Occult epidermal growth factor receptor-mutant lung adenocarcinoma complicated by prostatic metastasis: a case report

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Herein, we report a case of occult epidermal growth factor receptor (EGFR)-mutant lung adenocarcinoma complicated by prostatic metastasis. A 75-year-old male with >30 years of smoking history presented with lower back pain as the initial symptom. Respiratory symptoms, including cough and sputum production, were absent. PET–computed tomography revealed the presence of bone and prostatic metastases, without any lung abnormalities. Biopsies of the space-occupying bone and metastatic lesions suggested that the metastases originated from primary lung adenocarcinoma. Genetic testing indicated *EGFR* 21L858R(+). The patient had an abnormal serum carcinoembryonic antigen level but a normal prostate-specific antigen level. Following a multidisciplinary discussion, a diagnosis of occult primary lung adenocarcinoma complicated by bone and prostatic metastases (TxN0M1b, Stage IVB) was considered. Following targeted therapy with oral osimertinib, the patient achieved a partial response, with alleviation of pain symptoms alleviated and normalization of carcinoembryonic antigen levels. In the absence of tissue biopsy, such cases can often be misdiagnosed as prostate cancer complicated by multiple bone metastases. Hence, the present case highlights the importance of comprehensive diagnostic testing, including tissue biopsy, to accurately identify the underlying cause of metastatic disease. *Anti-Cancer Drugs* 36: 521–524

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Introduction

Distant metastases are commonly observed with lung cancer; the bones, liver, and brain are the most common metastatic sites, while prostatic metastasis is rare. Primary lung cancer usually presents with respiratory symptoms and is generally screened using contrast-enhanced chest computed tomography (CT). However, in few cases that lack space-occupying lung lesions, metastases serve as the primary clinical presentation. In such cases, diagnosis is dependent on biopsy and pathological examinations. Termed as occult lung cancer, these cases are often misdiagnosed, and account for approximately 2% of nonsmall cell lung cancer cases [1].

Herein, we report a case of occult primary lung adenocarcinoma with an epidermal growth factor receptor (EGFR)-sensitive mutation complicated by prostatic metastasis.

Case report

Informed consent

Written informed consent for publication of data and images was obtained from the patient.

Patient information

A 75-year-old male patient of Han ethnicity experienced lower back pain for 3 months with a numeric rating scale (NRS) score of 4–5 but had no other symptoms. He had a smoking history of >30 years with no family history of tumors.

Diagnostic assessment and therapeutic intervention

The patient was examined at a local hospital in March 2023. Chest CT detected no space-occupying lesions in bilateral lungs. Emission CT identified multiple bone metastases. Immunohistochemistry of lumbar spine biopsy revealed: PCK(+), Hep(–), GS(+), Villin(–), CDX-2(–), prostate-specific antigen (PSA)(–), TTF-1(+), CD138(+), CA19 – 9(–), CK19(+), CD56(–), Syn(+), CgA(+). Adenocarcinoma was diagnosed following a consultation at the West China Hospital of Sichuan University (Chengdu, China). The adenocarcinoma

