Clinical Case Report

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A rare subtype of meningioma

Case series of anaplastic meningioma and review of the literature

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Abstract

Rationale: Anaplastic meningioma, a rare subtype of meningioma, has malignant morphological characteristics and a World Health Organization (WHO) grade of III.

Patient concerns: In this report, we present findings from 6 cases of anaplastic meningioma.

Diagnoses: Pathological examination of the tumors, including hematoxylin and eosin staining and immunohistochemical staining, was performed. Of the six cases of anaplastic meningioma, two were recurrent tumors from original seminoma with a WHO grade of I. Histologically, three cases had carcinoma-like morphology, one case had sarcoma-like morphology, and two had two kinds of tissue structures: carcinoma-like tumor cell nests and areas with spindle tumor cells. Necrosis was detected in most cases (5/6). Ki67 index was high and varied from 20% to 70%.

Interventions: All the patients received surgery. 3 patients received adjuvant radiotherapy. 1 patient received chemotherapy.

Outcomes: 4 patients had no recurrence at follow-up of 19, 30, 46 and 54 months after the last surgery. 1 patient had recurrence 3 months after the last surgery. 1 patient died 12 days after the last surgery.

Lessons: This malignant subtype can be secondary to a WHO grade I meningioma after a long quiescent period. Necrosis was common in the tumor tissues, and Ki67 index was usually high. For patients with a history of meningioma, including benign cases, regular physical examination is important for early detection of tumor recurrence and malignant transformation.

Abbreviations: CT = computed tomography, EMA = epithelial membrane antigen, HE = hematoxylin and eosin, MRI = magnetic resonance imaging, WHO = World Health Organization.

Keywords: anaplastic meningioma, case series, meningioma

1. Introduction

Anaplastic meningioma is a rare type of malignant meningioma, accounting for less than 5% of all meningiomas.[1,2] The diagnostic criterion for anaplastic meningioma is that the tumor should have at least one of the following characteristics: carcinoma-, sarcoma-, or melanoma-like morphology, and a high mitotic index (≥20/10 high-power fields).[1] It commonly occurs in the convex surface of the cerebrum, and in rare cases, in the parietal region,[3] brain parenchyma,[4] and spinal cord.[5]

Anaplastic meningioma occurs mostly in adults, and is rare in children. Honda reported a case of anaplastic meningioma with metastasis to the lung in a 3-year-old boy.[6] The prognosis of patients with anaplastic meningioma is generally poor, mainly because of aggressive growth. However, it is not clear whether the clinical outcome of this tumor is worse in children than in adults.

In a study of 755 cases, Orton et al[7] found that the 5-year overall survival rate of patients with anaplastic meningioma was 41.4%. In addition, they found that the factors associated with poor prognosis included older age, high comorbidity score, and subtotal resection.[7] Moreover, a study by Moliterno et al[8] revealed that patients with primary anaplastic meningioma had better survival than those with anaplastic meningioma arising from low-grade meningioma.

Herein, we present the findings from 6 cases of anaplastic meningioma and a review of the relevant literature.

2. Case presentation

2.1. Clinical history

2.1.1. Case 1. The patient was a 64-year-old man with a 1-year history of weakness in his left lower extremities without any apparent cause. He developed a severe headache the day before he visited our hospital. A computed tomography (CT) scan showed a mass in the parietal and occipital lobe. The patient had no fever, convulsions, or weight loss.

2.1.2. Case 2. A 45-year-old man was referred to our hospital for further diagnosis and treatment because he had developed a subcutaneous mass above his left ear a month ago. The patient had a World Health Organization (WHO) grade I meningioma 10 years ago, which had been removed. The tumor recurred 3 years before his visit, and the patient underwent a second surgery.

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2.1.3. Case 3. A 77-year-old male patient was referred to our hospital because he had developed weakness of the right limbs and memory impairment 20 days prior. The symptoms progressively worsened. The patient had no headache, nausea, vomiting, or convulsions.

2.1.4. Case 4. The patient was a 33-year-old man with a 6-month history of right eyelid swelling and a 1-month history of discontinuous headaches. CT performed in a local hospital revealed a right intracranial mass. He visited our hospital for further diagnosis and treatment.

2.1.5. Case 5. A 91-year-old man had undergone surgery for a WHO grade I meningioma 20 years before he visited our hospital. The tumor recurred 13 years prior, and he underwent a second surgery. He experienced sudden-onset convulsions 6 months prior, and repeated convulsions for 25 days before his visit.

