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Computed tomographic features of lymphangioleiomyomatosis: Evaluation in 138 patients

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ABSTRACT

Purpose: The aim was to characterize the computed tomographic (CT) findings from Japanese patients with lymphangioleiomyomatosis (LAM).
Materials and methods: CT scans of the chest, abdomen, and pelvis from 124 patients with sporadic LAM (S-LAM, mean age, 37.4 years) and 14 patients with tuberous sclerosis complex (TSC)-LAM (mean age, 35.6 years) were analyzed.
Results: Pulmonary nodules (18.8%) and hepatic angiomyolipoma (AML, 24.3%) were more common in our patients than those in previous reports. Compared with TSC-LAM, S-LAM group had a higher frequency of pulmonary nodules (28.6% vs 32.3%, $P < 0.01$) and lower frequencies of air-space consolidation (21.4% vs 2.4%, $P < 0.01$), pneumothorax (28.6% vs 8.1%, $P = 0.02$), pulmonary hilar lymphadenopathy (14.3% vs 0.8%, $P < 0.01$), renal AML (85.7% vs 17.4%, $P < 0.01$), hepatic AML (71.4% vs 17.4%, $P < 0.01$), and retrocrural lymphadenopathy (14.3% vs 1.4%, $P = 0.04$). Axial lymphatic abnormalities (i.e., thoracic duct dilatation, lymphadenopathy, and lymphangioleiomyoma) were most common in the pelvis and tended to decrease in incidence with increased distance from the pelvis.
Conclusion: The incidence of some CT findings in Japanese patients differed from those in previous reports. Axial lymphatic abnormalities noted here suggest that the origin of LAM cells may be the pelvis.

1. Introduction

Lymphangioleiomyomatosis (LAM) is an uncommon disease in females of child-bearing age and is characterized by the proliferation of abnormal smooth muscle cells (LAM cells) in the lungs and along the axial lymphatic system of the thorax, retroperitoneum, and pelvic cavity. LAM occurs in approximately 30% of females with tuberous sclerosis complex (TSC-LAM), although LAM also occurs in females without TSC (i.e., sporadic LAM [S-LAM]) [1]. Both TSC-LAM and S-LAM are associated with mutations in the *TSC* genes. A diagnosis of LAM is usually made when warranted by clinical history and a pathognomonic appearance of pulmonary cysts on chest computed tomography (CT) or identification in a pathology report of LAM cells [2,3]. Recently, clinical and radiographic characteristics of patients with LAM were described based on the analyses of a large series of patients in National Heart, Lung, and Blood Institute (NHLBI) LAM registry [4–6]. In our country, clinicopathologic findings of 46 patients with LAM were already reported [2]; however,

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no comparable radiologic investigations have been done. Therefore, we retrospectively examined the CT images from a large series of Japanese patients with LAM to clarify the spectrum and prevalence of radiologic findings in our country.

2. Materials and methods

2.1. Patients

This retrospective study was approved by the ethics committee of our institution (JIRB21-134). We evaluated 138 females, including 124 patients with S-LAM (age range, 21–61 years; mean, 37.4 years) and 14 patients with TSC-LAM (age range, 25–50 years; mean, 35.6 years) who had undergone at least one of the following examinations at our hospital between May 1990 and November 2009: chest CT scans (138 patients; age range, 21–61 years; mean, 37.3 years), abdominal CT scans (72 patients; age range, 22–61 years; mean, 36.9 years), and pelvic CT scans (69 patients; age range, 22–61 years; mean, 37.0 years). All patients were studied when there was no evidence infection and large pneumothorax (the presence of a visible rim of $\geq$2 cm between the lung margin and the chest wall). Thirty-three of 138 patients had smoking history (mean, 7.6 pack-year). Each diagnosis was established based on biopsy findings of the lungs, lymphangioleiomyoma (LALM), lymph nodes (LNs), and uterus, respectively, in 92, 18, 3, and 1 patients. One patient was diagnosed based on a cytological study of the pleural fluid. Twenty-three patients did not undergo tissue biopsies, but had characteristic clinical pictures (recurrent pneumothorax and/or chylous pleural effusion) and CT findings (diffusely scattered thin-walled pulmonary cysts). Fourteen patients with TSC were diagnosed based on established clinical criteria [7].

