WHO Grade I Meningioma Metastasis to the Lung 26 Years after Initial Surgery: A Case Report and Literature Review

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Metastases from meningioma grade I are especially rare. We describe a case of a 65-year-old male with meningioma WHO grade I with a history of local recurrence and distant metastasis to the lung 26 years after the initial surgery. The original tumor was localized at the occipital low convexity and invaded into the venous sinus and posterior cranial fossa; it was resected. About 15 years later, the tumor recurred in the posterior cranial fossa and γ-knife radiosurgery was performed. About 4 years later, the recurrent tumor was resected at our hospital. Another 7 years later, the tumor recurred in the same area and right middle cranial fossa. All tumors except that inside the venous sinus were excised. All specimens obtained were classified as meningioma WHO grade I. Preoperative examination of the third operation revealed a nodule in the lower lobe of the right lung. The nodule grew gradually. Four months after the third surgery, partial resection of the right lung was performed. Histology indicated meningioma WHO grade I. The two lesions in the cranium and lung lesions were subjected to fluorescence in situ hybridization of the NF2 gene, and the three specimens had similar findings, genetically confirming them to be metastases of the intracranial meningioma. A literature review of past cases of meningioma progression revealed that the mean duration to metastasis is 12.5, 6.8, 3.7 years for grades I, II, and III, respectively. The current case therefore has an extended time frame.

Keywords: meningioma, extracranial metastasis, WHO grade I, lung, sinus invasion

Introduction

Intracranial meningiomas are the most common tumors of the central nervous system, accounting for 13–26% of all primary intracranial tumors;9 they are typically solitary and benign. Despite being pathologically benign, there are rare cases of metastases to extracranial sites, which take a course of malignancy.2–6 Distinct metastasis of a meningioma is extremely rare, at 0.15%,7 but this may be an underestimation.8 Because of the rare nature of extracranial metastases, no standard management protocol has been established and the prognosis for these patients is unknown.9,10 Most meningiomas are WHO grade I and about 7–15% and 2–4% of meningiomas are WHO grade II and III, respectively.11,12 In metastatic cases, there are more cases of grades II and III. We describe a case of WHO grade I meningioma that had metastasized to the lung and reviewed the relevant literature.

Case

The patient was a 65-year-old male who, 26 years previously, had undergone surgery (at a previous hospital) for occipital low convexity meningioma that had invaded the transverse sinus, sigmoid sinus, jugular vein, and posterior cranial fossa. Part of the tumor in the sinus was left untouched, the remainder of the tumor was excised and a subtotal resection was performed. The tumor was diagnosed as fibrous meningioma. Sixteen years after the operation, the tumor recurred in the posterior cranial fossa and γ-knife radiosurgery was performed at another hospital. A further 3 years later, the tumor recurred and the patient came to our hospital for a second surgery. The second operation was performed and the tumor was completely excised (Figs. 1A and 1B). Histological sections showed a proliferation of spindle cells with oval and elongated nuclei arranged in fascicular or whorl-like arrangements. No atypical features were detected and WHO grade I meningioma was considered (Fig. 1C). Seven years after the second operation, the patient suffered headaches and nausea. Magnetic resonance imaging (MRI) revealed a recurring tumor (size: 6.5 × 5.7 × 5.9 cm) in the location of the previous operation; there was also another tumor in the middle cranial fossa (5.0 × 4.7 × 3.8 cm) where the first operation had been executed (Figs. 2A and 2B). A third operation was scheduled and the preoperative examination was performed. A chest X-ray revealed a nodule shadow in the right middle lung field. In a chest computed tomography (CT), a 2 cm nodule was seen in the lower lobe of the right lung (Fig. 3A). At this time point, treatment for the intracranial tumor was performed which included embolization of the feeding artery and tumor resection (Simpson grade II; Figs. 2C and 2D). There was no macroscopically visible tumor infiltration into the bone, and no histological examination of tumor infiltration was performed. Histologically, the sections showed proliferation of meningothelial tumor cells with oval or elongated nuclei arranged in...
Fig. 1 (A) Pre-second operation. A tumor recurred in the posterior cranial fossa. (B) Radiologically, the tumor was completely resected. (C) The section shows proliferation of spindle cells with oval and elongated nuclei arranged in fasciculi (hematoxylin and eosin, 200×). Atypical features were not evident.