2.1.6. Case 6. The patient was a 65-year-old man with a 1-week history of weakness of the lower limbs, somnolence, and dizziness, with symptom aggravation 3 days before he visited our hospital.

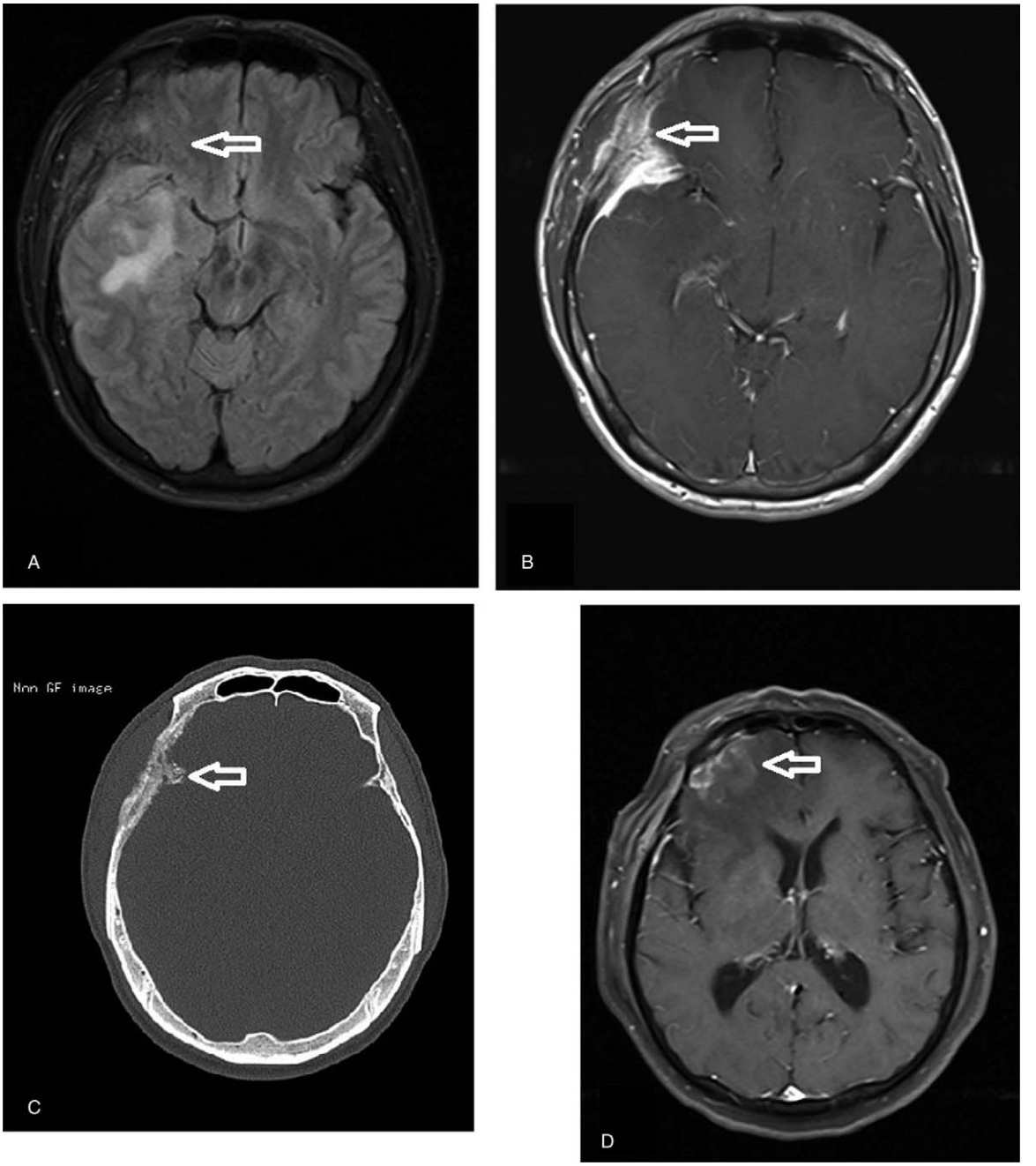

Figure 1. MRI and CT findings. A mass with short T1 and long T2 signals (A, B) was detected inside and outside the right frontotemporal skull plate. The mass was closely attached to the adjacent frontotemporal bone, and invaded the right temporal bone and the lateral orbital wall. The mass was also detected by CT. It showed slightly low density and invaded the right frontotemporal bone, sphenoid bone, and lateral orbital wall (C). A mass in the right frontal lobe near the frontal bone was detected in another patient by MRI. It had a short T1 signal and invaded the right frontal bone. CT = computed tomography, MRI = magnetic resonance imaging.

