CASE REPORT

Surgery and radiation therapy for brain metastases from classic biphasic pulmonary blastoma

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SUMMARY

Pulmonary blastoma, a rare malignant lung tumour, can metastasise to the brain. However, there is no evidence for any effective treatment. The aim of this report is to discuss the treatment options for pulmonary blastoma and confirm the necessity for a pathological diagnosis. A 75-year-old man was admitted with progressive right-sided hemiplegia and aphasia. MRI showed multiple brain tumours. A left frontal lobe lesion was surgically resected, after which he underwent whole brain radiation (30 Gy/10 fractions). He died of an acute exacerbation of interstitial pneumonia. On performing autopsy, partial responses in the brain metastases that had been irradiated were confirmed pathologically. Thus, we present pathological confirmation that surgery and radiation therapy have therapeutic effects on brain metastases from pulmonary blastoma.

BACKGROUND

Pulmonary blastoma, a rare malignant tumour of the lung, was first described by Barrett and Barnard.¹ It is subdivided into two categories; classic biphasic pulmonary blastoma (CBPB) and well-differentiated fetal adenocarcinoma (WDLA). CBPB is reported to comprise 0.25–0.5% of all primary lung tumours.² According to Larsen *et al*, patients with the WDLA subtype survive longer (median 34 months) than those with the CBPB type (median 11 months).³ In addition to the histological type, other indicators of poor prognosis are tumour recurrence, metastasis at initial presentation, and tumour size greater than 5 cm⁴: only the second of these was present in our case. Brain metastases were first reported by Barson *et al*.⁵ Because of the rarity of this tumour, treatment remains controversial and the efficacy of adjuvant chemotherapy and radiotherapy has not been well established.⁶ We report the case of a 75-year-old man with CBPB with brain metastases. This is the first reported case of confirmed partial pathological response in brain metastases from pulmonary blastoma after combined surgical and radiation therapy.

CASE PRESENTATION

A 75-year-old man with a history of non-specific interstitial pneumonia, hypertension and cerebrovascular disease was admitted to our institution in August 2011 for an acute exacerbation of interstitial pneumonia. At that time, no evidence of malignancy was found. In June 2012, he reported progressive difficulty in walking, and weakness in his right hand. A CT scan showed multiple brain tumours and he was admitted to the department of

neurosurgery. He had a smoking history of 135 pack-years and drank two glasses of Japanese spirits every day. He had no known drug allergies. On admission, vital signs were normal except for SpO₂ of 94% (on room air). Physical examination was normal except for rales heard in both lungs. On neurological examination, he was alert with no evidence of increased intracranial pressure. He had decreased muscle tone on the right side (3/5), but normal muscle tone on the left.

INVESTIGATIONS

Laboratory data were unremarkable. CT of the chest showed a right lower hilar lymph node enlargement accompanied by several enlarged mediastinal lymph nodes (figure 1A, B). No primary lesion was detected, but we suspected to find it in the lung field. There was a reticular shadow and ground glass opacity at the base of both lungs, which was caused by interstitial pneumonia. CT of the abdomen was unremarkable. Cranial CT showed a 38 mm lesion in the left and a 20 mm lesion in the right frontal lobe with surrounding oedema and evidence of intraleSIONAL haemorrhage. MRI suggested multiple brain metastases (figure 1C, D). A positron emission tomography scan showed accumulation in hila and mediastinal lymph nodes bilaterally, suggestive of metastases.

DIFFERENTIAL DIAGNOSIS

Differential diagnosis included other histological subtypes of lung cancer (squamous cell carcinoma, adenocarcinoma, small cell lung cancer, large cell carcinoma).

TREATMENT

Total resection of the left frontal tumour was attempted; however, a postoperative positron emission tomography scan showed residual tumour. Pathologically, a mixture of immature glandular formation and spindle cell proliferation was found (figure 2B–D). A diagnosis of metastasis from pulmonary blastoma was made. Postoperatively, the residual brain tumours were treated with whole brain radiation (30 Gy/10 fractions). Because the patient's Karnofsky Performance Scale score⁷ was 50 and he had interstitial pneumonia, no chemotherapy was initiated. He was able to sit in a wheelchair postoperatively and postradiation therapy.

