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Unique clinicopathological characteristics of pulmonary squamous cell carcinoma with part-solid nodule

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Abstract

Chest high-resolution computed tomography (HRCT) finding of part-solid nodule (PSN) is related to pulmonary adenocarcinoma (AC) with lepidic growth. We recently experienced a pulmonary squamous cell carcinoma (SCC) showing PSN pattern on HRCT. We present a 70-year-old man who had a small nodule with PSN pattern in the right lung field on HRCT. After clinical diagnosis of AC, lobectomy was performed. The tumour was pathologically diagnosed as SCC with lepidic growth. Histopathologically, the central area of the tumour showed keratinizing SCC, whereas the peripheral area revealed lepidic SCC cell growth between non-neoplastic type II pneumocytes and alveolar basement membrane. On the basis of the present case and five from the literature, SCC with lepidic growth had the following clinical characteristics: peripheral location, early stage detection, clinical misdiagnosis as AC, less progression, and favourable prognosis. This case may be a special type of SCC with less progression and favourable prognosis.

Introduction

High-resolution computed tomography (HRCT) has recently been widely used as an essential diagnostic tool for lung cancer in routine clinical practice. HRCT is especially useful for detection of small lung cancers. In addition, HRCT images can be used for differential diagnosis of histopathological types of small lung cancers based on the high spatial resolution of the images [1]. Ground-glass opacity (GGO) and part-solid nodule (PSN) are useful findings in HRCT images of small lung cancers. These findings are related to the histopathological types of adenocarcinoma (AC) in situ, early invasive AC, and lepidic AC, and usually exclude clinical diagnosis of squamous cell carcinoma (SCC).

We recently experienced a rare case of pulmonary SCC showing PSN finding on HRCT. Here, we present the clinicopathological details of the case along with a literature review.

Case Report

A 70-year-old man with a smoking history of 50 pack-years had a small nodule in the right lung field on chest X-ray during an annual health check-up (Fig. 1A). HRCT demonstrated a PSN in the peripheral area of segment 10 of the right lung (Fig. 1B, C). The total area of the PSN measured 25 × 20 mm and the solid area 21 × 20 mm. There was no distant metastasis or lymphadenopathy. In routine preoperative laboratory tests, carcinoembryonic antigen (2.2 ng/mL) and cytokeratin-19 fragment (1.2 ng/mL) were within normal ranges. After clinical diagnosis of well-differentiated AC of the right lung, stage IA3-cT1cN0M0 (Union for International Cancer Control TNM classification, version 8), we successfully performed right lower lobectomy and mediastinal lymph node dissection via video-assisted thoracic surgery.

The tumour was pathologically diagnosed as SCC with lepidic proliferation. Macroscopic and representative histopathological findings of the tumour are represented in Figure 2. We compared the HRCT image (Fig. 1B, C) and macroscopic and loupe-level findings of the resected tumour (Fig. 2A, B). The solid and GGO areas of the PSN on HRCT corresponded to central and peripheral areas of the tumour, respectively. Histopathological examination of