3. Materials and methods

Tumor samples were subjected to hematoxylin and eosin (HE), and immunohistochemical staining. Immunohistochemical staining was performed using an SP-kit (Maixin Biotechnology, Fuzhou, Fujian, China) according to the manufacturer's instructions. This study was approved by the institutional Ethics Committees of China Medical University and conducted in accordance with the ethical guidelines of the Declaration of Helsinki.

4. Results

4.1. Imaging and gross features

Figure 1 shows images obtained using magnetic resonance imaging (MRI) and CT. An MRI scan showed a mass with short T1 and long T2 signals inside and outside the right frontotemporal skull plate in Case 4 (Fig. 1A and B). The mass wrapped around the adjacent frontotemporal bone and invaded the right temporal bone and lateral orbital wall. CT indicated a mass with

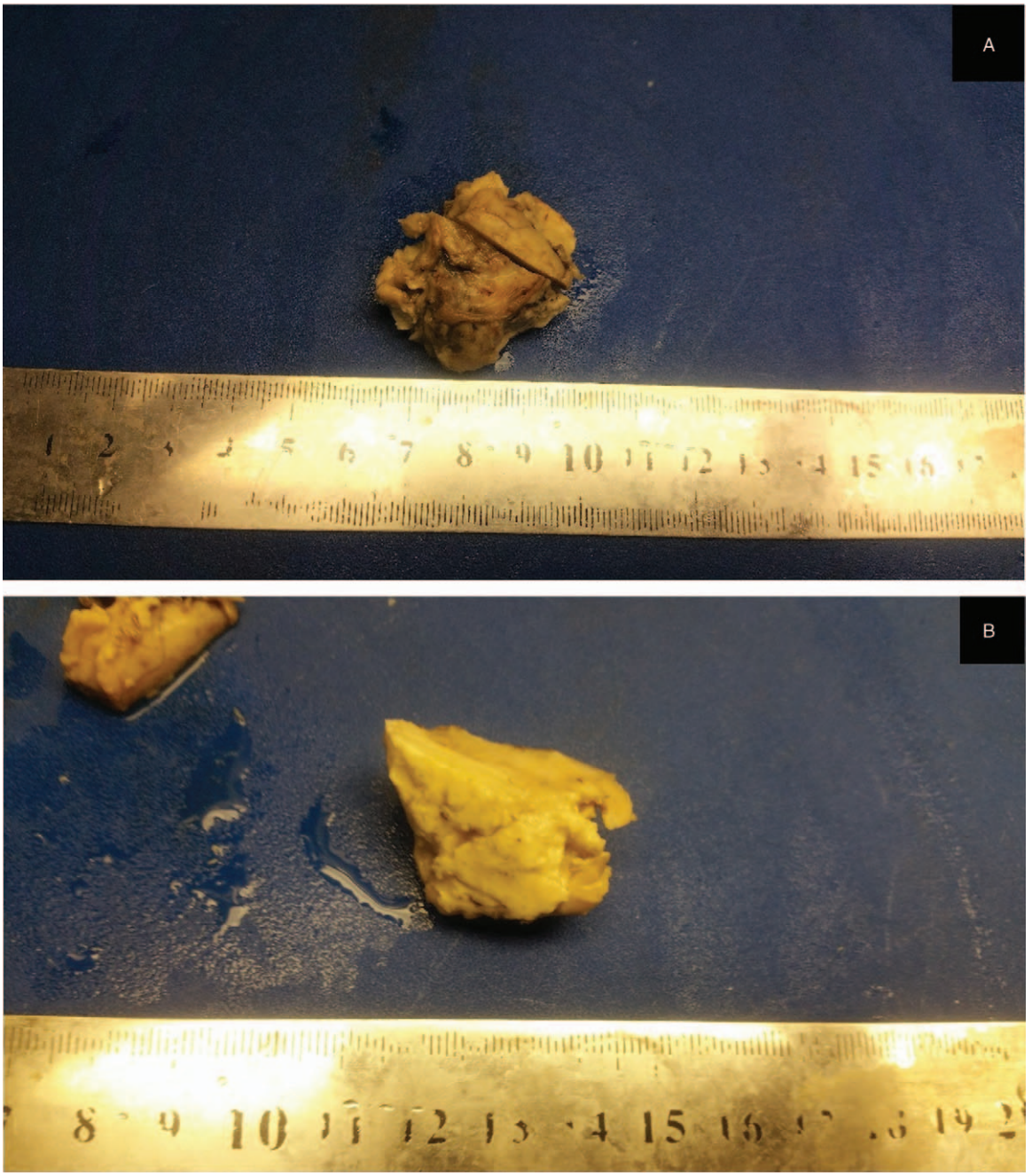

Figure 2. Gross features of the tumor. The mass, measuring about 4 cm × 3.0 cm × 2.5 cm, was cut into pieces. The surface of the tumor is rough, with adhesion between the mass and the surrounding tissue (A). The cut surface is gray yellow, with relative tenacious texture (B).

slightly low density, invading the right frontotemporal bone, sphenoid bone, and lateral orbital wall (Fig. 1C). An MRI scan showed a mass with short T1 signal in the right frontal lobe near the frontal bone in Case 6 (Fig. 1D), invading the right frontal bone. Figure 2 shows the gross tumor features of Case 6. A near globular mass, measuring approximately 4 cm × 3.0 cm × 2.5 cm, was cut into pieces. The surface of the mass was focally smooth. A local adhesion was observed between the mass and the surrounding tissue, which had a rough surface (Fig. 2A). The cut surface of the mass was gray yellow, with a relatively tenacious texture (Fig. 2B).

