

Lung metastasis from gastric cancer presenting as diffuse ground-glass opacities

Yuki Abe^a, Masaru Suzuki^{a,*}, Kosuke Tsuji^a, Mineyoshi Sato^a, Hirokazu Kimura^a, Hiroki Kimura^a, Kentaro Nagaoka^a, Emi Takakuwa^b, Yoshihiro Matsuno^b, Satoshi Konno^a

^a Department of Respiratory Medicine, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Sapporo, Japan

^b Department of Surgical Pathology, Hokkaido University Hospital, Sapporo, Japan

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ABSTRACT

Most metastatic lung tumors display well-defined, round, multiple nodular shadows, whereas the presence of diffuse ground-glass opacities on chest computed tomography generally suggests non-malignant conditions. Here, we report an unusual case of pulmonary metastasis from gastric cancer in which diffuse ground-glass opacities were observed in all lung segments. A 59-year-old man with a 3-month history of worsening chest pain and shortness of breath was referred to the pulmonary clinic. Chest computed tomography revealed low attenuation areas, suggesting emphysema, along with diffuse ground-glass opacities and interlobular septal thickening in both lungs. A transbronchial lung biopsy specimen revealed signet-ring cell carcinoma infiltrating the alveolar septa. Immunohistochemical staining of the cancer cells was positive for CDX-2, cytokeratin 7, and cytokeratin 20, and negative for surfactant apoprotein-A, TTF-1, and Napsin A. Gastrointestinal endoscopy revealed an ulcerative tumor in the stomach, and a biopsy from the tumor demonstrated malignant cells with similar morphology and immunophenotypes as those in the lungs. The final diagnosis was diffuse lung metastasis from gastric cancer. Our case shows that although multiple, well-defined nodules are typically considered to be the classic presentation of pulmonary metastasis, clinicians should also be aware of the possibility of pulmonary metastasis presenting as diffuse ground-glass opacities.

1. Introduction

Most metastatic lung tumors display well-defined, round, multiple nodular shadows. In contrast, the presence of diffuse ground-glass opacities (GGOs) on chest computed tomography (CT) generally suggests non-malignant conditions such as interstitial lung disease, diffuse alveolar hemorrhage, pulmonary alveolar proteinosis, or infection. Here, we report an unusual case of pulmonary metastasis from gastric cancer in which diffuse GGOs were observed in all lung segments.

2. Case presentation

A 59-year-old man with a 3-month history of worsening chest pain and shortness of breath was referred to the pulmonary clinic. He had a history of 82 pack-years of tobacco use. He had no notable medical history. On presentation, his oxygen saturation level was 96%, and his

lungs were clear to auscultation. Physical examination showed no remarkable findings other than left precordial tenderness. Serum cytokeratin 19 fragment, pro-gastrin-releasing peptide, and neuron-specific enolase were elevated (3.7 ng/ml, 115.3 pg/ml, 14.8 ng/ml, respectively), whereas other tumor markers, including carcinoembryonic antigen, carbohydrate antigen 19-9, squamous cell carcinoma-related antigen, and sialyl Lewis X, were all negative. Serum markers for interstitial pneumonia were not elevated (KL-6, 101 U/ml; surfactant protein-A, 21.3 ng/ml; surfactant protein-D, 25.1 ng/ml). Pulmonary function tests revealed airflow limitation (FEV₁/FVC, 62.8%) and reduced diffusion capacity (%DLco, 34.2%; %Kco, 38.0%). Chest CT revealed low attenuation areas, suggesting emphysema and diffuse GGOs along with interlobular septal thickening in both lungs (Fig. 1). Bronchoscopy revealed no obvious abnormalities in the lumen, and bronchoalveolar lavage from the right B5 showed no abnormal findings. Interstitial lung disease was initially suspected; however, transbronchial

Abbreviations: CT, computed tomography; GGO, ground-glass opacity; HRCT, high resolution computed tomography.

* Corresponding author. Department of Respiratory Medicine, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Kita 15, Nishi 7, Kita-ku, Sapporo, 060-8638, Japan.

E-mail address: suzumasa@med.hokudai.ac.jp (M. Suzuki).