Fig. 2 (A and B) Pre-third operation. The tumor recurred in the same place (6.5 × 5.7 × 5.9 cm) as for the previous operation and additionally, it expanded from the ridge of the resected site to the middle cranial fossa (5.0 × 4.7 × 3.8 cm). (C and D) Tumors were excised for Simpson grade II. (E and F) The sections show proliferation of meningothelial tumor cells with oval or elongated nuclei arranged in intersecting short fascicles or small whorl-like structures [hematoxylin and eosin, (E) 100×, (F) 200×].

Fig. 3 (A) In the chest CT, a 2 cm nodule was seen in the right lower lobe. (B and C) The section showed proliferation of spindle shaped tumor cells with round to oval nuclei forming intersecting short fascicles [hematoxylin and eosin, (C) 200×]. Necrosis was seen in the center of the tumor, but no other atypical features were evident. (D) NF2 gene fluorescence in situ hybridization (FISH) image. NF2 FISH predominantly demonstrated a single pair in the lung tumor. Arrows show one pair of red and green signals per cell. Red signal, NF2 (22q, 12.2); Green (FITC) signal, chromosome 22 centromere.

intersecting short fascicles or small whorl-like structures (Figs. 2E and 2F). No high mitotic figures were found (1 < 10 high power fields). Although a small focus of necrosis was seen in the posterior fossa specimen, it was considered to be an effect of vascular embolization. These findings were consistent with WHO grade I meningioma. Ki-67(MIB-1) labeling index of the posterior fossa and temporal lesions were 4.8% and 5.1%, respectively, making them slightly high. Since there is a tendency for tumorous lesions in the lung to expand, a thoracoscopic partial resection of the right lower lobe was performed 2 months after the third cranial surgery. Histologically, the section showed proliferation of spindle shaped tumor cells with round to oval nuclei forming intersecting short fascicles (Fig. 3C). Although, necrosis was seen in the center of the
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Discussion

Meningioma was found in the patient’s lung, 26 years after the first surgery. The lesion was histologically similar to the intracranial lesion, and pulmonary metastasis of the meningioma was suspected. Distant metastases of grade I meningioma are rare. Despite this rarity, primary meningioma may occur in the lung. In order to confirm the genetic identity of these tumors, FISH was performed, and it was found that the NF2 gene (22q 12.2) was deleted to the same degree in both intracranial and lung lesions (Table 1). Thus, we confirmed genetically and morphologically that the intracranial lesions and the pulmonary lesion were identical.

The higher the tumor grade, the higher the incidence of distant metastasis. The incidence of distant metastases in grades II and III are 5% and 30%, respectively. The route for distant metastasis includes hematogenous metastasis via the internal jugular vein system and paraspinal venous plexus, lymphogenous metastasis, and cerebrospinal fluid dissemination. As far as we are aware, there has been no report summarizing the time period until the occurrence of distant metastases or the course after distant metastasis for each grade. To examine these, we reviewed the English-language literature published since 2007 using the PubMed search engine with the terms (“meningioma” AND “metastasis”). This search was performed on January 31st, 2018. We excluded cases in which metastases were found first or where simultaneous primary tumor and metastasis were identified. Cases of suspected drop metastasis or cerebrospinal fluid dissemination were also excluded. We reviewed 35 articles and 48 (present case included) cases of meningioma metastasized to extracranial sites. The median age of the extracranial metastases was 61.5 years (range 3–82 years) with a female predominance (30 females, 17 males, and not described in one case). Regarding the WHO grade of the primary tumor, 19 (39.6%) cases were grade I, 14 (29.2%) cases were grade II, 12 (25%) cases were grade III, and 3 (6.3%) cases were not described. Regarding metastatic tumor grading, 12 (25%) cases were grade I, 15 (31.3%) cases were grade II, 19 (39.6%) cases were grade III, and two (4.2%) cases were not described. In 13 cases, pathological upgrade was confirmed at the time of distant metastasis from initial surgery. With regard to the time of upgrading, 10 cases were at the time of local recurrence, three cases were metastasis, and one case showed local recurrence and metastasis simultaneously.

