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【 CASE REPORT 】

The Value of ^{18}F-FDG PET in the Diagnosis of Intertrabecular Vertebral Metastasis in a Small Cell Lung Cancer Patient with a High Serum CEA Level

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Abstract:
We encountered a small cell lung cancer (SCLC) patient with intertrabecular vertebral metastasis (IVM). A 59-year-old man was admitted to our hospital with weight loss. ^{18}F-fluorodeoxyglucose positron emission tomography (FDG PET)-CT demonstrated the uptake of fluorodeoxyglucose in the hilum of the left lung and whole-body bones. Despite intensive support, the patient died within a month. Subsequent autopsy revealed a small lesion consisting of small round cells in the left lung. The cancer cells were found to have spread through the replacement of the bone marrow cells while sparing the trabecular bone. This case demonstrated the potential of ^{18}F-FDG PET for detecting IVM in SCLC patients.

Key words: small cell lung cancer, bone metastasis, intertrabecular vertebral metastasis, ^{18}F-fluorodeoxyglucose positron emission tomography, carcinoembryonic antigen

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Introduction

Lung cancer shows a marked propensity to metastasize to various organs, even in the early stages of the disease. Patients with bone metastasis, which accounts for approximately 40% of all cases, have a particularly poor prognosis (1, 2). Although intertrabecular vertebral metastasis (IVM) is rarely diagnosed in the clinical setting, it is one of the most common forms of bone metastasis encountered at autopsy in cancer patients (3, 4). Many imaging techniques fail to detect cancer cells in the marrow in patients with IVM, as the cancer cells diffusely infiltrate the bone marrow and spare the trabecular bone structure. However, ^{18}F-fluorodeoxyglucose positron emission tomography combined with computed tomography (^{18}F-FDG PET-CT) is able to directly reveal the presence of cancer cells, irrespective of whether the bone structure remains intact (5). Most small cell lung cancer (SCLC) patients with IVM show an elevated serum carcinoembryonic antigen (CEA) level (6, 7). We herein report the case of a patient with IVM in whom the primary lesion was a tiny SCLC. The serum CEA level was remarkably high and the accumulation of ^{18}F-FDG was demonstrated in the whole-body bones.

Case Report

A 59-year-old man without any prior significant medical history was admitted to our hospital complaining of body weight loss of 15 kg over the previous two months. He had a 40 pack-year smoking history and an Eastern Cooperative Oncology Group Performance Status of 3. Laboratory examinations revealed significantly elevated serum levels of CEA (1,720 ng/mL) and pro-gastrin releasing peptide (>70,000 pg/mL), both strongly indicating the presence of malignant disease. Although whole-body contrast-enhanced

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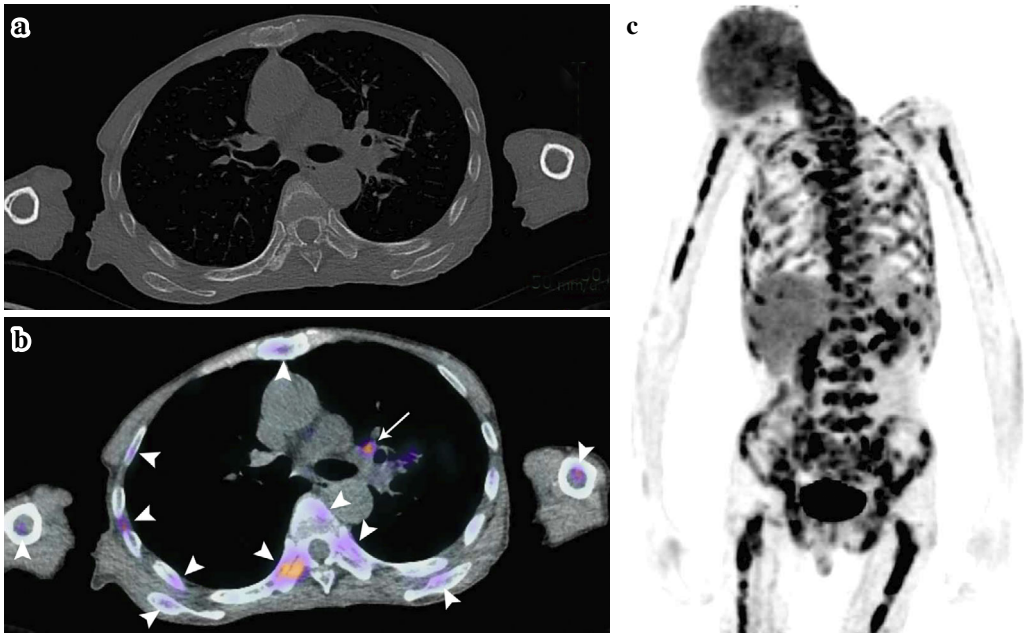

