ANTICANCER RESEARCH *41*: 4039-4043 (2021)
doi:10.21873/anticanres.15204

Sternal Metastasis of Brain Meningioma – A Case Report

SHUHEI MATSUMURA[1], TOSHIHIRO MATSUO[1], SHINJI HIRAI[2], TATSUYA KATAYAMA[2], TAKASHI NISHISAKA[3], ATSUSHI TOMINAGA[4], KEISUKE SHINBO[5], YU MOCHIZUKI[1], KOJI NISHIDA[1], MITSUHIRO NAKAMURA[1], RYOUSUKE MATSUSHITA[1], SHUHEI KAWAGUCHI[1] and NOBUO ADACHI[6]

Departments of [1]Orthopaedic Surgery, [2]Thoracic Surgery, [3]Pathology and Laboratory Medicine, [4]Neurosurgery, and [5]Plastic Surgery, Hiroshima Prefectural Hospital, Hiroshima, Japan; [6]Department of Orthopaedic Surgery, Hiroshima University, Hiroshima, Japan

Abstract. *Background: Metastases of meningiomas are infrequent and the site of extracranial metastasis such as the bone is extremely rare. Case Report: A 75-year-old male had a history of five sessions of surgery and gamma-knife treatment for brain meningioma over a period of 29 years. He visited our hospital because he noticed a swelling in his anterior chest 2 years and 6 months after the final treatment. After an open biopsy, histopathological analysis revealed the mass to be a metastatic grade II meningioma. We resected the tumor along with the sternum, ribs, pleura, and pericardium. The patient had recurrences in the thoracic cavity and pericardium postoperatively and received radiation therapy. He also had metastasis in the abdominal cavity, which spread rapidly. Conclusion: We report on a rare instance of metastasis to the sternum in a case of atypical meningioma, showing rapid growth and invasion after long-term treatment.*

Meningiomas are the most common primary central nervous system neoplasms and constitute >30% of all intracranial tumors (1). Most meningiomas are benign; therefore, extracranial metastases are infrequent and occur in only 0.1% of all cases (1-3). Meningiomas are classified by the World Health Organization grading scale into 3 types (grade I, II, and III), and about 20% of meningiomas are grade II (atypical) (4). Atypical meningiomas have an aggressive potential and possibility of distant metastasis. The most frequent site of extracranial metastasis is the lung, with other sites such as the bone being rare (5-7). Here, we report an extremely rare instance of metastasis to the sternum in a case of atypical (grade II) meningioma showing rapid growth and invasion after long-term treatment.

Correspondence to: Toshihiro Matsuo, MD, Ph.D., Department of Orthopaedic Surgery, Hiroshima Prefectural Hospital, 1-5-54 Ujinakanda, Minami-ku, Hiroshima 734-8530, Japan. Tel: +81 822541818, Fax: +81 822538274, e-mail: t-matsuo@hph.pref.hiroshima.jp

Key Words: Atypical meningioma, sternum, metastasis, rapid growth.

Case Report

A 75-year-old male underwent five sessions of surgery and gamma-knife treatment for brain meningioma over a period of 29 years. He visited our hospital because he noticed a swelling in his anterior chest 2 years and 6 months after the final gamma knife treatment. On physical examination, an elastic hard mass measuring 7 cm in diameter was palpated in the anterior chest. The mass adhered to the skin and was not mobile on palpation. Laboratory data were within normal limits. Computed tomography (CT) images showed cortical destruction and extraosseous extension in the distal part of the sternum (Figure 1). On magnetic resonance imaging, iso-signal intensity on T1-weighted images and high signal characteristics on T2-weighted images were observed (Figures 2 and 3). Apart from the sternum, no other site demonstrated an uptake on positron emission tomography (PET)-CT (Figure 4). After an open biopsy, histopathological analysis revealed the mass to be a metastatic grade II meningioma. Microscopically, the tumor was composed of proliferating epithelioid polygonal cells with mild cellular pleomorphism (Figure 5). Immunohistochemistry showed that the neoplastic cells were negative for BerEP4, EMA, CK7, CK20, S100, HMB-45, Melan A, and NSE but positive for cytokeratin AE1/AE3 and Ki-67 (30%). The mass grew rapidly without any pain over a period of three weeks after the biopsy, and measured 12 cm in size. CT images showed bone destruction and invasion of the surrounding soft tissue (Figure 6). We resected the tumor, including the skin flap measuring 13 cm, body of the sternum, bilateral third to seventh ribs, pleura, and the pericardium (Figure 7). Sternal reconstruction was performed with expanded polytetrafluoroethylene membrane titanium mesh (Figure 8) according to our previous report (8).

