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Case report

Lung cancer with post-fracture healing changes causing difficulty in staging

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ABSTRACT

In cases wherein metastatic disease diagnosis in lung cancer is difficult with imaging, tissue biopsy should be performed. A 77-year-old woman presented with a complaint of cough. Positron emission tomography-computed tomography showed a left lung tumor with fluorodeoxyglucose accumulation, multiple lymphadenopathies, and right-rib sclerotic lesion. Although the diagnosis was lung adenocarcinoma, the bone lesion required differentiation from traumatic changes. A costal biopsy showed bone lesions as post-fracture healing changes, leading to variation in the therapeutic strategy to curative. In patients with lung cancer, history of trauma, and bone lesions with fluorodeoxyglucose accumulation, aggressive tissue biopsy is recommended for accurate staging.

1. Introduction

The diagnosis of metastatic disease in lung cancer is generally based on imaging findings such as positron emission tomography-computed tomography (PET-CT) performed before the initial treatment. If the distant metastasis is a single lesion, the diagnosis should be made with particular caution because this diagnosis can serve as an indication for surgery, radiation therapy, and other curative treatments.

PET-CT may show increased fluorodeoxyglucose (FDG) accumulation in the presence of bone fracture or orthopedic intervention [1,2]. Therefore, bone metastasis cannot be evaluated with only PET-CT in patients with lung cancer and a history of bone fracture.

In the reported case, PET-CT showed a sclerotic bone lesion with FDG accumulation in the right 9th and 10th ribs, which was initially thought to be a multiple-bone metastatic lesion from lung cancer. However, costal biopsy results showed that the bone lesions were post-fracture healing changes.

Due to the change in the clinical stage, the treatment plan was changed from chemotherapy to combined chemoradiation for radical cure. We report the case to highlight the need for aggressive tissue biopsy to accurately assess bone metastases in lung cancer patients with a history of trauma.

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2. Case presentation

A 77-year-old woman visited our clinic with a chief complaint of a cough that lasted for 1 month. She had a history of injury to the right side of her chest due to a fall approximately 1 year before her visit.

Chest computed tomography (CT) showed a left lung tumor and mediastinal lymphadenopathy. PET-CT showed sclerotic bone lesions with FDG accumulation in the right 9th and 10th ribs in addition to lung tumor and mediastinal hilar lymph nodes (Fig. 1).

Physical examination on admission revealed blood pressure of 142/78 mmHg, pulse rate of 72 beats/min, temperature of 36.4 °C, and percutaneous oxygen saturation of 98% on room air. Her neck was supple, and the results of cardiovascular examination were normal with clear breath sounds.

Accordingly, she underwent bronchoscopy, and a biopsy of the left lower lobe mass revealed primary lung adenocarcinoma as the diagnosis (Fig. 2).

However, the right ribs showed sclerotic lesions, which are atypical for bone metastases of lung cancer, and CT-guided biopsy of the right 9th rib was performed because imaging evaluation alone was insufficient to diagnose metastatic lesions (Fig. 3).

Histopathological examination revealed bone remodeling with fibrosis in some lesions, which was considered post-fracture healing changes. No malignant cells were found in the tissue samples (Fig. 4).

She was finally diagnosed with lung adenocarcinoma cT3N3M0 cStage IIIB, and because bone metastasis was excluded, the treatment plan was changed from chemotherapy to radical chemoradiation.

She received chemoradiotherapy (2 Gy × 30 fractions with weekly carboplatin (AUC = 2) and weekly nab-paclitaxel (50 mg/body). She was then administered adjuvant durvalumab (10 mg/kg) every 2 weeks as maintenance therapy.

The tumor shrank after treatment and has not progressed since 2 years after treatment.

Written informed consent was obtained from the patient and her family for publication of this case report and accompanying images.

3. Discussion

Bone metastasis is observed in 30%–40% of patients with advanced lung cancer [3,4]. Bone is the most common single metastatic organ for lung adenocarcinoma (28.7%), with the spine being the most common site of bone metastasis, followed by the ribs [5]. Therefore, rib metastases are not uncommon in adenocarcinoma of the lungs.

If PET-CT shows a tumor with FDG accumulation in the ribs, a clinician could deem this to be a rib metastasis based on imaging studies alone. However, PET-CT displays FDG accumulation for bone trauma, inflammation, and degeneration as well, which can be mistaken for bone metastasis [6]; therefore, its use for final determination of malignancy is problematic. For the exclusion of bone metastases in lung cancer, relying only on diagnostic imaging may lead to missed diagnoses that affect treatment selection and patient prognosis [7]. Thus, even in lung cancer patients with imaging findings suspicious for bone metastases, a tissue biopsy is necessary to determine a treatment strategy if there is a possibility of complications of benign disease, such as post-fracture healing changes. CT-guided bone biopsy is the gold standard diagnostic procedure for patients with bone lesions, with success rates in the range of 69–90% if morphologically clear bone lesions can be identified [8]. Complications include slight