Figure 1. **a: Computed tomography failed to demonstrate any abnormal findings in the left lung hilar area or bones, whereas the uptake of FDG was distinctively increased. b: ^{18}F-FDG PET-CT demonstrated a higher uptake of FDG in the left lung hilum (arrow) and multiple bones (arrowheads). c: SPECT imaging by ^{18}F-FDG PET showed the increased spread in the whole-body bones where the uptake of FDG was increased.**

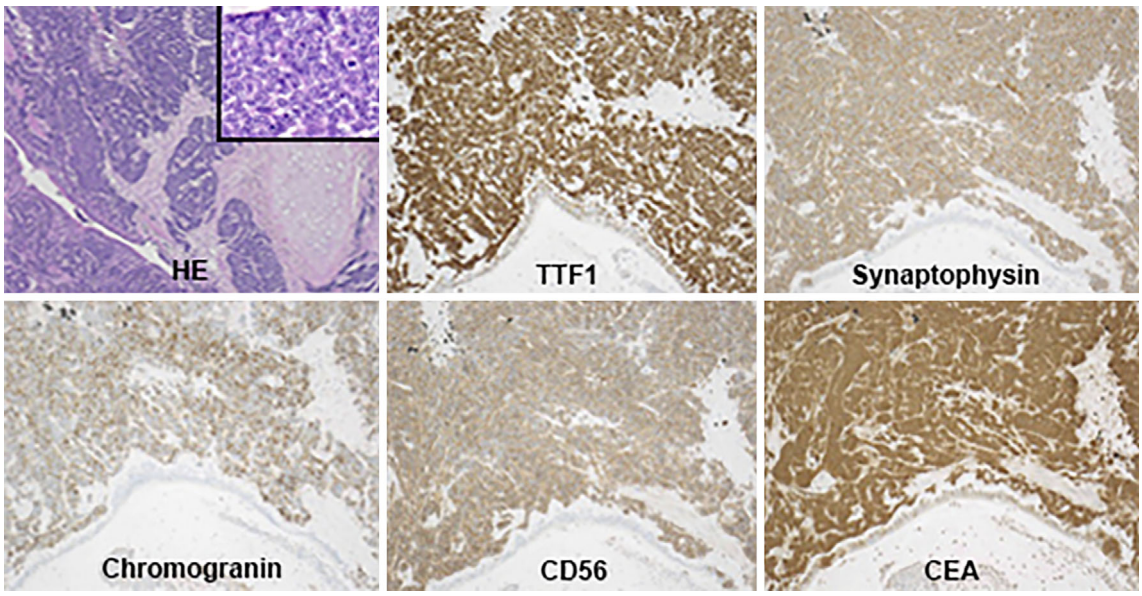

Figure 2. **Around the bronchial cartilage, Hematoxylin and Eosin staining showed solid to sheet-like tumor nests consisting of small round cells possessing nuclei with fine granular chromatin. The tumor cells were positive for chromogranin A, synaptophysin, CD56, and TTF-1, which was diagnostic for small cell cancer of the lung. The tumor cells also exhibited markedly high levels of CEA.**

computed tomography (CT) demonstrated no significant abnormalities, ^{18}F-FDG PET-CT revealed the distinct uptake of FDG by the left bronchial wall and the whole-body bones (Fig. 1). Despite intensive care, the patient's general condition progressively deteriorated, and he died within a month without further investigation. Subsequent autopsy and a pathologic investigation revealed a 5-mm tumor beside the left bronchus and along the bronchial wall. The tumor consisted of homogeneously proliferated small cells, which possessed nuclei with fine granular chromatin with no other non-small cell carcinoma components. These cells were positive for chromogranin A, synaptophysin, CD56, TTF1 and CEA (Fig. 2). There were multiple metastatic lesions in the liver and pancreas, and cancer cells had replaced the bone mar-