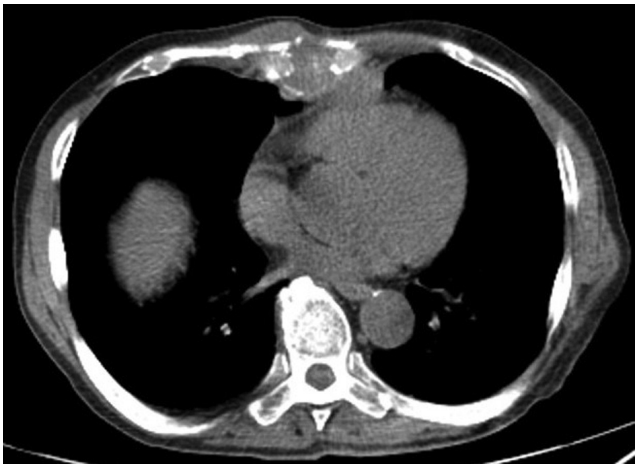

Figure 1. *Plain computed tomography image showing cortical destruction and extraosseous extension in the distal part of the sternum.*

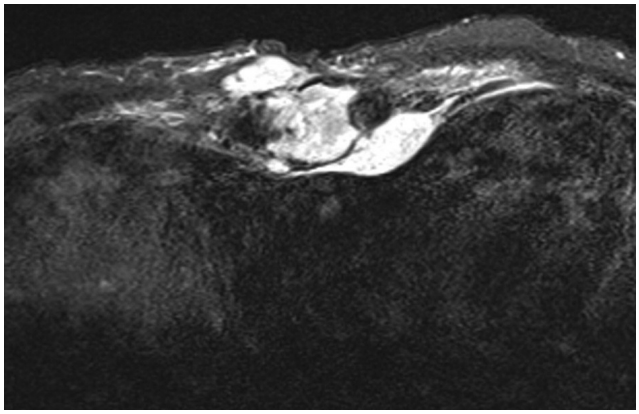

Figure 2. *T2-weighted axial magnetic resonanse (MR) image showing a very high signal of the sternum.*

Figure 3. *T1-weighted saggital magnetic resonanse image of the chest showing iso signal of the sternum.*

The defect was covered using an anterolateral thigh free flap and a tensorfascia lata musclocutaneous free flap (Figure 9). The patient experienced recurrences in the thoracic cavity and pericardium 2 months postoperatively and received radiation therapy (20 fractions of 40 Gy). He had a recurrence around the heart, outside of the irradiated field, 4 months postoperatively, and received radiation therapy (deep; 12 fractions of 30 Gy + superficial; 5 fractions of 20 Gy). He had a metastasis in the abdominal cavity that rapidly spread 6 months postoperatively. During radiation therapy, he suffered severe pneumonia and died.

Discussion

Meningioma is one of the most common benign tumors of the central nervous system; therefore, extracranial metastases from meningiomas are very rare (1-3). The most common metastatic site is the lung, followed by the liver and regional lymph nodes, whereas bone is considered a rare site of metastasis (5-7). Spinal and sacrum metastases have been reported as frequent sites of bony metastases (1, 3, 7, 8-12). However, to the best of our knowledge, there have been no reports of metastasis to the sternum, as seen in the present case.

Multiple treatments for local recurrence may cause metastasis of atypical meningioma (3, 13). The interval between the first treatment and metastasis to the bone can vary from 3 to 168 months (14, 15). Previous reports have revealed that the interval was shorter in patients with high-grade meningioma (grade II, III) than in those with low-grade meningioma (grade I) (3, 16). In the present case, the patient underwent surgery and gamma-knife treatment for brain grade II meningioma over a period of 29 years and noticed a mass formation owing to metastasis 2 years and 6 months after the final gamma-knife treatment, indicating that the interval was >31 years. Therefore, long-term follow-up may be necessary to suspect or identify metastases even in patients with high-grade meningioma.

