Case Report

Journal of INTERNATIONAL MEDICAL RESEARCH

Journal of International Medical Research
2016, Vol. 44(3) 742–752

DOI: 10.1177/0300060515618053
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Multiple pulmonary metastases in recurrent intracranial meningioma: Case report and literature review

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Abstract

Multiple pulmonary metastases from meningioma are rare. We report here a 59-year-old man with multiple pulmonary metastases from a recurrent intracranial meningioma. The primary intracranial tumour in the left occiput was totally excised in 2009. Pathological examination confirmed the diagnosis of atypical meningioma and adjuvant radiotherapy was given to help prevent recurrence. However, recurrence occurred in the left occipital region in 2011 and the meningioma was re-excised in 2012. At the same time, multiple metastases in the right pulmonary lobe were found and excised 3 months after the second craniotomy. The patient has not developed any further recurrence or metastases to date. Neurosurgeons should be aware of the occurrence of pulmonary metastases in patients with intracranial meningioma; potential predictive factors include atypical meningioma, venous sinus invasion, recurrence or previous intracranial surgery, and loss of heterozygosity.

Keywords

Meningioma, pulmonary, multiple metastases

Date received: 1 August 2015; accepted: 27 October 2015

Introduction

Meningiomas are the second most common primary intracranial neoplasms.[1] Most are benign tumours, with a low rate of recurrence after total resection.[2] However, it has been reported that 2–10% of meningiomas exhibit aggressive behaviour and 0.1–1% of all patients with primary meningiomas develop distant metastases.[2–4] The most

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frequent site for extracranial metastases is the lung, accounting for 61% of all meningioma metastases.[5] Here we report a rare case of multiple pulmonary metastases from a recurrent intracranial meningioma, together with a review of previous similar cases reported in the literature.

Case report

A previously healthy 56-year-old man was admitted to the Department of Neurosurgery, First Affiliated Hospital, Zhejiang, China, in June 2009 with dizziness and blurred vision for about 1 month. Magnetic resonance imaging (MRI) revealed a $4 \times 4 \times 5$ cm homogeneously enhancing tumour in the left occiput with adjacent brain parenchymal oedema, which was suggestive of a meningioma (Figure 1). Other laboratory and imaging examinations, including chest X-radiography and abdominal B-scan ultrasound, did not show any abnormalities.

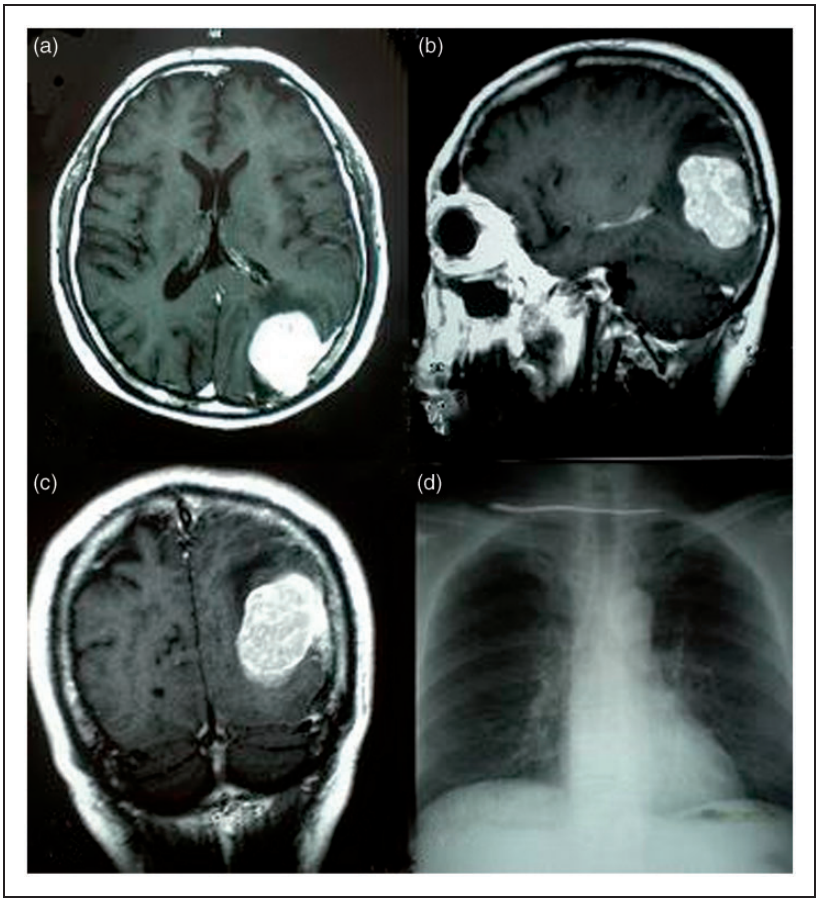

Figure 1. Preoperative magnetic resonance imaging in a male patient with intracranial meningioma: T1-weighted with contrast medium showing a homogeneously enhancing tumour in the left occiput: (a) axial; (b) sagittal; (c) coronal views. (d) Normal chest X-radiography taken before the first craniotomy in 2009.

