

Case Report

Recurrent meningioma with malignant transformation: a case report and literature review

Junwen Wang^{1*}, Lei Wang^{1*}, Bo Luo², Zhi Chen¹, Zuojun Xiong¹, Mingbo Fang¹, Jun Li¹

Departments of ¹Neurosurgery, ²Pathology, Wuhan Central Hospital Affiliated to Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430014, Hubei, P. R. China. *Equal contributors.

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Abstract: Meningiomas are common and mostly benign intracranial tumors, but may show a histological progression to malignancy. The mechanisms of malignant transformation remain unclear. Malignant meningiomas usually bear a high recurrence rate and unfavorable prognosis, and multiple surgical resections are required for the treatment. We report on a case of 51-year-old woman with a histologically benign intracranial meningioma. The patient had undergone multiple tumor resections and radiotherapy treatments. After multiple resections, the tumor demonstrated malignant transformation. A rapid tumor growth resulted in extensive tumor invasion of dura, brain and nasal sinus. Impaired brain function and subsequent intracranial hypertension caused serious headache, vomiting and coma. The patient survived 5 years following initial presentation. 3 subtotal resections of meningioma were performed. Radiotherapy was shown to be relatively ineffective during the course. The treatment strategies of recurrent meningiomas are briefly reviewed.

Keywords: Meningioma, recurrence, malignant transformation, surgery

Introduction

Meningiomas represent one of the largest subgroups of intracranial neoplasms, constituting approximately 36% of all primary tumors in this location [1]. Approximately 90% of meningiomas are benign. The WHO classifications defined the most frequent subtype as grade I meningioma and atypical and anaplastic neoplasms as grade II and III meningiomas, respectively [2, 3]. Surgical resection is considered to be the best treatment for most patients with meningioma [4]. Compared to WHO grade I meningioma, WHO grade II and III meningiomas have a significantly higher recurrence rate after both surgical and radiotherapy managements [3]. However, even WHO grade I meningiomas occasionally recur and can result in incurable disease [5]. Multiple surgical resections may be required in patients with recurrent meningioma. When repeated operations are required, the chance of cure is significantly reduced. Furthermore, multiple operations also carry an increased risk of intracranial infection and other postoperative complications. In rare

instances, a histological malignant transformation may occur and make the prognosis even worse [6].

We here report a case of orbitofrontal meningioma which at the time of presentation was histological benign. Location and invasion of bone and eye resulted in subtotal resection with later recurrences. There was a malignant transformation in the course of multiple recurrences. Extensive tumor invasion led to serious complications and finally the demise of the patient.

Case report

A 51-year-old non-smoking right-handed woman presented with a 3-year history of wild headache and gradually impaired vision of the right eye in August 2009. Cranial magnetic resonance imaging (MRI) revealed a 4 × 5 cm hard mass in the right orbitofrontal area; part of the tumor invaded into the posterior segment of the right eye (**Figure 1A, 1B**). Skull x-rays, cranial computed tomography (CT) and angiography confirmed the diagnosis.