The period of primary tumor operation to metastasis varied depending on the tumor grade. The mean period until metastasis in grades I, II, and III was 11.0, 5.4, and 2.0 years, respectively. The period until metastasis in our case was 26 years; this was fairly long compared with the mean period. Prognosis after metastasis was examined, and it was different depending on each grade. For grade I, there was one case of death with an unknown survival time, but there were no other deaths within the observation period in other cases. In grades II and III, the mean survival times were 3.3 and 0.98 years, respectively. Median survival period was 4 years and 1 year, respectively. Data indicate that when the tumor of a distant metastasis reached a high grade, the survival period was significantly shortened.

Known risk factors for metastasis and local recurrence are histopathological signs of malignant behavior. But this does not explain why grade I meningiomas metastasize. The pathophysiology leading to distant metastases may be a hematogenous spread originating from tumor invasion into the venous sinuses. In fact, 75% of patients with extracranial metastases of meningioma show an invasion of the venous sinus. In our review, five cases did not reveal any relationship between the sinus and tumor from the description and two cases were spinal meningioma. These seven cases were excluded when considering the association with the venous sinus. Invasion or contact with the venous sinus was observed in 60.1% (25/41) of cases. In this group, grade I accounted for 11/25 cases (44%). Grades II and III were 7/25 (28%) and 5/25 (20%), respectively. Not described was 2/25 (8%). In each grade, where an association with the sinus venous was observed, the association was as follows: grade I, 61%; grade II, 54%; and grade III, 62.5%. These results indicate that contact with the venous sinus has the potential to develop extracranial metastases. In addition, in recent years, there are reports that CD90 becomes highly expressed in meningioma metastasis, and that chromosomal instabilities such as deletion of chromosomes 22 and 1 are associated with distant metastasis.

Our case was histologically WHO grade I but the MIB-1 labelling index was slightly high. At the time of first surgery,
the tumor had already made extensive infiltration into the venous sinus and jugular vein. These factors may have contributed to meningioma WHO grade I metastasized to the lung.

Conclusion

We experienced a case of meningioma WHO grade I that had metastasized to the lung 26 years after initial surgery. Confirmation was made morphologically and also genetically. However, despite the histological features indicating WHO grade I, sinus invasion may be associated with metastasis. Our review shows that the histological grading of the primary tumor was related to the period to metastasis. Furthermore, grading of the distant metastasized tumor was related to survival time.

Limitation

In this case study, we considered the lung disease to be a metastasis, but we could not fully eliminate either metastasis or both primary. Because the somatic NF2 loss of heterozygosity was not examined, the possibility of meningiomatosis cannot be discounted.

Conflicts of Interest Disclosure

All authors declare no conflicts of interest.