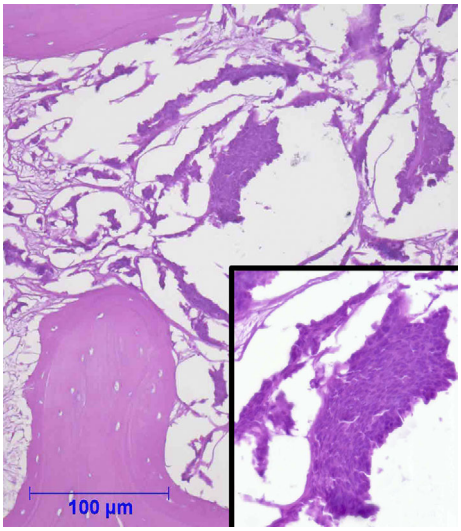

Figure 3. The cancer cells diffusely infiltrated the bone marrow. There was no bone destruction or new bone formation.

row cells in the whole-body bones but had spared the trabecular bone (Fig. 3). On this basis, the patient was retrospectively diagnosed as having SCLC with marked the expression of CEA, burdened by multiple metastatic lesions and IVM.

Discussion

Bone metastasis is classified into four types on the basis of the accompanying bone response: osteolytic, osteoplastic, mixed and IVM. Although IVM is the most common type of skeletal metastasis, reportedly accounting for approximately 34% of all cases of vertebral metastasis identified at autopsy (3), it is only rarely recognized in the clinical setting. IVM tends to be formed by medullary carcinomas that have a poor tumor stroma, such as SCLC, hepatocellular carcinoma and hematologic malignancies (3).

As IVM is a type of bone metastasis in which the trabecular bone structure is retained (3, 4), regular imaging techniques that detect structural deformation, such as fluoroscopy, CT and bone scintigraphy, often fail to reveal any abnormalities. Furthermore, serum markers of bone metabolism may be within the normal ranges (4). Thus, the possible presence of IVM should always be considered, even in situations where regular examinations do not point to bone metastasis.

As reported in the literature (4, 5), this case study clearly demonstrated the value of ^{18}F-FDG PET in the effective detection of cancer cell infiltration into the bone marrow in IVM. The sensitivity and specificity were reported to be 90.5-96.0% and 96.0-98.0%, respectively (8). MRI has also been reported to be effective. The MRI findings are reported to include a low signal intensity on T1-weighted images and a high signal intensity in T2-weighted images, with a detection rate of 94.6-100% (3, 9). Although no studies have compared ^{18}F-FDG PET scan and MRI in the detection of IVM, the use of ^{18}F-FDG PET would be advantageous for evaluations without a primarily target lesion.

In cases of SCLC with the expression of CEA, combined SCLC (CSCLC)-for example, SCLC combined with non-SCLC (NSCLC) components such as adenocarcinoma, squamous cell carcinoma, and large cell carcinoma-is another possible pathogenesis (10). CSCLC is classified as a subtype in the WHO classification of SCLC (11); it is reported, based on the examination of surgery or autopsy specimens, to consist of 13-28% SCLC (12-14). Although an NSCLC component was not detected in this case, it is important to perform a thorough investigation because treatment options may change depending on whether it includes an NSCLC component. On the other hand, ^{18}F-FDG PET and/or MRI would be relevant for screening for bone metastasis in SCLC with the expression of CEA, because IVM is frequently observed in SCLC (4), and because CEA positivity is a poor prognostic factor associated with disease progression and distant metastasis in SCLC (6, 7). CEA is an oncofetal protein detected in several pathophysiological processes related to cancer progression, including immunological defense, cell survival, and metastasis. Although CEA is not a specific marker of SCLC, it may be indicative of bone metastasis in SCLC, as it is reported to be detected in 32.7% of all SCLC cases (7), which is consistent with the frequency at which IVM is found at autopsy.

Treatment should be considered for each primary disease as there is no standard treatment specific for IVM. Although active treatment may not be possible due to the poor performance status of patients with IVM, as in the present case, carboplatin plus etoposide would be one possible treatment for SCLC with IVM, and has been reported to be feasible for elderly individuals and or patients with a poor performance status with advanced SCLC. A randomized controlled trial showed that the response rate and median survival time were 73% and 10.6 months, respectively, and adverse events were generally tolerable (15).

In conclusion, the present case illustrates that SCLC associated with a high serum concentration of CEA is highly malignant and has a poor prognosis. In such cases clinicians should consider the use of ^{18}F-FDG PET for the detection of latent IVM.

This case report was approved by the institutional Human Investigation Committee of Uonuma Institute of Community Medicine Niigata University Hospital. In accordance with the Declaration of Helsinki, written informed consent was obtained from the patient for publication of this case report.

The authors state that they have no Conflict of Interest (COI).

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