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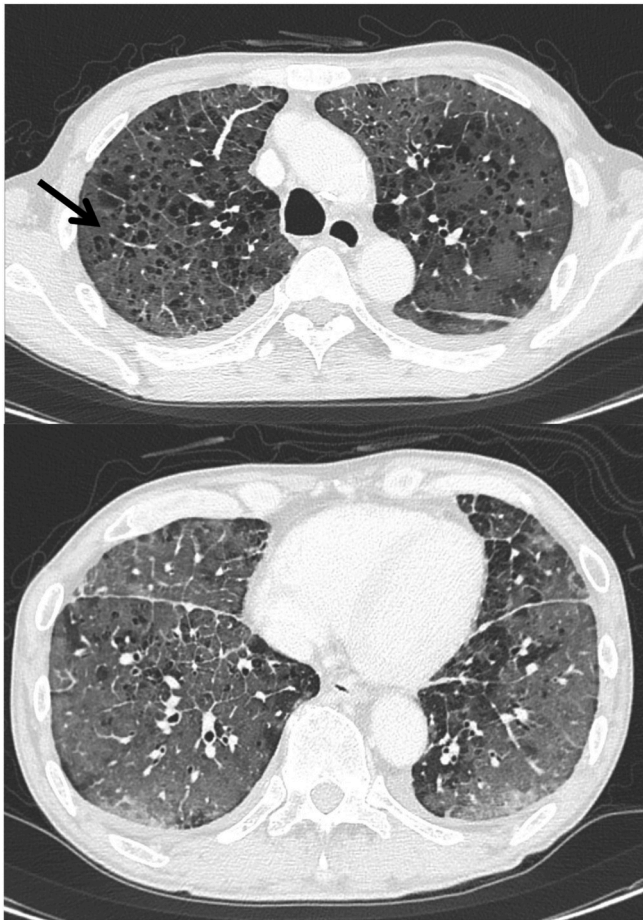


Fig. 1. Chest computed tomography scans on admission, showing multiple ground-glass opacities and interlobular septal thickening in both lungs. Arrow shows the location of one of the transbronchial lung biopsies, the right S2b.

lung biopsies obtained from multiple lesions showed an adenocarcinoma with a signet-ring morphology (negative for surfactant apoprotein-A, TTF-1, and Napsin A, and positive for CDX-2, cytokeratin 7, and cytokeratin 20) that infiltrated the alveolar septa in all specimens (Fig. 2). The tumor cells contained abundant intracellular mucin. Gastrointestinal endoscopy revealed an ulcerative tumor in the stomach. A biopsy of the tumor demonstrated malignant cells with similar morphology and immunophenotype as those in the lungs. The final diagnosis was diffuse lung metastasis from gastric cancer. The patient refused chemotherapy because his performance status worsened and he hesitated the side effects of systemic chemotherapy. At the patient's request, he was transferred to hospice care.

3. Discussion

The incidence of lung metastasis from gastric cancer is relatively low, and Kong et al. reported that only 0.96% of over 20,000 patients with gastric cancer were identified to have lung metastasis [1]. The most frequent pattern of lung metastasis was hematogenous metastasis presenting as multiple lung nodules (52.3%), followed by pleural metastasis (35.2%) and lymphangitic metastasis (26.4%) [1]. The median survival after the diagnosis of lung metastasis was only 4.0 months [1]; therefore,

the accurate diagnosis of thoracic manifestations in patients with gastric cancer is very critical for deciding optimal treatment options.

It is well known that the most common cancer manifesting with GGOs is primary adenocarcinoma in situ or minimally invasive adenocarcinoma of the lung, previously included in the category of bronchioalveolar carcinoma, which occasionally shows multiple or diffuse GGOs. Although metastatic lung tumors generally manifest as multiple and well-defined nodules, lung metastases presenting as multiple GGOs have been reported in several gastrointestinal cancers, including gastric cancer [2], pancreatic cancer [3], and colorectal cancer [4]. The size of the GGOs in these cases ranged from 5 to 20 mm in diameter. In addition to gastrointestinal cancers, diffuse GGOs have also been reported as a manifestation of neoplastic diseases, such as pulmonary diffuse large B-cell lymphoma [5,6], extranodal natural killer/T-cell lymphoma [7], methotrexate-associated lymphoproliferative disorder [8], breast cancer [9], and prostate cancer [10] in rare cases. However, to the best of our knowledge, metastatic lung tumors from gastrointestinal cancer presenting with such diffuse GGOs have not been reported till date.

