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CLINICAL STUDY – PATIENT STUDY

Clear cell meningioma with frequent chordoid features and aggressive behavior: a clinicopathologic study of ten cases at a single institution

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Abstract Clear cell meningioma is an uncommon variant of meningiomas that often occurs in young patients, shows a proclivity for spinal intradural extramedullary and cerebellopontine angle, and follows an aggressive clinical course. We render clinicopathologic features of ten cases of this rare tumor to further elucidate its behavior. Fifteen specimens of clear cell meningioma belonging to ten patients were obtained at a single institution from 2001 to 2009. Correlations of histologic parameters, immunohistochemical study, and clinical features were assessed. This series included eight men and two women with a mean age of 62.1 years at the first surgery. The mean post-operative follow-up period was 3.9 years. Four patients (40%) had single or multiple local tumor recurrences. The mean time to recurrence was 2.3 years. Seven tumors (46.7%) were combined with chordoid features. There was a wide range of MIB-1 labeling indices (4.4–33.5%, mean 15.8%), which were higher in recurrent tumors, tumors with chordoid features, and tumors with necrosis. There was no correlation between MIB-1 labeling indices and brain invasion. The study illustrates aggressive behavior of clear cell meningioma and frequently combined chordoid features in our cases.

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Introduction

Meningiomas are common intracranial tumors that originate from the arachnoidal cap cell of the meninges and have a large variety of histopathologic appearances. Most of the variants are merely descriptive and carry no prognostic significance. However, some subtypes, such as chordoid and clear cell, have unique clinical associations or prognostic implications. In the 2000 and the 2007 revision of WHO classification of tumors of central nervous system, clear cell meningioma (CCM) joined chordoid meningioma and atypical meningioma in a grade II category [1, 2], due to a high rate of recurrence.

Histopathologically, CCM is composed of polygonal cells with centrally oval to round nuclei and clear, glycogen-rich cytoplasm, forming sheetlike or lobular growth pattern, in moderate cellularity, against a backdrop of blocky collagenous and hyalinized stroma. The tumor cells bear great resemblance to that of hemangioblastoma, and metastatic clear cell renal cell carcinoma. By comparison, chordoid meningioma is composed of epithelioid or spindle cells, forming cords or nests, in a pale, basophilic mucoid matrix. The tumor cells bear great resemblance to physaliferous cells of chordoma, featuring vacuolated cytoplasm.

The present study was undertaken to document the clinicopathologic correlation of ten cases of clear cell meningioma with frequent combination of chordoid features, operated at the Chang Gung Memorial Hospital-Kaohsiung Medical Center during 2001–2009.

Materials and methods

All the cases shown in this study represented materials from the surgical pathology files of the Chang Gung Memorial Hospital-Kaohsiung Medical Center from 2001 to 2009. Clinical data, which included age, sex, presenting symptoms, tumor size, location of involvement, treatment and clinical follow-up, were obtained from the medical records. Surgical specimens were promptly fixed in neutral buffered formalin, paraffin embedded, and routinely processed. Routine hematoxylin–eosin-stained sections were generated from formalin-fixed, paraffin-embedded tissue, which was cut to 3 μm-thick. Special stains for periodic acid-Schiff (PAS) with and without diastase, mucicarmine, and Alcian blue at pH 2.5 were applied to all cases.

Immunohistochemical stains were performed using standard reagents and techniques on an i6000 Automated Staining System (BioGenex, San Ramon, CA). The following antibodies were used for immunohistochemistry: epithelial membrane antigen (EMA) (clone GP1.4, Novocastra; steam in citrate buffer, 1:400), cytokeratin high molecular weight (HMW) (clone 34βE12, Neomarkers; steam in citrate buffer, 1:100), cytokeratin low molecular weight (LMW) (clone AE1, Neomarkers; steam in citrate buffer, 1:100), podoplanin (Santa Cruz; steam in citrate buffer, 1:50), D2-40 (DAKO; steam in citrate buffer, 1:100), vimentin (clone V9, Neomarkers; steam in citrate buffer, 1:400), CD10 (clone 56C6, Novocastra; steam in citrate buffer, 1:100), glial fibrillary acidic protein (GFAP) (clone ZCG29, Invitrogen, steam in citrate buffer, 1:150), S100 (polyclonal, DAKO; 1:1000), and MIB-1 antigen (clone MIB-1, DAKO; steam in citrate buffer, 1:100). Inactivation of endogenous peroxidase activity was obtained by incubating sections in 3% H_2O_2 for 15 min. Localization of bound antibodies was performed with a non-biotin polymeric technology (Super Sensitive™ Polymer-HRP Detection System, BioGenex, San Ramon, CA). Immunoreactions were visualized using 3,3′-diaminobenzidine tetrahydrochloride (ZYMED®, Invitrogen, Carlsbad, CA). Appropriate positive controls for each antibody were run in parallel. The immunostained slides were then assessed for both extent and intensity of staining. The percentage of tumor with positive staining was estimated first. Next, the intensity of staining was semiquantitatively scored from 0 to 3+. The rough percentage of tumor with positive staining and the semiquantitative measure of staining intensity were then tabulated for each specimen (Table 3).