The patient underwent total resection of the tumour. Histological examination of the mass revealed sheet-like growth and lobular arrangement of the tumour cells, with atypia and mitotic figures (Figure 2a); the skull was invaded locally and blood sinusoids were seen in the interstitial tissue. Immunohistochemical staining demonstrated that the tumour cells were positive for vimentin, epithelial membrane antigen, Ki-67 (>25%) and progesterone receptor, but negative for S100. Pathological examination confirmed the diagnosis of atypical meningioma (World Health Organization grade II).[6] Subsequently, the patient underwent adjuvant radiotherapy to help prevent recurrence. The postoperative course was uneventful and the patient's preoperative dizziness and blurred vision abated.

In December 2011, a small mass was noticed by the patient in the left occipital scalp. By April 2012 this had become much larger and the patient was readmitted to hospital. MRI showed a $5 \times 5 \times 5$ cm homogeneously enhancing tumour in the left occiput region, suggestive of a recurrent meningioma. The patient also underwent whole-body [^{18}F]-2-fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography, which revealed multiple lesions in the right pulmonary lobe, the largest of which was 2.6×2 cm and located in the inferior lobe, with lymphadenectasis in the right hilus (Figure 3). These multiple lesions were thought to be lung neoplasms or metastases from an unknown primary. A second craniotomy was performed and a well-demarcated subcutaneous mass was seen that had invaded the subcutaneous

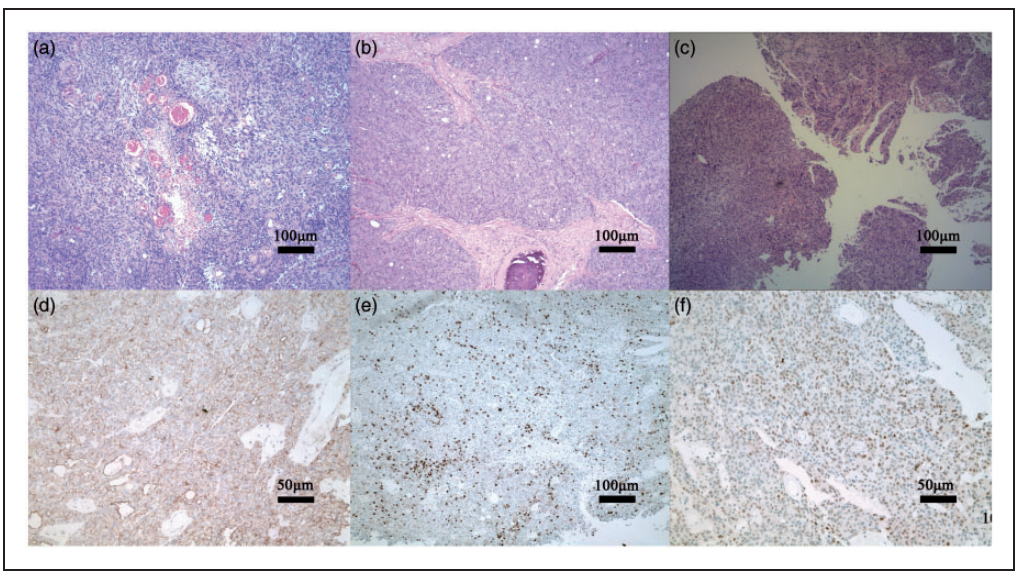

Figure 2. Histopathology of resected tumours in a male patient with intracranial meningioma and pulmonary metastases, showing sheet-like growth and lobular arrangement of the tumour cells, with atypia and mitotic figures: (a) primary meningioma; (b) recurrent meningioma; (c) pulmonary metastasis, showing giant cells. Haematoxylin and eosin. Immunohistochemical staining in recurrent meningioma showing tumour cells positive for epithelial membrane antigen (d), Ki-67 (e) and progesterone receptor (f). The colour version of this figure is available at: http://imr.sagepub.com.

