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<center>Serial CT and lung function testing in pulmonary Langerhans cell histiocytosis</center>

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Lung HRCT analysis and methods used to determine the semi-quantitative nodular and cystic scores.

The lung CTs were obtained with different multidetector helical scanners during breath holding at the end of inspiration with the patient lying in the supine position. All of the patients underwent HRCT, with a reconstructed section thickness of 1 mm or less and a high-spatial frequency algorithm. The images were obtained at window levels appropriate for the pulmonary parenchyma (widths of -600-1600 HU).

The different pulmonary abnormalities were classified as micronodules (<5 mm), nodules (5-10 mm), cavitary nodules, and thick- and thin-walled cysts. Each lung was divided into 3 areas, from the lung apices to the domes of the diaphragm: the upper level was from the lung apex to the carina, the middle level was between the carina and the lower pulmonary veins, and the lower level was from below the lower pulmonary veins to the diaphragm. Each zone was assessed for the presence, type and extent of lung abnormalities.

The following values were attributed to the extent of the nodular lesions (including micronodules, nodules and cavitary nodules): 0 (no nodules), 1 (mild), 2 (moderate), and 3 (diffuse nodules) (fig.E1). The global nodular CT score was obtained by adding the nodular scores for the lung zones defined above. Thus, the nodular HRCT score for the entire lung could vary from 0 to a maximum value of 18.

The extent of the cystic lesions (including thick- and thin-walled cysts) was assessed for each of the defined lung areas on the HRCT and classified by the percentages of the lung

surface analyzed: 0 (no cyst); 1 (<25%); 2 (25-49%); 3 (50-75%); and 4 (>75%) (fig.E2). The maximal value of the cystic HRCT score for the entire lung was 24.

The patients were divided into 3 subgroups based on their CT nodular scores (low (0-6), intermediate (7-12), and high (13-18)) and into 4 subgroups to reflect the extent of their cystic lung lesions (low (≤6), intermediate (7-12), high (13-18) and very high (19-24) CT cystic score). Transitions in the nodular or cystic HRCT scores from one subgroup to another during follow-up were considered significant.

Figure Legends

FIGURE E1 Representative sections used for calculating the lung HRCT nodular scores: A

(rare, score value=1), B (moderate, score value=2), and C (diffuse, score value=3).

FIGURE E2 Representative sections used for calculating the lung HRCT cystic scores, expressed as a percentages of the lung surface analyzed: A (<25%, score value=1), B (25-49%, score value=2), C (50-74%, score value=3) and D (≥75%, score value=4)