In addition to the mitotic index, cell proliferation was assessed by immunohistochemical staining for MIB-1 antigen. The MIB-1 labeling index (LI) was calculated in regions of maximal activity and expressed as percentage of nuclear staining. Based on the 2007 revision of new WHO classification of tumors of central nervous system [2], histologic features of atypia include a mitotic index $\geq$4/10 high-power fields (HPF) or the presence of at least three of the following variables: increased cellularity, small cell with a high nuclear: cytoplasmic ratio, prominent nucleoli, uninterrupted patternless or sheet-like growth, and foci of spontaneous or geographic necrosis. The mitotic index was defined as the maximal number of mitoses observed in any ten consecutive HPF (1 HPF = 0.16 mm^2). Histologic malignancy was defined by the presence of obviously malignant cytology or an exceptionally high mitotic index ($\geq$20/10 HPF).

Table 1 Summary of clinical data

Case no.	Age (years)/sex	Tumor size (cm)/ location	Extent of surgery	Radiotherapy	Clinical outcome
1	79/M	6.1/parasagittal	Subtotal resection	Yes	Alive, AWT, RD, 3.7 years[a]
2	77/M	6.0/parasagittal	Total resection	No	Alive, ANT, 2.3 years[a]
3	71/F	5.0/convexity	Total resection	No	Alive, ANT, 0.8 year[a]
4	56/M	5.2/frontal base	Total resection	Yes	Alive, AWT, RD (0.6, 2.4, 3.0 years), 5.0 years[a]
5	69/F	3.8/tentorium	Total resection	Yes	Alive, ANT, 1.2 years[a]
6	56/M	5.0/parasagittal	Total resection	No	Alive, ANT, 1.3 years[a]
7	59/M	3.2/parasagittal	Total resection	No	Alive, ANT, 7.0 years[a]
8	47/M	2.5/parasagittal	Subtotal resection	Yes	Alive, AWT, RD (3.0 years), 5.7 years[a]
9	88/M	6.0/parasagittal	Subtotal resection	No	Unknown, RD (2.7 years), 2.9 years[a], LTF
10	19/M	3.0/cavernous sinus	Subtotal resection	Yes	Alive, AWT, RD (2.3 years), 8.6 years[a]

F Female, *M* Male, *AWT* Alive with tumor, *ANT* Alive without tumor, *RD* Recurrent disease, *LTF* Lost to follow-up

[a] Time from first surgery at our hospital to last visit

Results

Clinical features

The essential clinical information of all ten cases is summarized in Table 1. This series included eight men and two women with a mean age of 62.1 years (range from 19 to 88 years) at the first surgery. There was no pediatric case. The ten primary tumors were distributed in sites where common meningiomas normally occur, including six at parasagittal area, one at convexity, one at frontal base, one at tentorium, and one at cavernous sinus. There was no spinal case. The tumors ranged from 2.5 to 6.1 cm in diameter, and the mean diameter was 4.6 cm. The common initial symptoms included hemiparesis, conscious change, headache, epilepsy, and visual disturbances. The duration of symptoms ranged from 1 day to 5 years (mean, 1 year). No systemic manifestations were found.

