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Case report

Diffusion-weighted magnetic resonance imaging-directed biopsy of a metastatic bone tumor: Lung adenocarcinoma with *ALK* rearrangement

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ABSTRACT

A previously healthy 44-year-old Japanese man with a 5-month history of lumbago presented to the emergency department with acute respiratory failure caused by pneumonia, and was immediately intubated. Computed tomography revealed a lung mass, pleural effusion, and multiple osteolytic lesions; however, the results of thoracentesis and bronchial brushing were not definitive. We performed a bone tumor biopsy guided by diffusion-weighted magnetic resonance imaging (DW-MRI) with mechanical ventilation, which enabled the diagnosis of *ALK* rearrangement-positive lung adenocarcinoma. In the era of precision medicine requiring proper biological tissue collection, DW-MRI was critical for identifying the biopsy site safely and with high precision.

1. Introduction

The introduction of precision medicine has dramatically advanced oncological management and helped produce individualized treatment. In clinical practice, it has become increasingly important to collect adequate viable specimens for histopathological, molecular, and genetic assessment to investigate relevant biomarkers. However, the invasiveness of the biopsy itself is burdensome, especially for patients with poor performance status. Therefore, it is necessary to develop biopsy methods that have better efficacy and safety yet are less invasive. Herein, we report a patient with lung adenocarcinoma harboring *ALK* rearrangement who presented with acute respiratory failure because of undiagnosed neoplasms, and who was also complicated with pneumonia. The patient underwent pathological and genomic tests on a bone metastasis biopsy obtained with good precision and safety owing to the use of diffusion-weighted (DW) magnetic resonance imaging (MRI) for guidance.

2. Case presentation

A previously healthy 44-year-old Japanese non-smoking man presented to the emergency department of our hospital after experiencing a wet cough and fever for 2 weeks as well as dyspnea over the previous 24 hours. He had initially developed back pain and loss-of-appetite over the previous 5 months. As the symptoms gradually worsened, he became unable to walk 2 months prior and became bedridden 1 month later. He presented to the orthopedic outpatient clinic and underwent pelvic MRI 1 day before admission. He was then referred to the National Cancer Center for suspected primary bone tumors.

On admission, the following data were recorded: temperature, 37.8 °C; pulse rate, 158 beats/min; blood pressure, 114/92 mmHg; respiratory rate, 25 breaths/min; and oxygen saturation (digital pulse oximetry), 76% at rest while breathing ambient air. Arterial blood gas analysis revealed a pH of 7.289, $PaCO_2$ of 61.4 mmHg, PaO_2 of 83.3 mmHg and HCO_3^- concentration of 28.6 mmol/L under bag-valve-mask ventilation with a 15 L oxygen flow per minute. Chest roentgenography revealed right-sided white-out hemithorax (Fig. 1). The patient was immediately administered antibiotics and intubated with mechanical ventilation, which stabilized his vital signs. Further investigation was then performed. Contrast-enhanced whole-body computed tomography (CT) revealed a large mass with inhomogeneous enhancement in the right lung, as well as pleural effusion, consolidation in both lungs, and multiple osteolytic lesions, mainly in the spine and pelvic bones (Fig. 2). Bronchoscopy revealed purulent sputum and extrinsic compression of the right lower lobe of the bronchus intermedius. Bronchial washings and brush cytology, as well cytological analysis of the right pleural effusion, were suggestive of but not conclusive for malignancy (class III). Two days post-admission, we performed a pelvic bone tumor biopsy with CT guidance as well as fused DW and T1-weighted MRI (Fig. 3). The specimen was identified as an

Abbreviations: DW, diffusion-weighted; MRI, magnetic resonance imaging; CT, computed tomography

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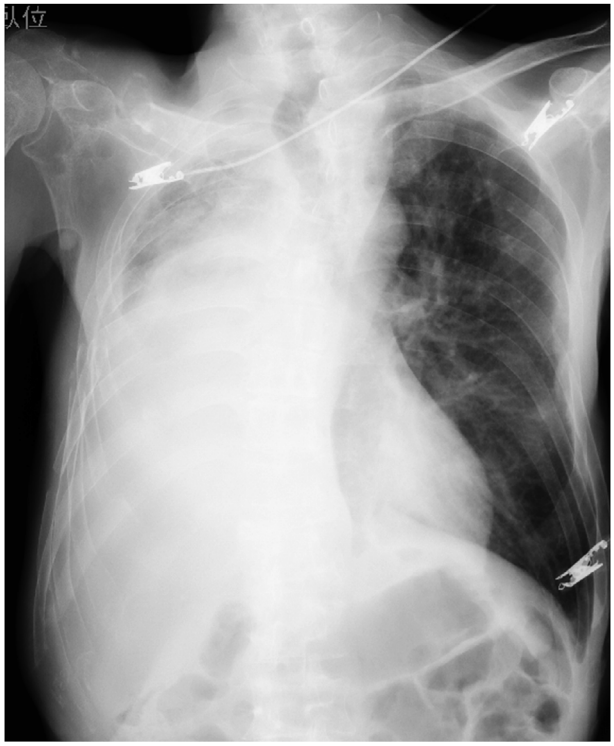