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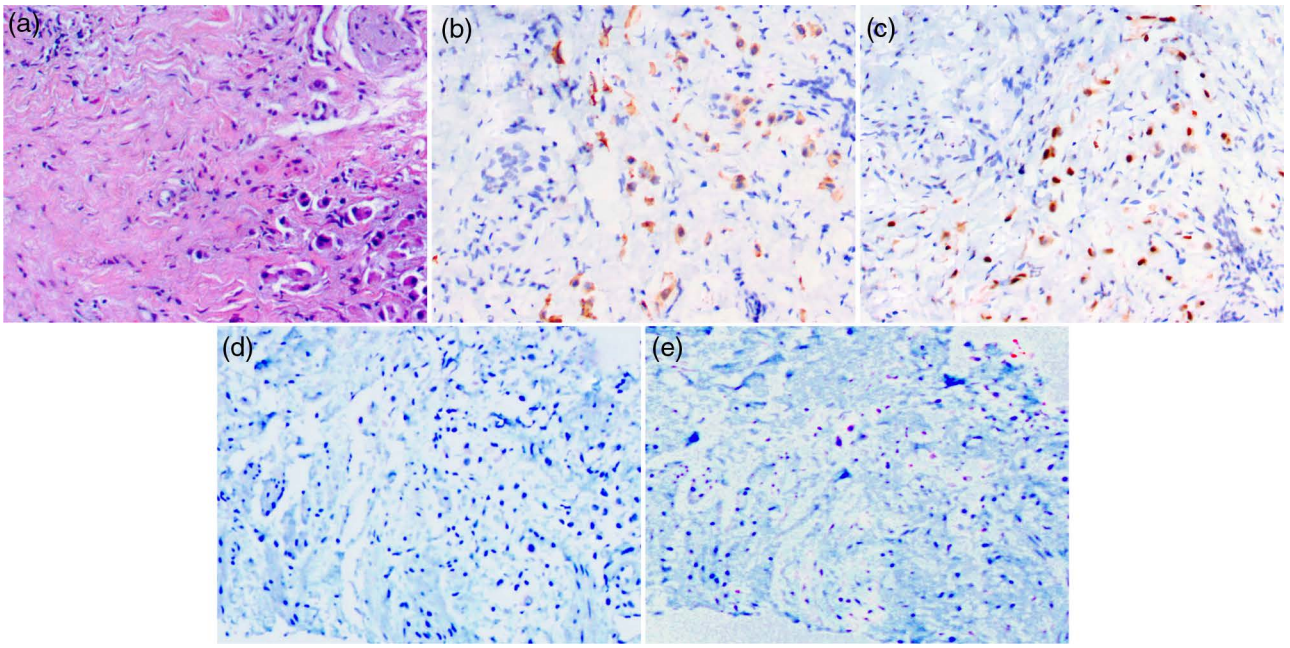
Fig. 1



(a) Pathological examination of prostate tissue (HE stain). Immunohistochemistry analysis: (b) CK positivity (+), (c) TTF-1 positivity (+), (d) NKX-3.1 negative, and (e) PSA negative.

