CASE REPORT

Successful gefitinib treatment administration via gastrostomy tube in a patient with non-small cell lung cancer with dysphagia

Tomohiro Suzumura,¹ Kimio Yonesaka,^{1,2} Hiroshi Tsukuda,¹ Masahiro Fukuoka¹¹Izumi Municipal Hospital, Izumi-shi, Japan²Kinki University School of Medicine, Osaka-sayama, Japan**Correspondence to**Dr Kimio Yonesaka,
yonesaka2002@yahoo.co.jp

Accepted 21 February 2014

SUMMARY

A 72-year-old woman with dysphagia was diagnosed with lung adenocarcinoma and metastatic meningeal tumour that impaired the medulla. Owing to a bulky tumour beside the medulla, radiosurgical control of the meningeal tumour was achieved before systemic therapy. Genomic examination of the tumour revealed an existing epidermal growth factor receptor (EGFR) exon 19 deletion, for which an EGFR tyrosine kinase inhibitor such as gefitinib was the standard therapy. However, because of dysphagia, the patient was unable to orally ingest gefitinib. Gefitinib was delivered via gastrostomy tube as a suspension after spontaneous dissolution in hot water. One month later, the patient's symptoms, including dysphagia, were drastically improved and she had recovered sufficiently to orally ingest gefitinib. Gefitinib-associated toxicity comprises only mild liver dysfunction and skin rash. CT scanning and MRI detected drastic shrinkage of the primary lung and meningeal tumours. The patient continued to take gefitinib and has remained symptom-free for 9 months.

BACKGROUND

Lung cancer is currently the most common lethal malignancy instead of the most common malignancy. The progressive ageing of society has increased the morbidity associated with lung cancer in developed nations. Lung cancer is usually diagnosed at a non-curative advanced stage in which standard chemotherapy prolongs survival and improves the quality of life (QOL). Non-small cell lung cancer (NSCLC) comprises 85% of all lung cancers. NSCLC, especially non-squamous cell carcinoma, often possesses specific oncogenic mutations to which cancer cells become addicted for their own proliferation and survival. The epidermal growth factor receptor (EGFR) is frequently expressed as receptor-type tyrosine kinase in NSCLC. Mutations in the tyrosine kinase domain-coding portion of the EGFR gene lead to constitutive kinase activation, followed by intracellular growth and signal transduction. Gefitinib is the first selective inhibitor of the EGFR tyrosine kinase. Gefitinib binds to an ATP-binding site on the EGFR tyrosine kinase and competitively inhibits tyrosine kinase activation. EGFR gene mutation-addicted tumours were significantly sensitive to gefitinib in preclinical and clinical studies. In randomised clinical trials, gefitinib significantly prolonged the progression-free survival of patients with NSCLC

with the EGFR mutation, compared with cytotoxic chemotherapy.^{1–3} Currently, gefitinib is among the standard first-line therapies for advanced NSCLC with the EGFR mutation. In particular, patients with the EGFR mutation and extremely poor performance statuses (PSs) benefit from first-line gefitinib treatment.^{4,5}

CASE PRESENTATION

A 72-year-old woman presented to her family physician with a 1-week progressive history of dysphagia and dysarthria. Brain MRI detected a meningeal tumour beside the medulla (figure 1A). She was referred to a neurosurgeon for meningeal tumour treatment. Neurosurgeons considered the meningeal tumour to be a metastasis of a cancer or primary meningeal tumour. Because a bulky tumour was located beside the medulla, radiosurgical control of the meningeal tumour was preferentially achieved prior to systemic therapy. She urgently underwent opposing portal irradiation therapy of 12 Gy in four fractions and subsequently stereotactic radiation therapy of 21.6–24 Gy in six fractions for the meningeal tumour. The patient's symptoms, particularly dysphagia, did not improve after the radiosurgery and rapidly increased general fatigue caused her to remain in bed for nearly an entire day. At that time, her physical condition declined to an Eastern Cooperative Oncology Group (ECOG) PS of 4. She was referred to us to receive palliative therapy for the advanced cancer. A chest radiograph showed multiple patchy shadows in the bilateral lung and a chest CT scan detected a solid primary tumour (3 cm at the longest diameter) in the upper lobe of the left lung, some metastases in the bilateral lung and lymph node metastases in the left hilum and mediastinum (figure 2A). Bronchoscopic sampling of the left lung primary tumour revealed lung adenocarcinoma. We evaluated the tumour sample for EGFR genome mutations and the analysis revealed an exon 19 deletion in the tumour.

TREATMENT

As the patient experienced severe dysphagia due to meningeal metastasis that impaired the medulla, oral administration of gefitinib in tablet form was impossible. We attempted to perform a percutaneous endoscopic gastrostomy and administer gefitinib via gastrostomy tube. According to a simple suspension method, a 250 mg gefitinib tablet was

CrossMark

To cite: Suzumura T, Yonesaka K, Tsukuda H, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-202705

Figure 1 Brain MRIs revealing a meningeal tumour beside the medulla before (A) and post (B) gefitinib treatment.

dissolved in hot water without crushing and was subsequently administered to the patient daily.

