

CASE REPORT

Complete remission of liver metastasis in a lung cancer patient with epidermal growth factor mutation achieved with Icotinib

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Keywords

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Abstract

A 65-year-old Chinese male was referred to our hospital for epidermal growth factor receptor (EGFR)-mutated advanced non-small cell lung cancer (NSCLC). Aggressive combined therapy with surgical resection of the right upper lung lesion and chemotherapy was performed. One month later, continued Icotinib treatment was used as magnetic resonance imaging revealed liver metastasis (LM). Interestingly, complete remission of the patient's LM lesions was achieved in six months. To our knowledge, this is the first report documenting a successful case of an NSCLC patient with LM treated with Icotinib after receiving a radical resection for pulmonary carcinoma. Our experience could provide a treatment strategy for patients with similar disease.

Introduction

Cancer is the leading cause of death worldwide, with about 20% related to lung cancer. The most common extra-pulmonary sites of distant metastasis in non-small cell lung cancer (NSCLC) patients are the brain, bone, adrenal gland, and liver. In the past decade, epidermal growth factor receptor-tyrosine kinase inhibitors (EGFR-TKIs) have become widely used for the treatment of advanced NSCLC. However, the effect of EGFR-TKI treatment in patients with EGFR-mutated lung adenocarcinoma with liver metastasis (LM) after surgical resection of the lung cancer lesions is unclear.

Case report

In February 2015, a 65-year-old asymptomatic male smoker was admitted to our hospital, after being diagnosed with lung cancer at Sir Run Run Shaw Hospital. The patient denied any other medical history. On hospital admission, physical examination and laboratory test results were normal. A chest computed tomographic scan revealed

an oblong lesion in the right upper lobe of the lung measuring 3.4 cm × 1.6 cm × 2.1 cm and the right hilar lymph nodes were enlarged (Fig 1a,b). Bronchoalveolar lavage was performed and histopathologic examination indicated NSCLC. No distant metastases were found outside the lung during examination. After obtaining the patient's informed consent, a radical resection of the right upper pulmonary carcinoma and mediastinal lymph node dissection by video-assisted thoracic surgery was performed. Histopathologic examination showed a 3.0 cm × 2.0 cm middle to well-differentiated adenocarcinoma of the right upper lobe (Fig 1g). Thirty-eight resected lymph nodes were detected and 10 were positive. The right upper lobe lesion carried an EGFR exon 19 deletion (Fig 1h). According to the 2015 National Comprehensive Cancer Network guidelines for NSCLC, chemotherapy was intravenously administered (pemetrexed 800 mg day 1 + cisplatin 40 mg days 2–3) after the surgery. However, in March 2015, magnetic resonance imaging (MRI) revealed multiple lesions detected in the liver, which were considered to be metastases (Fig 1c,e). Considering that the right