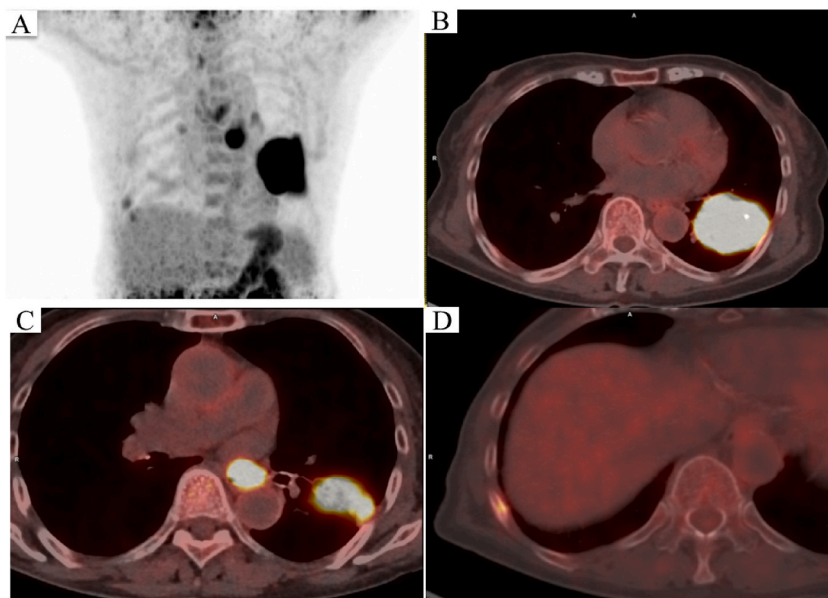


Fig. 1. Fluorodeoxyglucose positron emission tomography-computed tomography -PET/CT of lung lesions. Fluorodeoxyglucose shows accumulation in the left lung tumor, mediastinal lymphadenopathy, and the right 9th and 10th ribs.

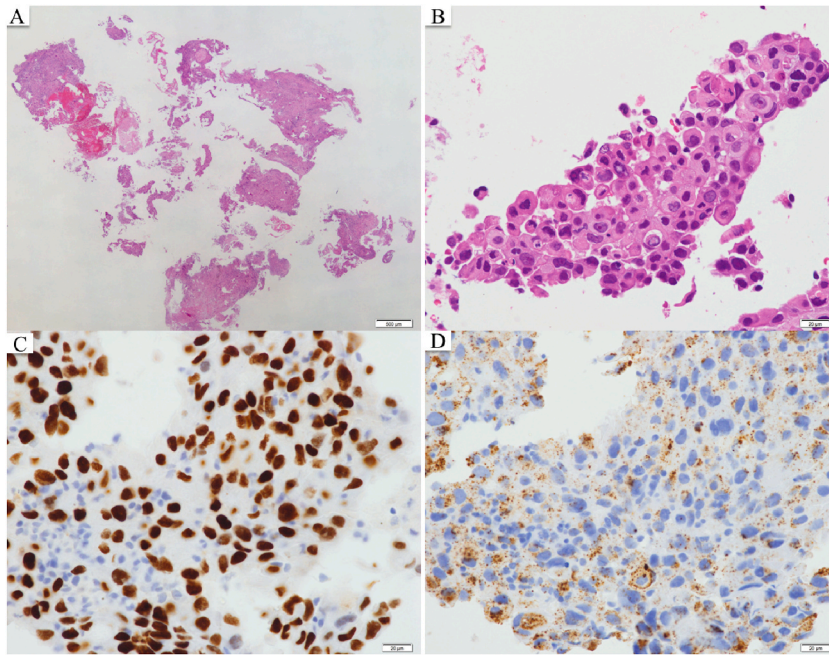


Fig. 2. Computed tomography-guided biopsy of the right 9th rib tumor. After local anesthesia using 1% xylocaine on the skin surface, muscle layer, and periosteum, a 3-mm skin cut was made and the subcutaneous skin was bluntly dissected. A computed tomography-guided needle biopsy was then performed in a trajectory tangential to the thoracic cavity.

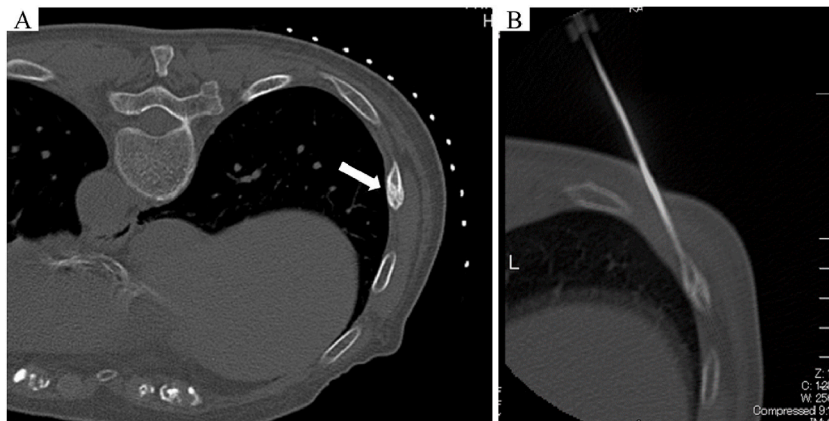


Fig. 3. Histological examination of the lung tumor. Atypical cells proliferating with a solid or nests pattern are seen. Nuclear maldistribution and mucus-like material are observed. Immunohistochemical analysis shows that the tumor cells are positive for thyroid transcription factor-1 (TTF-1) and napsin A. [(A): hematoxylin and eosin (H&E) staining, bar: 200 μ m], [(B): H&E staining, bar: 50 μ m], [(C): TTF-1 staining, bar: 100 μ m], [(D): napsin A staining, bar: 200 μ m].