2.2. CT technique

All chest CT scans were obtained at the end of inspiration by the patient in a supine position. The scanning protocol consisted of reconstruction of 1–5-mm collimation sections with a high spatial frequency algorithm at 1- or 2-cm intervals. Contrast material-enhanced abdominal and pelvic CT scans were performed in 62 and 60 patients, respectively, 100 ml of iohexol [Omnipaque 300] (Daiichi-Sankyo, Tokyo, Japan) or of iopamidol [Iopamiron 300] (Bayer Schering Pharma, Osaka, Japan). The remaining patients did not receive intravenous contrast material due to a history of either allergic reactions or poor renal function.

2.3. CT image analysis

Four radiologists, each with over 15 years of experience in chest, abdominal, and pelvic CT imaging, worked independently and had knowledge of the diagnosis (LAM only). These observers, all of whom were blinded to any other clinical information about the patients, were divided into two groups and reviewed the images in random order. Disagreements regarding the CT findings were resolved by consensus between the two groups. The CT scans were obtained on a variety of scanners. Images were evaluated on the film images or a monitor: (chest, 30 patients on film images and 108 patients on a monitor; abdomen, 27 patients on film images and 45 patients on a monitor; and pelvis, 25 patients on film images and 44 patients on a monitor) at window settings appropriate for viewing the lung (window level from −500 to −800 HU; window width from 1000 to 2000 HU), the mediastinum (window level from 15 to 40 HU; window width from 300 to 400 HU), and the abdomen and pelvis (window level from 15 to 40 HU; window width from 300 to 400 HU).

2.4. Chest CT image interpretation

Pulmonary cysts, noncalcified pulmonary nodules, ground-glass opacity, air-space consolidation, thickening of the bronchovascular bundles, interlobular septal thickening, thoracic duct dilatation, pneumothorax, pleural effusion, and lymphadenopathy (of the pulmonary hilum, mediastinum, supraclavicular, and/or axillary regions) were evaluated (see online supplementary materials for further details).

2.5. Abdominal and pelvic CT image interpretation

The abdominal and pelvic CT findings included hepatic and renal masses, LALM, lymphadenopathy (of the retrocrural space, upper abdomen, pelvis, and inguen), and ascites. Hepatic and renal masses were considered to represent angiomyolipomas (AMLs) if they contained fat. More information is provided in the online supplementary material.

2.6. Lymphatic lesions

Solitary masses found in LAM patients were considered to be possible LALMs or lesions of lymphadenopathy. Therefore, we defined "lymphatic lesions" as those involving thoracic duct dilatation, lymphadenopathy, LALM, and/or solitary masses and evaluated the frequency of such lesions in each part of the body.

2.7. Statistical analysis

The interobserver variation of the extent of pulmonary cysts was evaluated using Spearman's rank correlation coefficient. The interobserver variation of the extent and size of various abnormalities was evaluated using a linear regression analysis and Bland–Altman plots [8]. The interobserver variations among findings and the predominant distribution were analyzed using the k-statistic. Interobserver agreement was then classified as poor (0.00–0.20), fair (0.21–0.40), moderate (0.41–0.60), good (0.61–0.80), or excellent (0.81–1.00). The frequencies of various findings were compared using the Chi-square test with appropriate Fisher exact test, and the extent of pulmonary cysts was compared between the S-LAM and TSC-LAM groups using the unpaired t-test. All statistical analyses were performed using the SPSS software program (version 16.0, SPSS Inc., Chicago, IL, USA). The data are expressed as the mean $\pm$ standard deviation (SD). A P-value of less than 0.05 was considered to indicate a significant difference.

3. Results

3.1. Observer agreement

Regarding the chest CT findings, there was moderate to excellent agreement with respect to the extent and size of the pulmonary cysts (Spearman rank correlation coefficient, $r = 0.607–0.942$; $P < 0.001$) and fair to excellent agreement for the extent and size of abnormal lesions (linear correlation coefficient, $r = 0.352–0.942$; $P < 0.001$). Agreement was fair to excellent for the presence of abnormal findings and the characteristics of distribution ($k = 0.228–1.00$); an exception was the presence of pulmonary nodules ($k = 0.200$). Regarding abdominal and pelvic CT findings, the existence of abnormal findings generated good to excellent agreement ($k = 0.655–1.00$) and excellent agreement for the size of abnormal lesions (linear correlation coefficient, $r = 0.947–0.966$, $P < 0.001$), with the exception of the size of intrapelvic solitary masses ($r = 0.215$, $P = 0.580$) (see online supplementary materials for further details). Bland–Altman plots of the two groups' measurements of the extent of pulmonary cysts are shown in Fig. 1.

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