman's Rho (ϱ).

Statistical analysis was performed using SPSS v.15. Significance was set at a p value of less than 0.05. Microsoft Excel software was used for the anatomic distribution tables.

To assess intra-observer and inter-observer reliability, the semi-quantitative scoring terms were calculated by a kappa statistic. A kappa value of 0 to 0.20 was considered poor, 0.21 to 0.40 fair, 0.41 to 0.60 moderate, 0.61 to 0.80 good, and 0.81 to 1.00 excellent.

Results

Over the 12-month study period, 21 consecutive patients (median age 48 [Q1-Q3: 39-64] years, 13 females) with antisynthetase syndrome and varying degrees of ILD, followed-up at our outpatient clinic were studied. No patients were lost during the study. Seventeen patients tested positive to anti-Jo-1, two to anti-PL-12, and two more to anti-PL-7. These patients were classified as having probable or definite DM (13 cases) or PM (6 cases); the remaining patients (2 cases) had pure antisynthetase-associated ILD, without myositis.

Descriptive analysis

A median of 59 (Q1-Q3: 58-63) sonographic points were examined per patient, and a median of 26 (Q1-Q3:

18-36) points showed B-lines, representing 44.1% (95% CI 29.9%-60.7%) of all sonographic points studied. The kappa value for intraobserver and interobserver reliability to assess ultrasound points was 0.83 and 0.76 respectively. B-lines were most often found in the lower posterior and upper anterior areas (Fig. 2). Ten bronchopulmonary segments (Q1-Q3: 7-13) were affected by any sign of interstitial lung disease. The median Warrick score was 15 (Q1-Q3: 13-22), with ground glass opacities affecting the largest number of segments (median 10 [Q1-Q3: 6-12]), followed by irregular pleural margins (median 6 [Q1-Q3: 4-10]), and septal/subpleural lines (median 6 [Q1-Q3: 0-10]).

Correlations between pulmonary function testing, HRCT findings and US lung comets

A correlation coefficient of 0.135 (p=0.559) was found between the percentage of US points with B-lines and the Warrick's score. When correlation with the different components of Warrick's score was analysed, only the number of HRCT segments showing ground glass opacities was related to the percentage of US points with B-lines (Rho=0.502; p=0.02). The correlation coefficient between the number of HRCT affected bronchiopulmonary segments and the percentage of sonographic points with any B-lines was 0.401 (p=0.07).

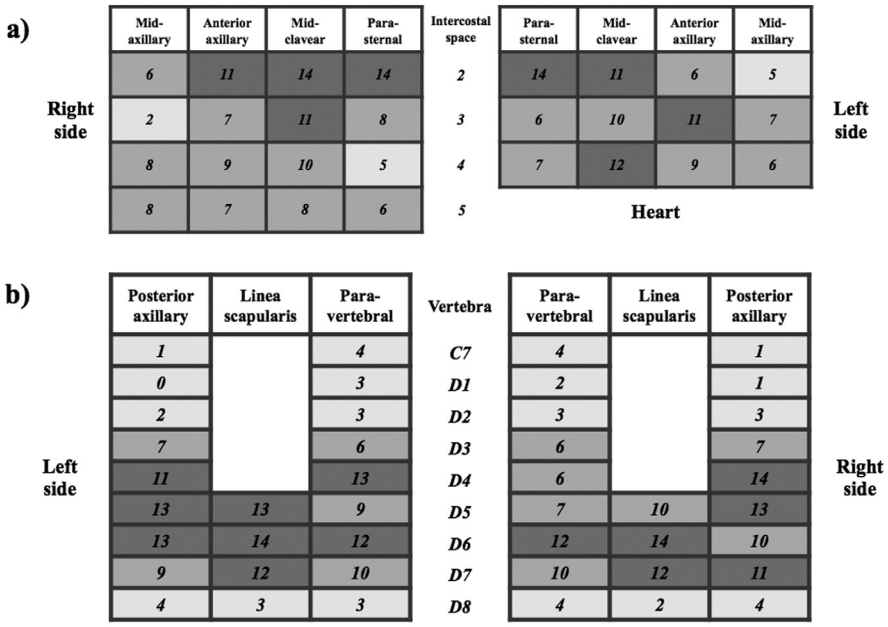

Fig. 2. Anatomic distribution of the B-lines. Each field contains the absolute frequency of positive sonographic points of our sample of patients. Lower posterior and upper anterior areas were the most often affected.

Discussion

In this study performed in a cohort of patients with the antisynthetase syndrome, a good correlation was found between the presence of ground glass opacities on HRCT and the percentage of sonographic points showing B-lines. Several recent studies have focussed on assessing ILD with chest US in patients with connective tissue disorders, mainly systemic sclerosis (3). To the best of our knowledge, only two patients with antisynthetase syndrome have been studied in this manner (11, 12).

Gargani *et al*. reported a good correlation between pulmonary interstitial fibrosis and US B- lines, mainly in patients with systemic sclerosis (3). Although similar results were obtained when patients with other connective tissue disorders and ILD were analysed, the small number of cases studied precludes generalising the data obtained (11, 12). Thus, there is a need to investigate the performance of US in a relatively large cohort of patients diagnosed with antisynthetase-associated ILD to ascertain the utility of this technique for evaluating ILD in these patients.

Ground glass opacities can be considered an early chest HRCT finding in some cases of ILD. Several studies have related the presence of ground glass opacities with the existence of non-specific interstitial pneumonia (NSIP), which seems to be the most representative pathological finding in patients with antisynthetase-associated ILD (13-15). Therefore, a correlation between ground glass opacities and percentage of sonographic B-lines would support the utility of chest US in the initial assessment and follow-up of ILD in patients with antisynthetase syndrome. Considering that ground glass opacities seem to be a surrogate marker of alveolitis and/or NSIP, which seems to respond to immunosuppressive therapy, the possibility that this finding could be detected by US imaging, a widely available, inexpensive and non-ionising technique deserves consideration.

Our study has the limitation of a relatively small number of patients included. It should be seen as an exploratory study on chest US evaluation in antisynthetase-associated ILD that is, to some extent, confirmatory of the results previously reported in systemic sclerosis and other connective tissue disorders.

Despite these limitations, the correlation between ground glass opacities and ultrasound B- lines can be considered a relevant finding. Although chest HRCT is now considered the reference standard test for diagnosing ILD, serial examinations with this technique expose the patient to undesirable ionizing radiation exposure. Therefore, other techniques should be considered in the assessment and follow-up of ILD. Chest US may be a good option in patients with antisynthetase syndrome.

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