Metastasis is the process of dissemination of the tumor cells from the primary lesion *via* the bloodstream to establish

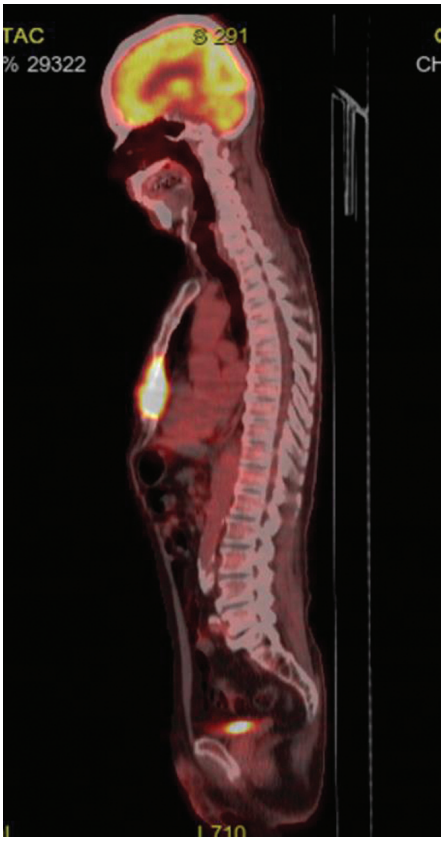

Figure 4. *Positron emission tomography-computed tomography showing no uptake other than the sternum.*

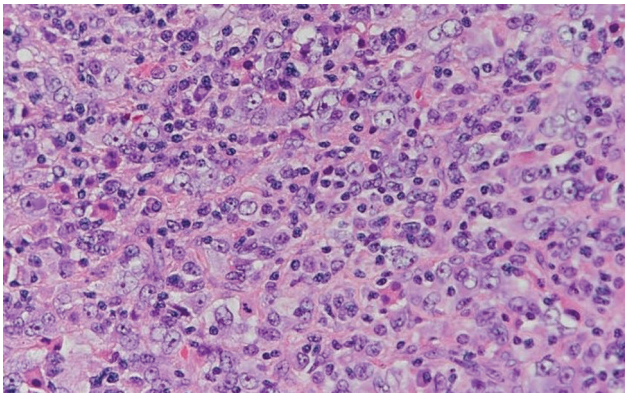

Figure 5. *High-power view of the histopathological specimen showing proliferation of epithelioid polygonal cells (hematoxylin-eosin; ×400).*

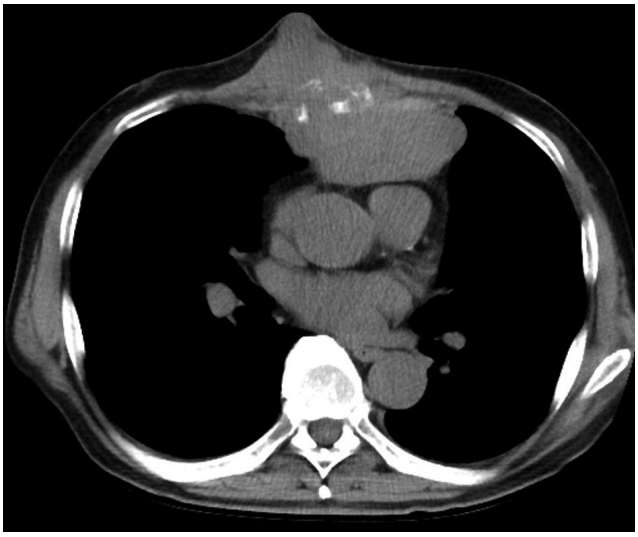

Figure 6. *Plain computed tomography image after three weeks of biopsy showing bone destruction and invasion to the surrounding soft tissue.*

