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CLINICAL ARTICLE - BRAIN TUMORS

Clinical features of clear cell meningioma: a retrospective study of 36 cases among 10,529 patients in a single institution

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Abstract
Background Clear cell meningioma (CCM) is a rare subtype of meningioma. We present the largest series of 36 CCMs and evaluate several prognostic factors of patient's clinical outcome.
Methods Thirty-six patients with pathologically confirmed CCM among a total of 10,529 meningioma patients were retrospectively reviewed.
Results CCM constituted 0.3 % of the intracranial meningiomas and 1.4 % of the intraspinal meningiomas. The male-to-female ratio (36 vs 64 %) for CCMs was similar to that for total meningiomas (28 vs 72 %) patients (chi-squared test, p=0.3). The mean age at diagnosis of CCM patients (29.3±18.4 years) was significantly younger than that of total meningiomas (49.8±11.9 years) patients (t-test, p=0). During the follow-up, 15 patients (42 %) suffered from tumor recurrence. The recurrence time ranged from 10 months to 12 years, with a median time of 29 months. Kaplan-Meier survival analysis showed that patients after total resection (Simpson grades I and II) had significantly longer progression-free survival (PFS) time than those after subtotal resection (Simpson grades III and IV) (log-rank test, p=0.006). However, age (≤20 years or >20 years, p=0.9), gender (p=0.3), postoperative radiotherapy (p=0.4), progesterone receptor staining (positivity or negativity, p=0.2), and Ki-67 index (≤5 % or >5 %, p=0.4) did not have significant effects on patients' PFS time.
Conclusions The proportion of CCM in spinal meningiomas is likely to be much larger than that in intracranial meningiomas. CCMs should be resected totally when possible to decrease the risk of recurrence or prolong patient's PFS time.

Keywords Clear cell meningioma · Clinical features · Prognosis · Retrospective study

Clear cell meningioma (CCM) is a rare subtype of meningioma. It represents only 0.2–0.8 % of all meningiomas [1, 2]. Histologically, it is characterized by sheets of polygonal cells with clear cytoplasm, which is the expression of a high glycogen concentration [3]. CCM was firstly described by Manivel and Sung in 1990 [4]. It was classified as a grade I lesion in 1993 because of its bland histological appearance [2]. However, CCM was found to behave aggressively with a high rate of local recurrence and cerebrospinal fluid metastasis, and it was changed to grade II in 2000 [5]. To date, more than 100 CCMs have been reported in the English literature [6]. Most of them were isolated case reports except for several series [2, 5–9]. The clinical features of CCM are still not clear. Here, we present the largest series of 36 CCMs and evaluate several prognostic factors of patient's clinical outcome.

Patients and methods

Search methods and case definition

Review of the records of Beijing Tian Tan Hospital for the period from 2008 to 2015 identified 36 patients with pathologically confirmed CCM among a total of 10,529

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meningioma patients. Data regarding the clinical presentation, radiological imaging, pathologic results, and treatment outcome of CCM patients were retrospectively reviewed. The microscopic pathologies of 36 CCMs were reviewed by two independent neuropathologists (L.L. and J.L.) according to the 2007 WHO grading system. The age and gender information of 10,529 meningioma patients were also collected for the purpose of comparison. We searched PubMed for relevant articles with the term "clear cell meningioma" in the title. Studies with more than seven cases were carefully reviewed.

Ethical committee approval and follow-up

This retrospective study was approved by the Beijing Tian Tan Hospital institutional review board. CCM patients were followed-up through the telephone interview or an outpatient department. Generally, patients were told to get cranial enhanced magnetic resonance imaging (MRI) examination at 3, 6, and 12 months after the operation; then they received cranial radiological examination every 1 or 2 years thereafter. Patients might also get additional radiological examination if they got suspicious symptoms that might be associated with tumor recurrence. Progression of CCM was defined as the radiological regrowth of the tumor. Progression-free survival (PFS) was defined as the time between initial surgery and tumor progression on radiology.

Statistical analysis

To select prognostic factors associated with longer PFS, the Kaplan-Meier survival analysis and log-rank test were used. The chi-squared test was used for the comparison of gender distribution in CCM and meningioma patients. Student's independent *t*-test was used for the comparison of mean age at diagnosis in CCM and meningioma patients. A p value <0.05 was considered statistically significant. The analyses were performed using the SPSS statistical software, version 19 (SPSS, Chicago, IL, USA).

Results

Demographics

A total of 10,529 meningioma patents were treated in our institution from 2008 to 2015, CCM constituted 0.3 % of all meningiomas. Of the 36 CCM patients, 30 cases were intracranial and 6 cases were intraspinal. Of the 10,529 meningioma patients, 10,102 cases were intracranial and 427 cases were intraspinal. Thus, CCM constituted 0.3 % of the intracranial meningiomas and 1.4 % of the intraspinal meningiomas (chi-squared test, p=0.003). The clinical characteristics of 36 CCM patients are summarized in Tables 1 and 2. The age at diagnosis of CCM patients ranged from 4 to 77 years; the mean age was 29.3±18.4 years, which was significantly younger than that of total meningioma patients (49.8±11.9 years) (*t*-test, p=0, Fig. 1a–c). Of the 36 CCM patients, 13 were male and 23 were female; the male-to-female ratio (36 vs 64 %) was similar to that of total meningiomas (28 vs 72 %) patients (chi-squared test, p=0.3, Fig. 1d).

