Ipsilateral breast metastasis from lung adenocarcinoma harboring anaplastic lymphoma kinase or ROS1 rearrangement and significant response after targeted therapy: report of two cases

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To the Editor: A 43-year-old female patient was admitted to our department for a 6-month history of paroxysmal cough in July 2013. She was diagnosed with right lower lung adenocarcinoma (cT2aN3M1b, stage IV, anaplastic lymphoma kinase [ALK]+) with bone metastasis in other hospital and came to participate a phase III trial of crizotinib (No. NCT01639001).

Computed tomography (CT) scan revealed a mass in the right lower lung, two masses in the right breast located in lower and outer quadrant, upper and inner quadrant separately. We further identified the nature of two masses in the right breast by needle biopsy. Immunohistochemistry (IHC) showed ALK(+) thyroid transcription factor-1 (TTF-1) (+), NapsinA(+), P63(−), estrogen receptor (ER−), progesterone receptor (PR−), C-erbB-2(−), P53(+), CK5 (+), E-cadherin(+), Ki-67(+), MMG(−), FISH using a probe specific to the ROS1 locus (Vysis locus specific identifier ROS1 dual-color, break-apart rearrangement probe; Abbott Molecular, Abbott Park, IL) also showed ROS1 translocation [Figure 1H]. The patient was diagnosed as lung adenocarcinoma with multiple metastases including breast, bone, and brain (T4N3M1b stage IV) harboring with ROS1 rearrangement.

The patient was enrolled in a Phase II study of crizotinib (NCT01945021). She received crizotinib treatment from April 15, 2014 and get a PR with significant shrinkage of the tumor lesion in lung and disappearance of the tumor lesions in breast [Figure 1I and 1J]. However, there was no obvious improvement of the central nervous system lesions and she died 8 months later.

Breast metastasis from extra-mammary malignancies is rare and it just makes up approximately 2% of all malignant mammary neoplasms.[1] ER, PR are the representative markers of primary breast cancer and TTF-1 was the immunoreactive markers for lung adenocarcinoma.[2]

Previous studies have reported that epidermal growth-factor receptor (EGFR) mutations were detected in both the primary lung lesion and breast metastases. In our cases, both the primary lung lesion and breast metastases are...
immunohistochemically positive for ALK or ROS1 rearrangement, and the rearrangements were both confirmed by FISH. We believed that driven genes mutations, including EGFR/ALK/ROS1, were useful biomarkers to identify primary breast cancer from lung cancer breast metastases.\(^3\)

What’s more, targeted tyrosine kinase inhibitor, crizotinib, has been approved by the FDA to treat non-small cell lung cancer patients with ALK or ROS1 rearrangement. It has a response rate of nearly 60% and 7.7 to 8.1 months median progression-free survival (PFS) in ALK positive patients and a 72% objective response rate and 19.2 months median PFS in ROS1 positive patients.\(^4,5\)

It is important to detect EGFR/ALK/ROS1 gene mutation in patients with both lung and breast lesions to identify which is the primary lesion and make more precise treatment.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

None.

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