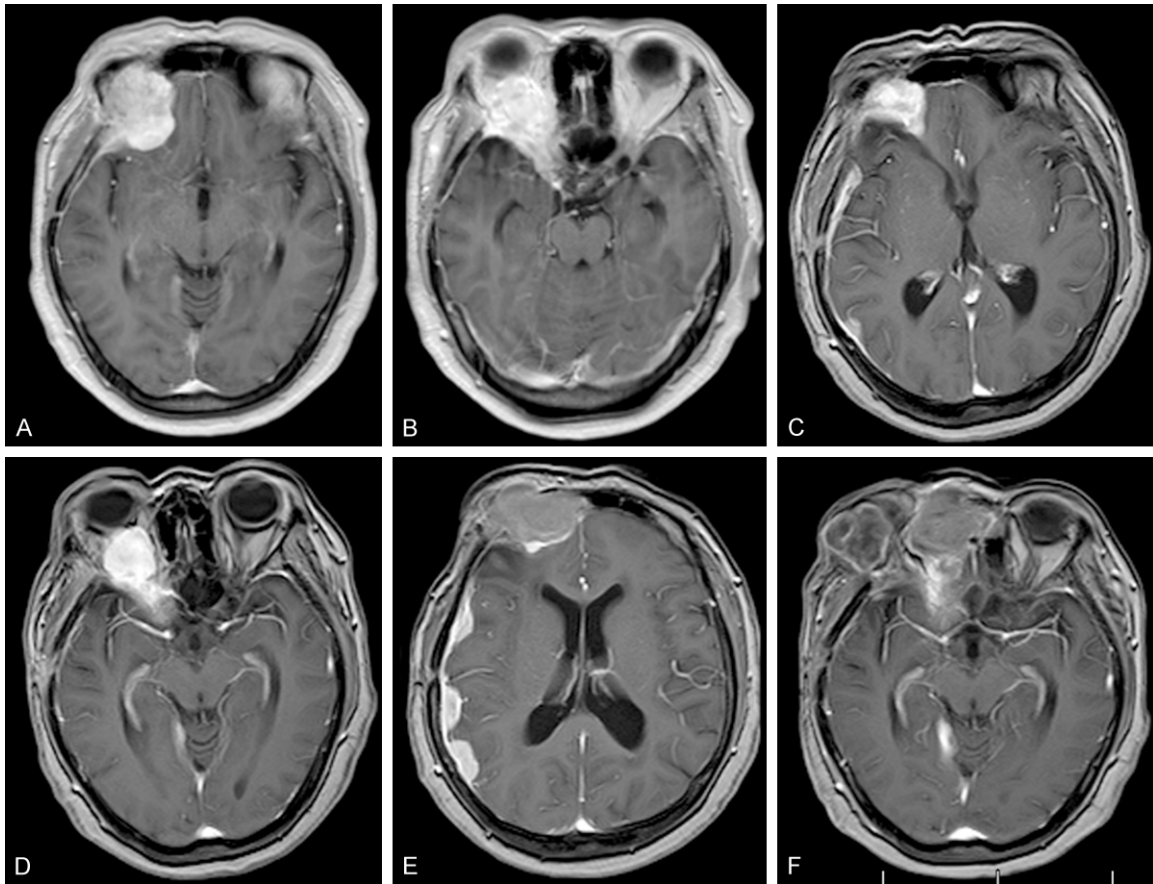


Figure 1. Magnetic resonance Imaging (MRI) scans of the meningioma in our patient. A, B. Axial T1-weighted image with gadolinium contrast (T1-Gd) MRI scans in 2009 revealed a hard tumor mass in the right orbitofrontal area, the tumor partially invaded into the posterior segment of the right eye. C, D. T1-Gd MRI scans in 2012 showed a small local recurrence of the meningioma in the right orbitofrontal area, and the residual primary tumor in the posterior segment of the right eye. E. T1-Gd MRI scan in 2013 demonstrated multiple recurrences, involving the right orbitofrontal convexity, dura, and brain. F. T1-Gd MRI scan in 2014 showing the recurrent meningioma with rapid growth and the invasion into nasal sinus.

Two months after the initial presentation, she underwent the first surgery. Because of the local bone, dura and right eye infiltration, a subtotal tumor resection was carried out by right frontal craniotomy. The tumor was observed to involve the right eye, orbitofrontal bone and dura during the surgery. Three years later the patient returned with a small local recurrent lesion in the right orbitofrontal convexity (**Figure 1C, 1D**), and a second subtotal resection was performed. After the second surgery, the patient underwent a 6 months procedure of single-fraction gamma knife radiotherapy at marginal (12 Gy) and maximum (18 Gy) doses. In 2013, cranial MRI revealed a big recurrent tumor mass with frontal and temporal dural metastasis (**Figure 1E**) and another surgical resection was conducted. Only 5 months after

the third surgery, the cranial MRI revealed an even bigger recurrent tumor mass with dura, brain and sphenoid sinus invasion (**Figure 1F**). The patient suffered from serious headache and vomiting subsequently and fell into coma soon. The patient died 8 days after the coma.