OUTCOME AND FOLLOW-UP

A month after discharge, the patient was hospitalised for an acute exacerbation of interstitial pneumonia for which he was treated with antibiotics

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Figure 1 Radiographic findings. (A) Chest CT showing interstitial pneumonia and hilar lymph node enlargement. (B) Chest CT showing a 2 cm nodular lesion (arrow) that was interpreted as inflammatory change in the right lung periphery. Subsequent autopsy showed this to be the primary pulmonary blastoma. (C) Brain MRI T1-enhanced coronal view showing enhanced bilateral tumour deposits (arrows). The left-sided lesion is 46 mm in diameter. (D) Brain MRI T1-enhanced axial view showing enhancement of tumour deposit on the left side of the brain (arrow).

Figure 2 Histological findings. (A) Pathology of the primary lesion in the lung showing a biphasic appearance with immature glandular structures (arrow) and proliferation of spindle-shaped cells (inside the circle) (H&E stain; $\times 40$). (B) Pathology of a brain metastasis (surgical specimen) showing a structure similar to that found in the lung specimen (A). An immature glandular structure is seen inside the circle (H&E stain; $\times 40$). (C) Pathology of a brain metastasis (surgical specimen) showing an immature glandular structure with epithelial characteristics in which duct formation is positive for cytokeratin AE1/AE3 (H&E stain; $\times 200$). (D) Pathology of a brain metastasis (surgical specimen) showing proliferation of spindle-shaped cells, which are positive for vimentin and have mesenchymal characteristics (H&E stain; $\times 200$).

Figure 3 Histology of brain metastasis after radiation. (A) Tissue from the right temporal lobe (basal ganglia): much of the 2 mm tumour is necrotic, presumably because of radiation therapy. However, some viable tumour tissue is visible in the left upper part of the field (arrow) (H&E stain; $\times 4$) (B) High-power view of the viable component of the tumour (H&E stain; $\times 100$).

and prednisolone. This treatment was ineffective and he died 5 days after admission. MRI performed on this admission showed a decrease in the volumes of both frontal lobe masses consistent with a partial response.

At autopsy, a 2 cm mass was found in the right lung together with mediastinal lymph node metastases (figure 2A). A 2 mm focus of viable tumour was found in the right frontal lobe; no other lesions were found (figure 3A, B). Based on these findings, we concluded that the combination of surgery and radiation therapy had resulted in a pathologically confirmed partial response. Written informed consent for publication of this case report and any accompanying images was obtained from the patient after completion of radiation.

DISCUSSION

Pulmonary blastoma has a poor prognosis, the 5-year survival rate being only 16%.⁸ Histologically, the tumour consists of epithelial and mesenchymal components. Because of its histological characteristic of intratumoural heterogeneity and its rarity, this tumour is extremely difficult to diagnose preoperatively by either non-invasive or invasive techniques.⁹ Because there have been so few reported cases, the optimal treatment is yet to be

determined. In particular, the treatment for brain metastases is controversial.⁶

In our case, because the tumour had malignant epithelial components with glandular structures in a small proportion of the sample, the frozen section diagnosis provided during surgery was adenocarcinoma. For multiple brain metastases from lung adenocarcinoma, whole brain radiation is a treatment option. Because of the rarity of this condition, there are no large-scale studies supporting use of radiation therapy for brain metastases from pulmonary blastoma. However, radiation therapy has been used as adjuvant therapy after resection of brain metastases from pulmonary blastoma.^{6 10} There are also some reports of favourable responses to radiation therapy used alone.^{11–13}

This is the first reported case of pulmonary blastoma with brain metastases in which relief of neurological symptoms was obtained by surgical and radiation therapy and the therapeutic effects were confirmed by pathological evaluation.

Learning points

- Surgical and radiation therapy can be of therapeutic effect for brain metastases from pulmonary blastoma.
- It is important to make an accurate histopathological diagnosis before starting treatment.
- Although pulmonary blastomas characteristically present as large primary tumours, the primary may be smaller than the metastases, as was true in this case.

Contributors KK handled the case with KY and HS. YS discussed the pathology of the disease and contributed to the design. KK wrote the draft of the case, and the clinical part was revised by KY and HS. The pathological part was revised by YS. The final version was approved by all the authors.

Competing interests None.

Patient consent Obtained.

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