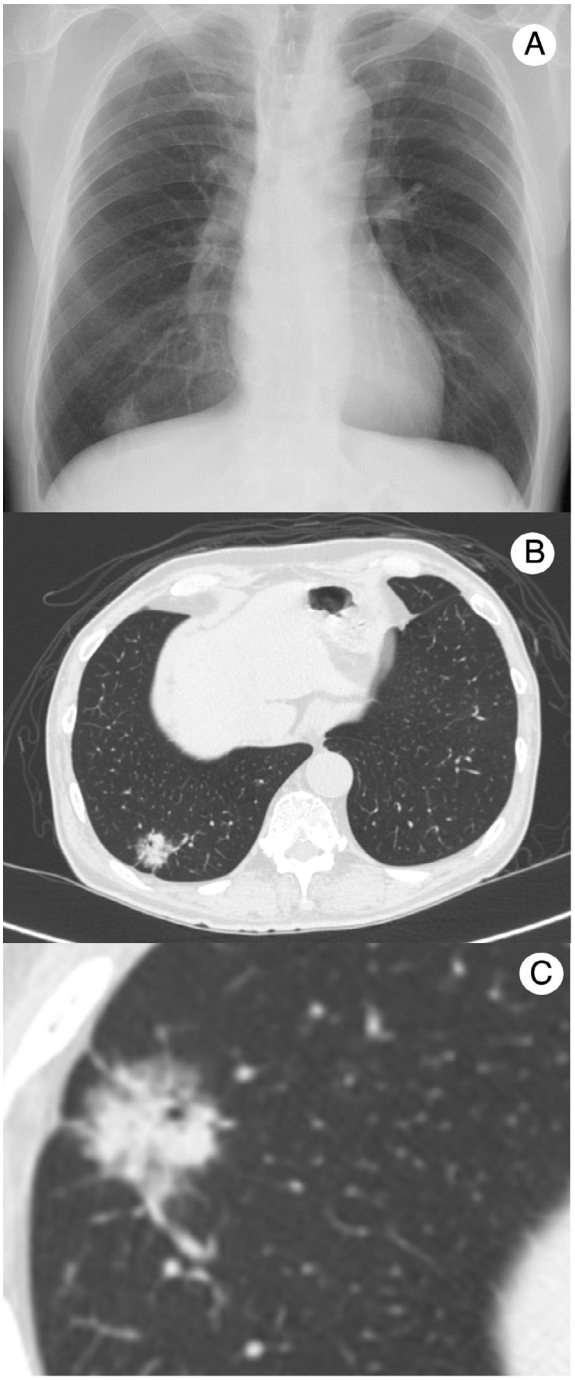

Figure 1. (A) Chest X-ray revealed a small nodule in the right lung field. (B, C) Chest high-resolution computed tomography showed a part-solid nodule measuring 25 × 20 mm (total size) and 21 × 16 mm (solid size) in the S10 area of the right lung.

the central area of the tumour indicated the typical finding of invasive SCC with keratinization (Fig. 2C). In the peripheral area of the tumour, we detected a lepidic growth pattern represented by carcinoma cells between

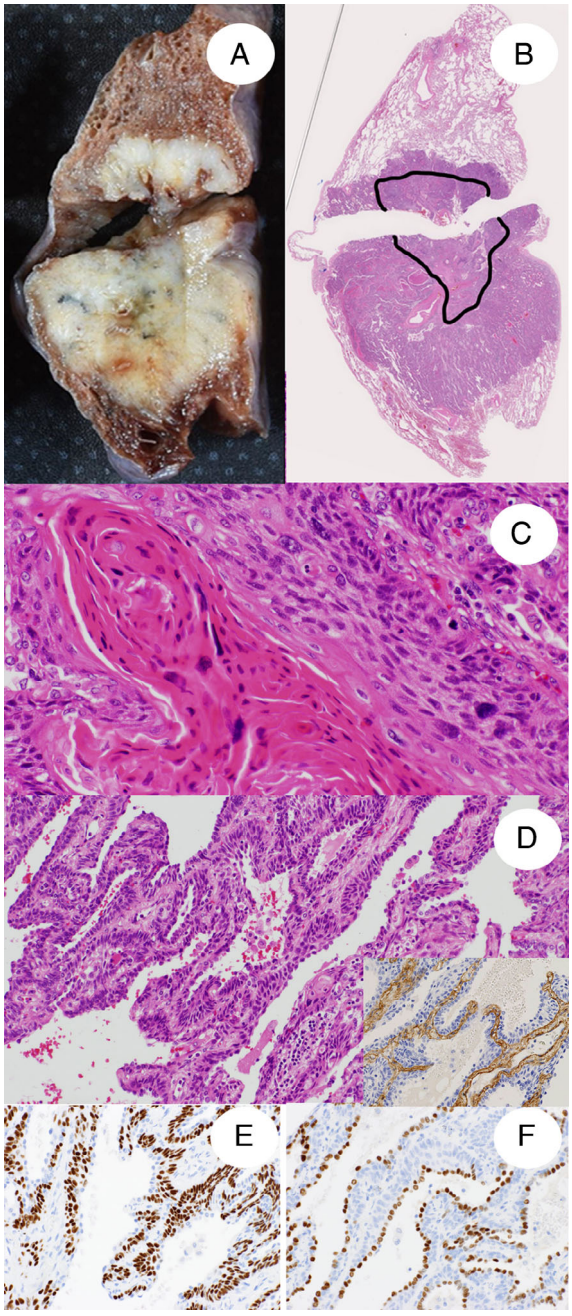

Figure 2. Macroscopic findings (A), loupe image (B), and representative histopathological findings of haematoxylin and eosin sections (C, D). The central area circled by a black line (B) indicates the histopathology of keratinizing squamous cell carcinoma (SCC) (C) (original magnification: 100×). The peripheral area outside the black line (B) reveals lepidic growth of carcinoma cells between non-neoplastic type II pneumocytes and alveolar basement membrane (D) (original magnification: 100×). Also, immunohistochemical staining of type 4 collagen clearly indicates lepidic growth (inserted image in D). Immunohistochemical staining of p40 and thyroid transcription factor 1 highlights SCC cells in lepidic growth covering non-neoplastic type II pneumocytes (E, F) (original magnification: 200×).

non-neoplastic type II pneumocytes and the alveolar basement membrane (Fig. 2D). Tumour-infiltrating lymphocytes were scanty in whole tumour tissue. On immunohistochemical staining, tumour cells had squamous cell differentiation shown by positivity of p40 (Fig. 2E) and negativity of thyroid transcription factor 1 (TTF-1). There was no difference of p40 positive rate of carcinoma cells between central and peripheral lepidic lesions. A monolayer of reactive type II pneumocytes was highlighted by TTF-1 positivity, and was covered by lepidic spreading of carcinoma cells (Fig. 2F). Ki-67 index in central solid and in peripheral lepidic lesions was about 40% and 10%, respectively.