After 14 days of gefitinib administration, a chest radiographic examination detected tumour shrinkage. After 35 days, a chest CT revealed significant tumour shrinkage (figure 2B). After 40 days, the symptoms, especially dysphagia, were remarkably improved and the patient began oral gefitinib intake. MRI detected drastic shrinkage of the medulla tumour (figure 1B). The patient developed mild liver dysfunction (grade 2, according to the Common Terminology Criteria for Adverse Events V4.0) due to gefitinib toxicity and thus we planned to discontinue the treatment. After her liver dysfunction improved, gefitinib was administered every second day.

OUTCOME AND FOLLOW-UP

Nine months after beginning the gefitinib treatment, the patient continued to ingest gefitinib orally. She remained symptom-free, with an ECOG PS of 0. Gefitinib-associated toxicity comprises only manageable mild liver dysfunction and skin rash. CT scan and MRI indicated good responses in both the lung and meningeal tumours.

DISCUSSION

In this case, gefitinib administration via gastrostomy tube was proven beneficial even in a patient with severe dysphagia. EGFR tyrosine kinase inhibitors, including gefitinib, were developed as

orally administered agents. In this case, gefitinib was delivered once daily via gastrostomy tube in suspension form after spontaneous dissolution in hot water (55°C) for 10 min. An alternative administration manner would potentially influence the pharmacokinetics of gefitinib, although a pharmacokinetic analysis has not been reported in NSCLC. However, in a healthy volunteer, gefitinib administration via nasogastric tube achieved a bioavailability of 99.1%, relative to the whole tablet.⁶ In a comparison of tablets ingested by drinking and via nasogastric tube, the estimate-of-treatment ratios were close to 1.0 for the area under the curve (1.006 and 0.928, respectively) and the peak concentration (C_{max}; 1.012 and 0.964). There appeared to be no clinical significant differences in absorption or elimination between the preparations.

In this case, gefitinib achieved steady tumour shrinkage within 1 month; therefore, the patient was able to ingest gefitinib orally. Gefitinib administration via a gastrostomy tube might impair the QOL because of physical and mental discomfort. However, the good, steady response of gefitinib minimised the discomfort of the gastrostomy tube. Patients with NSCLC with poor PS have few treatment options. For PS 3 patients with NSCLC, chemotherapy is not always recommended because of concerns about severe toxicity. However, in cases of poor PS NSCLC with EGFR mutations, gefitinib was reported to be an efficient treatment option with which the QOL and symptoms were improved with tolerable toxicity.⁷

Figure 2 Chest CT scans showing multiple nodules in the bilateral lung fields before (A) and post (B) gefitinib treatment.

Learning points

- ▶ Patients with non-small cell lung cancer with poor performance status have few treatment options.
- ▶ The administration of a simple gefitinib suspension via a gastrostomy tube allows for an improved quality of life.
- ▶ This case demonstrates the benefit of gefitinib administration via a tube in patients with dysphasic lung adenocarcinoma with epidermal growth factor receptor mutations.

Acknowledgements The authors wish to thank the staff of the pharmaceutical department in their hospital for collecting information about the simplified suspension method, the certified nurse specialist in cancer chemotherapy nursing for practicing the administration method and Dr Nobuko Yanagawa at Tane General Hospital.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Mok TS, Wu YL, Thongprasert S, *et al.* Gefitinib or carboplatin-paclitaxel in pulmonary adenocarcinoma. *N Engl J Med* 2009; 361:947–57.
- 2 Mitsudomi T, Morita S, Yatabe Y, *et al.* Gefitinib versus cisplatin plus docetaxel in patients with non-small-cell lung cancer harbouring mutations of the epidermal growth factor receptor (WJTOG3405): an open label, randomised phase 3 trial. *Lancet Oncol* 2010;11:121–8.
- 3 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.
- 4 Inoue A, Kobayashi K, Usui K, *et al.* First-line gefitinib for patients with advanced non-small-cell lung cancer harboring epidermal growth factor receptor mutations without indication for chemotherapy. *J Clin Oncol* 2009; 27:1394–400.
- 5 Maemondo M, Minegishi Y, Inoue A, *et al.* First-line gefitinib in patients aged 75 or older with advanced non-small cell lung cancer harboring epidermal growth factor receptor mutations: NEJ 003 study. *J Thorac Oncol* 2012; 7:1417–22.
- 6 Cantarini MV, McFarquhar T, Smith RP, *et al.* Relative bioavailability and safety profile of gefitinib administered as a tablet or as a dispersion preparation via drink or nasogastric tube: results of a randomized, open-label, three-period crossover study in healthy volunteers. *Clin Ther* 2004;26:1630–6.
- 7 Goss G, Ferry D, Wierzbicki R, *et al.* Randomized phase II study of gefitinib compared with placebo in chemotherapy-naïve patients with advanced non-small-cell lung cancer and poor performance status. *J Clin Oncol* 2009;27:2253–60.

Copyright 2014 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow