

Case Report

An unusual subtype of meningioma: report of 3 cases of papillary meningioma and review of the literature

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Received September 20, 2017; Accepted May 24, 2018; Epub August 15, 2018; Published August 30, 2018

Abstract: Background: Papillary meningioma is a rare subtype of meningioma most often occurs in young people. It usually shows aggressive growth pattern and was considered as tumor of WHO III which is different from the common meningioma. Case presentation: Here we report 3 cases of this rare subtype of meningioma in 2 males and a female, who are all adults. Grossly, the tumors had no clear boundary and showed invasive growth. Histologically, the tumor cells all formed the characteristic capillary-surrounding pseudo papillary structures. The tumors were mainly composed of epithelioid tumor cells with eosinophilic cytoplasm and pale-dyed nucleus with low mitotic index. The immunostaining showed that all the tumors have bidirectional differentiation of mesenchymal tissue and epithelium with positive EMA and vimentin staining. Ki67 index was relative high and about 10%-15%. All the patients received tumor resection and 2 patients also received adjuvant radiotherapy. No recurrence occurred at 6-40 months follow-up. Conclusions: According to the findings, the 3 cases were diagnosed as papillary meningioma. We suggest that distinguishment of this rare type from the normal one, and timely surgery and adjuvant radiotherapy are critical for improving patients' outcomes. Close follow-up is necessary as recurrence is common in this rare subtype.

Keywords: Meningioma, papillary meningioma, case report

Background

Meningiomas are common neoplasms originating from dura mater which are mostly benign [1, 2]. Meningiomas account for about 24-30% of intracranial primary tumors [1]. People who are above middle age are prone to meningiomas, and the peak age is between 51-70 years [1]. Tumors present in children are usually more aggressive [1]. The incidence of meningioma in female is far higher than that of male, suggesting that the pathogenesis of meningioma may be related to hormone [1]. Another important cause of meningioma is radiation therapy [1]. The common sites of meningioma include intracranial, orbital, and spinal, and rare sites include intraventricular, epidural, and all organs of the body [1]. Meningiomas usually grow slowly and cause symptoms mainly by pressing surrounding tissues, such as headache and epilepsy [1, 3]. Most meningiomas have a good

prognosis, and only about 20% of the tumors recur within 20 years after surgery [1]. The common meningiomas usually are benign tumors, but there are several rare subtypes which show aggressive growth including papillary meningioma [1, 4]. These rare subtypes are listed as World Health Organization (WHO) II or III because the tumors are easy to relapse, have high invasiveness, or can metastasize. Papillary meningioma is one of these rare subtypes of meningioma. According to Brignolio's paper, papillary meningioma only account for 1% (8/750) of meningioma [5]. Unlike common meningioma, papillary meningioma has no well-defined gender preference [6, 7]. Middle age people are prone to this kind of meningioma [6, 8]. Malignant meningiomas can metastasize and the common sites include the lung, bone, and liver [1]. In Ludwin's report of 17 cases of papillary meningioma, 3 cases had distant extraneural metastases, among which 2 cases

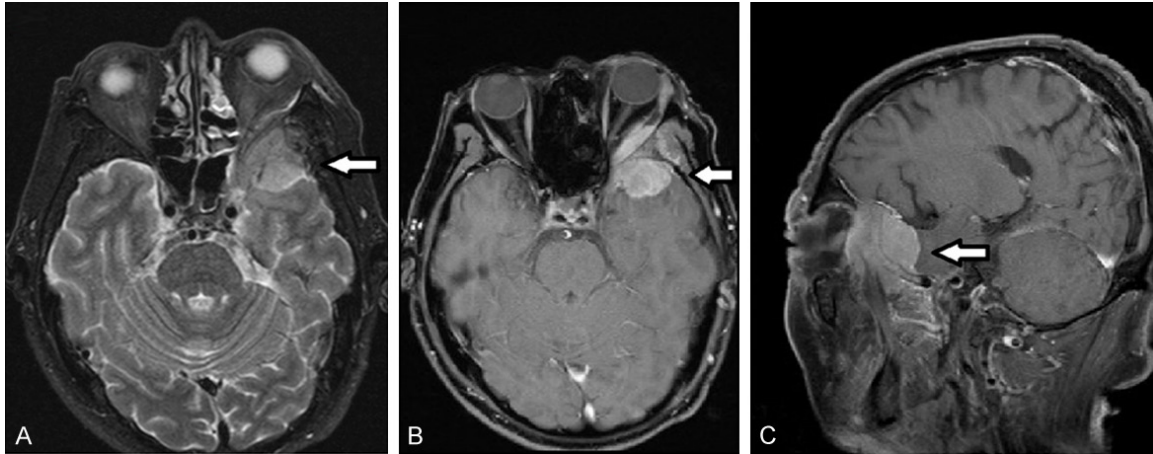


Figure 1. The imaging of the tumor of case 1. The MRI shows that the mass (the arrows) was centered on the left sphenoid large wing, and grew into the middle cranial fossa and the left orbital muscle cone (A-C). The left lateral orbital wall and the large wing of the sphenoid bone were invaded, and the left lateral rectus muscle was displaced by compression of the tumor (A-C). (A and B) shows the cross section, and (C) shows the sagittal section of the tumor. T2-weighted image shows the mass had slightly long T2 signal intensity (A). T1-weighted/STIR images show moderate enhancement of the signals in the mass (B, C).

metastasized to the lung and 1 to the liver [9]. The prognosis of this subtype is generally poorer than common meningioma [6, 10, 11]. Careful differentiation from the common type, an appropriate diagnosis and thus an appropriate treatment in time is crucial for improving the prognosis of the patients. In the current paper, we report 3 cases of rare papillary meningioma in adults and give a summary of this subtype of meningioma of the literature.

Case presentation

Clinical history

Case 1. A 64-year-old man referred to our hospital for left proptosis accompanied by foreign-body sensation 2 months ago. The movement of the eye is restricted in all directions. After using Eye drops to drip to the eyes the symptom hadn't changed. His symptom aggravates one month ago accompanied by decreased vision and pain of the left eye. Neurological examination showed no positive sign. Liver and kidney function and blood cell examination were normal. The patients received tumor resection and adjuvant radiotherapy. The symptoms showed dramatic improvement after the surgery and after a 40 months follow-up, no relapse occurred.

Case 2. A 73-year-old man referred to our hospital for epileptic seizure accompanying loss of consciousness and limb spasm without

obvious cause 4 days ago. The seizures usually relieved after a few minutes. Neurological examination showed no positive sign. The blood test only showed a slight rise of eosinophils ($0.74 \times 10^9/L$). Liver function test showed higher GGT (117 U/L), lower ALB (30.9 g/L) and lower TP (52.2 g/L). The patient received surgery and antiepileptic therapy. No recurrence occurred at a 21 months follow-up.

Case 3. A 47-year-old woman referred to our hospital for headache, dizziness, nausea and vomit two weeks ago. No positive sign was detected by neurological body examination. The blood test only showed a slight rise of monocytes ($0.64 \times 10^9/L$), eosinophils ($1.58 \times 10^9/L$), and basophils ($0.07 \times 10^9/L$), and a slight decrease of lymphocyte percentage (15.4%) and hemoglobin concentration (97 g/L). The liver and kidney function test was normal. The patient received surgery and adjuvant radiotherapy. Postoperative recovery was good and the symptoms including dizzy and nausea disappeared. MRI was performed a month after the surgery and no residual tumor was found. No recurrence occurred at a 6 months follow-up.

Materials and methods

The blocks of the resected samples were cut into sections and stained with alum haematoxylin and eosin for morphological examination under light microscope. The immunohisto-

Case report of papillary meningioma

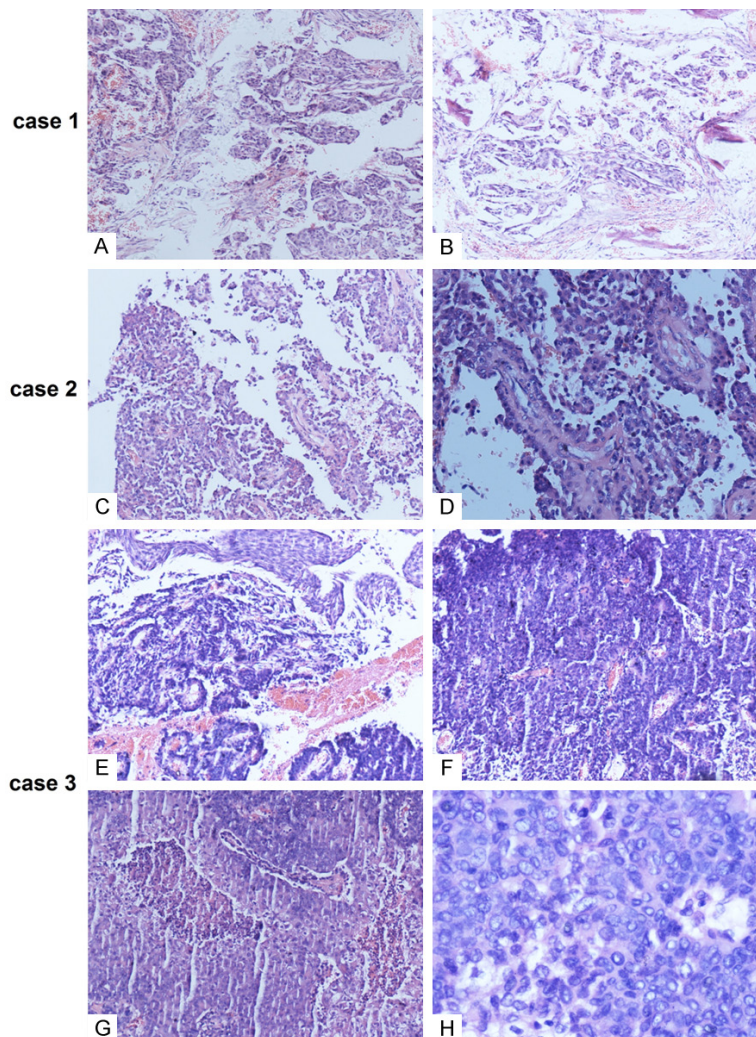


Figure 2. Histological features of the tumors (HE staining). All the tumors show characteristic pseudo papillary structure around the blood vessels (A-H). The tumor cells invade the bones (B). In some areas, the tumor cells were densely arranged in sheets (F). Necrosis was seen in the tumor tissues (G). (A, B: $\times 100$; C-G: $\times 200$; H: $\times 400$).

chemistry was performed as described previously according to the instruction the producer [12]. The sections were incubated with the primary antibodies including: EMA (1:100, DAKO), Ki-67 (1:200, DAKO) and vimentin (1:100, DAKO) overnight at 4°C. 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.

Results

Imaging and gross features

Case 1. The Magnetic Resonance Imaging (MRI) scan displayed a mass centered on the

left sphenoid bone greater wing in the left middle cranial fossa and orbit (**Figure 1**). The boundary between the mass and greater wing of sphenoid bone and the outside wall of the left orbital. The patient received surgery and the tumor was found in sphenoid ridge and invade cavernous sinus and rock bone sinus. The tumor was about 2 cm $\times$ 2 cm $\times$ 1 cm. The cut surface was grey-yellow with moderate hardness. No lymph node metastasis or distant metastasis was detected.

Case 2. The patient was examined with Computed Tomography (CT) and MRI scan in the local hospital, displaying a mass in the left frontal lobe of the brain. The patient received surgery in our hospital and the tumor was found to be originated from the dura mater and closely attached to the brain and the boundary with the brain was not clear. The tumor was about 6 cm $\times$ 5 cm $\times$ 4 cm. The cut surface was grey-white with moderate hardness. No lymph node metastasis or distant metastasis was detected.