4.2. Microscopic features

Histopathological features of the tumors are listed in Figure 3. Tumor tissues of Case 1 (A) and Case 5 (L) were composed of 2 different areas: spindle cells and focal carcinoma-like cell nests. The tumor cells of Case 1 had large nucleoli (B) and those of Case 5 had medium-sized nucleoli (M). Tumor cells of Cases 2, 3, and 4 formed cell nests with carcinoma-like morphology (C, E, G), and the tumor cells had medium-sized nucleoli (D, F, H). The tumor cells of Case 4 invaded bond and muscle tissues (J, K). Tumor cells of case 6 had sarcoma-like morphology and invaded brain tissues (N). The tumor cells had medium-sized nucleoli (P). Necrosis was detected in all cases except case 1 (C, E, I, N, O). Large patchy necrosis was found in 4 cases: Cases 2, 3, 4, and 6.

4.3. Immunophenotype

Results of tumor immunostaining are shown in Figure 4. Tumors from all 6 cases were positive for epithelial membrane antigen (EMA) and vimentin immunostaining, which indicated bi-directional tumor differentiation. EMA immunostaining was generally focally positive and strong in 2 cases (Cases 2 and 6) and weak in 4 cases (Cases 1, 3, 4, and 5). Vimentin immunostaining was generally diffuse and strong, except in Case 3, where vimentin immunostaining was relatively weak. The Ki67 index varied from 20% to 70%, and was 30%, 70%, 20%, 30%, 50%, 60% in Cases 1–6, respectively (Fig. 4 and Table 1).

5. Discussion

Most anaplastic meningiomas occur in adults, although some rare cases have been reported in children.[9] In the present study, the patients were all adults, with ages ranging from 33 to 91 years. Anaplastic meningiomas are usually highly invasive and grow rapidly.[10] Ahmeti et al[10] reported a case of an anaplastic meningioma that destroyed most of the calvarial bone. In a case