bleeding and pain [8], but numerous studies have reported that percutaneous bone biopsy has a very low complication rate [9]. In this case, as in previous reports, there were no notable complications other than mild pain after examination.

In the acute phase after fracture, increased FDG uptake at the fracture site has been reported in PET-CT [1,2]. Zhuang et al. reported that the acute increase in FDG accumulation after traumatic fracture or orthopedic intervention is not persistent for more than 3 months [10]. However, the results of the current case suggest that FDG accumulation persists even 1 year after injury. Thus, bone biopsy should be actively attempted in lung cancer patients with a history of traumatic injury, even if the injury occurred more than 3 months ago. Judging bone metastasis solely on the basis of PET-CT results may lead to an incorrect assessment.

In general, non-small-cell lung cancer (NSCLC) causes osteolytic bone metastases, but it has been reported that 16% of patients with NSCLC can present with sclerotic bone metastases at initial diagnosis [11], suggesting that sclerotic changes are not a rare metastatic pattern in NSCLC. Furthermore, the sensitivity of FDG-PET has been reported to be decreased in sclerotic bone metastases [12], and the possibility of bone metastases should be considered in NSCLC when sclerotic lesions are found in the bone, even if FDG accumulation is poor. In the current case, the FDG accumulation observed in sclerotic bone lesions was difficult to differentiate

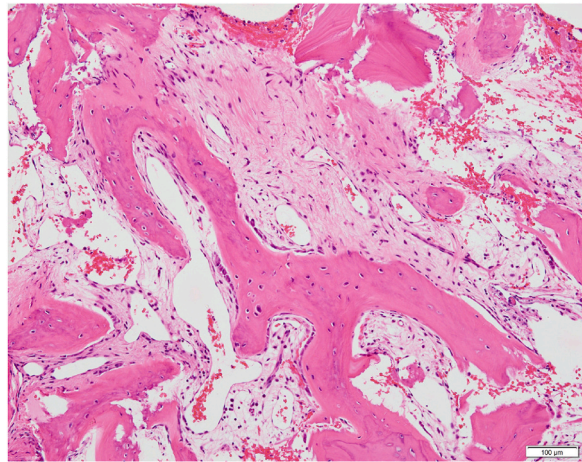


Fig. 4. Histological examination of the bone puncture biopsy. This section shows the tissue of lamellar bone with focal remodeling, fibrosis, and pre-existing hematopoietic cells, with no apparent carcinomatous components (H&E staining, bar: 100 µm).

from bone metastases. At the time of the diagnosis, the patient was diagnosed with cStageIV advanced stage lung cancer with multiple bone metastases, but aggressive bone biopsy revealed that the bone lesions were post-healing changes from rib fractures. Her clinical stage was changed to cStage III, so she could select chemoradiotherapy for curative cancer treatment.

Recently, the efficacy of durvalumab as a consolidation therapy for chemoradiotherapy has been demonstrated; it significantly prolonged the primary endpoint of progression free survival (16.8 vs. 5.6 months) and overall survival (not reached vs. 28.7 months) compared with placebo [13,14]. Therefore, consolidation therapy with durvalumab after chemoradiotherapy is recommended for the treatment of unresectable stage III NSCLC.

In NSCLC, stage III is a group of patients in which a certain percentage of patients can be cured, whereas patients with stage IV exhibiting distant metastasis are not likely to be cured and the primary aim of treatment is to delay progression. Therefore, accurate differentiation between clinical stages is particularly important to improve patient prognosis.

4. Conclusion

In the reported case, PET-CT at the initial examination showed lesions with FDG accumulation in multiple bones, which were initially thought to be multiple-bone metastatic lesions from lung cancer. However, costal biopsy results showed that the bone lesions were post-fracture healing changes. This finding made it possible to change the treatment plan from chemotherapy to combined chemoradiotherapy aimed at curative treatment. FDG accumulation in bone lesions may be observed in lung cancer patients with a history of trauma. In addition, FDG accumulation after fracture may persist for more than 1 year after injury. When evaluating bone metastases in lung cancer patients with a history of trauma, aggressive tissue biopsy should be considered for accurate staging and prevention of missed opportunities for curative treatment.

Disclosures

The authors state that they have no conflict of interest in regard to this manuscript.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Written informed consent was obtained from the patient and her family for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Availability of data and material

Not applicable.

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Authors' contributions

All authors read and approved the final manuscript.

Declarations of interest

None.

Declaration of competing interest

The authors declare that there is no conflict of interest in relation to this manuscript.

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