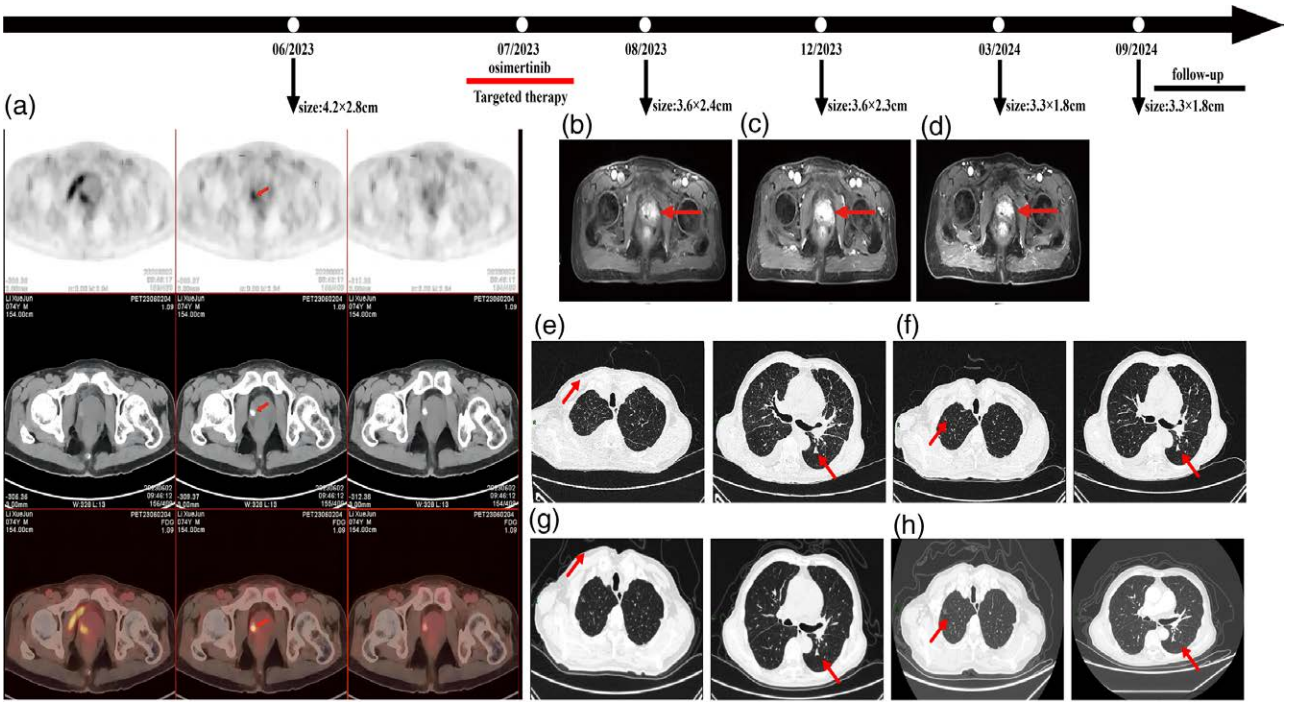
was thought to originate from the lung based on: PCK(+), CK7(+), CK20(−), CK8/18(+), CK19, TTF-1(+), NapsinA(+), CDX-2(−), SATB2(−), GATA3(−), CD56(−), Syn(−), CgA(−), SALL4(−), PSA(−), PAX8(−), HEPPAR-1(−), GPC3(+−), GS(−), AFP(−), KI-67(+, 5–10%). Next-generation sequencing (NGS) was performed. At this point, the patient sought medical attention at Sichuan Cancer Hospital (Chengdu, China). PET/CT indicated: (1) multiple small nodules in bilateral lungs with no increased radiotracer uptake; (2) multiple bone metastases throughout the body, and (3) a space-occupying prostatic lesion measuring 4.2 × 2.8 cm. Signs of malignant lesions were absent elsewhere in the body. Prostate biopsy revealed: NKX-3.1(−), Ki-67(+, approximately 2%), CK5/6(−), P63(−), TTF-1(+), CKpan(AE1/AE3)(+), suggesting metastasis of lung adenocarcinoma (Fig. 1). NGS indicated EGFR exon 21 c.2573T>Gp.L858R with a copy number of 4.3%. PD-L1 expression was negative. Serum carcinoembryonic antigen (CEA) and PSA levels were 45.35 ng/ml and 2.53 ng/ml, respectively.

The patient was diagnosed with bone and prostatic metastatic adenocarcinoma. On reviewing the contrast-enhanced chest CT scan, a small nodule measuring approximately 0.3 cm was observed in the dorsal segment of the lower lobe of the left lung. Following a multidisciplinary discussion, a diagnosis of lung adenocarcinoma with an occult primary lesion (TxN0M1b, stage IV) complicated by a sensitive gene mutation was considered. First-line targeted therapy with osimertinib (80 mg qd) was initiated on 13 July 2023. Before this, patients only received symptomatic treatment with no relief from pain.

Follow-up and outcomes

After 1 month of targeted therapy, contrast-enhanced pelvic MRI revealed a mass shadow measuring approximately 3.6 × 2.4 cm in the prostate. CEA level was >60 μg/L. The patient experienced significant alleviation in pain symptoms, with an NRS score of 1–2. Reexamination after 4 months of continued therapy revealed persistent scattered nodules in bilateral lungs. However, the space-occupying prostatic lesion had shrunk to 3.6 × 2.3 cm. CEA level and NRS score were 14.53 ng/ml and 1, respectively. After 8 months of oral osimertinib, reexamination revealed persistent scattered nodules in bilateral lungs. The space-occupying prostatic lesion had shrunk to 3.3 × 1.8 cm. CEA level and NRS score were 3.8 ng/ml and 0, respectively. Hence, a partial response to treatment was seen. Currently, the patient is continuing oral osimertinib with regular follow-up (Fig. 2). At the September 2024 imaging examination, the patient's efficacy was evaluated as SD, and reported a severe oral ulcer. Subsequently, the patient underwent surgery for an inguinal hernia in October, and recovered well after surgery, and is still maintaining targeted therapy.