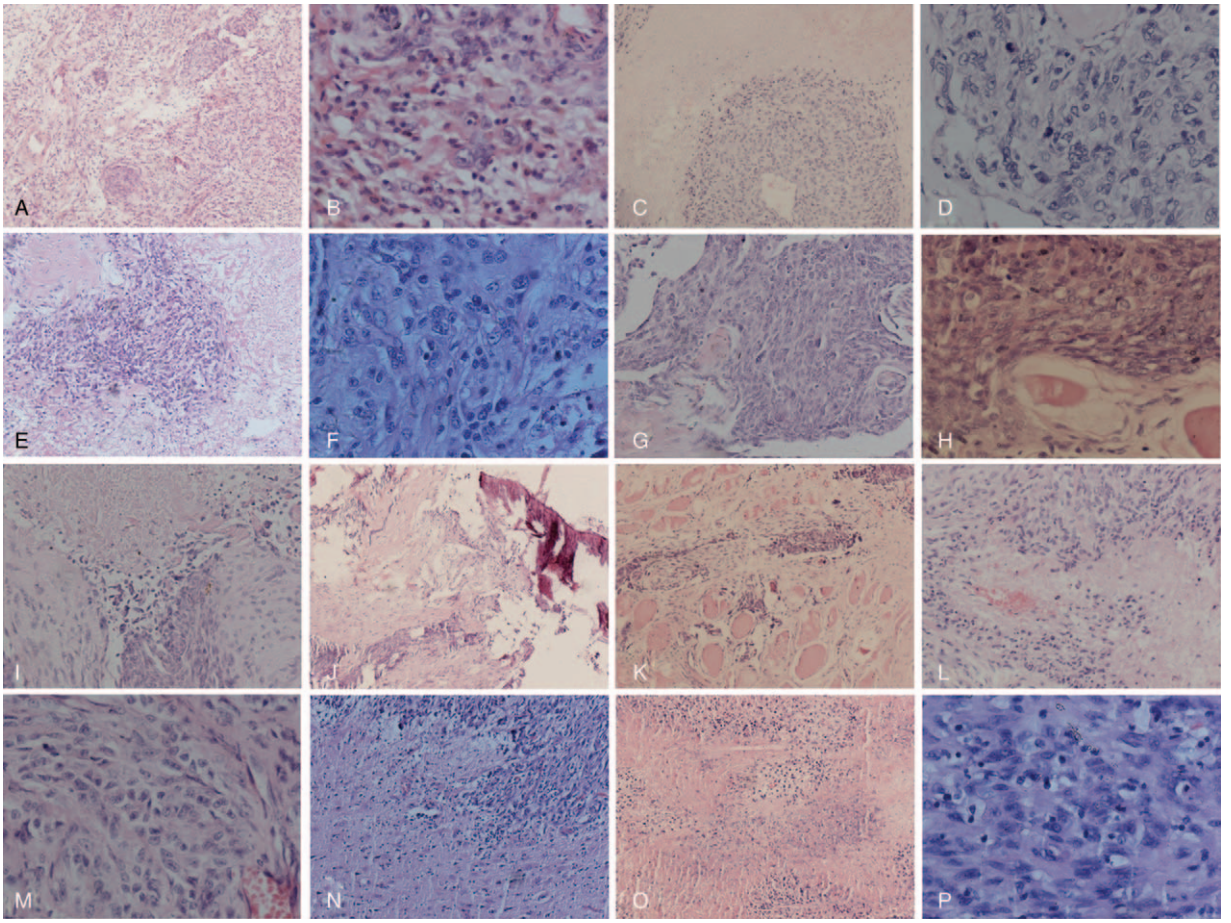

Figure 3. Microscopic features of the tumors. Tumor tissues of Case 1 and 5 had 2 kinds of tumor cells: carcinoma-like cells and spindle cells (A, L). The tumor cells in Case 1 had large nucleoli (B). Tumor cells of Cases 2, 3, and 4 formed nests with carcinoma-like morphology (C, E, G). Necrosis was observed in the tumor tissues in 5 cases: Cases 2, 3, 4, 5, and 6 (C, E, I, L, and O, respectively). The tumor cells of Cases 2, 3, 4, 5, and 6 had medium-sized nucleoli (D, F, H, M, P). In Case 4, the tumor cells invaded bone (J) and muscles (K). In Case 6, the tumor cells invaded brain tissues (N). (A, C, E, K, N, O: magnification × 100; G, L, I, J: magnification × 200; B, D, F, H, M, P: magnification × 100).