Histological examination of the resected tumor tissue from the first operation demonstrated the classic features of meningiothelial meningioma (WHO grade I) (**Figure 2A**). The tumor tissue from the second operation revealed an atypical meningioma (WHO grade II) with signs of rare mitoses which were generally benign (**Figure 2B**). Sections from the third operation showed an anaplastic meningioma (WHO grade III). Mitoses, nuclear atypia and cellular pleomorphism had increased enough to imply a

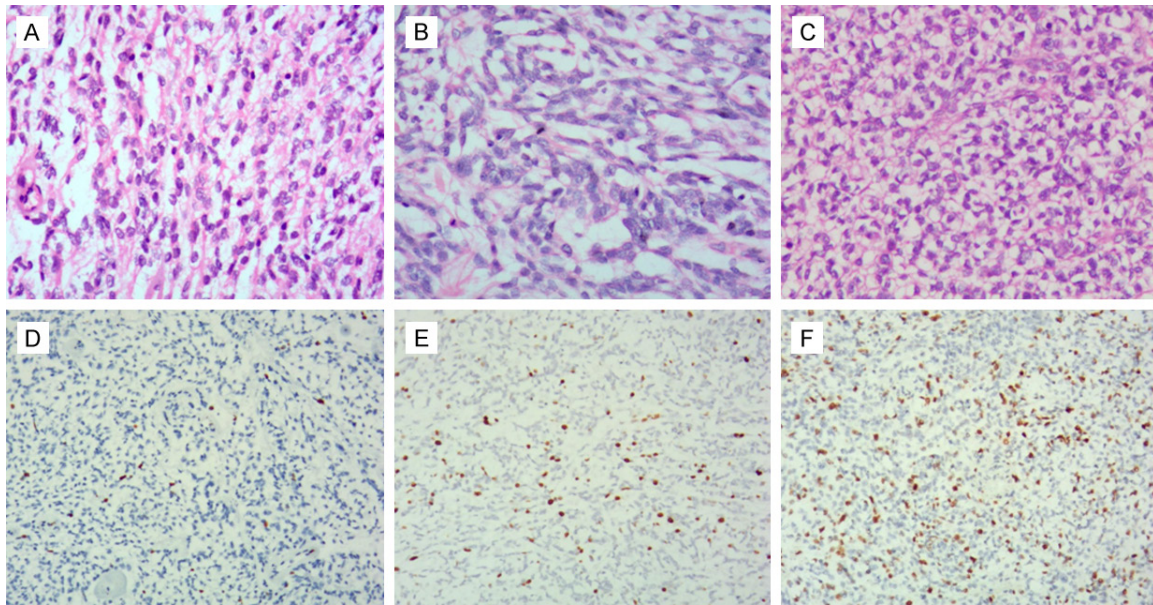


Figure 2. Histopathological findings of meningioma specimens. A. The tumor specimen from the first operation (2009) demonstrated a benign meningiothelial pattern with whorls (H&E \times 200). B. The tumor section from the second operation (2012) showed an increased clear cell component with rare mitoses, which were generally benign (H&E \times 200). C. The tumor resected in the third operation (2013) revealed abundant mitoses, nuclear atypia and cellular pleomorphism, indicating an anaplastic meningioma (H&E \times 200). D-F. Ki-67 staining of meningioma specimens. The Ki-67 index was <2% in 2009, 5% in 2012, and 35% in 2013.

malignant transformation (**Figure 2C**). All specimens showed positive staining of epithelial membrane antigen (EMA) and vimentin (Vim). The Ki-67 staining index was <2%, 5% and 35% in specimen 1-3, respectively (**Figure 2D-F**).

Discussion

The majority of meningiomas are benign. However, atypical and anaplastic meningiomas are more aggressive, especially anaplastic meningiomas, which are rare but bear a high recurrence rate and unfavorable prognosis [3]. Because meningiomas originate from the arachnoid villi, the location of tumor mass can be in any part of skull [7]. Thus, the symptoms can be various accordingly, including headache, seizure, hemiparesis, and even cranial neuropathysuch as vision loss [8]. Meningiomas are usually located in the skull vault and the skull base; to be specific, the parasagittal area is the most frequent, followed by the flax, the cavernous sinus, the tuberculum sellae, the lamina cribrosa, the foramen magnum, and the torcular zones [9]. Parasagittal meningiomas make up 17% to 20% of all the subtypes and most often involve the frontal lobe [4]. They can be asymptomatic for a long time and grow to a

considerable size. And when the symptoms show, jacksonian seizures of the lower limbs and headache are most apparent. If the meningioma advanced, papilledema and homonymous hemianopia may occur [10]. There is more serious situation that tumor mass can invade directly into the posterior segment of eye and terminate its vision. The patient in our case had the tumor in the orbitofrontal area, and the major symptoms at the admission were headache and impaired vision, which partially accorded with statistical features.