Symptoms and location

Of 36 CCM patients, most patients were sporadic and two patients (patients 10 and 19) had neurofibromatosis 2 (NF2). Preoperative symptoms of CCM patients were usually caused by tumor compression. Preoperative duration ranged from 1 month to 3 years, with a median duration of 3 months. Most spinal CCMs were located in the lumbosacral area. Of the 30 intracranial CCMs, the most common location was supratentorial (14 cases), followed by CPA or petrous apex region (11 cases), and infratentorial (5 cases).

Radiological findings

The MRI characteristics of CCM were similar to those of other types of meningiomas. Most CCMs appeared as isointense or slightly hyperintense on T1-weighted images and isointense or slightly hyperintense on T2-weighted images. The tumors were usually heterogeneously enhanced after the contrast administration. Two tumors (patients 17 and 22) extended from the cerebellopontine angle (CPA) to the region of Meckel's cave and were misdiagnosed as trigeminal schwannoma preoperatively. One tumor showed hypointense on T1-weighted image and hyperintense on T2-weighted image without evident enhancement, mimicking cholesteatoma (patient 5, Fig. 2).

Treatment

Twelve patients (33 %) underwent subtotal resection (Simpson grades III and IV) and 24 patients (67 %) underwent total resection (Simpson grades I and II). During the operation, CCM tumors were usually found to be firm and hypervascular like other types of meningiomas. Seven tumors (19 %) were found to erode the skull or sacrum bone. Most tumors were attached to the dura mater. One intracranial (patient 9, Fig. 3) and one spinal (patient 34) CCM were absent of dural attachment. Most spinal CCMs were intradural extramedullary; one spinal CCM was extradural and extended outward through the intervertebral foramen (patient 33, Fig. 4). Nine patients received postoperative radiotherapy, including gamma knife surgery (GKS) in four cases.

Table 1 Clinical features of 36 patients with clear cell meningioma

No.	Sex/age (years)	Preoperative symptoms	Preoperative duration	Location	EOR	RT	Recurrence	Follow-up	Ki-67
1	F/13	Diplopia	2 months	Right petrous apex-parasellar region	Subtotal		12 months: second OP 30 months: third OP + GKS	8 years/alive	
2	M/42	Facial numbness & tinnitus	4 months	Left petrous apex-parasellar region	Subtotal		48 months: second OP	6 years/alive	
3	F/7	Hearing loss & facial palsy	3 months	Left CPA	Total	RT	15 months: second OP + RT	7 years/alive	
4	F/21	Epilepsy	2 months	Right frontal lobe	Total		None	7 years/alive	
5	F/28	Hearing loss	5 months	Right CPA	Total		None	6 years/alive	
6	F/23	Headache	2 months	Left CPA	Subtotal		15 months: second OP 28 months: third OP + RT 60 months: fourth OP	6 years/alive	
7	M/19	Headache	3 months	Left frontal lobe	Total		None	5 years/alive	Negative
8	F/20	Visual deficieny	7 months	Sellar region	Total		None	5 years/alive	
9	M/15	Headache & epilepsy	3 months	Left frontal parietal lobe	Total	RT	10 months: second OP + GKS 36 months: third OP + RT + CH	4 years/dead	
10	F/42	Walking instability	8 months	Left petrous apex -parasellar region	Total	RT	None	4 years/alive	
11	F/10	Hearing loss	1 year	Right petroclival region	Total		144 months: second and third operation (multiple recurrence)	15 years/alive	10 %
12	F/22	Epilepsy	3 months	Parafalx	Subtotal	GKS	29 months: second OP	4 years/dead	10–30 %
13	F/29	Epilepsy	2 months	Right frontal lobe	Total		None	3 years/alive	5 %
14	M/30	Headache & limb weakness	2 years	Right frontal parietal lobe	Total		14 months: second OP + RT 29 months: third OP	3 years/alive	0–12 %
15	F/50	Limb numbness	3 months	Right parietal lobe	Subtotal		34 months: second OP + RT 60 months: third OP	7 years/alive	
16	F/20	Headache	1 month	Right frontal lobe	Subtotal		12 months: second OP 24 months: third OP	2 years/alive	5 %
17	M/27	Dizziness	2 months	Left middle-posterior cranial fossa	Subtotal	GKS	None	2 years/alive	
18	F/63	Headache	1 month	Left temporal lobe	Total	RT	None	2 years/alive	
19	M/34	Body examination		Ventral aspect of the medulla oblongata	Total		None	1 year/alive	3 %
20	M/19	Water choking	1 month	Left jugular foramen	Subtotal		35 months: second OP + GKS	5 years/alive	5 %
21	F/6	Headache	2 months	Left middle-posterior cranial fossa	Total		96 months: second OP (extracranial recurrence) 103 months: third OP + Cyber knife (extracranial recurrence)	10 years/alive	
22	F/38	Facial numbness	6 months	Left middle-posterior cranial fossa	Total		None	1 year/alive	6 %
23	M/29	Headache	3 months	Anterior cranial fossa	Total		24 months: second OP	3 years/alive	
24	F/14	Limbs weakness	2 months	Middle-posterior cranial fossa (both-side)	Total		None	1 year/alive	
25	M/77	Headache	6 months	Left parietal lobe	Subtotal	GKS	None	8 months/alive	5 %
26	F/65	Headache	1 month	Left frontal lobe	Total		None	6 months/alive	

Table 1 (continued)

No.	Sex/age (years)	Preoperative symptoms	Preoperative duration	Location	EOR	RT	Recurrence	Follow-up	Ki-67
27	M/40	Dysphagia	3 months	Cerebellum	Subtotal	GKS	34 months: second OP + RT	3 years/alive	15 %
28	F/37	Dizziness	2 months	Left jugular foramen	Subtotal		34 months: second OP + RT	3 years/alive	1–2 %
29	M/64	Headache	1 month	Parafalx	Total	RT	None	3 months/alive	3 %
30	F/48	Dysphagia	1 year	Foramen magnum	Total		None	3 months/alive	3 %
31	M/21	Limb pain	4 months	L5	Total		None	5 months/alive	5–15 %
32	F/43	Limb pain	3 years	L3-S3	Subtotal		None	10 month/alive	5 %
33	F/7	Limb pain	6 months	T11-L1	Total		None	9 months/alive	20 %
34	F/7	Limb pain	1 month	L2-4	Total		None	2 years/alive	10 %
35	M/4	Limb pain & weakness	6 months	T11-12	Total		None	2 years/alive	
36	F/20	Limb pain	3 months	L4-5	Total		None	2 months/alive	5–10 %

F female, *M* male, *CPA* cerebellopontine angle, *EOR* extent of resection, *RT* radiotherapy, *GKS* gamma knife surgery, *CH* chemotherapy, *OP* operation

Histological findings

Most CCMs showed benign histological features, and only one had significant mitotic figures (patient 15). The histological diagnosis was aided by immunostaining. Most tumors were positive for vimentin and EMA, and negative for S-100, GFAP and CK. Progesterone receptor (PR) staining was available in 16 cases: eight were positive and eight were negative. The Ki-67 indexes were available in 19 cases, and they varied from negative to 30 %. Nine cases were below 5 %, and ten cases were above 5 %.

Recurrence and survival analysis

Follow-up time of CCM patients ranged from 2 months to 15 years, with a median time of 3 years. During the follow-up, 15 patients (42 %) suffered from tumor recurrence. Most of them were local recurrence, multiple recurrences were found in only one patient (patient 11). Imaging study of the entire neuroaxis was not performed to evaluate the possible spinal metastasis. But patients did not have relevant symptoms that might be associated with tumor occurrence in other parts of the body. The recurrence time after the first operation ranged from 10 months to 12 years, with a median time of 29 months. Kaplan-Meier survival analysis showed that patients after total resection had significantly longer PFS time than those after subtotal resection (log-rank test, $p=0.006$, Fig. 5). Of 12 patients receiving subtotal resection, 9 (75 %) patients got tumor recurrence; of 24 patients receiving total resection, 6 (25 %) patients got tumor recurrence. However, age (≤20 years or >20 years, $p=0.9$), gender ($p=0.3$), postoperative radiotherapy ($p=0.4$), PR staining (positivity or negativity, $p=0.2$), and Ki-67 index (≤5 % or >5 %, $p=0.4$) did not have a significant effect on patient's PFS time. After recurrence, patients usually received repeated operation and/or radiotherapy. Most patients stayed alive to the last date of follow-up, and two patients died of the disease.

Discussion

CCM is a rare variant of grade II meningioma with distinctive histological features [6]. Previous studies indicated that it constituted 0.2–0.8 % of all meningiomas, which was similar to the result of our study (0.3 %). Recent studies found that CCM occurred equally in the intracranial and spinal region [6, 10]. However, the total spinal meningiomas are much less common than their intracranial counterparts. Our study showed that the proportion of CCMs among spinal meningiomas was almost 5 times that of the proportion of CCMs among intracranial meningiomas (1.4 vs 0.3 %), which could explain this interesting phenomenon. It should be noted that our institution performed far more cranial op-

Table 2 Clinical, demographic, and pathological characteristics of 36 patients with clear cell meningioma

Characteristics		Value
Age at diagnosis (years)	Range	4–77
	Mean	29.3±18.4
Gender	Male	13 (36 %)
	Female	23 (64 %)
Preoperative duration	Median	3 months
	Range	1 month–3 years
Location	Supratentorial	14 (39 %)
	CPA or petrous apex	11 (31 %)
	Infratentorial	5 (14 %)
	Intraspinal	6 (17 %)
Extent of resection	Subtotal	12 (33 %)
	Total	24 (67 %)
Postoperative RT	Yes	9 (25 %)
	No	27 (75 %)
Recurrence frequency	0	21 (58 %)
	1	8 (22 %)
	2	6 (17 %)
	3	1 (3 %)
Recurrence interval	Median	29 months
	Range	10 months–12 years
Follow-up time	Median	3 years
	Range	2 months–15 years
Ki-67 index	≤5 %	9 (47 %)
	>5 %	10 (53 %)
PR staining	Positive	8 (50 %)
	Negative	8 (50 %)

Values represent number of cases (%) unless otherwise indicated. All means are expressed ± SD

CPA cerebellopontine angle, *RT* radiotherapy, *PR* progesterone receptor

erations than spinal operations. Thus, the data in our study could not reflect the real ratio of total intracranial meningiomas to the spinal ones.

Like the other types of meningioma, CCM has a female predilection. The ratio of females to males having CCM was not significantly different from that for total meningiomas (1.8 vs 2.5, p=0.3, Fig. 1d). It has been considered to be attributed to the sex hormones. Previous reports indicated that the female bias did not exist in CCM childhood cases [7]. CCM has also been reported to progress rapidly during pregnancy [11, 12]. All these indicate an important role of female sex hormones in the occurrence of CCM. Different from other types of meningiomas, CCMs tend to have a predilection toward younger patients [2, 6, 13]. Childhood cases of CCM are common [3, 7, 14]. Our study also found that the mean age at diagnosis of CCM patients was significantly younger than that of the total meningioma patients (29.3±18.4 years vs 49.8±11.9 years, p=0, Fig. 1c).

CCMs usually have some preferred locations. The CPA is the most common intracranial area affected [1], which is seldom seen in other meningiomas [6]. In our study, CCM at the CPA or petrous apex region constituted 31 % of all CCMs. Most spinal CCMs were located in the lumbar region [15, 16], like the six patients in our study. Most CCMs are based in the dura, a few nondura-based CCMs have also been reported [17]. Two tumors in our study were also found to be nondura-based (patients 9 and 34). Clinical symptoms of CCM are mainly due to an increased intracranial pressure or a direct tumor compression. Inflammatory syndrome has also been rarely reported in patients with intracranial CCM [18, 19]. CCMs usually have similar radiological features to other types of meningiomas [20]. Wang et al. [6] reported CCM tended to have marked heterogeneous enhancement, apparent dural tail sign, prominent peritumoral edema, cystic components, and bone involvement. Despite its bland histological appearance, CCM is known for its aggressive behaviors with local recurrence and cerebrospinal fluid metastasis [7]. In six large series of CCM, the recurrence rates were reported to be 61, 50, 62.5, 22.2, 40, and 60 %, respectively [2, 5–8, 21]. This is similar to the result of our study (42 %). In contrast, the 5-year PFS rates for benign (WHO grade 1) and atypical

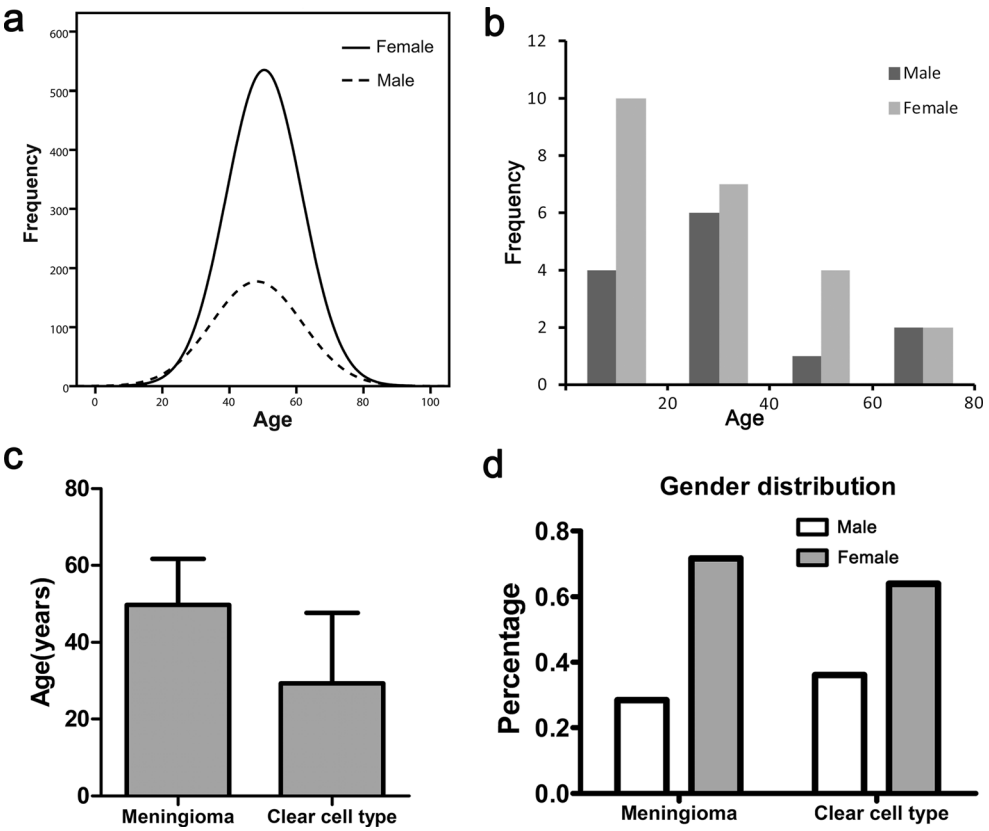

Fig. 1 Graph depicting gender and age distribution for CCM and total meningioma patients. **a** Distribution of age at diagnosis in total male (*dotted line*) and female (*solid line*) meningioma patients. The trendlines are normal curves. **b** Distribution of age at diagnosis in male and female CCM patients. **c** The mean age at diagnosis of CCM patients is significantly younger than that of total meningioma patients (*t*-test, $p=0$). **d** The ratio of male to female CCM patients is similar to that in total meningioma patients (chi-squared test, $p=0.3$)

(WHO grade 2) meningiomas were reported to be 97.5 and 69.7 % in one large series study [22]. Many patients in our study were followed-up for a relatively short time; the recurrence rate might be larger when longer follow-ups are performed. The reported average time of recurrence varied from 5.3 months to 2.3 years [5, 20]. The median recurrence time in our study was 29 months. Although multiple recurrences of CCM were common [2], only one patient in our study got multiple recurrences. Metastasis through the cerebrospinal fluid circulation has also been reported occasionally [2, 10, 13]. The imaging study of the entire neuroaxis was not performed in our study, so we could not evaluate the spinal metastasis rate. But our patients did not show any symptoms that might be associated with spinal tumor occurrence during the follow-up.

Currently there are no definite predictors of clinical outcome for CCM. Several studies showed that CCM patients after gross total resection had lower recurrence rate and longer PFS time than those after subtotal resection [6, 7]. This is consistent with the results of our study (Fig. 5). To avoid

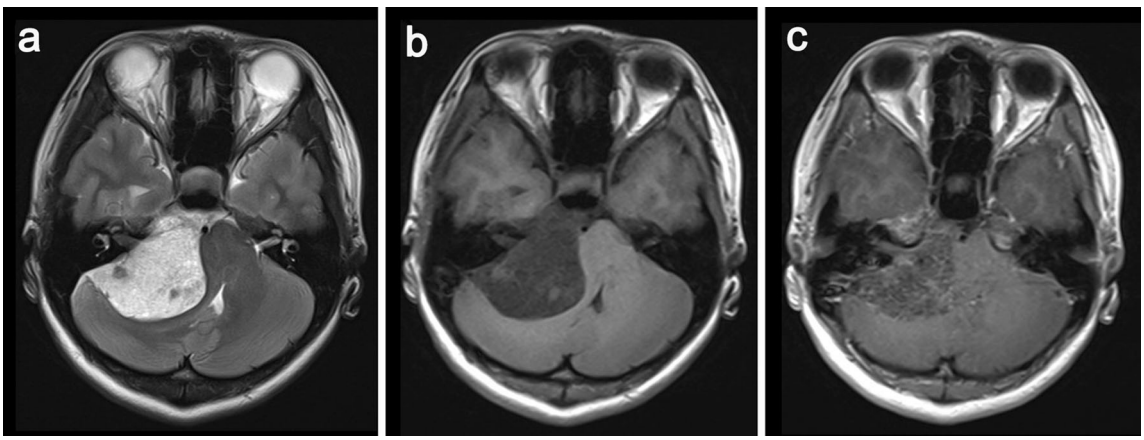

Fig. 2 Patient 5. CCM at right CPA mimicking cholesteatoma. **a** T2-weighted image. **b** T1-weighted image. **c** Enhanced T1-weighted image

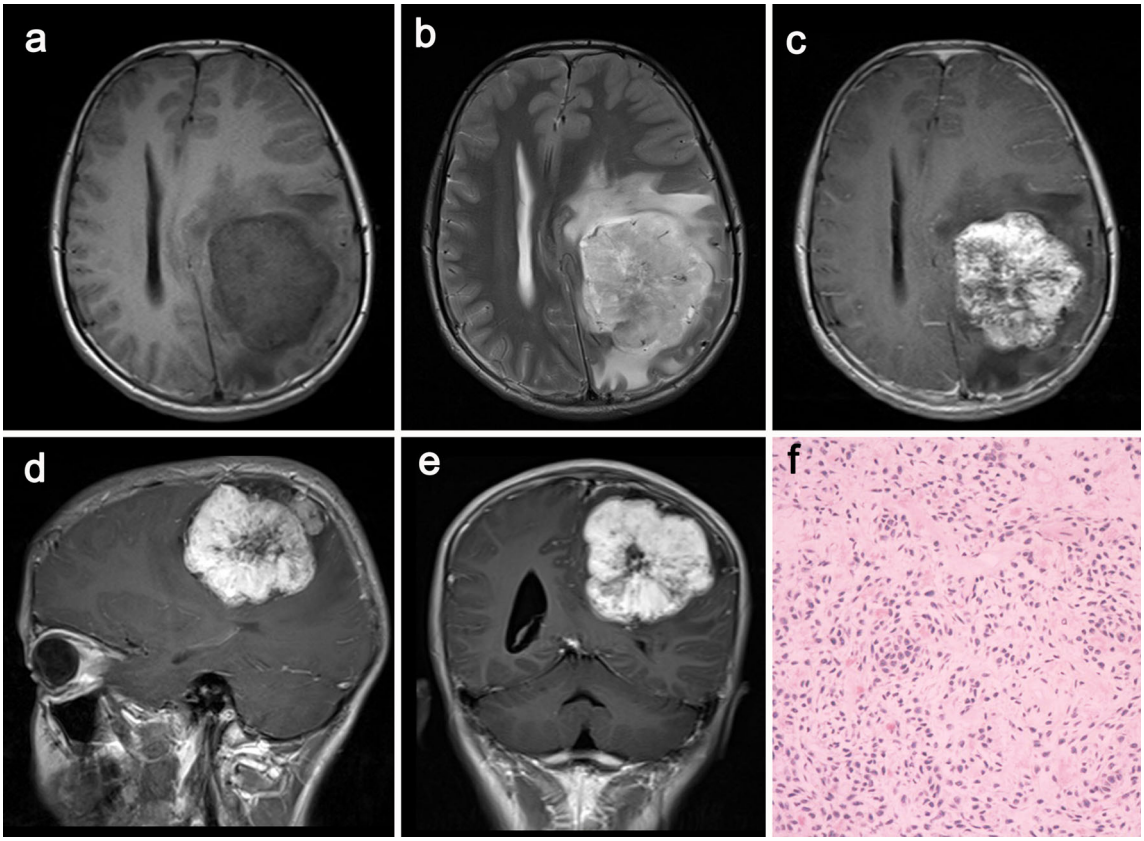

Fig. 3 Patient 9. One nondura-based CCM at left frontal parietal lobe. The tumor shows hypointense on T1-weighted image (**a**) and hyperintense on T2-weighted image (**b**). The tumor is heterogeneously enhanced after the contrast administration (**c**–**e**). Note that there is thin brain parenchyma between the tumor and the dura mater. Pathological examination (**f**) reveals the diagnosis of clear cell meningioma (HE staining, ×100)

distant tumor recurrence, Kuster et al. [23] suggested minimizing tumor cell spread during the CCM operation; Kobayashi et al. [24] suggested resecting tumors en bloc, without rupturing the tumor capsule. Some studies found that childhood patients seemed to have higher recurrence rates and shorter PFS time [25, 26]. However, in our study, age (≤20 years or >20 years) did not have a significant effect on the PFS time (p=0.9). The role of adjuvant radiotherapy in

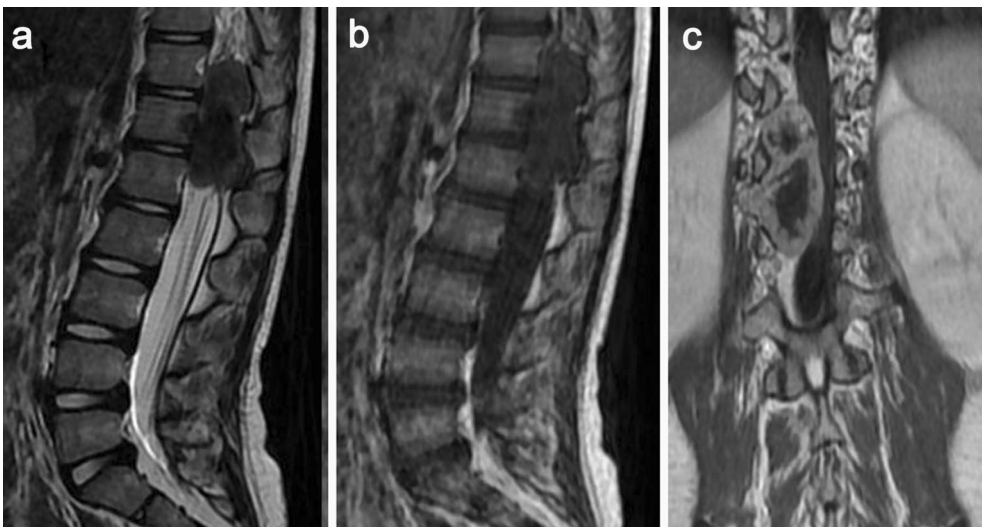

Fig. 4 Patient 33. One extradural spinal CCM extends outward through the intervertebral foramen. The tumor shows hypointense on T2-weighted image (**a**) and isointense on T1-weighted image (**b**). The tumor is heterogeneously enhanced after the contrast administration (**c**)

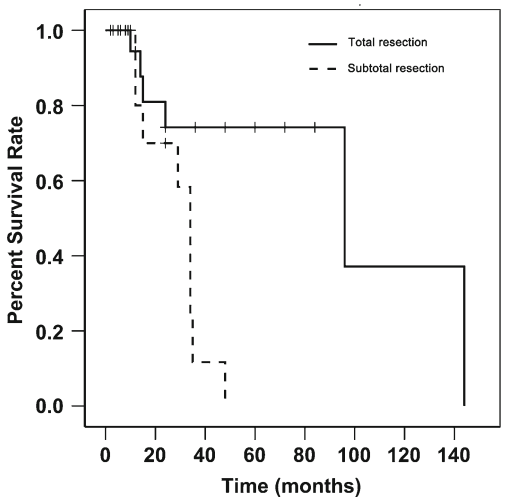

Fig. 5 Kaplan-Meier plots of PFS for CCM patients after total (Simpson grades I and II) or subtotal (Simpson grades III and IV) resection (log-rank test, $p=0.006$)

CCM remains controversial [7, 25]. Due to CCM's aggressive behavior, some authors suggested postoperative radiotherapy (gamma-knife surgery or common radiotherapy) despite total resection of the tumor [27, 28]. Postoperative radiotherapy could get satisfactory treatment effects in some CCMs; some tumors could even decrease in the volume [29]. However, some tumors still recurred despite radiotherapy [1, 25]. In our study, 9 patients received postoperative radiotherapy, and they did not have significantly longer PFS time than other patients. Considering the potential harm of radiotherapy, especially in childhood patients, some authors suggested radiotherapy reserved for cases of local recurrence or subtotal resection [20, 26, 30]. Ide et al. [31] and Hori et al. [27] reported that radiosurgery with a marginal dose of 16 Gy might not be sufficient to control CCM. On the other hand, chemotherapy does not appear to have a significant role in the management of CCM, although it is also a suggested adjuvant therapy [10]. In our study, only one patient received chemotherapy after the recurrence; he did not recover well and died of the tumor (patient 9). Considering CCM's propensity for distant relapse, postoperative regular MRI scans of the entire neuraxis should be performed every 3–6 months for the first several years to monitor for recurrence [7, 28].

Zorludemir et al. [2] reported that no histological predictors were associated with recurrence or clinical outcome in CCM. CCMs usually show benign histological characteristics, and CCM with anaplastic features have been reported occasionally [28, 32, 33]. Some CCMs could progress to anaplastic meningiomas after recurrence [27]. The relationship between prognosis and anaplastic histological features in CCMs still remains to be clarified [28]. Some studies found that CCMs with higher Ki-67 indexes were more likely to recur [7]. However, some studies did not find this association [1, 9]. In our study, the Ki-67 indexes did not significantly affect the patients' PFS time (≤5 % or >5 %, $p=0.4$). Kwon et al. [34] reported that high expression of MMP-9 tended to decrease the PFS time for CCM, although not significantly. PR expression was documented in 77 % of CCM [11]; Kobayashi et al. [24] thought PR positivity might predict a favorable prognosis for CCM. In our study, PR staining was available in 16 patients (positivity rate 50 %), and this did not significantly affect the patients' PFS time. Besides, some authors thought that brain invasion of the CCM was accountable for high recurrence rate [7].