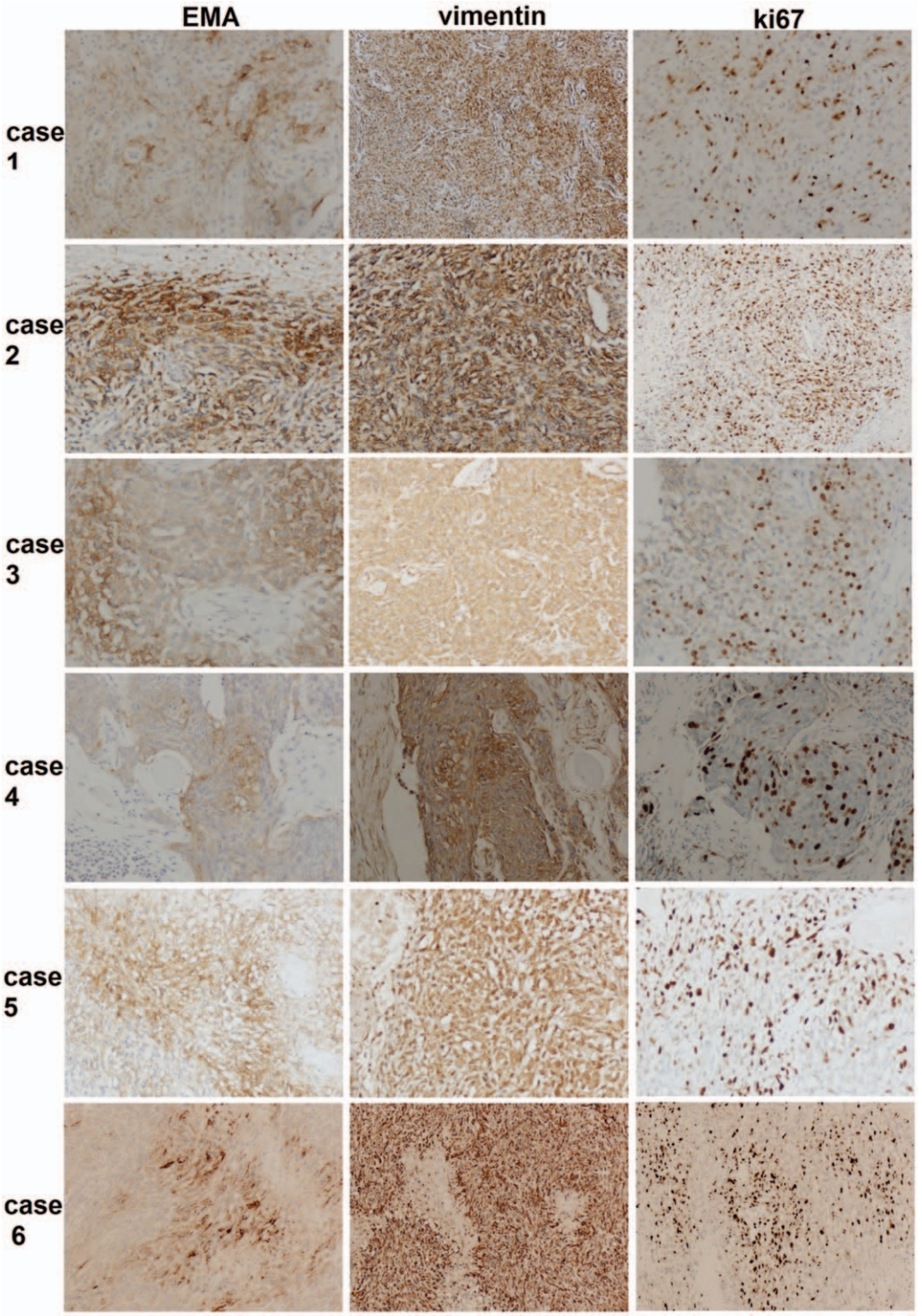

Figure 4. Results of tumor immunostaining. The tumor cells in all cases were positive for epithelial membrane antigen (EMA) and vimentin. EMA immunostaining was focal and weak in Cases 1, 3, 4, and 5, and focal and strong in Cases 2 and 6. Vimentin immunostaining was generally diffuse and strong, with weak staining only in Case 3. The Ki67 index was high in all cases: 30%, 70%, 20%, 30%, 50%, and 60% in Cases 1–6, respectively (magnification × 200). EMA=epithelial membrane antigen.

reported by Güngör et al,[11] a giant intracranial tumor invaded extracranial soft tissue and formed a cutaneous mass. Consistent with these previous reports, the tumors in the current study were aggressive, invading brain, bone, and muscle tissues. The recurrence of anaplastic meningioma is very common, with recurrence rates of 50% to 80%.[12] Kawahara et al[12] reported a rapid recurrence of this tumor < 2 months after surgery for removal of the primary tumor. However, distant metastasis of anaplastic meningioma is rare. In a study of 168 cases of atypical and anaplastic meningioma, Kessler et al[2] found that the rate of

Table 1

Histopathological features of the 6 cases of anaplastic meningioma.