Fig. 1. Frontal anteroposterior chest roentgenography revealing right middle and lower lobe atelectasis, as well as infiltration into the left lung.

adenocarcinoma that was found to be anaplastic lymphoma kinase-positive by immunohistochemistry (Fig. 4); break-apart fluorescence in situ hybridization confirmed *ALK* rearrangement. The patient's respiratory condition gradually improved with antibiotics and supportive treatment, and he was extubated on day 9. Palliative chemotherapy with alectinib for stage IV lung adenocarcinoma (cT3N2M1c) commenced on day 19, which resulted in a partial response with amelioration of respiratory symptoms and back pain. He regained the ability to walk and was discharged on day 56; his serological carcinoembryonic antigen levels decreased from 3733.3 ng/mL at admission to 280.5 ng/mL. He is currently continuing treatment at the outpatient clinic.

3. Discussion

In the new era of precision medicine, molecular targeted therapies for lung cancers harboring *EGFR* mutation, *ALK* rearrangement, and *ROS1* rearrangement are generally less toxic and have higher response and overall survival rates than conventional cytotoxic chemotherapy [1]. Therefore, such treatments can be administered to patients who have poor performance statuses [2,3].

In our patient, lung cancer was not diagnosed until it had progressed to stage IV. The patient was complicated with pneumonia and was admitted to our department with an Eastern Cooperative Oncology Group performance status score of 4 under mechanical ventilation. While biopsy samples should be acquired promptly to establish a treatment strategy for presumptive neoplasms, it was not feasible to obtain a biopsy from our patient's presumptive primary tumor in the lung because of the risk of post-procedural complications, including pneumothorax and airway bleeding, because he was in acute respiratory failure and under positive-pressure ventilation. As soon as the patient's condition allowed, we selected the pelvic bone, which had osteolytic lesions of various sizes, as the extrathoracic biopsy site. Moreover, we used DW-MRI guidance to identify the viable parts of the tumor for biopsy collection, because large and heterogeneous tumor