References

1) Whittle IR, Smith C, Navoo P, Collie D: Meningiomas. Lancet 363: 1535–1543, 2004
2) Fyrdychowicz C, Holland H, Hantmann H, et al.: Two cases of atypical meningioma with pulmonary metastases: a comparative cytogenetic analysis of chromosomes lp and 22 and a review of the literature. Neuropathology 35: 175–183, 2015
3) D’Aiuto M, Veronesi G, Pelosi G, et al.: Two-year survival after multiple bilateral lung metastasectomy for cranial meningioma. Ann Thorac Surg 80: 1129–1130, 2005
4) Kanzaki R, Higashiyama M, Fujiwara A, et al.: Surgical resection of pulmonary metastases from meningioma: report of a case. Surg Today 41: 995–998, 2011
5) Kaminski JM, Movsas B, King E, et al.: Metastatic meningioma to the lung with multiple pleural metastases. Am J Clin Oncol 24: 579–582, 2001
6) Fabbri A, Nuzzo C, Vidiri A, et al.: Bone and lung metastases from intracranial meningioma. Anticancer Res 26: 3835–3837, 2006
7) Adlakha A, Rao K, Adlakha H, et al.: Meningioma metastatic to the lung. Mayo Clin Proc 74: 1129–1133, 1999
8) Surov A, Gottschling S, Bolz J, et al.: Distant metastases in meningioma: an underestimated problem. J Neurooncol 112: 323–327, 2013
9) Honda Y, Shirayama R, Morita H, Kusuhara K: Pulmonary and pleural metastasis of intracranial anaplastic meningioma in a 3-year-old boy: a case report. Mol Clin Oncol 7: 633–636, 2017
10) Paix A, Waissi W, Antoni D, Adeduntan R, Noël G: Visceral and bone metastases of a WHO grade 2 meningioma: a case report and review of the literature. Cancer Radiother 21: 55–59, 2017
11) Perry A, Stafford SL, Scheithauer BW, Suman VJ, Lobhe CM: Meningioma grading: an analysis of histologic parameters. Am J Surg Pathol 21: 1455–1465, 1997
12) Maier H, Ofner D, Hittmair A, Kitz K, Budka H: Classic, atypical, and anaplastic meningioma: three histopathological subtypes of clinical relevance. J Neurosurg 77: 616–623, 1992
13) Forest F, Berremla SA, Gynes C, et al.: Metastatic meningiomas: an unusual clinical and pathological diagnosis with highly variable outcome. J Neurooncol 120: 411–421, 2014
14) Abboud M, Haddad G, Kattar M, Aburiziq I, Geara FB: Extraneuronal metastases from cranial meningioma: a case report. Radiat Oncol 4: 20, 2009
15) Cho BR, Yoon WS: Pulmonary metastases from benign calvarial meningioma: a case report. Br J Neurosurg 31: 276–278, 2017
16) Corniola MV, Lands BD, Migliorini D, et al.: Rapidly growing pulmonary metastasis from anaplastic meningioma with lethal outcome: a case report. J Neurol Surg B 78: e129–e134, 2017
17) Ito K, Imagama S, Ando K, et al.: Intrapulmonary meningioma with malignant transformation and distant metastasis. Nagoya J Med Sci 79: 97–102, 2017
18) Koessler RA, Garzon-Muvdi T, Yang W, et al.: Metastatic atypical and anaplastic meningioma: a case series and review of the literature. World Neurosurg 101: 47–56, 2017
19) Zhao P, Li N, Cao J, Lin X, Liang C: Rhabdoid meningioma arising concurrent in pulmonary and intracranial with a rare malignant clinical progression: case report and literature review. World Neurosurg 107: 1046.e137–1046.e22, 2017
20) Chua FH, Low SY, Tham CK, Ding C, Wong CF, Nolan CP: Disseminated extracranial metastatic meningioma. J Clin Neurosci 33: 214–216, 2016
21) Leemans J, Van Calenbergh F, Sciot R, Debie- Rychter M, Decaluwe H, Nackaerts K: Pulmonary metastasis of a meningioma presenting as a solitary pulmonary nodule: 2 case reports. Acta Clin Belg 71: 107–110, 2016
22) McCarthy C, Hofer M, Vlychou M, et al.: Metastatic meningioma presenting as a malignant soft tissue tumour. Clin Sarcoma Res 6: 23, 2016
23) Mindermann T: Paraneoplastic symptoms caused by extracranial meningioma metastases? Surg Neurol Int 7: 106, 2016
