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Comparison of thin-section CT and pathological findings in small solid-density type pulmonary adenocarcinoma: Prognostic factors from CT findings

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ABSTRACT

Objective: We divided pulmonary adenocarcinoma of ≤20 mm into air-containing and solid-density types based on a percentage reduction of the maximum tumor diameter in the mediastinal window image compared to the area in the lung window image on thin-section (TS) CT of ≥50% (air-containing type) and <50% (solid-density type). No relapse occurred in patients with air-containing type. The prognosis of solid-density type may be poor even when the tumor size is 20 mm or smaller. We investigated whether CT findings for these tumors could serve as prognostic factors.
Methods: The subjects were 105 patients with solid-density type pulmonary adenocarcinoma that was identified on TSCT and found to have a diameter of 20 mm or smaller after surgical resection during the period from April 1997 to November 2004. Notches, air bronchogram, pleural retraction, spiculation, venous involvement, and ground glass opacity were examined on TSCT, and their associations with pathological findings (i.e., pleural invasion, lymphatic permeation, vascular invasion, lymph node metastasis, and Noguchi's classification) and relapse were investigated using chi-square test and Cox proportional hazards model.
Results: The incidence of relapse was significantly higher in cases with notches. The incidence of notches increased with tumor growth and notches were frequent in Noguchi type D tumors, reflecting poorly differentiated adenocarcinoma. Lymphatic permeation and type D cases were independent factors associated with a poor prognosis using Cox proportional hazards model.
Conclusions: TSCT findings may be useful for prediction of the prognosis of solid-density type pulmonary adenocarcinoma.

1. Introduction

Discovery of peripheral-type small lung cancer is increasingly common due to the recent introduction of computed tomography (CT) screening and advances in diagnostic imaging devices. Most such cases are adenocarcinoma [1]. The increased number of cases suggests that criteria are needed to establish a treatment policy. A small tumor size suggests a favorable prognosis, but cases of peripheral-type small lung cancer include a malignant subgroup. Patz et al. reported that the tumor size was not correlated with the disease stage or prognosis in lung tumors of ≤30 mm [2], and Noguchi et al. pathologically classified pulmonary adenocarcinoma of ≤20 mm into 6 types and showed the presence of a group with a poor prognosis [3].

We have investigated the relationship of thin-section (TS) CT and pathological findings with the prognosis of small pulmonary adenocarcinoma [4–10]. We divided tumors of ≤20 mm into air-containing and solid-density types based on a percentage reduction of the maximum tumor diameter in the mediastinal window image compared to the area in the lung window image on TSCT of ≥50% (air-containing type) and <50% (solid-density type). Postoperative relapse did not occur in cases with the air-containing type, whereas relapse occurred in about 25% of cases with the solid-density type. This classification permits pathological differentiation of non-invasive tumors that retain the alveolar framework and alveolar air space (air-containing type) from invasive tumors in which the alveolar framework is destroyed and the alveolar air space is lost due

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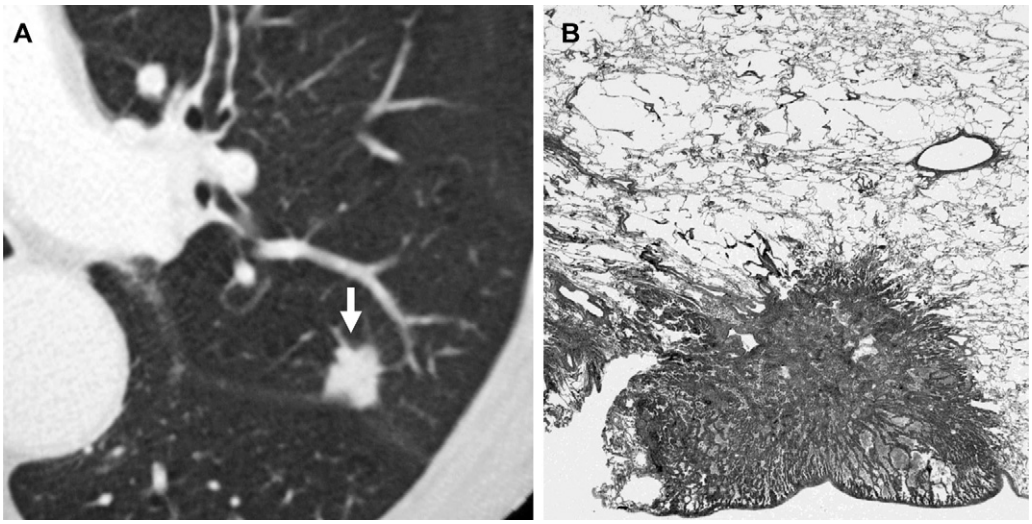

Fig. 1. (A) TSCT scan showing a nodule with a notch (arrow) on a lung window image. (B) Pathologic specimen showing papillary adenocarcinoma with a compressive growth pattern (hematoxylin–eosin, original ×6).

to collagen fibrotic foci (solid-density type). There are several other methods for differentiation based on CT images, but our classification appears to reflect the outcome with higher precision compared to other approaches [9].