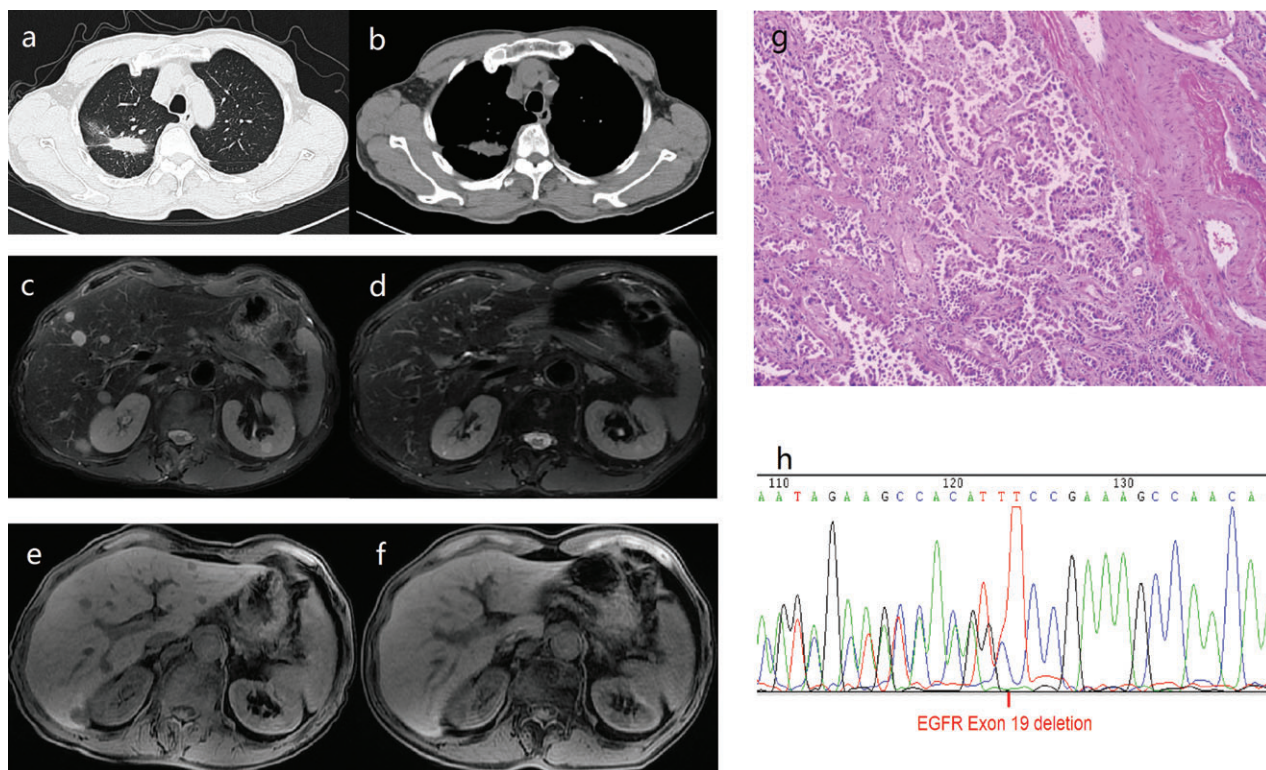


Figure 1. (a,b) Computed tomographic scan obtained February 2015, showing an oblong lesion in the right upper lobe measuring 3.4 cm × 1.6 cm × 2.1 cm. (c,e) Liver magnetic resonance imaging (MRI) obtained March 2015, showing multiple lesions in the liver. (d,f) Liver MRI after six months of Icotinib treatment; the multiple lesions in the liver have vanished. (g) Histopathologic examination of the oblong lesion in the right upper lobe showed middle to well-differentiated adenocarcinoma (hematoxylin and eosin; ×100). (h) Epidermal growth factor receptor (EGFR) exon 19 microdeletion (delE746-A750) detected by direct Sanger sequencing of biopsied samples from the right upper lobe lesion.

upper lung cancer was positive for EGFR mutations, the patient began treatment of 375 mg Icotinib daily, from March 2015. Interestingly, after six months of therapy, liver MRI showed that the multiple lesions had vanished (Fig 1d,f). The patient is currently receiving maintenance Icotinib treatment and no new metastases have been found in 16 months.

Discussion

The incidence of LM in NSCLC patients is 20–40%.^{1,2} Patients with an EGFR mutation tend to have synchronous LM.³ For the past few years, many trials have demonstrated that advanced NSCLC patients with EGFR mutations could clinically benefit from receiving first-line treatment with EGFR-TKIs, such as afatinib, gefitinib, or erlotinib.^{4–6} Nevertheless, in stage IV lung adenocarcinoma patients, LM predicts poorer PFS and OS, despite treatment of susceptible gene mutations with first-line EGFR-TKIs.⁷ Although patients with liver metastasis on initial diagnosis have shorter PFS and OS than patients without liver metastasis,

they could also benefit from first-line treatment with EGFR-TKIs. To our knowledge, no case of LM lesions in an NSCLC patient achieving complete remission by Icotinib treatment after radical resection of pulmonary carcinoma has previously been reported.