24) Singh R, Ryan C, Chohan MO, Tisnado J, Hadjigeorgiou G, Biilsky MH: Intracranial meningioma with vertebral or intraspinal metastasis: report of 2 cases and review of the literature. J Neurosurg Spine 25: 775–781, 2016
25) Klingler JH, Krüger MT, Kogias E, Bredecke SM, Hubbe U, Scheiwe C: Minimally invasive resection and vertebroplasty for an osteolytic C-1 metastasis of malignant meningioma: case report. J Neurosurg Spine 23: 602–606, 2015
26) Parameshwaran Nair R, Vinod, Sarma Y, Naylor B, Kaur Dil S, Tripathi PK: Metastatic rhabdoid meningioma of the parotid - Mimicking primary salivary gland neoplasm. Int J Surg Case Rep 6C: 104–106, 2015
27) Strong MJ, Garces J, Tang W, Ware ML: Benign sacral metastatic meningioma: a rare entity. Ochsner J 15: 200–202, 2015
28) Wang KD, Su YB, Zhang Y: Recurrent intracranial meningioma with multiple pulmonary metastases: a case report. OncoLett 10: 2765–2768, 2015
29) Tao CY, Wang JJ, Li H, You C: Malignant intraventricular meningioma with craniospinal dissemination and concurrent pulmonary metastasis. World J Surg Oncol 12: 238, 2014
30) Dmytriw AA, Gullane P, Bartlett E, Perez-Ordonez B, Yu E: Parotid gland metastasis originating from malignant meningioma. Clin Imaging 37: 740–747, 2013
31) Lanfranchi M, Nikpoor N: Detection of meningioma metastasis to liver and lung using somatostatin receptor scintigraphy. Clin Nucl Med 38: 668–670, 2013
32) Lambertz N, Koehler J, Schulte DM, et al.: Multivisceral systemic metastases from an intracranial anaplastic meningioma: a case report and review of literature. Clin Neurosurg Neurosci 113: 592–595, 2011
33) Rampurwala M, Pazoski M, Schauer P: Delayed hepatic metastasis from a benign fibroblastic meningioma thirty-one years after surgical resection of the intracranial tumor. J Clin Oncol 29: e214–e215, 2011
34) Taieb G, Campello C, Renard D, et al.: Multifocal extracranial meningioma metastases. Arch Neurol 68: 388–389, 2011
35) Wang Z, Kong M, Li J, Xiao W, Zheng S: Intraspinal rhabdoid meningioma metastasis to the liver. J Clin Neurolsci 18: 714–716, 2011
36) Estanislau ES, Carvalho GT, Reis BL, et al.: Malignant meningioma with extracranial metastases. Arq Neuropsiquiatr 67: 730–732, 2009
37) Sujit Kumar GS, Chacko G, Chacko AG, Haran RP: Multiple extracranial metastases from intradiploic meningioma. Neurol India 57: 96–97, 2009
38) Lee GC, Choi SW, Kim SH, Kwon HJ: Multiple extracranial metastases of atypical meningiomas. J Korean Neurosurg Soc 45: 107–111, 2009
39) Psaras T, Pantazis G, Steger V, Meyermann R, Honegger J, Beschorer R: Benign meningioma developing late lung metastases: case report and review of the literature. Clin Neuropathol 28: 453–459, 2009
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40) Azene EM, Gai QW, Tabar SP, Morrison AL, Meisenberg B: Metastasis of a histologically benign—appearing meningioma to the iliac bone. *J Clin Oncol* 26: 4688–4690, 2008

41) Gladin CR, Salsano E, Menghi F, et al.: Loss of heterozygosity studies in extracranial metastatic meningiomas. *J Neurooncol* 85: 81–85, 2007

42) Asioli S, Senetta R, Muldi E, et al.: “Benign” metastatic meningioma: clinico-pathological analysis of one case metastasising to the lung and overview on the concepts of either primitive or metastatic meningiomas of the lung. *Virchows Arch* 450: 591–594, 2007

43) Figueroa BE, Quint DJ, McKeever PE, Chandler WF: Extracranial metastatic meningioma. *Br J Radiol* 72: 513–516, 1999

44) Scognamiglio G, D’Antonio A, Rossi G, et al.: CD90 expression in atypical meningiomas and meningioma metastasis. *Am J Clin Pathol* 141: 841–849, 2014

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