Follow-up information was available in all patients. The mean post-operative follow-up period was 3.9 years (range from 0.8 to 8.6 years). Four patients (40%) had single or multiple tumor recurrences. The mean time to recurrence was 2.3 years (range from 0.6 to 3.0 years). The pattern of recurrence was local recurrence without CSF seeding or extracranial metastasis. All in all, there were six tumors completely removed with total resection and nine tumors partially removed with subtotal resection. Among the nine tumors partially removed, four tumors were located at parasagittal area involving posterior aspect of the superior sagittal sinus, three tumors were located at frontal base, and two tumors were located at cavernous sinus. Five patients received post-operative radiation therapy, including a stereotactic radiosurgery for one patient (case 10).

Light microscopy and immunohistochemistry

There were ten primary and five recurrent intracranial clear cell meningioma specimens totally. The diagnostic parameters are summarized in Table 2. The immunoprofile is summarized in Table 3. The patterns of clear cell, chordoid and anaplastic morphologies and characteristics, and immunohistochemical findings are illustrated in Figs. 1, 2, 3 and 4. On microscopic examination, the tumors were composed of sheets of polygonal cells in a blocky collagenous and hyalinized stroma. The tumor cells bore centrally oval to round nuclei and abundant clear cytoplasm. The cytoplasmic clearing was PAS-positive yet diastase sensitive, consistent with glycogen accumulation. The clear cell elements constituted 10–100% of tumor areas. Sweeping, uninterrupted sheeting appearance was appreciated in eight specimens (53.3%) where clear cell elements were over 98% of the tumor areas; otherwise, they were alternating or intermingled with chordoid subtype. Meningothelial features were indistinct for most cases, with only one tumor (6.7%) consisting of vague whorl formation and two tumors (13.3%) harboring few psammoma bodies. On the other hand, features of chordoid meningioma with epithelioid or spindle cells, forming cords, cribriforms or nests, in a pale, basophilic mucoid matrix, were present in seven tumors (46.7%). The physaliferouslike cells featuring vacuolated cytoplasm were also noted. Eight specimens (53.3%) exhibited brain invasion. Necrosis was noted in eleven tumors (73.3%); nine (60%) geographic and two (13.3%) spontaneous, respectively.

There was a wide range of MIB-1 labeling indices (4.4–33.5%, mean 15.8%), which increased following tumor recurrence. The MIB-1 LI were higher in recurrent tumors (8.1–33.5%, mean 21.7%) tumors versus primary tumors (4.4–25.2%, mean 12.8%), tumors with chordoid features (6.8–33.3%, mean 22.0%) versus tumors without chordoid features (4.4–33.5%, mean 10.3%), and tumors with necrosis (4.4–33.5%, mean 18.7%) versus tumors without necrosis (5.3–10.5%, mean 7.6%), but were lower in tumors with brain invasion (4.4–33.5%, mean 13.4%) versus without brain invasion (5.3–30.1%, mean 18.5%).

All tumors showed diffuse positive immunoreactivity with vimentin (100%) and EMA (100%). One tumor (6.7%) was focally positive for HMW. One tumor (6.7%) was focally positive for LMW. Twelve tumors (80%) were positive for podoplanin (both membranous and cytoplasmic). Twelve tumors (80%) were positive for D2-40 (both membranous and cytoplasmic). Two tumors (13.3%) were focally positive for CD10 (membranous staining). One tumor (6.7%) was focally positive for GFAP. Two tumors (13.3%) were positive for S100 (both nuclear and cytoplasmic).

Discussion

Meningiomas are common intracranial tumors, which constitute 13–26% of all primary intracranial tumors [1, 2]. The majority is slowly growing, and follows a benign clinical course. There are, however, rare meningiomas that meet atypical or anaplastic criteria, or belong to chordoid, clear cell, papillary or rhabdoid subtype, and show an aggressive clinical behavior. Clear cell meningioma (CCM) was coined by Scheithauer [3] in 1990 as a unique variant of meningiomas with distinct histological features. In fact, the case reported by Harkin and Leonard [4] in 1988 as meningioma with giant amianthoid collagen fibers was probably the first case, followed by cases of Manivel and Sung [5], and Shiraishi [6] as glycogen-rich meningioma. In the 1993 World Health Organization (WHO) classification of tumors of central nervous system [7], CCM was classified as a grade I meningioma, because of