Histologically, CCM appears as a solid cellular neoplasm mostly composed of clear glycogen rich cells [8]. CCM should be differentiated from other lesions with clear cell appearance, such as oligodendrogliomas, hemangioblastomas, seminomas, pleomorphic xanthoastrocytomas, lipid-rich glioblastomas, renal cell carcinoma metastases, and ependymomas [35]. The mechanisms underlying the aggressive clinical behavior of CCM still need to be elucidated. Prayson et al. [21] reported that even a minor clear cell component (10 %) in meningiomas might indicate a higher risk of recurrence. The etiology of CCM is still not clear. Some genetic mutations may be implicated in the CCM tumor genesis. SMARCE 1 mutation has been found in some CCMs [14, 36]. CCMs have also been reported in some NF2 patients [2, 8], and Hartmann et al. [37] reported 22 % NF2 mutations in CCMs by single strand conformational polymorphism. Some CCMs were found in patients with multiple meningiomas [38, 39]. Familial occurrences of CCM have also been reported occasionally [13, 40].

Conclusions

The proportion of CCMs in spinal meningiomas is likely to be much larger than that in intracranial meningiomas. CCM has a female predilection, and the ratio of female to male in CCM is similar to that in total meningiomas. The mean age at diagnosis of CCM patients was significantly younger than that of the total meningioma patients. CCM patients have a high rate of recurrence. CCMs should be resected totally when possible to decrease the risk of recurrence or prolong the patient's PFS time.

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Compliance with ethical standards

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Conflict of interest None.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study format consent is not required.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

1. Ohba S, Sasaki H, Kimura T, Ikeda E, Kawase T (2010) Clear cell meningiomas: three case reports with genetic characterization and review of the literature. Neurosurgery 67:E870–E871, **discussion E871**
2. Zorludemir S, Scheithauer BW, Hirose T, Van Houten C, Miller G, Meyer FB (1995) Clear cell meningioma. A clinicopathologic study of a potentially aggressive variant of meningioma. Am J Surg Pathol 19:493–505
3. Ahn ES, Chin LS, Gyure KA, Hudes RS, Ragheb J, DiPatri AJ Jr (2005) Long-term control after resection and gamma knife surgery of an intracranial clear cell meningioma: case report. J Neurosurg 102:303–306
4. Manivel JC, Sung JH (1990) Pathology of meningiomas. Pathol Annu 25(Pt 2):159–192
5. Chen HK, Wu YT, Lin YJ, Lin JW (2011) Clear cell meningioma with frequent chordoid features and aggressive behavior: a clinicopathologic study of ten cases at a single institution. J Neurooncol 103:551–559
6. Wang XQ, Huang MZ, Zhang H, Sun FB, Tao BB, Feng BH, Liao CL, Kochanski R, Hua XM, Li ST (2014) Clear cell meningioma: clinical features, CT, and MR imaging findings in 23 patients. J Comput Assist Tomogr 38:200–208
7. Chen H, Li XM, Chen YC, Wu JS, Dou YF, Wang Y, Xu J, Zhong P, Jiang CC, Wang XQ (2011) Intracranial clear cell meningioma: a clinicopathologic study of 15 cases. Acta Neurochir (Wien) 153: 1769–1780
8. Jain D, Sharma MC, Sarkar C, Suri V, Garg A, Singh M, Sharma BS, Mahapatra AK (2007) Clear cell meningioma, an uncommon variant of meningioma: a clinicopathologic study of nine cases. J Neurooncol 81:315–321
9. Rousselot C, Francois P, Jan M, Bergemer AM (2010) Report of seven cases of clear-cell meningioma and a literature review. Ann Pathol 30:73–82
10. Dhall SS, Tumialan LM, Brat DJ, Barrow DL (2005) Spinal intradural clear cell meningioma following resection of a suprasellar clear cell meningioma. Case report and recommendations for management. J Neurosurg 103:559–563
11. Baxter DS, Smith P, Stewart K, Murphy M (2009) Clear cell meningioma presenting as rapidly deteriorating visual field and acuity during pregnancy. J Clin Neurosci 16:1502–1504
12. Kasper EM, Hess PE, Silasi M, Lim KH, Gray J, Reddy H, Gilmore L, Kasper B (2010) A pregnant female with a large intracranial mass: reviewing the evidence to obtain management guidelines for intracranial meningiomas during pregnancy. Surg Neurol Int 1:95
13. Lee W, Chang KH, Choe G, Chi JG, Chung CK, Kim IH, Han MH, Park SW, Shin SJ, Koh YH (2000) MR imaging features of clear-cell meningioma with diffuse leptomeningeal seeding. AJNR Am J Neuroradiol 21:130–132
14. Raffalli-Ebezant H, Rutherford SA, Stivaros S, Kelsey A, Smith M, Evans DG, Kilday JP (2015) Pediatric intracranial clear cell meningioma associated with a germline mutation of SMARCE1: a novel case. Childs Nerv Syst 31:441–447
15. Carra S, Drigo P, Gardiman M, Perilongo G, Rigobello L (2001) Clear-cell meningioma in a 22-month-old male: a case report and literature review. Pediatr Neurosurg 34:264–267
16. Liu PI, Liu GC, Tsai KB, Lin CL, Hsu JS (2005) Intraspinal clear-cell meningioma: case report and review of literature. Surg Neurol 63:285–288, **discussion 288–289**
17. Payano M, Kondo Y, Kashima K, Daa T, Yatsuka T, Kida H, Nakayama I, Yokoyama S (2004) Two cases of nondura-based clear cell meningioma of the cauda equina. APMIS 112:141–147
18. Cassereau J, Lavigne C, Michalak-Provost S, Ghali A, Dubas F, Fournier HD (2008) An intraventricular clear cell meningioma revealed by an inflammatory syndrome in a male adult: a case report. Clin Neurol Neurosurg 110:743–746
19. Sato T, Sugiyama T, Kawataki T, Sato E, Horikoshi T, Sugita K, Kinouchi H (2010) Clear cell meningioma causing castleman syndrome in a child. J Neurosurg Pediatr 5:622–625
20. Zhang J, Shrestha R, Li J, Shu J (2013) An intracranial and intraspinal clear cell meningioma. Clin Neurol Neurosurg 115: 371–374
21. Prayson RA, Chamberlain WA, Angelov L (2010) Clear cell meningioma: a clinicopathologic study of 18 tumors and examination of the use of CD10, CA9, and RCC antibodies to distinguish between clear cell meningioma and metastatic clear cell renal cell carcinoma. Appl Immunohistochem Mol Morphol 18:422–428
22. Nowak A, Dziedzic T, Krych P, Czernicki T, Kunert P, Marchel A (2015) Benign versus atypical meningiomas: risk factors predicting recurrence. Neurol Neurochir Pol 49:1–10
23. Kuster O, Schittenhelm J, Schwartz O, Meyermann R, Schuhmann MU (2012) Paediatric clear cell meningioma with multiple distant recurrences after presumed intra-operative cell spread. Childs Nerv Syst 28:925–931
24. Kobayashi Y, Nakamura M, Tsuji O, Iwanami A, Ishii K, Watanabe K, Hosogane N, Tsuji T, Kameyama K, Toyama Y, Chiba K, Matsumoto M (2013) Nondura-based clear cell meningioma of the cauda equina in an adult. J Orthop Sci 18:861–865
25. Balogun JA, Halliday W, Bouffet E, Kulkarni AV (2013) Spinal clear cell meningioma in a 3-year-old: a case report. Pediatr Neurosurg 49:311–315
26. Colen CB, Rayes M, McClendon J Jr, Rabah R, Ham SD (2009) Pediatric spinal clear cell meningioma. Case report. J Neurosurg Pediatr 3:57–60
27. Hori S, Hayashi N, Ishizawa S, Hayashi S, Sato H, Nagao S, Akioka N, Nagai S, Nishikata M, Endo S (2012) Clear cell meningioma with histologically aggressive appearance and clinically aggressive behavior: a case report. Neuropathology 32:415–419
28. Tong-tong W, Li-juan B, Zhi L, Yang L, Bo-ning L, Quan H (2010) Clear cell meningioma with anaplastic features: case report and review of literature. Pathol Res Pract 206:349–354
29. Boet R, Ng HK, Kumta S, Chan LC, Chiu KW, Poon WS (2004) Lumbosacral clear-cell meningioma treated with subtotal resection and radiotherapy. J Clin Neurosci 11:432–436
30. Ranjan R, Sethuraman S (2010) Supratentorial clear cell meningioma in a child: a rare tumor at unusual location. J Pediatr Neurosci 5:141–143
31. Ide M, Yamamoto M, Hagiwara S, Tanaka N, Kawamura H (2004) Rapid regrowth of intracranial clear cell meningioma after craniotomy and gamma knife radiosurgery—case report. Neurol Med Chir (Tokyo) 44:321–325
32. Subramanyam S, Wojno TH, Grossniklaus HE (2012) Malignant (anaplastic) transformation of orbital clear cell meningioma. Ophthal Plast Reconstr Surg 28:e3–e4
33. Wu T, Yang Q, Li Z, Cai F, Zhu S, Zhang F (2012) Clinicopathological analysis of clear cell meningioma. Nan Fang Yi Ke Da Xue Xue Bao 32:131–134