Case 3. The patient was examined with CT scan in the local hospital, displaying that there was a cystic mass in the right cerebellum which was first considered as hemangioblastoma, considering the site and cystic change. Surgical records showed that the tumor located in the upper surface of the right cerebellar hemisphere. It originated from the transverse sinus of the tentorium and right side of torcular, and closely attached to the cerebellar surface. The tumor was about 2 cm $\times$ 1 cm $\times$ 0.5 cm and the cut surface was grey-white and soft with cystic change.

Microscopic features

Figure 2 shows the histological features of the tumors. In all the 3 cases, the tumor cells forms

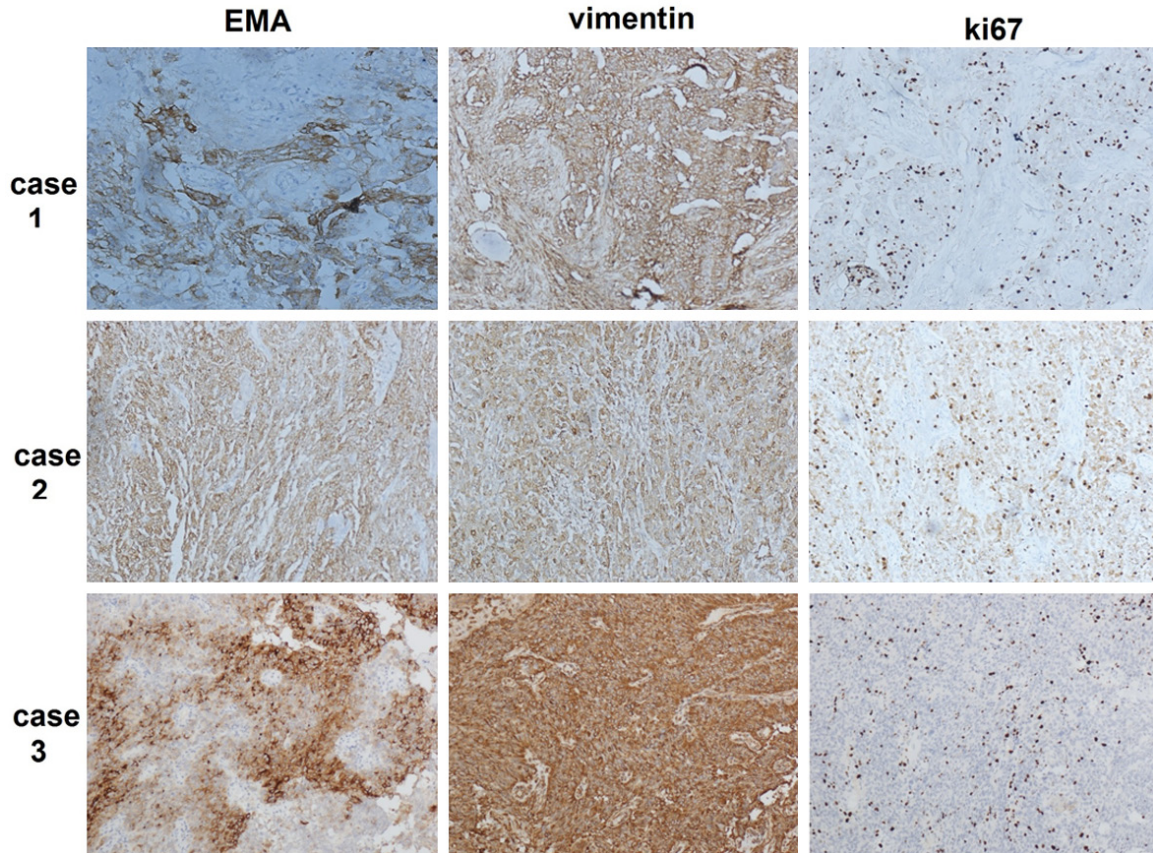


Figure 3. Immunostaining pattern of the tumors. The tumor cells of the 3 cases were all positive for EMA and vimentin. Ki67 index was 15%, 10% and 10% respectively. (Magnification: case 1: EMA, Ki67: $\times 200$; vimentin: $\times 400$; case 2: EMA, vimentin: $\times 400$; Ki67: $\times 200$; case 3: EMA, vimentin, Ki67: $\times 400$).

a pseudo papillary structure around the blood vessels which is a characteristic pathological change (A, B, C, D, E). In some areas, the tumor cells were arranged densely and the pseudo papillary structures were very tight and looks like cell sheets (F). The tumor cells invade the adjacent bones indicating an aggressive growth pattern (B). Necrosis can be seen in the tumor tissues of case 3 (G). The tumor cells are mainly epithelioid with round or ovoid pale-dyed nucleus and eosinophilic cytoplasm (H). Mitotic index are very low in all these cases lower than 1/10 HPF.

Immunophenotype

Figure 3 shows the immunostaining pattern of the tumors. The tumor cells of all the 3 cases show positive immunostaining of EMA and vimentin, which indicate a bidirectional differentiation of mesenchymal tissue and epithelium of the tumor. Ki67 index was about 10%~15% in these tumors.

Discussion

Papillary meningioma is a rare subtype of meningioma which belong to tumors of WHO III [1]. Histologically, the characteristic feature of papillary meningioma is the pseudo papillary structure. There are also some other difference in microscopic findings from the common type. Pasquier's study of 7 cases of papillary meningiomas indicated that psammoma bodies in this subtype was unusual but the necrosis is common [13]. Due to the epithelioid structure, the main differentiations include metastasing carcinomas. The epithelial marker CK is positive in carcinoma but negative or only focally positive in papillary meningioma. Depending on sites and types, the carcinoma can also be positive for some specific antibodies, such as TTF-1, PAX-8, CDX-2, which are all negative in papillary meningioma. Glioma, which is the most common intracranial malignant tumor, should also be differentiated, though the pseudo papillary structure was usually not seen in

Case report of papillary meningioma

Table 1. Clinicopathological features of the tumors

Case	Features			
	Age	Sex	Location	Tumor size
Case 1	64	Male	Left temporal pole	2 cm × 2 cm × 1 cm
Case 2	73	Male	Left frontal lobe	6 cm × 5 cm × 4 cm
Case 3	47	Female	Cerebellum	2 cm × 1 cm × 0.5 cm

this tumor. Another differentiation is ependyoma which are common malignant intracranial tumors perivascular pseudorosettes which is somewhat similar as the pseudo papillary structure in papillary meningioma. However, glioma and ependyoma are commonly positive for GFAP, not like papillary meningioma.

Both children and adults can suffer from papillary meningioma, but the most patients are middle-aged. In 1975, Ludwin reported 17 cases of papillary meningiomas and the ages of the patients range from 3 to 67 years [9]. Shuangshoti's analyzed 123 cases of papillary meningiomas and the patients' mean age was 35 years [8]. In Fong's study the mean age of the patient with papillary meningioma was 32.3 years [14]. The mean age of patients with this tumor in Wang's report was 40 (6-55) years [6]. In Yu's study, the ages of the eight patients range from 24 to 54 years [15]. In the summary of the literature in **Table 2** [8, 10, 16-28], the youngest patient is 6 months old who had a tumor involved the oculomotor nerve [16]. There was also a 3 year-old patient who had a tumor in the posterior fossa which relapsed 6 months after the surgery and intracranial metastases occurred 2 months latter [11]. In the current paper, the 3 patients are all adults and the ages are relative high. In the 17 cases of papillary meningiomas in Wang's paper, the most common location of the tumors was the cerebral convexity which was consistent with Li's study [6, 29]. The maximum diameters of the tumors range from 2 to 8 cm in Yu's paper [15]. As we summarized in **Table 1**, the maximum diameters of the tumors range from 1.4 cm to 10 cm which was similar as Yu's study [15].

The patient usually has oppressive symptoms, without obvious neurological signs. Some patients may have abnormal signs such as nerve palsy on neurological examination depending on the tumor sites [18]. In Jiang's case, after a second tumor surgery, the patient had no recur-

rence of the tumor at 2 years follow-up, but symptom of limb weakness persisted [19]. In this study, the patients mainly suffer from the symptoms due to compression of brain tissue and cranial nerves by the tumors. The treatment of meningiomas usually is resection, and

there is no consensus on whether the patient will be treated with radiotherapy after a total resection of the tumor [14]. The patient with papillary meningioma of the jugular foramen in Yu's paper had no relapse after surgery on a 4-year follow-up [18]. As the extent of resection is closely related to the prognosis of the patient, it is necessary to perform postoperative imaging to determine whether the tumors are totally removed. Yu's study investigated the MRI findings of papillary meningioma and found that most of the tumors (7/8) had no clear boundary with the surface of brain, which indicate that MRI is useful for understand the aggressive growth pattern of this subtype of meningioma [15]. According to Fong's study, patients with papillary meningioma underwent total resection and radiotherapy had better prognosis than total resection alone, indicate the significant roles of radiotherapy [14]. Moreover, patients who do not have complete resection of the tumor usually need radiotherapy [14]. Some studies didn't show sex difference for the tumor [6, 7]. In Wu's paper the patient with intraspinal papillary meningioma received surgery and radiotherapy and a 15 months follow-up indicated no relapse of the tumor [17].

Patients with papillary meningioma usually have poorer prognosis than the common meningioma. In Wang's study all the 30 patients underwent partial resection and 57.1% of the patients receiving total resection had recurrence of the tumors [7]. Half of the patients (17 cases) died after 3 years who underwent total tumor resection in Wang's study [6]. The patient with papillary meningioma in the brain stem had a recurrence 9 months after the gross total tumor resection in Jiang's paper [19]. Papillary meningioma doesn't relapse only due to local recurrence, but also can metastasis. Kim reported a patient with papillary meningioma which spreaded in the pia mater, and the patient died 60 days after the surgery [20]. Li's study also reported 3 cases of papillary meningioma with cerebrospinal fluid dissemination

Case report of papillary meningioma

Table 2. Case summary of papillary meningioma in the literature

Author, study location, publication year and reference	Gender	Age (year)	Site	Size	Outcome: Recurrence/follow-up time
Wu, Beijing Tiantan Hospital, 2016 [17]	Female	44	Cervical spine	1.4 × 1.8 × 1.5 cm	No/15 months
Yu, the first hospital of Jilin University, 2015 [18]	Male	21	Jugular foramen	3.0 × 2.5 × 1.0 cm	No/4 years
Zhang, Chinese PLA General Hospital, 2014 [24]	Male	16	Left temporal region	Not sure (giant)	Died the second day after the operation
Jiang, Sun Yat-sen University Cancer Center, 2012 [19]	Male	23	Brainstem	3.5 × 2.5 × 2.0 cm	No/2 years
Kim, Kyung Hee University College of Medicine, 2011 [20]	Male	43	Falcotentorium	3.1 × 2.8 × 2.9 cm	Died on the following day
Avninder, Safdarjang Hospital, New Delhi, 2007 [27]	Male	16	Anterior cranial compartment	10 × 8 × 2 cm	No/15 months
Erkutlu, Gaziantep University School of Medicine, 2009, [21]	Male	29	Posterior fossa meninges	Unknown	Spinal drop metastases/32 months
Zhi, First Affiliated Hospital, Sun Yat-sen University, 2009 [10]	Female	23	Left temporal lobe	Unknown	Unknown
Miyajima, Kitasato University School of Medicine, 2007 [22]	Male	13	Tentorium cerebelli	Unknown	Unknown
Buschmann, Kantonsspital St. Gallen, 2005 [25]	Female	15	Infratentorial	2.5 × 1.2 × 1.5 cm	Yes/4 years
Go, Fukuoka University School of Medicine, 2000 [23]	Female	48	Parasagittal	Unknown	Yes/within 1 year
	Female	35	A high convex tumor	Unknown	unknown
	Male	57	Parasagittal	Unknown	unknown
Meinsma-vdTuin, University Hospital AZG, 2000 [26]	Unknown	19	Spinal	Unknown	Yes/6 months
Bouvier, CHU Timone, 1999 [11]	Male	3	Posterior fossa	Unknown	Twice/6 and 8 months after operation
Benchetrit, hôpital Pasteur, 2013 [28]	Male	16	Right frontal	Unknown	Unknown
Piatt, Duke University Medical Center, 1986 [16]	Unknown	6 months	Oculomotor nerve	Unknown	Unknown
Shuangshoti, Faculty of Medicine, Chulalongkorn University, 1993 [8]	Female	54	Optic nerve sheath	Unknown	Unknown