Table 2 Summary of the histopathologic findings

Case no.	Increased cellularity	Small cell with a high N/C ratio	Prominent nucleoli	Sheet-like growth pattern	Necrosis	Mitotic count (/10HPF)	Malignant cytology	MIB-1 labeling index (%)	Percentage of clear cell morphology (%)	Additional morphology
1	Yes	Yes	Yes	No	Yes, geographic	7	Absent	12.5	30	Chordoid
2	Yes	Yes	Yes	No	Yes, geographic	12	Absent	19.7	40	Cordoid
3	Yes	Yes	Yes	No	Yes, geographic	6	Absent	6.8	45	Chordoid, BI(+)
4	Yes	Yes	Yes	No	Yes, geographic	15	Absent	25.2	30	Chordoid
4[a]	Yes	Yes	Yes	No	Yes, geographic	16	Absent	26.4	25	Chordoid
4[b]	Yes	Yes	Yes	No	Yes, geographic	22	Present	30.1	10	Chordoid
4[c]	Yes	Yes	Yes	No	Yes, geographic	25	Present	33.3	10	Chordoid, BI(+)
5	No	No	No	Yes	Yes, geographic	15	Absent	33.5	100	No additional morphology, BI(+)
6	No	No	No	Yes	No	7	Absent	9.3	100	No additional morphology, BI(+)
7	No	No	No	Yes	No	3	Absent	5.4	98	Vague whorl formation, BI(+)
8	No	No	No	Yes	Yes, spontaneous	5	Absent	6.1	99	Psammoma body, BI(+)
8[a]	No	No	No	Yes	Yes, spontaneous	7	Absent	8.1	99	Psammoma body, BI(+)
9	No	No	No	Yes	Yes, geographic	2	Absent	4.4	100	No additional morphology, BI(+)
10	No	No	No	Yes	No	4	Absent	5.3	100	No additional morphology
10[a]	No	No	No	Yes	No	8	Absent	10.5	100	No additional morphology

BI Brain invasion

[a] First recurrence, [b] second recurrence, [c] third recurrence

Table 3 Immunohistochemical results

Case no.	Antibody								
	EMA	HMW	LMW	Podoplanin	D2-40	Vimentin	CD10	GFAP	S100
1	100%, 3+	5%, 3+	10%, 2+	70%, 2+	60%, 2+	100%, 3+	0	0	0
2	100%, 2+	0	0	80%, 3+	60%, 2+	100%, 3+	0	5%, 1+	0
3	80%, 3+	0	0	70%, 2+	60%, 2+	70%, 2+	10%, 2+	0	0
4	80%, 2+	0	0	70%, 2+	60%, 2+	90%, 2+	0	0	0
4[a]	80%, 2+	0	0	60%, 2+	50%, 2+	90%, 2+	0	0	0
4[b]	70%, 2+	0	0	50%, 2+	50%, 2+	90%, 2+	0	0	0
4[c]	60%, 2+	0	0	50%, 2+	50%, 2+	90%, 2+	0	0	0
5	100%, 3+	0	0	30%, 2+	30%, 2+	90%, 2+	0	0	5%, 1+
6	80%, 2+	0	0	0	0	100%, 3+	0	0	0
7	80%, 2+	0	0	70%, 2+	70%, 2+	100%, 3+	5%, 1+	0	50%, 2+
8	70%, 2+	0	0	0	0	100%, 2+	0	0	0
8[a]	60%, 2+	0	0	0	0	100%, 2+	0	0	0
9	70%, 2+	0	0	60%, 2+	70%, 2+	100%, 3+	0	0	0
10	60%, 2+	0	0	80%, 2+	60%, 2+	90%, 2+	0	0	0
10[a]	60%, 2+	0	0	50%, 2+	50%, 2+	90%, 2+	0	0	0

The extent of immunohistochemical staining is expressed semiquantitatively: the percentage of the tumor cells with observable staining, followed by the intensity of staining (1+, 2+ or 3+)