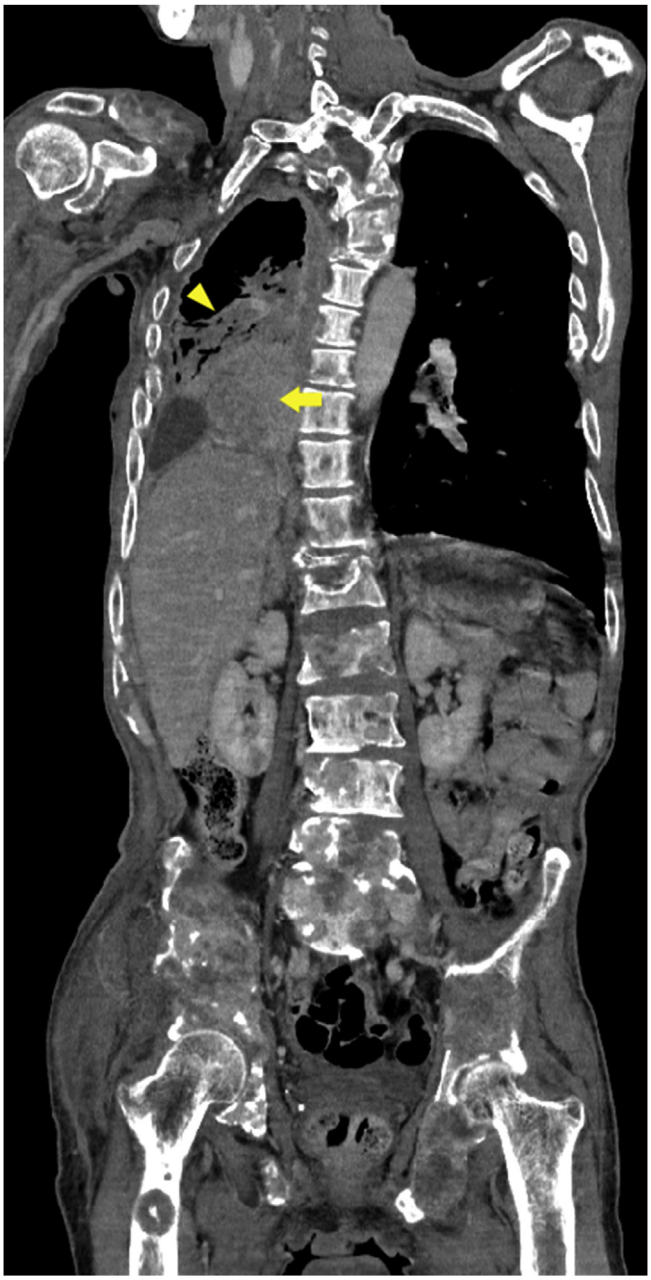

Fig. 2. Frontal view of contrast-enhanced whole body computed tomography (mediastinal window) revealing a large mass with inhomogeneous enhancement (arrow), consolidation with air bronchogram (arrowhead), and pleural effusion in the right lung. Multiple osteolytic lesions, especially in the spine and pelvic bones, are also visible.

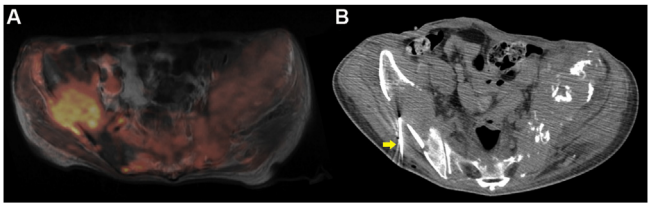

Fig. 3. The tumor biopsy was directed by diffusion-weighted image sequences and guided by computed tomography. (A) A fusion image of axial T1-weighted and diffusion-weighted image sequences shows a high signal intensity area in the right iliac bone. It suggests that the area was more cellular and viable than the other pelvic bone osteolytic lesions. (B) The tumor biopsy was directed to the high signal intensity area with the patient in a prone position (arrow; biopsy needle). (Note: this image is upside down).

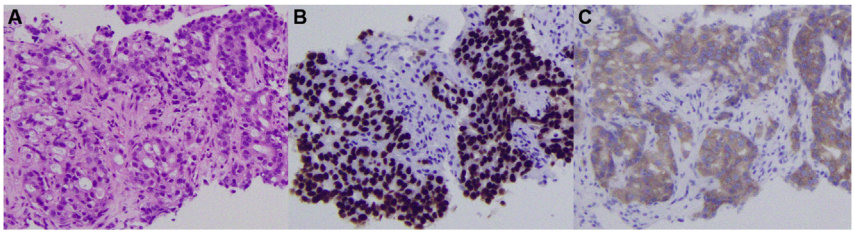

Fig. 4. Histopathological examination of the tumor biopsy shows adenocarcinoma (A, hematoxylin and eosin staining). The tumor cells expressed thyroid transcription factor-1 (B) and anaplastic lymphoma kinase protein (C). (All micrographs × 200).

masses frequently contain inviable parts and have great potential for sampling error.

Until recently, DW-MRI was used to evaluate intracranial diseases, especially cerebral infarctions. Its application to extracranial lesions was technically problematic and not always practical. However, with advances in MRI techniques, DW-MRI has become more broadly applicable in clinical oncology, and can now better detect lesions present in the trunk, especially the abdomen and pelvis [4]. Furthermore, within head and neck tumors, DW-MRI can differentiate between the viable and necrotic areas, and it has the potential to help select the best biopsy site [5].

Concerning chest tumors, artifacts resulting from physiologic motions, such as breathing and heart pulsation, had been a barrier for DW-MRI application until about a decade ago. However, to date, this technique has been used for the characterization, grading, and staging of lung carcinoma, and is potentially a new prognostic marker; a lower apparent diffusion coefficient value of a lung cancer is associated with higher pathological tumor grade and metastatic lymph nodes [6,7]. DW-MRI has also aided in pinpointing the optimal biopsy site by differentiating central lung carcinoma from post-obstructive atelectasis [6,8–10] and viable tumors from central necrosis in a patient with pyothorax-associated lymphoma [11]. DW-MRI can provide qualitative information about the degree of tissue cellularity and integrity of cellular membranes [12]. Many malignant tumors consist of tissues with a high density of atypical cells with intact membranes [12]; therefore, areas of high signal intensity on DW-MRI should be biopsied for high diagnostic accuracy.

4. Conclusions

It has become increasingly important to collect adequate viable specimens in the current era of precision medicine in oncology. Hence, functional DW-MRI data combined with the anatomical details provided by morphologic sequences and CT are of critical value, especially in patients with high-volume tumors that presumably contain an inviable component, to determine the biopsy site.

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Declarations of interest

The authors declare no competing interests related to this case report.

Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.rmcr.2018.05.024.

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