34. Kwon MJ, Sung CO, Kang SY, Do IG, Suh YL (2013) Differential expression of extracellular matrix-related genes in rare variants of meningioma. Hum Pathol 44:260–268
35. Carlotti CG Jr, Neder L, Colli BO, dos Santos MB, Garcia AS, Elias J Jr, Chimelli LC (2003) Clear cell meningioma of the fourth ventricle. Am J Surg Pathol 27:131–135
36. Evans LT, Van Hoff J, Hickey WF, Smith MJ, Evans DG, Newman WG, Bauer DF (2015) SMARCE1 mutations in pediatric clear cell meningioma: case report. J Neurosurg Pediatr 1–5
37. Hartmann C, Sieberns J, Gehlhaar C, Simon M, Paulus W, von Deimling A (2006) NF2 mutations in secretory and other rare variants of meningiomas. Brain Pathol 16:15–19
38. Kuzeyli K, Cakir E, Usul H, Karaarslan G, Kadir Reis A, Temiz C, Baykal S (2003) Clear cell meningioma: case report and literature review. J Clin Neurosci 10:264–266
39. Lista-Martinez O, Santin-Amo JM, Facal-Varela S, Rossi-Mautone E, Rivas-Lopez LA, Amaro-Cendon S (2012) Multifocal clear cell meningioma in the sacral and lumbar spine. Case report and literature review. Neurocirugia (Astur) 23:259–263
40. Li Z, Zhang Y, Wang E, Wang Z, Li W, Huang S, Li J (2012) Intracranial clear cell meningioma in two children with blood relations: two case reports and literature review. Childs Nerv Syst 28: 2143–2151