Features case	Mitosis	Necrosis	Nucleolus	Ki67
1	>10/10HPF	None	Single, large	30%
2	>20/10HPF	Large patchy necrosis	Single, medium sized	70%
3	>5/10HPF	Large patchy necrosis	Single, medium sized	20%
4	>1/10HPF	Large patchy necrosis	Single, medium sized	30%
5	>10/10HPF	Small patchy necrosis	Single, medium sized	50%
6	>1/10HPF	Large patchy necrosis	Single, medium sized	60%

extracranial metastases was about 3%. Corniola et al[13] reported a case of anaplastic meningioma with pulmonary metastasis 2 years after surgery, resulting in the patient's death. In a case reported by Lambertz et al,[14] a patient with anaplastic meningioma developed multiple metastases in both lungs after the first surgery; this patient also had liver metastases. Nishida et al[5] reported an anaplastic meningioma in a very rare site, the spinal cord, with subsequent metastasis to the mediastinal lymph nodes. Moubayed et al[15] also reported a case of anaplastic meningioma metastasizing to the mediastinal lymph nodes. The patient had a cervical lump, which was found to be a metastatic anaplastic meningioma after removal of the primary intracranial tumor. The prognosis of anaplastic meningioma is generally poor because of frequent recurrence and occasional metastasis, and the median survival time is <2 years.[12,16]

The primary treatments for anaplastic meningioma are resection and adjuvant radiotherapy.[17] A study by Orton et al[7] indicated that adjuvant radiotherapy improved survival in patients with anaplastic meningioma. Another study by Garzon-Muvdi et al[18] also indicated an association between radiotherapy and improved clinical outcomes. A study by Moubayed et al[15] showed that radiation therapy was also effective for lymph node metastatic tumors. The effect of chemotherapy on anaplastic meningioma remains inconclusive. Lucchesi et al[19] reported a positive outcome in a 2-year-old patient with anaplastic meningioma who received chemotherapy for soft tissue sarcomas. A phase II trial revealed that sunitinib was efficacious in patients with anaplastic meningiomas.[20] Hydroxyurea, a medication used in the treatment of a variety of malignant tumors, has been used in combination with radiotherapy and chemotherapy for the treatment of malignant meningioma. However, the efficacy of hydroxyurea has not been substantiated in most studies. Gurberg et al[21] reported that, in a patient with anaplastic meningioma, hydroxyurea resulted in a radiologic response. In a patient with anaplastic meningioma arising from a WHO grade I meningioma, treatment with octreotide resulted in remission.[22] In addition, radiopeptide therapy had been shown to be effective for metastatic anaplastic meningioma.[23] Moreover, a study by Puchner et al[17] indicated that bevacizumab treatment resulted in regression of anaplastic meningioma.

The findings of our study indicate that a high Ki67 index is a common feature of anaplastic meningiomas. A study by Bruna et al[24] revealed that the Ki-67 index was an independent indicator of poor prognosis in patients with anaplastic meningioma. Another study by Ikeda and Yoshimoto,[25] indicated that a higher Ki-67 index was associated with tumor recurrence. The same study showed that EMA expression decreased as the degree of tumor malignancy increased.[25] In the present study, EMA immunostaining in the tumor cells was generally focal and weak in most cases (4/6).

Anaplastic meningioma can be a result of malignant transformation of meningioma with a WHO grade of I or II.[26] Rammo et al[22] reported a meningioma progressing from WHO grade I to III after 12 years. In the present study, 2 patients had a history of WHO grade I meningioma, supporting the possibility of malignant transformation.

6. Conclusion

Anaplastic meningioma is a malignant meningioma subtype with malignant morphological features. Necrosis and a high Ki67 index are common features in this rare tumor subtype, which may be secondary to a WHO grade I meningioma. Our findings indicate that regular physical examination is important in patients with a history of meningioma, including benign cases, to enable early detection of recurrence and malignant transformation of meningioma.

Author contributions

Conceptualization: Hongyi Cao, Biying Jiang, Chuifeng Fan.
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Formal analysis: Yang Zhao.
Investigation: Biying Jiang, Yang Zhao.
Resources: Hongyi Cao.
Supervision: Chuifeng Fan.
Validation: Chuifeng Fan.
Writing – original draft: Hongyi Cao, Biying Jiang, Yang Zhao.
Writing – review & editing: Chuifeng Fan.