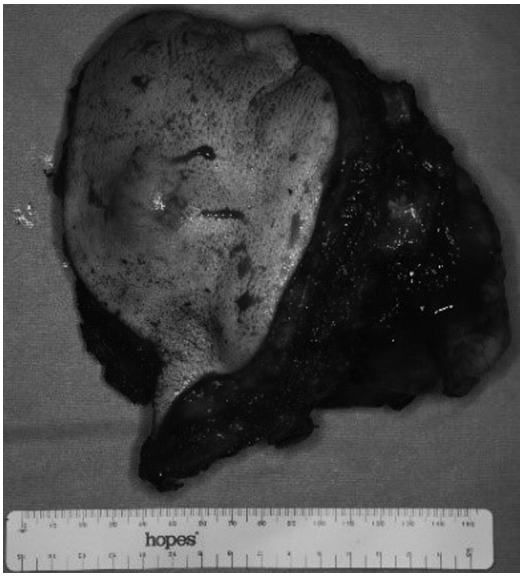

Figure 7. *Resected tumor including the skin flap measuring 13 cm, body of sternum, ribs, pleura, and pericardium.*

new growth in different organs (17). Recently, circulating tumor cells (CTCs) have been reported to play an important role in metastatic relapse *via* the vascular system and may have the potential to form metastases (18, 19). Tumor cell dormancy may be due to the microenvironment, response to treatment, or the immune system (20). CTC is present in the peripheral blood; when this cell type is present in the bone marrow, it is referred to as disseminated tumor cell (DTC). CTCs, which remain in the bone marrow as DTCs, and DTCs, which circulate in the peripheral blood as CTCs, can persist as dormant cells in the absence of cell division and apoptosis (21-23). Bone marrow DTCs may exist in specific

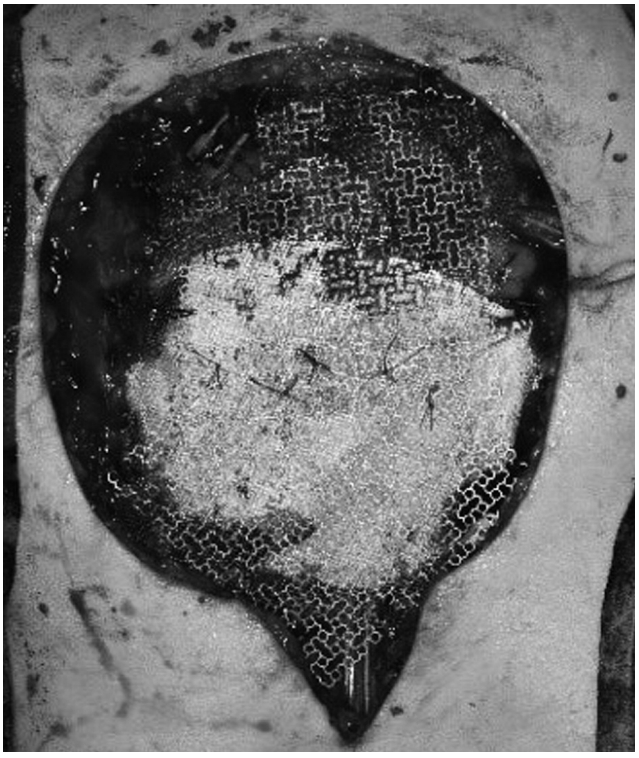

Figure 8. *Sternal reconstruction by using expanded polytetrafluoroethylene (ePTFE) membrane titanium mesh pleura.*

Figure 9. *Covering of anterolateral thigh free flap and tensor fascia lata musculocutaneous free flap.*

organ niches and enhance the survival of DTCs, and may remain dormant before developing into clinically detectable metastases (24). CTC may stay in the bone marrow as DTC. DTC may equally circulate in the peripheral blood as CTC. We, therefore, hypothesized that meningiomas with DTCs in the course of their metastatic growth may sometimes exhibit a prolonged time lag after the first treatment as in the present case (31-year interval).

The therapy for high grade meningioma consists of surgical resection and focal radiation depending on the complexity of the individual case, and there is no established therapy for metastatic meningiomas (25, 26). The role of chemotherapy as a subsequent treatment option for recurrence remains inconclusive in the literature (12, 27). In the present case, we were unable to retard the progression of this disease despite intensive radiation therapy.

In the present case, bone metastasis occurred during long-term treatment for primary meningioma over a period of 30 years. After metastasis, rapid growth and severe progression happened abruptly. This case presents with a very low incidence; hence, a high index of suspicion is required for early diagnosis and prevention of clinical entity with proper treatment.

Conflicts of Interest

The Authors declare that they have no competing interests in relation to this report.