[a] First recurrence, [b] second recurrence, [c] third recurrence

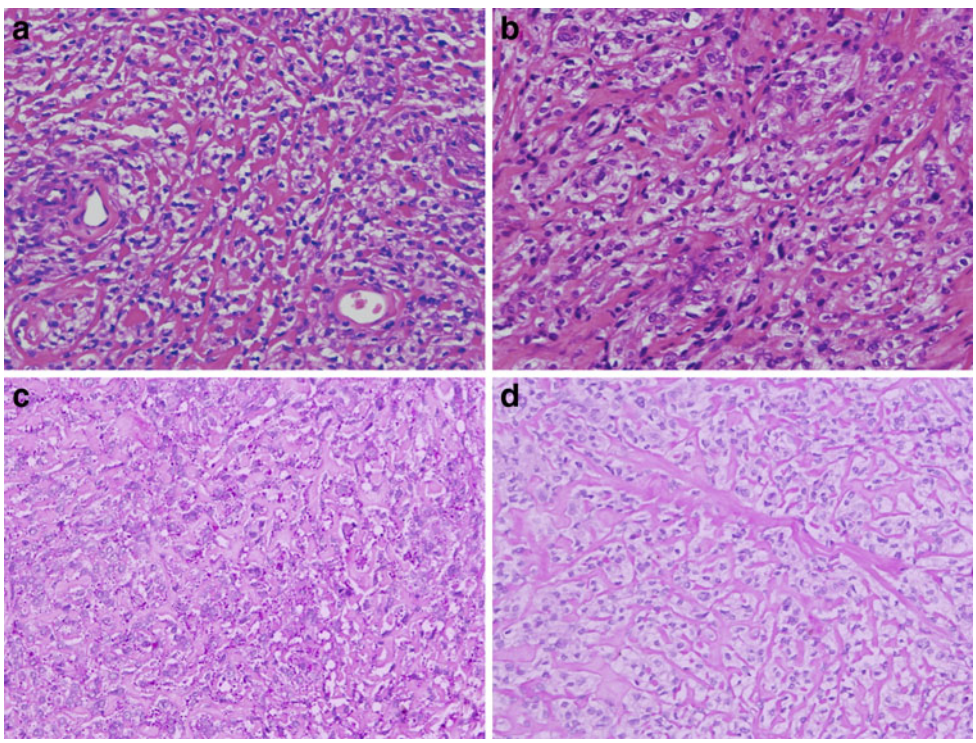

Fig. 1 (case 7) **a** Sheets of clear cells divided by collagenous septa (H&E, ×200), **b** vague whorl formation (H&E, ×200), **c** glycogen-rich cytoplasm (PAS, ×200), **d** absence of glycogen after diastase digestion (PAS-D, ×200)

its bland histological appearance. It was reclassified as a grade II meningioma in the 2000 WHO classification of tumors of central nervous system [1], due to a high rate of recurrence and aggressive clinical course. The grade II status of CCM remained unchanged in the 2007 revision of WHO classification of tumors of central nervous system [2]. CCM comprises 0.2% of meningiomas [8]. To the best of our knowledge, 105 cases of CCM have been published