[29]. Wang's study of 30 cases shows that the extent of resection and radiotherapy were prognostic factors [7]. Erkutlu reported a case of papillary meningioma in the posterior fossa which developed spinal drop metastases 32 months after the surgery [21]. The authors suggest the possibility of cerebrospinal fluid seeding during surgery and CSF sampling for early detection of metastatic tumor cells [21]. Zhi's study reported a case of papillary meningioma in the lateral ventricle which metastasized to the subarachnoid space [10]. Fukushima presented a rare case of papillary meningioma which had multiple lung metastasis and received successful resection of the remote metastasizing tumors [30]. Kros reported a case of papillary meningioma which metastasized to the pleura [31]. The factors impacting the prognosis of patients with meningioma mainly include the histological type and grade, the extent of resection and the adjuvant therapy, such as radiotherapy [14, 24]. In Fong's investigation, about half of the patients with papillary meningioma had relapse of the tumor after surgery and 28% had distant metastases [14]. The recurrence rate of tumors was relative lower in the patients underwent total resection than partial resection which indicate that the extent of resection is an important factor to impact the prognosis of the patient [14]. Zhang described a case of papillary meningioma in the left temporal region with abnormal vessels which were suggested to be considered as important factor for the patient's prognosis [24].

With the increase of histological grade, the recurrence rate increased obviously and the average survival time of the tumors with malignant histological features is less than 2 years [9]. Brignolio analyzed 8 cases of papillary meningiomas and suggested that the pathological malignant features such as necrosis, high mitotic index and pleomorphism were associated with the poor outcomes of the patients [5]. A patient with an infratentorial papillary meningioma experienced a recurrence 4 years after the tumor resection and the histological malignancy of the tumor increased [25]. What is to be noted that different subtype of meningioma can coexist. Kochanski reported a extremely rare case of meningioma with collision of two unusual subtypes, namely anaplastic and papillary meningioma [32].

Ki67 index is a very important indicator of tumor growth. The mean Ki67 index was 6.9% in Wang's report and 12% in Avninder's study [6, 27]. In this study, the Ki67 index was about 10% to 15% in the 3 cases which was also relative high. Whether there is a correlation between Ki67 index of this tumor and the prognosis of patients is still controversial. Li's study indicates that MIB-1 index is a prognostic factor [29]. But Wang's study didn't find a significant association between MIB-1 index and patients' prognosis [7].

Conclusion

Papillary meningioma is a very rare subtype of meningioma which has aggressive growth pattern.

The main cause of death is relapse of the tumor due to local recurrence or distant metastasis. Early detection and appropriate treatment including total resection and adjuvant radiotherapy are critical for improving the prognosis of the patients.

Acknowledgements

This work was supported by grants from the National Natural Science Foundation of China (No. 81472599 to Chuifeng Fan).

Disclosure of conflict of interest

None.

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Case report of papillary meningioma

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Case report of papillary meningioma

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