The prognosis of solid-density type adenocarcinoma is poor even if the lesion is smaller than 20 mm, but subgroups with favorable and poor prognoses may be present among these cases. In this study, we investigated TSCT and pathological findings for solid-density type pulmonary adenocarcinoma to examine possible associations with prognosis.

2. Materials and methods

We retrospectively reviewed TSCT scan findings and pathologic specimens from 283 consecutive patients who underwent surgical resection for peripheral adenocarcinomas ≤20 mm in diameter during the period from April 1997 to November 2004 at Kanagawa Cancer Center. Of these 283 patients for whom ≥5 years have passed since surgery, 153 had air-containing type pulmonary adenocarcinoma on TSCT and 130 had solid-density type. No relapse occurred in 153 patients with air-containing type. In the 130 patients with solid-density type, 25 patients underwent compromised limited resection because of pulmonary hypofunction, and 105 patients underwent lobectomy combined with systematic hilar and mediastinal node dissection. We investigated these 105 patients this time.

All patients underwent physical examination, chest roentgenography, CT scan of the chest and abdomen, bone scintigraphy, and MRI of the brain for the staging and evaluation of resectability before the operation. No chemotherapy or radiotherapy was performed before or after surgery. This study was approved by our institutional review board after confirmation of informed consent by the patients for us to review their records and images. Chest CT scan images were obtained by a commercially available scanner (X-Vigor/Real or Aquilion M/16 CT scanner; Toshiba Medical Systems; Tokyo, Japan). Conventional CT scan images were obtained serially from the thoracic inlet to the lung bases at 120 kV peak spacing, 512 × 512 pixel resolution, and 1-s scanning time. TS images targeted to the tumor were obtained serially at 120 kVp and 200 mA, with 2-mm section thickness, pitch 1, section spacing of 1–2 mm, 512 × 512 pixel resolution, and 1-s scanning time, using a high-spatial-reconstruction algorithm with a 20-cm field of view. These images were printed as photographs on each sheet of films using a mediastinal window level setting (level, 40 Hounsfield units [HU]; width, 400 HU) and a pulmonary window level setting (level, −600 HU; width, 1600 HU). While contrast medium (60 mL) was infused IV during imaging, lesion sites were translocated in a helical scan mode with a CT scan table speed of 2 mm/s; TSCT scan images were obtained at one breath hold (120 kVp; 200 mA). The time interval between CT scan examination and subsequent surgery was ≤2 weeks in all patients. All CT scan images were reviewed by four thoracic oncologists who were not informed of the pathologic findings. They obtained the maximum dimension of the tumor using a pulmonary window level setting and the maximum dimension of the tumor using a mediastinal window level setting from the TSCT scan images.

The excised lung was distended and fixed by infusion of formalin from the bronchus. The specimen including the maximum cross-sectional area of the tumor was sliced into sections at intervals of a few millimeters in the same direction as the CT image and stained with hematoxylin–eosin.

Preoperative TSCT lung window images were evaluated based on the presence or absence of a notch, air bronchogram, pleural retraction, spiculation, venous involvement, and ground glass opacity (GGO) (Figs. 1–4). The association of these findings with relapse was analyzed using the Kaplan–Meier method followed by a log-rank test. Notches on CT are generally defined as concave cuts, but we strictly included only those in which blood vessels or bronchus was present in the cut. The association of imaging findings with relapse was investigated using a Cox proportional hazards model.

Pleural invasion, lymphatic permeation, vascular invasion, and lymph node metastasis were investigated and Noguchi's classification was determined in pathological preparations of the resected specimens. The association with of these findings with relapse was also investigated using a Cox proportional hazards model. Associations between the imaging and pathological findings were examined using a chi-square test for independence.

3. Results

The patient background is shown in Table 1. There were 53 male and 52 female patients, and the median age was 63 years old. The pathological stage was Ia in 82 cases, Ib in 8, IIa in 6, and IIIa in 9. Relapse occurred in 23 cases (21.9%).

The TSCT findings are shown in Table 2. On lung window imaging, the median tumor size was 18 mm (8–20 mm). Notches were