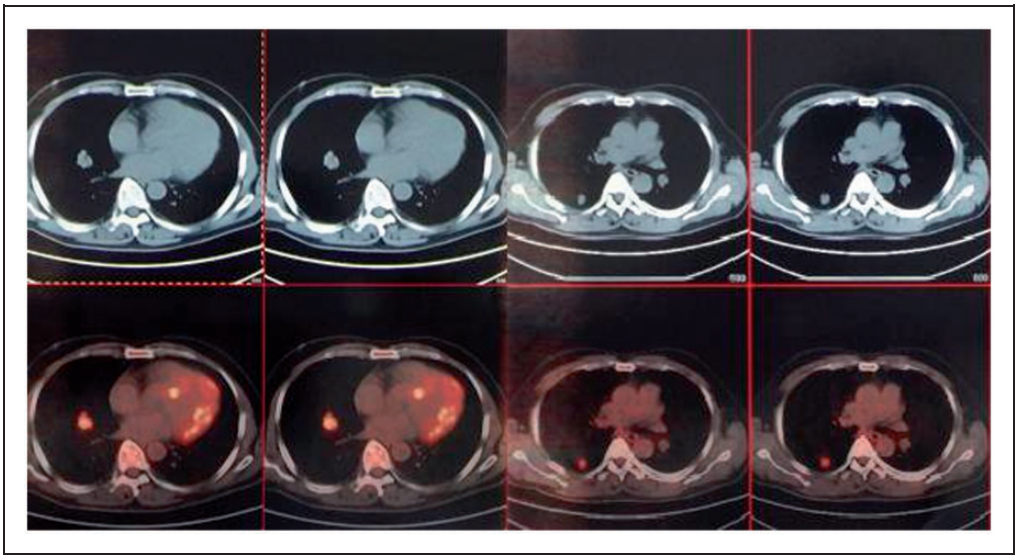

Figure 3. Whole-body [^{18}F]-2-fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography showing multiple lesions in the right pulmonary lobe in a male patient with intracranial meningioma. The colour version of this figure is available at: http://imr.sagepub.com.

tissues, local skull and meninges. The tumour and the invaded meninges and skull were totally removed surgically. The postoperative pathological diagnosis was the same as before (Figure 2b,d–f).

The patient subsequently underwent removal of the lesions in the right lung 3 months after the second craniotomy. Unexpectedly, histological examination revealed different sized tumour cells arranged in sheets, with atypia and giant cells (Figure 2c). Immunohistochemical staining demonstrated that the tumour cells were positive for epithelial membrane antigen, Ki-67 (> 10%) and progesterone receptor, but were negative for S100, CK7, CK14, CD20 and CD3. The pathological diagnosis was metastatic meningioma. Because of residual lymphadenectasis in the right hilus after the thoracotomy, the patient was recommended to undergo chemotherapy but he refused. He therefore received radiotherapy at a dose of 60 Gy for the residual lymphadenectasis. Although the treatment given was not optimum, the patient has not developed any further recurrences or metastases to date.

The patient gave written consent for this case to be published.

Discussion

Multiple pulmonary metastases from intracranial meningiomas are rare. To the best of our knowledge, 35 cases of intracranial meningiomas with multiple pulmonary metastases have been reported since 1960 (Table 1),[7–34] with almost balanced sex distribution (18 male and 17 female cases), despite the fact that meningiomas are more common in women[35] and metastatic meningiomas are more common in men.[36] The median age of these patients was 50 years (age range 21–84 years. The interval from the time of detection of the primary intracranial meningioma to the detection of pulmonary metastases ranged between 2 months and 26 years, but five cases of

Table 1. Reported cases of multiple pulmonary metastases in intracranial meningioma.

Reference	Age, years	Sex	Interval, years[a]	Metastases, *n*[b]	Size, mm[c]	Location[d]	Histology	Treatment[e]	Outcome
Kruse[7]	21	Male	10	6	50	Right occipitoparietal	Meningothelial	Partial resection	Died of convulsion
Aumann et al.[8]	45	Female	5	Multiple	20	Left frontal parasagittal	Transitional	Total resection	NA
LeMay et al.[9]	56	Female	10	Multiple	NA	NA	Benign	Partial resection	Died of disease 3 years after thoracotomy
Fukushima et al.[10]	50	Male	8	9	NA	Left posterior fossa with skull invasion	Papillary	Total resection and radiotherapy	NA
Ng et al.[11]	66	Male	Concurrent	Multiple	15	Parasagittal region of the left precentral gyrus	Transitional	NA	Died of acute myocardial infarction
Hishima et al.[12]	25	Female	Prior to intracranial tumour	Multiple	50	Right parietal region adjacent to the falx	Meningothelial	Partial resection	NA
Murrah et al.[13]	53	Female	10	9	45	Left frontal hemispheric convexity	NA	Partial resection	Alive with disease 2 years after thoracotomy
Adlakha et al.[14]	70	Male	Concurrent	Multiple	NA	Left frontal parasagittal	Psammomatous	Resection	No evidence of disease 7 years after thoracotomy
	39	Female	6	Multiple	NA	Left parietal parasagittal	Atypical	Partial resection and gamma knife radiosurgery	Died of disease 10 years after initial presentation
Figueroa et al.[15]	50	Female	5	Multiple	NA	Left cranial fossa	Transitional	Total resection and radiotherapy for metastases	Alive with disease 32 years after radiotherapy

(continued)

Table 1. Continued.