References

[1] David NL, Hiroko O, Otmar DW, et al. WHO Classification of Tumors of the Central Nervous System. 4th edn.IARC Press, Lyon:2007.
[2] Kessler RA, Garzon-Muvdi T, Yang W, et al. Metastatic atypical and anaplastic meningioma: a case series and review of the literature. World Neurosurg 2017;101:47–56.
[3] Najjar MW, Abdul Halim NH, Sukhon FR, et al. Anaplastic meningioma presenting as a left parietal mass: a case report. Am J Case Rep 2017; 18:1166–70.
[4] Nayil K, Makhdoomi R, Malik R, et al. Intraparenchymal anaplastic meningioma in a child: a rare entity. Asian J Neurosurg 2015;10: 111–3.
[5] Nishida N, Kanchiku T, Imajo Y, et al. A case of an anaplastic meningioma metastasizing to the mediastinal lymph nodes. J Spinal Cord Med 2016;39:484–92.
[6] Honda Y, Shirayama R, Morita H, et al. Pulmonary and pleural metastasis of intracranial anaplastic meningioma in a 3-year-old boy: a case report. Mol Clin Oncol 2017;7:633–6.
[7] Orton A, Frandsen J, Jensen R, et al. Anaplastic meningioma: an analysis of the National Cancer Database from 2004 to 2012. J Neurosurg 2017;1–6. doi: 10.3171/2017.2.JNS162282. [Epub ahead of print].
[8] Moliterno J, Cope WP, Vartanian ED, et al. Survival in patients treated for anaplastic meningioma. J Neurosurg 2015;123:23–30.
[9] Benesch M, Kleinert R, Spork E, et al. Case 2. Anaplastic meningioma in a 3 1/2-year-old girl. J Clin Oncol 2001;19:274–6.
[10] Ahmeti H, Maslehaty H, Petridis AK, et al. Extensive growth of an anaplastic meningioma. Case Rep Neurol Med 2013;2013:527184.
[11] Güngör S, Gökdemir G, Tarıkçı N, et al. Intracranial anaplastic meningioma presenting as a cutaneous lesion: a case report of a cutaneous meningioma. Dermatol Online J 2012;18:6.
[12] Kawahara Y, Nakada M, Hayashi Y, et al. Anaplastic meningioma with extremely rapid recurrence. Neurol Med Chir (Tokyo) 2011;51:386–8.
[13] Corniola MV, Landis BN, Migliorini D, et al. Rapidly growing pulmonary metastasis from anaplastic meningioma with lethal outcome: a case report. J Neurol Surg Rep 2017;78:e129–34.

[14] Lambertz N, Koehler J, Schulte DM, et al. Multivisceral systemic metastases from an intracranial anaplastic meningioma: a case report and review of literature. Clin Neurol Neurosurg 2011;113:592–5.
[15] Moubayed SP, Guertin L, Lambert C, et al. Successful treatment of anaplastic meningioma metastatic to cervical lymph nodes. Head Neck 2013;35:E115–8.
[16] Riemenschneider MJ, Perry A, Reifenberger G. Histological classification and molecular genetics of meningiomas. Lancet Neurol 2006;5:1045–54.
[17] Puchner MJ, Hans VH, Harati A, et al. Bevacizumab-induced regression of anaplastic meningioma. Ann Oncol 2010;21:2445–6.
[18] Garzon-Muvdi T, Yang W, Lim M, et al. Atypical and anaplastic meningioma: outcomes in a population based study. J Neurooncol 2017; 133:321–30.
[19] Lucchesi M, Buccoliero AM, Scoccianti S, et al. A successful case of an anaplastic meningioma treated with chemotherapy for soft tissue sarcomas. CNS Oncol 2016;5:131–6.
[20] Kaley TJ, Wen P, Schiff D, et al. Phase II trial of sunitinib for recurrent and progressive atypical and anaplastic meningioma. Neuro Oncol 2015;17:116–21.
[21] Gurberg J, Bouganim N, Shenouda G, et al. A case of recurrent anaplastic meningioma of the skull base with radiologic response to hydroxyurea. J Neurol Surg Rep 2014;75:e52–5.
[22] Rammo R, Rock A, Transou A, et al. Anaplastic meningioma: octreotide therapy for a case of recurrent and progressive intracranial disease. J Neurosurg 2016;124:496–500.
[23] Sabet A, Ahmadzadehfar H, Herrlinger U, et al. Successful radiopeptide targeting of metastatic anaplastic meningioma: case report. Radiat Oncol 2011;6:94.
[24] Bruna J, Brell M, Ferrer I, et al. Ki-67 proliferative index predicts clinical outcome in patients with atypical or anaplastic meningioma. Neuropathology 2007;27:114–20.
[25] Ikeda H, Yoshimoto T. Immunohistochemical study of anaplastic meningioma with special reference to the phenotypic change of intermediate filament protein. Ann Diagn Pathol 2003;7: 214–22.
[26] Cimino PJ. Malignant progression to anaplastic meningioma: neuropathology, molecular pathology, and experimental models. Exp Mol Pathol 2015;99:354–9.