Authors' Contributions

TM, SM, SH, TK, KS, KN, MN, SK, and AT performed surgeries and treatments. TN, TM, SM, SH, TK, KN, MN, RM and SK analyzed the pathology and clinical course. TM, SM, SH and TN took the lead in writing the manuscript with support from TK, AT, KS, YM, KN, MN, RM and SK. All Authors discussed the clinical results, critically revised the report, commented on drafts of the manuscript and approved the final manuscript. NA and YM supervised the findings of this case and helped to draft the manuscript.

References

1 Kessler RA, Garzon-Muvdi T, Yang W, Weingart J, Olivi A, Huang J, Brem H and Lim M: Metastatic atypical and anaplastic meningioma: A case series and review of the literature. World Neurosurg *101*: 47-56, 2017. PMID: 28143726. DOI: 10.1016/j.wneu.2017.01.070

2 Modha A and Gutin PH: Diagnosis and treatment of atypical and anaplastic meningiomas: a review. Neurosurgery *57(3)*: 538-50;

discussion 538-50, 2005. PMID: 16145534. DOI: 10.1227/01.neu.0000170980.47582.a5

3 Singh R, Ryan C, Chohan MO, Tisnado J, Hadjigeorgiou GF and Bilsky MH: Intracranial meningioma with vertebral or intraspinal metastasis: report of 2 cases and review of the literature. J Neurosurg Spine *25(6)*: 775-781, 2016. PMID: 27420397. DOI: 10.3171/2016.5.SPINE151457

4 Louis DN, Ohgaki H, Wiestler OD, Cavenee WK, Burger PC, Jouvet A, Scheithauer BW and Kleihues P: The 2007 WHO classification of tumours of the central nervous system. Acta Neuropathol *114(2)*: 97-109, 2007. PMID: 17618441. DOI: 10.1007/s00401-007-0243-4

5 Fabi A, Nuzzo C, Vidiri A, Ciccarese M, Felici A, Cattani F and Cognetti F: Bone and lung metastases from intracranial meningioma. Anticancer Res *26(5B)*: 3835-3837, 2006. PMID: 17094409.

6 Frydrychowicz C, Holland H, Hantmann H, Gradistanac T, Hoffmann KT, Mueller W, Meixensberger J and Krupp W: Two cases of atypical meningioma with pulmonary metastases: a comparative cytogenetic analysis of chromosomes 1p and 22 and a review of the literature. Neuropathology *35(2)*: 175-183, 2015. PMID: 25376227. DOI: 10.1111/neup.12177

7 Ward AL, Risman A, Segar S, Sharma S and Vender JR: Atypical intracranial meningioma with metastasis to C7 vertebral body: a case report. World Neurosurg *122*: 593-598, 2019. PMID: 30465962. DOI: 10.1016/j.wneu.2018.11.067

8 Hirai S, Nobuto H, Yokota K, Matsuura Y, Uegami S, Sato K, Mitsui N, Sugita T and Hamanaka Y: Surgical resection and reconstruction for primary malignant sternal tumor. Ann Thorac Cardiovasc Surg *15(3)*: 182-185, 2009. PMID: 19597395.

9 Olson PN, Mitchell SL, Goswitz J and Griffiths HJ: Case report 853. Meningioma metastatic to the spine. Skeletal Radiol *23(5)*: 405-407, 1994. PMID: 7939845. DOI: 10.1007/BF02417004

10 Palmer JD, Cook PL and Ellison DW: Extracranial osseous metastases from intracranial meningioma. Br J Neurosurg *8(2)*: 215-218, 1994. PMID: 7917096. DOI: 10.3109/02688699409027971

11 Pinsker MO, Buhl R, Hugo HH and Mehdorn HM: Metastatic meningioma WHO grade II of the cervical spine: case report and review of the literature. Zentralbl Neurochir *66(1)*: 35-38, 2005. PMID: 15744627. DOI: 10.1055/s-2004-836245

12 Paix A, Waissi W, Antoni D, Adeduntan R and Noël G: Visceral and bone metastases of a WHO grade 2 meningioma: A case report and review of the literature. Cancer Radiother *21(1)*: 55-59, 2017. PMID: 28237610. DOI: 10.1016/j.canrad.2016.09.012

13 Kanthan R and Senger JL: Distant metastases from meningiomas-a myth or reality? Ann Clin Pathol 1(1): 1001, 2013.

14 Chamberlain MC and Glantz MJ: Cerebrospinal fluid-disseminated meningioma. Cancer *103(7)*: 1427-1430, 2005. PMID: 15690330. DOI: 10.1002/cncr.20926