Reference	Age, years	Sex	Interval, years[a]	Metastases, *n*[b]	Size, mm[c]	Location[d]	Histology	Treatment[e]	Outcome
Travitzky et al.[16]	41	Female	19	Multiple	80	NA	Malignant	Total resection and radiotherapy	No evidence of disease 6 months after doxil-induced regression of metastases
Teague and Conces[17]	64	Male	2	3	45	Biparietal	Atypical	Resection	NA
D'Aiuto et al.[18]	71	Male	13	37	60	Right temporo-occipital	Atypical	Resection	No evidence of disease 24 months after thoracotomy
Erman et al.[19]	34	Female	8	Multiple	NA	Left frontal-parasagittal	Meningotheliomatous/ atypical	Partial resection and radiotherapy	Died of disease shortly after thoracotomy, radiotherapy and chemotherapy of the metastases
Yekeler et al.[20]	43	Male	0.2	Multiple	30	Right convexity	NA	Resection	NA
Fabi et al.[21]	57	Male	12	Multiple	35	Right frontal	Malignant	Total resection and radiotherapy	Alive with disease 6 months after diagnosis of metastases
Gladin et al.[22]	47	Male	11	3		Right frontal	Transitional	Total resection	NA
Asioli et al.[23]	58		12	Multiple	30	NA	Meningothelial	Resection	Alive with disease 18 months after thoracotomy
Ishibashi et al.[24]	68	Male	26	Multiple	60	NA	NA	Resection	NA
Psaras et al.[25]	65	Female	15	Multiple	NA	Falx cerebri and superior sagittal sinus	Meningothelial	Total resection and radiotherapy	No evidence of disease 12 months after thoracotomy

(continued)

Table 1. Continued.

Reference	Age, years	Sex	Interval, years[a]	Metastases, *n*[b]	Size, mm[c]	Location[d]	Histology	Treatment[e]	Outcome
Estanislau et al.[26]	75	Male	6	Multiple	NA	Right temporoparietal	Atypical	Total resection	Died about 30 days after radical resection surgery of cervical metastasis
Alexandru et al.[27]	67	Male	NA	NA	NA	Bifrontal	Anaplastic	Partial resection	NA
	26	Female	NA	NA	NA	Multiple supratentorial	Anaplastic	Partial resection	NA
	84	Female	NA	NA	NA	Right frontal	NA	Total resection	NA
	38	Male	NA	NA	NA	Right and left sphenoid, cavernous sinus	Atypical	Partial resection	NA
	52	Female	NA	NA	NA	Right frontal, left parietal and right occipital	Atypical	Partial resection	NA
	57	Male	NA	NA	NA	Right parietal and right occipital	Anaplastic	Partial resection	NA
Sabet et al.[28]	62	Female	Concurrent	Multiple	NA	Left frontal	Anaplastic	Partial resection and radiotherapy	NA
Cheng et al.[29]	46	Male	Concurrent	4	NA	Right parietal	Benign	Total resection	No evidence of disease 5 months after chemotherapy and staged operations for pulmonary lesions
Nakano et al.[30]	34	Male	0.3	Multiple	20	Falx and superior sagittal sinus	Transitional	Total resection	NA
Nakayama et al.[31]	25	Female	Concurrent	Multiple	30	Right parietal	Meningothelial	Total resection	No evidence of disease 7 years after last surgery

(continued)

Table 1. Continued.

