CASE REPORT

A bone metastasis of non-small cell lung carcinoma with prominent clear cell features

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SUMMARY

We report the case of a 78-year-old man with multiple bone tumours and three round, smooth nodules in the right lung. He was referred to our hospital because of the left femoral neck pathological fracture. The histological characteristics of the femoral tumour corresponded to clear cell carcinoma, and bone and lung lesions were regarded as metastatic from an unknown primary site, since there was no clinical evidence of renal carcinoma. His general conditions gradually declined, and he died 2 months after the operation. At autopsy, no neoplasia lesion was found in the kidneys. Although clear cell components were histologically dominant in the affected organs such as the lungs, bones and liver, neoplastic tubular structures also existed. Immunohistochemically, atypical cells were positive for napsin-A. The final diagnosis was adenocarcinoma of the lung origin with prominent clear cell features.

BACKGROUND

Clear cell carcinoma is the most frequent histological subtype of renal cell carcinoma, and most metastatic clear cell bone tumours have come from a renal cell carcinoma. In contrast, it might not be widely known among oncologists, other than respiratory oncologists, that non-small cell lung carcinoma (NSCLC) occasionally has prominent clear cell features and produces metastases with these same clear cell features. We could not find a well-described, published report of metastatic clear cell bone tumour from a non-renal primary site. It would be beneficial to recognise that NSCLC has capability of causing bone metastasis with mainly or purely clear cell features.

Figure 2 Postoperative radiograph and left proximal femoral specimens. (A) A hip prosthesis was fixed with cement after tumour resection. (B) The left femoral head and proximal femur were removed. Histological examination revealed no atypical cells in the left femoral head.

CASE PRESENTATION

A 78-year-old man with gradually increasing pain of the left hip was admitted to a nearby hospital because of a fracture of the left femoral neck. Radiographs showed a vaguely osteoblastic lesion in the left proximal femur, and CT revealed three round, smooth nodules in the right lung (figure 1). Bone and lung lesions were regarded as metastases at that time, but surveillance including gastrointestinal endoscopies could not reveal the primary

Figure 1 Images at the time of the first visit to the previous hospital. (A) A plain radiograph showing a femoral neck fracture and sclerotic changes in the left femoral head and proximal femur demonstrated by a white arrow. (B) A metastatic tumour with low signal on a T1-weighted image is located diffusely in the left proximal femur demonstrated by a white arrow. (C) and (D) CT reveals three round to oval nodules with clear borders in the right lung demonstrated by white arrows.

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Figure 3 Microscopic findings of the left proximal femoral specimen. H&E staining of specimens from the left proximal femur (A) shows uniform sheets of atypical cells with a proliferation in a solid, alveolar manner. Tumour cells are positive for epithelial membrane antigen (B) and vimentin (C), and partially positive for CD10 (D).

malignancy. The patient was referred to our institution for further examination and treatment.

At the time of admission to our hospital, laboratory data showed moderate increases in prostate-specific antigen (PSA) at 36.2 ng/mL (normal range <4.0 ng/mL) and squamous cell carcinoma antigen at 3.9 ng/mL (normal range <1.5 ng/mL). To improve the patient's disability and for histological diagnosis, we resected the tumour and replaced the joint with a prosthesis (figure 2). Histologically, tumour tissue was composed of uniform sheets of atypical cells with necrosis, and H&E staining showed proliferation in a solid, alveolar manner. Immunohistochemically, tumour cells were positive for epithelial membrane antigen and vimentin, partially positive for CD10 and negative for CK7 and CK20 (figure 3). Prostate biopsy provided no evidence of prostate carcinoma. The possibility of renal cell carcinoma as a primary carcinoma was considered, but fluorodeoxy-glucose positron emission tomography and enhanced CT did not detect any malignant lesions in the kidneys. He was diagnosed with bone and lung

metastases of unknown origin, but could not undergo further cancer treatment due to his deteriorating general conditions.