Discussion

HRCT is a type of computed tomography (CT) with a small field of view and provides higher image quality, which yields images related to the histological changes in bronchial and alveolar structures. Therefore, HRCT is useful for screening non-neoplastic and neoplastic pulmonary lesions such as emphysema, interstitial pneumonia, and lung cancer. Most lung cancers show findings of GGO, PSN, or solid nodule. GGO on HRCT is related to histological findings of preserved alveolar structure with air spaces and thickened stroma. Therefore, the pulmonary lesions showing GGO pattern on HRCT include diseases with preserved alveolar structure, such as non-specific small inflammatory disease, AC in situ, or minimally invasive AC [1]. Pulmonary lesions with PSN on HRCT indicate combined patterns of central solid areas with surrounding GGO, and are related to diseases such as early invasive AC, lepidic carcinoma, or invasive AC with lepidic growth pattern. In rare cases, adenosquamous carcinoma and collision tumour of AC and SCC can present with a PSN pattern on HRCT.

SCCs usually reveal a solid nodule pattern on HRCT, and do not show GGO or PSN patterns, because most SCCs are invasive tumours without lepidic growth. However, some SCCs with emphysematous change can show HRCT imaging findings that resemble PSN pattern caused by a central solid area of tumour and surrounding non-neoplastic alveolar component with inflamed and fibrously thickened stroma. Our present case revealed invasive, well-differentiated SCC with keratinization of the central area and lepidic carcinoma cell growth at the peripheral area. Carcinoma cells with a lepidic growth pattern were seen along the alveolar basement membrane beneath non-neoplastic pneumocytes. SCC with a GGO or PSN pattern caused by lepidic growth of carcinoma cells is extremely rare. We only found five previous case

Table 1. Summary of previous cases of SCC with GGO or PSN.

Reference	Age and gender	Location in the lung	Findings and clinical diagnosis of HRCT	Follow-up period before resection	TMN	Background of the lung	History of smoking	Prognosis
Kimura (2002) [2]	65, M	Periphery in LLL	GGO (15 mm) No description	Six years	cT1N0M0	No disease	90 pack-years	No description
Kobayashi (2006) [3]	54, M	Middle in RUL	PSN (25 mm) AC	No	cT1N0M0	No disease	70 pack-years	FD (36 months)
Atsumi (2010) [4]	61, F	Middle in LLL	GGO (15 mm) No description	No	pTisN0M0	No disease	No smoking	FD (five months)
Sakaizawa (2015) [5]	68, F	Periphery in RUL	GGO (36 mm) AC	Nine years	No description	No disease	No smoking	FD (48 months)
Terada (2017) [6]	77, M	Periphery in RLL	GGO (24 mm) AC	1.5 years	cT1aN0M0	Pneumoconiosis	35 pack-years	FD (19 months)
Present case	70, M	Periphery in RLL	PSN (25 mm) AC	No	cT1cN0M0	No disease	50 pack-years	FD (12 months)

AC, adenocarcinoma; FD, free of disease; GGO, ground-glass opacity; HRCT, high-resolution computed tomography; LLL, left lower lobe; PSN, part-solid nodule; RLL, right lower lobe; RUL, right upper lobe; SCC, squamous cell carcinoma.

reports (Table 1), all of which were from Japan [2–6]. The patients had clinical characteristics such as peripheral tumour location, detection at an early stage, smoking history, less progression, and favourable prognosis. All cases except for one with no description were misdiagnosed preoperatively as AC. Except for one case with pneumoconiosis, there was no significant background lung disease. Histopathological findings of these cases were characteristically similar to those of our case; namely, carcinoma cells in lepidic growth pattern involving the alveoli beneath reactive pneumocytes. The characteristic lepidic growth pattern has been described in two previous reports without HRCT study, and one of them reported that the incidence of such cases was <4% in peripherally located small pulmonary SCC [7,8].

In conclusion, we present a rare case of SCC with lepidic proliferation presenting with a PSN pattern on HRCT. On the basis of our present case and five others from the literature, we make clinicopathological characteristics of SCCs with lepidic growth clear. We need to recognize that such cases can be misdiagnosed as AC by HRCT and may be a special type of SCC with less progression and favourable prognosis.

Disclosure Statement

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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