CASE REPORT

An unusual response with long term survival using erlotinib in NSCLC lung with brain metastases

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SUMMARY

We present a case of a middle-aged woman with adenocarcinoma of the lung and metastatic brain lesions. In view of her poor general condition and poor compliance to first-line chemotherapy, the patient was kept on tablet erlotinib after whole brain radiotherapy. This novel treatment resulted in a dramatic response with radiological regression in both the primary lung

lesion and metastatic intracranial lesions translating in unexpected and ongoing 24-month survival.

BACKGROUND

Lung cancer is the leading cause of cancer-related death worldwide.¹ Non-small cell lung cancer (NSCLC) accounts for about 80% of all lung

Figure 1 CT scan (plain and contrast) of the head showing a peripheral enhancing hypodense mass lesion in the region of the cerebellar vermis, measuring approximately 2.4 cm x 2.1 cm, with a compressed fourth ventricle, and another similar mass in the right occipitoparietal region, measuring approximately 3.2 cm x 2.4 cm, compressing the occipital horn of the right lateral ventricle.

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Figure 2 Chest X-ray showing an irregular opacity in the left suprahilar region.

cancers and approximately half of the patients present with advanced disease at the time of diagnosis.² Tyrosine kinase inhibitors (TKIs) are found to be effective drugs, improving progression-free survival (PFS), as compared to traditional chemotherapy.^{3–6} About 20–30% of patients with primary lung carcinoma present with brain metastases and have poor prognosis.⁷ Response to chemotherapy and radiotherapy is seen in only 50–60% of patients with unresectable brain metastases.⁸ Traditionally, brain metastases have been treated with whole brain radiotherapy (WBRT) with a response rate of only 15–30% and a median survival of about 6–8 months. Chemotherapy has not shown any benefit over WBRT in survival of patients with brain metastases. Whereas the mutations in epidermal growth factor receptor (EGFR) have been shown to predict response rate and survival in patients with NSCLC who have been treated with erlotinib and gefitinib.^{9–10} However, their effect on metastatic lung carcinoma, especially on the brain, is controversial.

CASE PRESENTATION

A 43-year-old postmenopausal woman, a non-smoker with no comorbidities, presented to our radiation oncology clinic in July 2013, with headache and vomiting for 15 days. The headache was persistent and vomiting was projectile in nature, suggesting

raised intracranial pressure. On general examination, mild pallor and dyspnoea (respiratory rate 20 breaths/min) were present. Further, left-sided fine crepitation was observed in the lower lobe, suggesting an infective component, with the rest of the findings being normal. On central nervous system examination, the patient was well oriented with intact cranial nerves and no gross motor or sensory deficit.

INVESTIGATIONS

On investigation, contrast-enhanced CT (CECT) of the head in July 2013 showed a peripheral enhancing hypodense mass lesion in the region of the cerebellar vermis, measuring approximately 2.4 cm×2.1 cm, with a compressed fourth ventricle, and another similar mass in the right occipitoparietal region, measuring approximately 3.2 cm×2.4 cm, compressing the occipital horn of the right lateral ventricle ([figure 1](#)). Chest X-ray showed an irregular opacity in the suprahilar region ([figure 2](#)), suggestive of a neoplastic lesion, which was further corroborated by CECT scan of the thorax—suggestive of an ill-defined heterogeneously enhancing lesion in the left hilar and suprahilar regions ([figure 3](#)). Owing to the patient's stage 4 metastatic disease and poor general condition, a quick and minimally invasive approach in the form of fine-needle aspiration cytology (FNAC) was performed. FNAC from the lung lesion confirmed the diagnosis of adenocarcinoma. The patient was immediately taken up for treatment and no further EGFR testing was performed.