Following a traditional therapeutic method, the patient may receive chemotherapy, radiofrequency ablation, or transcatheter arterial chemoembolization after undergoing radical resection of pulmonary carcinoma. However, because the tumor was positive for an EGFR mutation of exon 19 deletion in our case, we developed a strategy that involved continued Icotinib treatment for the liver lesions after radical resection of the pulmonary carcinoma.

Early clinical data has shown that EGFR-TKIs, including icotinib, gefitinib, and erlotinib, are mainly metabolized in the liver. Liver dysfunction may contribute to drug overexposure.^{8–10} Thus, it could be hypothesized that drug overexposure may lead to the higher curative effect of EGFR-TKIs in patients with liver dysfunction caused by LM.

In our case, the patient underwent radical resection of the pulmonary carcinoma before receiving EGFR-TKI treatment. It could be hypothesized that resection of the

pulmonary carcinoma leads to a higher curative effect of EGFR-TKIs, as it lightens the tumor load on the patient; however, further study needs to be conducted to confirm this hypothesis.

This case demonstrated the curative effect of EGFR-TKIs for NSCLC patients with LM, after radical resection for pulmonary carcinoma. Doctors could consider this treatment strategy for patients with similar disease. To date, the patient is still alive, receiving Icotinib treatment, with no further metastasis. Further study is warranted.

Disclosure

No authors report any conflict of interest.

References

- 1 Quint LE, Tummala S, Brisson LJ *et al.* Distribution of distant metastases from newly diagnosed non-small cell lung cancer. *Ann Thorac Surg* 1996; **62**: 246–50.
- 2 Hoang T, Xu R, Schiller JH, Bonomi P, Johnson DH. Clinical model to predict survival in chemo-naïve patients with advanced non-small cell lung cancer treated with third-generation chemotherapy regimens based on Eastern Cooperative Oncology Group data. *J Clin Oncol* 2005; **23**: 175–83.
- 3 Tseng SE, Chiou YY, Lee YC, Perng RP, Jacqueline WP, Chen YM. Number of liver metastatic nodules affects treatment options for pulmonary adenocarcinoma patients with liver metastases. *Lung Cancer* 2014; **86**: 225–30.
- 4 Rosell R, Carcereny E, Gervais R *et al.* Erlotinib versus standard chemotherapy as first-line treatment for European patients with advanced EGFR mutation-positive non-small-cell lung cancer (EURTAC): A multicentre, open-label, randomised phase 3 trial. *Lancet Oncol* 2012; **13**: 239–46.
- 5 Maemondo M, Inoue A, Kobayashi K *et al.* Gefitinib or chemotherapy for non-small-cell lung cancer with mutated EGFR. *N Engl J Med* 2010; **362**: 2380–8.
- 6 Sequist LV, Yang JC, Yamamoto N *et al.* Phase III study of afatinib or cisplatin plus pemetrexed in patients with metastatic lung adenocarcinoma with EGFR mutations. *J Clin Oncol* 2013; **31**: 3327–34.
- 7 Wua KL, Tsai MJ, Yang CJ *et al.* Liver metastasis predicts poorer prognosis in stage IV lung adenocarcinoma patients receiving first-line gefitinib. *Lung Cancer* 2015; **88**: 187–94.
- 8 Li J, Zhao M, He P, Hidalgo M, Baker SD. Differential metabolism of gefitinib and erlotinib by human cytochrome P450 enzymes. *Clin Cancer Res* 2007; **13**: 3731–7.
- 9 Miller AA, Murry DJ, Owzar K *et al.* Phase I and pharmacokinetic study of erlotinib for solid tumors in patients with hepatic or renal dysfunction: CALGB 60101. *J Clin Oncol* 2007; **25**: 3055–60.
- 10 Chen J, Zheng X, Liu DY *et al.* Therapeutic effects and adverse drug reactions are affected by icotinib exposure and CYP2C19 and EGFR genotypes in Chinese non-small cell lung cancer patients. *Asian Pac J Cancer Prev* 2014; **15**: 7195–200.