Because meningiomas do not have the typical symptoms, imaging techniques are important for the diagnosis of meningiomas. Among them, MRI and CT are most frequently used. Meningiomas show highly characteristic features in CT and MRI images: a 'dural tail' indicates the anchoring point of tumor mass and dura and a 'mottling' structure means the high vascularization of the tumor mass [11]. Sometimes, other imaging techniques are also employed to confirm the diagnosis, for example, angiography can be used to exclude the possibility of aneurysm or other cerebrovascular diseases.

Although diagnosis from imaging is easy and useful, pathologic diagnosis seems to be more important because histologic grading of meningiomas has prognostic and therapeutic implications. Anaplastic meningioma is the rare and most aggressive subtype. The prognosis for anaplastic meningiomas is the worst among the 3 grades, with an average survival of less than 2 years [12]. However, even the benign meningiomas may show a histological progression to malignancy, the mechanism underlying malignant transformation remains unclear. The procedure of malignant transformation may take 2 to 16 years according to previous research [1, 6, 13]. For our patient, it took 4 years to accomplish malignant transformation. The patient lived only 1 year after confirming the diagnosis of malignant meningioma.

Surgical resection is a reliable approach in treating meningioma in most cases. Total resection is the best management for the cure of the tumor and the least chance of recurrence. Total resection is often curative but may not be feasible based on factors such as extent, location, and bony or dural infiltration of the lesion. A subtotal resection may significantly increase the postoperative recurrence rate [4]. For local recurrences, treatment options include repeated surgical resection, radiotherapy and chemotherapy. Repeated surgical resection could be more radical resection or palliative subtotal resection. Radical resection can provide better relief but carry significantly higher surgical risk, which may endanger the patient. Subsequent subtotal resection can provide palliative relief when a radical resection is too dangerous to be performed, but there is a greater risk for repeated recurrences. Alternative nonsurgical treatments of recurrent meningiomas has been employed. The most frequent nonsurgical managements are radiotherapy and chemotherapy. There is no consensus for the role of radiotherapy and chemotherapy in therapeutic management. Concerning WHO grade III meningiomas, radiotherapy is considered necessary because of their potential for recurrence and aggressive behavior. Chemotherapy has not shown any convincing effect on atypical and anaplastic meningiomas and should be reserved for recurrent meningiomas when all standard therapies have failed [14, 15].

Metastasis of meningiomas is uncommon. Even when they show malignant histological

features, metastases is rare [6]. Malignant histology is more often expressed as infiltration rapid growth which increases the risk of local recurrences following surgical resection. However, metastasis can occur through the cerebrospinal fluid, blood, or lymphatic spread, but dissemination during surgery is not considered among them. Dura, brain and lung are the most frequent locations for meningioma metastasis. Unfortunately, no reliable predictors have been found for the metastasis of meningiomas. The majority of reported metastatic meningiomas had malignant histological characteristics at the time of presentation. Only a few exceptional cases have been reported so far [5, 13, 16]. Interestingly, for our patient, the initial presentation of the meningioma in 2009 was benign. Samples from recurrent lesion in 2012 still showed benign features. Substantial evidence had indicated the malignant transformation for the sections of repeated recurrent tumor in 2013. Combining with the published studies, a preliminary conclusion made is metastasis of meningiomas may not require histological malignancy.

As regards Ki-67 immunolabelling, there is controversy in the literature and considerable variation in Ki-67 immunolabelling of meningiomas has been reported [17-19]. However, most researchers have quoted 10% as a prognostic factor for tumoral progression. In our case, the Ki-67 index reached a high level of 40%, which was in accordance with the rapid tumor growth. Although it is undeniable that Ki-67 index helps neuropathologists to determine the aggressiveness of the tumor, no therapeutic decision is proposed on the basis of Ki-67 index alone.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Jun Li, Department of Neurosurgery, Wuhan Central Hospital Affiliated to Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430014, Hubei, P. R. China. Tel: +49 15756847006; E-mail: t0102082@hotmail.com

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