OUTCOME AND FOLLOW-UP

The patient received supportive care, but he passed away 2 months after the admission to our institution.

Autopsy revealed multiple lesions in the lungs, liver, adrenal glands, stomach, thyroid gland, small intestine, spine and subcutaneous tissue, but we found only benign cysts in the kidneys (figures 4 and 5). Microscopic examination clarified latent prostate cancer with a Gleason score of 7 (3+4), which was clearly different from metastatic lesions in other organs including lungs. Almost all lesions were histologically similar to the metastatic lesion in the left femur, but neoplastic tubular structures were also seen in the adrenal glands and spine. Immunohistochemically, atypical cells in the lungs and adrenal glands were positive for CAM5.2 and vimentin, partially positive for napsin-A, only slightly positive for CD10 and negative

Figure 4 Images of the kidneys. Fluorodeoxy-glucose positron emission tomography (FDG-PET)/CT (A), plain CT (B) and enhanced CT (C), delayed phase, showing no possible malignant lesions in the kidneys other than cysts without abnormal uptake of FDG.

Figure 5 Macroscopic findings at autopsy. No malignancy was revealed in 7 mm slices of the kidneys ((A): the right kidney and (B): the left kidney). Multiple, yellowish-white nodules were detected in the lungs, and a white arrow points to the largest mass regarded as a primary lesion in the right lung (C). Similar masses were identified in the adrenal glands (D).

for CK7, CK20, chromogranin A, synaptophysin, PSA and TTF-1 (figure 6). With the existence of neoplastic tubular structures and partial positivity of napsin-A, and finding no malignant lesion in the kidneys, our final diagnosis was pulmonary adenocarcinoma with prominent clear cell features. Although clear cell adenocarcinoma was another possibility, the lack of intracytoplasmic mucin production ruled out this.

DISCUSSION

NSCLC with prominent clear cell features has been reported. The first report dates back to 1964, when Morgan and Mackenzie¹ examined a series of 13 lung clear cell carcinomas and found that all cases had some portion of poorly differentiated adenocarcinoma. In 1980, Katzenstein *et al*² reported proportions of clear cell carcinoma component in 348

Figure 6 Microscopic findings at autopsy. An H&E-stained autopsy specimen from the prostate (A) shows an incidental prostatic adenocarcinoma. All other lesions have similar, clear cell carcinoma-like characteristics with H&E stain including the lung lesions (B). However, the atypical cells are immunohistochemically positive for napsin-A (C), and neoplastic tubular structures existed in lesions of the adrenal glands (D) and spine.

specimens of NSCLC, and high proportions of over 50% and over 90% were shown in 15 cases (4%) and only one case (0.3%), respectively.

Imaging characteristics of clear cell-dominant NSCLC have not been well discussed, but it might mimic metastatic pulmonary lesions. A case report from Kitada *et al*³ in 2010 had a CT image of lung clear cell carcinoma showing a lobular nodule with a distinct border. The primary lung lesions in our case were also well defined on CT. It can be difficult to differentiate

NSCLC with prominent clear cell features from a lung metastasis of other cancers through CT.

This case indicates that NSCLC can occasionally cause clear cell carcinoma-like metastasis. If bone metastasis is histologically clear cell dominant, the possibility of NSCLC as well as renal cell carcinoma should be considered even if the lung lesion seems to be metastasis.

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Contributors .JI and YY were involved in the treatment of the patient. JI was also involved in writing the manuscript. SM and MS performed the autopsy and examined it. YY and MS were involved in reviewing and editing the manuscript.

Competing interests None.

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Learning points

- ▶ Non-small cell lung carcinoma (NSCLC) may have prominent clear cell features.
- ▶ CT image of NSCLC with high proportion of clear cell carcinoma components can mimic lung metastases from other origins.
- ▶ Encountering clear cell-dominant bone metastasis with pulmonary lesion, we should consider the possibility of NSCLC as well as renal cell carcinoma even if the lung lesion seems to be metastasis.

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