Reference	Age, years	Sex	Interval, years[a]	Metastases, *n*[b]	Size, mm[c]	Location[d]	Histology	Treatment[e]	Outcome
Ocque et al.[32]	47	Male	NA	Multiple	NA	NA	Atypical	NA	NA
	44	Female	NA	Multiple	NA	NA	Anaplastic	NA	NA
Frydrychowicz et al.[33]	45	Female	5	Multiple	NA	Left frontal	Atypical	Surgery and radiotherapy	NA
Golemi et al.[34]	65	Male	NA	Multiple	NA	NA	Atypical	Surgery and gamma knife radiosurgery	NA
Present case	59	Male	3	Multiple	26	Left occiput	Atypical	Total resection and radiotherapy	No evidence of disease 3 years after thoracotomy

[a]Interval from time of detection of primary intracranial meningioma to detection of pulmonary metastasis.
[b]Number of pulmonary metastases.
[c]Size of largest pulmonary metastasis.
[d]Location of intracranial meningioma.
[e]Treatment of intracranial meningioma.
NA, data not available.

pulmonary metastases were found concurrently with the primary intracranial meningioma[11,14,28–30] and one pulmonary lesion was identified first;[12] none of the 35 patients reported had obvious pulmonary symptoms such as cough or haemoptysis. Mostly the multiple metastases were located in both lungs; six cases, including the present case, were limited to the right lung[9,12,22,26,31] and one case of metastases was limited to the left lung.[28] The size of the largest metastasis was usually >20 mm in diameter.

The mechanism of multiple pulmonary metastases from intracranial meningiomas is unclear: there seems to be no constant relationship between the presence of metastases and the histological pattern of the intracranial meningioma. However, compared with meningiomas that do not metastasize at all or have a single metastasis, there are some predictive factors for multiple pulmonary metastases. First, atypical meningiomas have a greater tendency to be associated with multiple pulmonary metastases.[14,17–19,26,27,32–34] Venous sinus invasion may be another risk factor for multiple pulmonary metastases,[8,11,12,14,19,25,27,30] although in some cases, including the present case, the intracranial meningioma did not invade the sinuses. Prior surgery may damage the blood–brain barrier, promoting the spread of tumour cells. Intracranial tumour recurrence after the first craniotomy may be predictive of multiple metastases.[9,12,15–19,22,25,27,31,33] Furthermore, loss of heterozygosity at 9p, 1p and 22q has been reported to be a potential predictor of multiple pulmonary metastases.[22]

Multiple pulmonary metastases are usually misdiagnosed as primary or metastatic adenocarcinoma, malignant mesothelioma or melanoma. Yekeler et al.[20] reported that similar signal features on MRI of pulmonary metastases and primary intracranial meningioma, including being isointense on T1- and T2-weighted images and late-phase contrast-enhanced T1-weighted images, might be predictive for diagnosis. Therefore, enhanced pulmonary computed tomography or MRI is recommended for patients with intracranial meningioma and risk factors for multiple pulmonary metastases. If available, positron emission tomography/computed tomography (PET/CT) is also valuable for diagnosis and follow-up after surgery.[28,34] However, PET/CT is not able to identify the cytopathology of pulmonary tumours, so the role of PET/CT in determining the presence of pulmonary metastatic meningioma remains controversial.

The standard treatment for multiple pulmonary metastases from intracranial meningioma has not been established by controlled studies. Commonly, the primary intracranial tumour is treated by surgical resection and postoperative radiotherapy is given for the prevention of local recurrence. It may be possible to perform thoracotomy to surgically remove the pulmonary metastases. However, if this is not feasible, chemotherapy is a valuable option for multiple pulmonary metastases. Travitzky et al.[16] reported that treatment with pegylated liposomal doxorubicin was associated with nearly complete resolution of a pulmonary metastasis in a patient with malignant meningioma. Other chemotherapies, including anthracyclines and alkylating agents, have shown some antitumour effect.[21] Sabet et al.[28] reported radioreceptor therapy using the radiolabelled somatostatin analogue ^{177}Lu-DOTA-octreotate improved the health-related quality-of-life in a patient who had undergone multiple surgical resections and percutaneous radiation.

Due to the rarity of multiple pulmonary metastases in meningioma, it is difficult to study the long-term outcome. In most of the published reports, patients were alive with disease for >18 months or without evidence of disease for >12 months after thoracotomy. Nakayama et al.[31] reported a patient who had pulmonary and pleural metastases

three times, and underwent resection of intracranial recurrences twice, who was alive 21 years after the first operation. The patient presented here has not developed any further recurrence or metastases to date.

In conclusion, blood-borne spread of tumour cells through venous channels is the most likely mechanism of pulmonary metastases in patients with meningioma. Atypical meningiomas, potential sinus invasion, tumour recurrence and loss of heterozygosity at 9p, 1p and 22q may be predictive of multiple pulmonary metastases. Treatment is mainly by surgical resection, with chemotherapy as a valuable option for multiple pulmonary metastases that cannot be totally removed. Enhanced pulmonary computed tomography is recommended for patients with intracranial meningioma and potential risk factors for multiple pulmonary metastases.

Declaration of conflicting interest

The authors declare that there are no conflicts of interest.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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