Two underlying pathologies of lung metastasis associated with GGOs on CT have been reported. First, Kundu et al. reported the histological findings of a surgical lung biopsy specimen of lung metastasis arising from gastric signet-ring cell carcinoma [2]. In this report, solid clusters of tumor cells containing large amount of mucin were found to be infiltrating alveolar septa with destruction of the alveolar structure, suggesting the association between the infiltration of mucinous tumor cells into the alveolar septa and formation of GGOs on CT. This tumor growth pattern is similar to the interstitial growth pattern that has been observed in metastatic sarcoma and primary lung cancer, and malignant cells that have weak intercellular adhesions are thought to be associated with the interstitial growth pattern [11,12]. Second, Okita et al. reported a case of lung metastasis from malignant melanoma and histopathological examination of tissue obtained by surgical lung biopsy showed proliferating melanoma cells that replaced and covered the alveolar epithelium with little destruction of the alveolar structure [13]. Such lepidic growth of tumor cells is often found in primary adenocarcinoma in situ or minimally invasive adenocarcinoma of the lung. In the present case, mucinous carcinoma cells apparently infiltrated the alveolar septa (interstitial growth pattern); therefore, the first mechanism seemed to result in the diffuse GGO appearance on chest CT in this case.

4. Conclusions

Although the presence of diffuse GGOs on chest CT generally suggests non-malignant situations, the present case indicate that physicians should pay attention to metastatic cancer in the differential diagnosis of diffuse GGOs.

Author contributions

All authors contributed to the conception and design of the study; collection, analysis, and interpretation of data; and drafting, critical revision, and final approval of the manuscript.

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Declarations of interest

None.

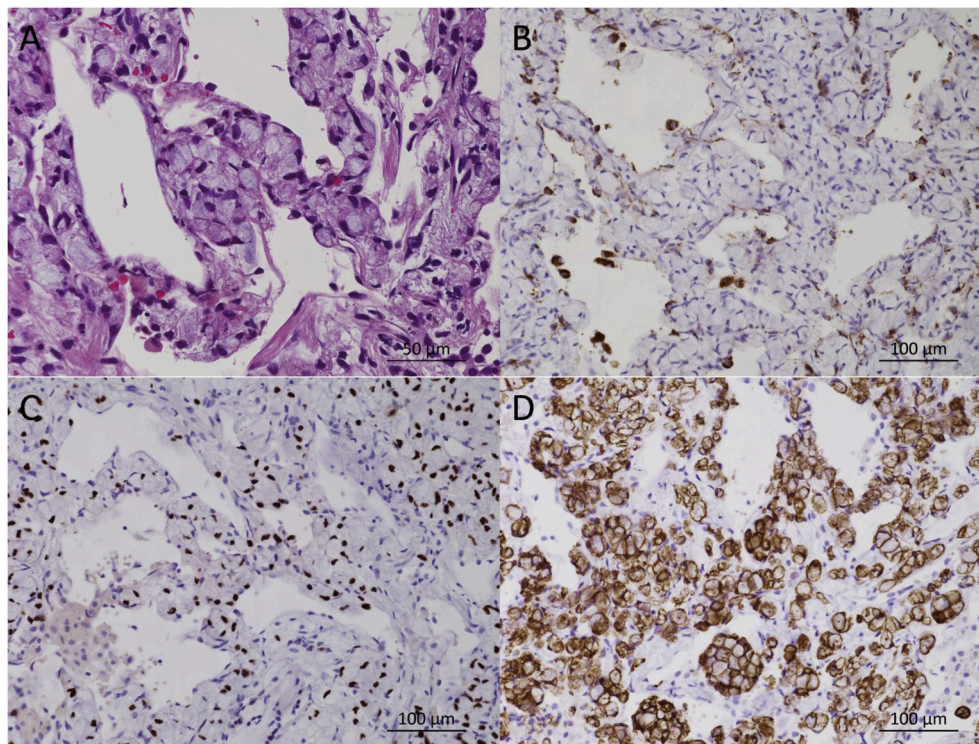


Fig. 2. (A) Histological examination of the lung tissue obtained using a transbronchial lung biopsy demonstrating infiltration of signet-ring cell carcinoma cells into the alveolar septa (hematoxylin and eosin staining). (B–D) Immunohistochemical staining of tumor cells, negative for Napsin A (B) and positive for CDX-2 (C) and cytokeratin 20 (D).

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