TREATMENT

In view of the histopathological diagnosis of adenocarcinoma, lung chemotherapy with pemetrexed (500 mg) and cisplatin (50 mg) was started followed by palliative WBRT. The prescribed dose was 30 Gy in 10 fractions. A second cycle of chemotherapy was subsequently given. Meanwhile, the patient experienced a worsening of symptoms after 1 week. She improved with conservative management. In the light of her poor compliance to chemotherapy and progression of the primary lung lesion, the patient was started on tablet erlotinib 150 mg once daily.

OUTCOME AND FOLLOW-UP

The erlotinib was well tolerated by the patient, with significant radiological response in both, primary lung ([figure 4](#)) and metastatic brain lesions ([figures 5 and 6](#)). At the time of writing this report, the patient was absolutely asymptomatic and on tablet

Figure 3 Contrast-enhanced CT scan of the thorax showing a well-defined heterogeneously enhancing lesion in the left hilar and suprahilar regions.

Figure 4 Contrast-enhanced CT scan of the thorax after 11 months showing complete disappearance of the left hilar lesion.

erlotinib once a day. CECT of the brain showed complete remission of the intracranial lesions ([figure 7](#)). At the same time, CECT of the thorax showed complete disappearance of the lung lesion ([figure 4](#)). The patient was free of neurological as well as respiratory symptoms and her performance status had increased as well.

DISCUSSION

The role of erlotinib in brain metastasis secondary to NSCLC of the lung has been evaluated in various studies. Lai *et al*¹¹ reported one of the first cases of NSCLC with EGFR mutation and brain metastases showing complete remission with WBRT followed by oral tablets of erlotinib. Fekrazad *et al*¹² reported

Figure 5 Contrast-enhanced CT of the brain after 4 months showing resolution of the initial lesion.

Figure 6 Contrast-enhanced CT of the brain after 10 months showing complete resolution and initial calcification around the primary disease.

on a patient who underwent WBRT for brain metastases that developed secondary to NSCLC, and later received erlotinib on intracranial recurrence. The patient demonstrated complete

remission of the brain metastases, however, whether such response was due to erlotinib or due to the delayed effects of WBRT is debatable. Sperduto *et al*,¹³ in a multicentre phase III

Figure 7 Contrast-enhanced CT of the brain after 15 months showing calcification and postradiotherapy changes.

trial, Radiation Therapy Oncology Group (RTOG) 0320, on 126 patients, compared the addition of erlotinib and temozolomide to WBRT and stereotactic radiosurgery (SRS) boost. They showed erlotinib and temozolomide are both equally ineffective in improving OS and PFS. These results were similar to that of a phase II trial conducted by Welsh *et al*,¹⁴ with the caveat being—neither of the trials had selected patients on the basis of EGFR mutation. In both trials, there was improvement in overall survival (OS) and PFS but it was not statistically significant. Thus the evidence for use of erlotinib in metastatic lung carcinoma, especially with unknown receptor status, is not robust enough.

Traditionally, brain metastases have been associated with dismal outcome with median survival of 6–11 months as reported in various case series. WBRT remains the standard treatment with a renewed interest in addition of either a SRS boost or TKI such as erlotinib, or both, to improve the outcome in such patients. Single agent erlotinib may be an excellent option in treating progressive brain lesions in metastatic adenocarcinoma of the lung, especially in patients with poor compliance to chemotherapy. In the light of improvement in OS—24 months and ongoing—as seen in our case, randomised

studies adequately powered to establish the efficacy of erlotinib in multiple brain metastases secondary to NSCLC lung are needed to reinforce the confidence in day to day treatment practice.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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Learning points

- Erlotinib is a viable, effective and safe agent for empirical use in non-small cell lung cancer of the lung with brain metastases, even with unknown epidermal growth factor receptor status.
- In this case, the addition of erlotinib to traditional whole brain radiotherapy improved overall survival and progression-free survival.
- The role of erlotinib becomes even more valuable in patients with low performance status or those non-compliant to chemotherapy.
- Complete radiological remission, as seen in this case, is rather uncommon, but such encouraging results may justify the empirical introduction of erlotinib in carefully selected patients.

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