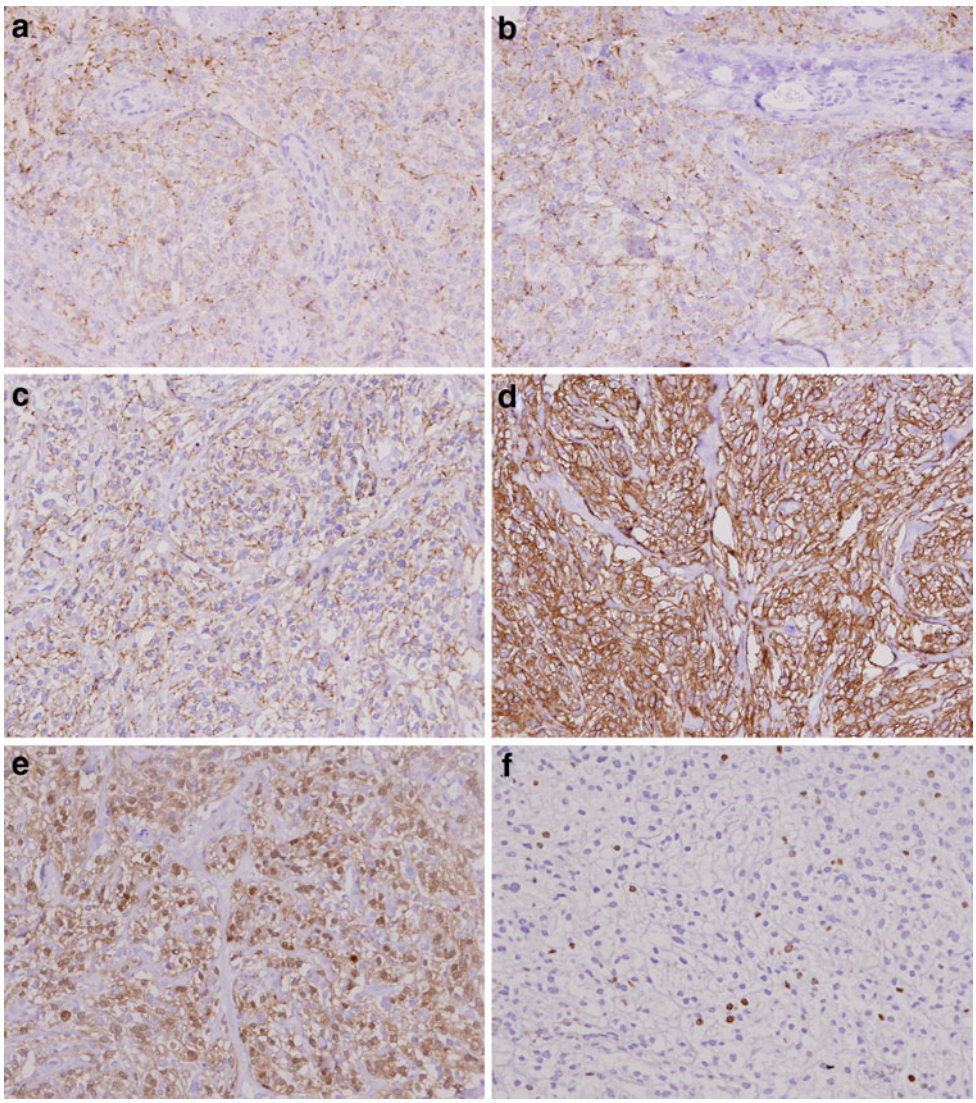

Fig. 2 (case 7) Immunohistochemical findings. The tumor cells show membranous and cytoplasmic positivity for **a** D2-40 (×200), and **b** podoplanin (×200), membranous positivity for **c** EMA (×200), cytoplasmic positivity for **d** vimentin (×200), nuclear and cytoplasmic positivity for **e** S100 (×200), and expression of **f** MIB-1 labeling index (×200)

in the English literature, largely in the form of isolated case reports [9–14], with only four series [8, 15–17]. There are 66 intracranial cases (53 adult and 13 pediatric), including 12 cases involving cerebellopontine angle (5 adult and 7 pediatric). The intraspinal cases total 39 in number (24 adult and 15 pediatric). The mean age is 36.8 years. The male:female ratio is 1:1.5.

Zorludemir et al. [8] published the first series of clear cell meningioma in 1995, which was comprised of 14 tumors in 13 cases, with emphasis on glycogen-rich clear cell morphology, often young age, a predilection for spinal intradural and cerebellopontine angle, and an aggressive clinical course. Recurrence was noted in 61% of the cases, local discontinuous spread in 15%, and widespread cranial to spinal metastasis in 8%. Three patients (23%) were dead of disease. Jain et al. [15] published the second series of clear cell meningioma in 2007, which was comprised of 9 cases with recurrence noted in 22.2% of the cases. Among the ten cases we reported**,** four patients (40%) had single or multiple tumor recurrences.

Prayson et al. [17] published an 18-case series of CCM with emphasis on differentiation from metastatic clear cell renal cell carcinoma. In their cases, the clear cell elements constituted 10–100% (mean 40.6%) of tumor areas. In our cases, the clear cell elements comprised 10–100% (mean 65.7%) of tumor areas, with eight specimens (53.3%) where clear cell elements were over 98% of the tumor areas, and seven specimens (46.7%) where clear cell elements were combined with chordoid features**.**

The main differential diagnosis for CCM with frequent chordoid components includes metastatic renal clear cell carcinoma, hemangioblastoma, chondroid chordoma, low-grade chondrosarcoma, and chordoid glioma. For that matter, immunohistochemical evaluation with a panel of EMA, cytokeratins, podoplanin, D2-40, vimentin, CD10, GFAP, and S100 is of the ultimate importance. D2-40 is a