Fig. 2



(a) PET/computed tomography (CT) image obtained during the initial consultation. The image showed a space-occupying lesion of the prostate, with a maximum diameter of 4.2 cm. Enhanced radiotracer uptake suggested a malignant tumor. (b–d) Follow-up images of the prostatic lesion. Assessment of treatment effectiveness revealed partial response. (e) Contrast-enhanced CT scan obtained during the initial consultation. Small nodules were seen in bilateral lungs, with the nodule in the dorsal segment of the left lower lobe having a diameter of approximately 0.3 cm; (f–h) Contrast-enhanced chest CT images, obtained in July 2023, August 2023, November 2023, March 2024, and September 2024, did not reveal any lung lesions. CEA, carcinoembryonic antigen; CT, computed tomography; NGS, next-generation sequencing; NRS, numeric rating scale; NSCLC, non-small cell lung cancer; PR, partial response; PSA, prostate-specific antigen.

Discussion

Prostatic metastases in lung cancer are relatively rare, with few reported cases [2]. Gilmour *et al.* [2] described a case of advanced lung adenocarcinoma with negative genetic test results complicated by brain metastasis. Prostatic metastasis occurred after chemoradiotherapy and immunotherapy, and palliative radiotherapy was administered [2]. The rest of the reported cases were negative for the driver mutation. Hence, the present case represents the first report of prostatic metastasis from driver gene mutation-positive primary lung cancer.

In the present case, obvious space-occupying lesions in the lungs and prominent respiratory symptoms were absent. The patient presented with lower back pain. Multiple chest imaging examinations revealed the presence of small lung nodules. In the absence of a biopsy, a diagnosis of bone metastasis from advanced prostate cancer would be considered. Given the occurrence of occult lung cancer in this case, diagnosis was highly dependent on accurate tissue biopsy and pathological examinations.

Tissue pathology and NGS indicated a close correlation with primary lung cancer. The L858R mutation is a common EGFR mutation, accounting for approximately 21.5% of all EGFR mutations, and occurs more frequently in nonsmokers and females. However, herein, the patient was a male with a long history of smoking, making the occurrence of this mutation a rare event.

NGS analysis involved deep sequencing of 230 genes. A class I genetic variant *EGFR* L858R was detected. Abnormalities were found in *FANCM*, *MLH1*, and *TSC2* with mutation frequencies of 48.5%, 52%, and 48%, respectively. They are associated with the risk of breast and colorectal cancer and abnormal cell proliferation, respectively [3–5]. However, correlations with the occurrence of occult lung lesions and prostatic metastasis in the patient remain unclear. Additionally, CEA levels correlated strongly with tumor burden and sensitivity to treatment. However, further research is required to determine the link to prostatic metastasis.

Conclusion

After targeted therapy, the patient experienced a gradual improvement in CEA levels and pain symptoms and a reduction in the space-occupying prostatic lesion, with partial response, confirming advanced lung

adenocarcinoma with an occult primary lesion. If imaging results from the initial consultation had been the sole basis for diagnosis, diagnosis of prostate cancer complicated by multiple bone metastases would have been more likely. Therefore, the present case can provide a reference for accurate clinical diagnosis and treatment of occult lung cancer.

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This study was approved by the Ethics Committee for Medical Research and New Medical Technology of Sichuan Cancer Hospital (SCCHEC-02-2024-107, June 18, 2024).

Written informed consent for publication of data and images was obtained from the patient.

The data supporting the results of this study can be obtained from the corresponding authors upon request.

F.Y.: conceptualization, data curation, investigation, visualization, methodology, project, writing—original draft, writing—review and editing. X.Z.: investigation, writing—original draft, writing—review and editing. H.X., Y.Z., and Y.W.: investigation, writing—review and editing. J.Z.: conceptualization, funding acquisition, methodology, formal analysis, project administration, supervision, visualization, writing—original draft, writing—review and editing.

Conflicts of interest

There are no conflicts of interest.

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