15 Chuang HC, Lee HC and Cho DY: Intracranial malignant meningioma with multiple spinal metastases – a case report and literature review: case report. Spine (Phila Pa 1976) *31(26)*: E1006-E1010, 2006. PMID: 17172988. DOI: 10.1097/01.brs.0000245952.71265.9b

16 Liu Y, Li J, Duan Y, Ye Y, Xiao L and Mao R: Subcutaneous metastasis of atypical meningioma: Case report and literature review. World Neurosurg *138*: 182-186, 2020. PMID: 32145423. DOI: 10.1016/j.wneu.2020.02.128

17 Obiorah IE and Ozdemirli M: Incidental metastatic meningioma presenting as a large liver mass. Case Reports Hepatol *2018*: 1089394, 2018. PMID: 29854500. DOI: 10.1155/2018/1089394

18 Cristofanilli M, Budd GT, Ellis MJ, Stopeck A, Matera J, Miller MC, Reuben JM, Doyle GV, Allard WJ, Terstappen LW and Hayes DF: Circulating tumor cells, disease progression, and survival in metastatic breast cancer. N Engl J Med *351(8)*: 781-791, 2004. PMID: 15317891. DOI: 10.1056/NEJMoa040766

19 Alix-Panabières C and Pantel K: Challenges in circulating tumour cell research. Nat Rev Cancer *14(9)*: 623-631, 2014. PMID: 25154812. DOI: 10.1038/nrc3820

20 Osisami M and Keller ET: Mechanisms of metastatic tumor dormancy. J Clin Med *2(3)*: 136-150, 2013. PMID: 26237067. DOI: 10.3390/jcm2030136

21 Luzzi KJ, MacDonald IC, Schmidt EE, Kerkvliet N, Morris VL, Chambers AF and Groom AC: Multistep nature of metastatic inefficiency: dormancy of solitary cells after successful extravasation and limited survival of early micrometastases. Am J Pathol *153(3)*: 865-873, 1998. PMID: 9736035. DOI: 10.1016/S0002-9440(10)65628-3

22 Aguirre-Ghiso JA: Models, mechanisms and clinical evidence for cancer dormancy. Nat Rev Cancer *7(11)*: 834-846, 2007. PMID: 17957189. DOI: 10.1038/nrc2256

23 Naumov GN, MacDonald IC, Weinmeister PM, Kerkvliet N, Nadkarni KV, Wilson SM, Morris VL, Groom AC and Chambers AF: Persistence of solitary mammary carcinoma cells in a secondary site: a possible contributor to dormancy. Cancer Res *62(7)*: 2162-2168, 2002. PMID: 11929839.

24 Pein M and Oskarsson T: Microenvironment in metastasis: roadblocks and supportive niches. Am J Physiol Cell Physiol *309(10)*: C627-C638, 2015. PMID: 26377313. DOI: 10.1152/ajpcell.00145.2015

25 Surov A, Gottschling S, Bolz J, Kornhuber M, Alfieri A, Holzhausen HJ, Abbas J and Kösling S: Distant metastases in meningioma: an underestimated problem. J Neurooncol *112(3)*: 323-327, 2013. PMID: 23404622. DOI: 10.1007/s11060-013-1074-x

26 Forest F, Berremila SA, Gyenes C, Ginguéné C, Kassir R, Sulaiman A, Pasquier B, Porcheron J and Péoc'h M: Metastatic meningiomas: an unusual clinical and pathological diagnosis with highly variable outcome. J Neurooncol *120(2)*: 411-421, 2014. PMID: 25081976. DOI: 10.1007/s11060-014-1567-2

27 Dalle Ore CL, Magill ST, Yen AJ, Shahin MN, Lee DS, Lucas CG, Chen WC, Viner JA, Aghi MK, Theodosopoulos PV, Raleigh DR, Villanueva-Meyer JE and McDermott MW: Meningioma metastases: incidence and proposed screening paradigm. J Neurosurg *132(5)*: 1447-1455, 2019. PMID: 30952122. DOI: 10.3171/2019.1.JNS181771

Received June 18, 2021
Revised July 1, 2021
Accepted July 2, 2021