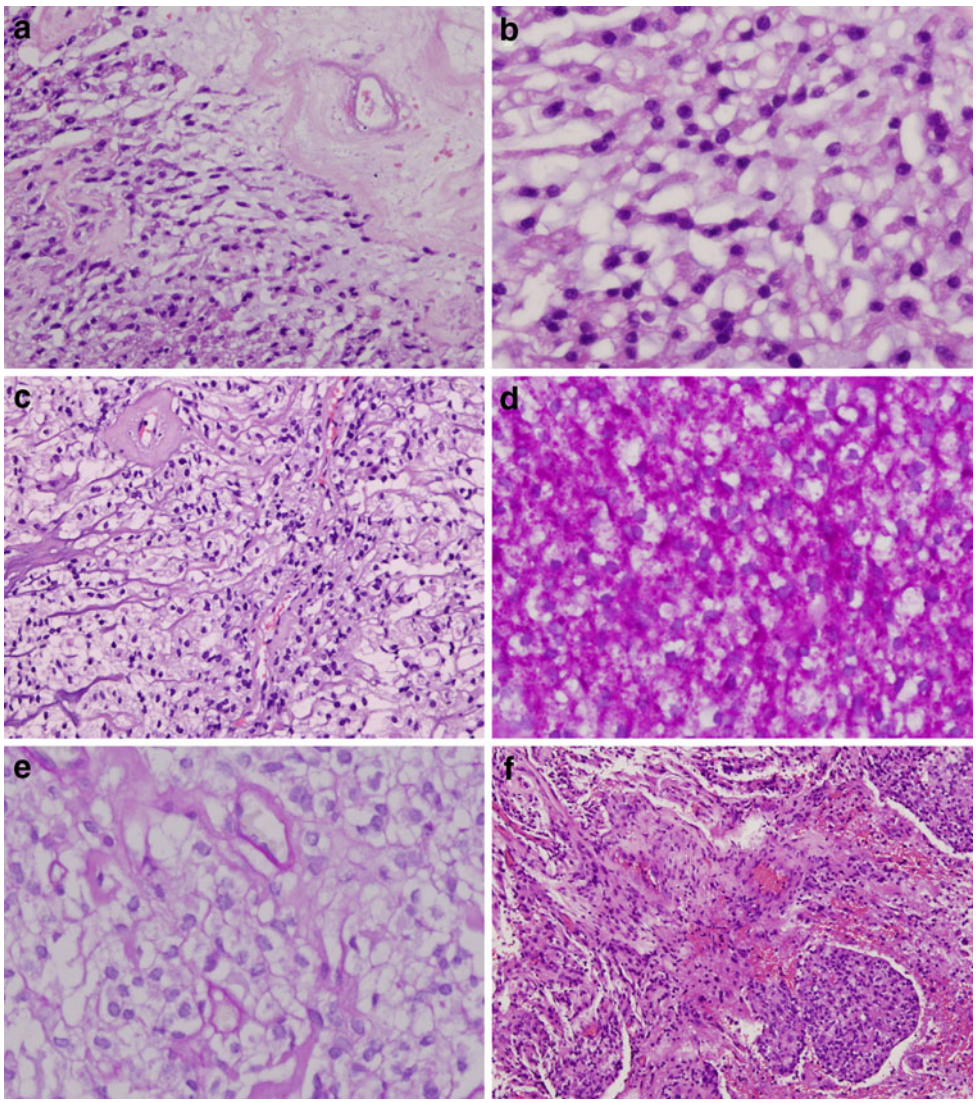

Fig. 3 (case 3) **a** Epithelioid cells arranged in cords against mucoid matrix with geographic necrosis (H&E, ×200), **b** physaliferouslike cells with vacuolated cytoplasm (H&E, ×400), **c** sheets of clear cells divided by fibrous septa (H&E, ×200), **d** glycogen-rich cytoplasm (PAS, ×400), **e** absence of glycogen after diastase digestion (PAS-D, ×400), and **f** brain invasion (H&E, ×100)

monoclonal antibody that was initially developed against M2A, a 38-kd, mucin-type transmembrane glycoprotein, and fetal testis-related antigen, now known as podoplanin [18–20]. D2-40 has been used in the clinical setting as a selective marker of lymphatic endothelium [20, 21] and in the identification of various normal and neoplastic tissues [22]. Within the CNS, D2-40 stains both non-neoplastic (choroid plexus epithelium, ependyma, subependymal area, leptomeninges, and cerebellar Purkinje cells) and neoplastic (ependymomas, choroid plexus papillomas, meningiomas, gliomas, medulloblastomas, and hemangioblastomas) tissues [23, 24]. D2-40 was also reported to stain normal cartilage, true chondroid tumors, chordoid meningiomas, and chordoid gliomas, but not chordomas [25].

Intracranial metastasis of renal clear cell carcinoma is one of the most typical problems in clinical practice. It poses greater challenge to diagnosis than any other entity. The tumor cells are positive for cytokeratins, EMA, vimentin and CD10, but negative for podoplanin and D2-40. Hemangioblastoma is an uncommon tumor that occurs sporadically or in familial forms associated with von Hippel-Lindau disease. The tumor may appear yellow owing to its rich lipid content. It is positive for podoplanin and D2-40, but negative for EMA. S100 has been well established as a chondroid marker, and both chordomas and chondrosarcomas typically express this protein. Although a minority of CCM is positive for S100, the staining is mostly focal or patchy in nature**.** Chordoma expresses epithelial markers such as cytokeratins and EMA, but is negative for podoplanin and D2-40. EMA is the most effective antibody for differentiating CCM from low-grade chondrosarcoma, which is positive for podoplanin and D2-40, but negative for EMA. Because cytokeratins and EMA also highlight chordoid glioma, the most telling marker turns out to be GFAP, with strong, diffuse staining supportive of chordoid glioma. Vimentin is very limited in

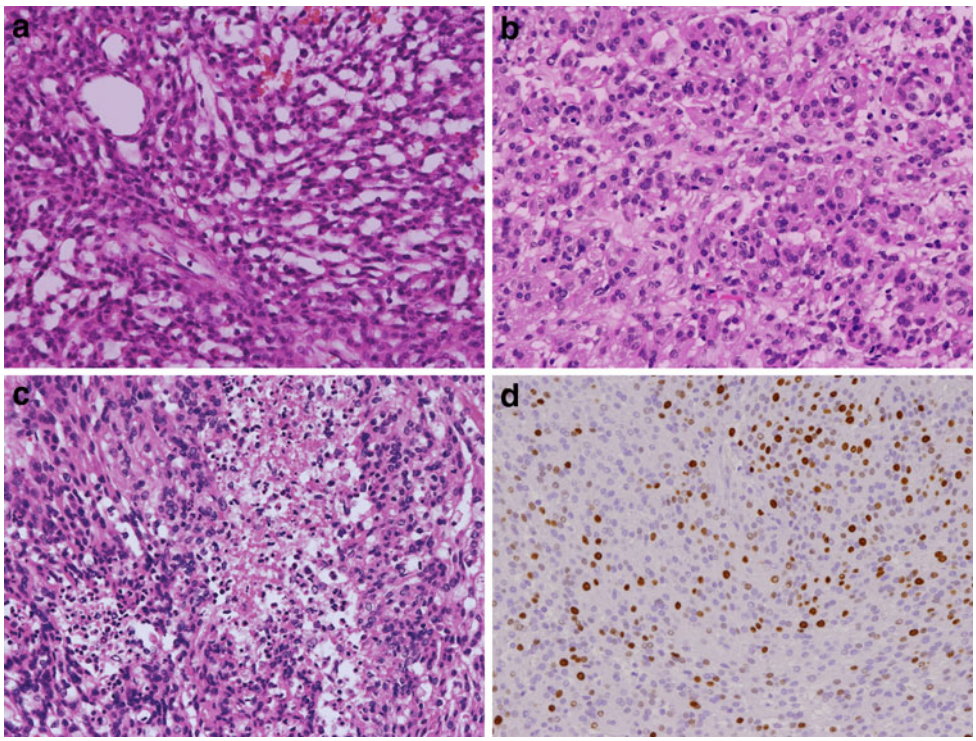

Fig. 4 (case 4) **a** Epithelioid cells arranged in cribriforms against mucoid matrix (H&E, ×200), **b** epithelioid cells arranged in nests against mucoid matrix (H&E, ×200), **c** anaplastic change with necrosis (H&E, ×200), and **d** high MIB-1 labeling index (×200)

utility due to poor specificity, and is shared by many entities.

Although CCM or chordoid meningioma with anaplastic change is exceptional [13, 26], a transformation or progression from any kind of grade II meningioma to anaplastic meningioma, at times through recurrence, as seen in one of our cases, makes perfect sense. Wu et al. [13] reported two adult cases of CCM with anaplastic features at presentation. Bollag et al. [26] reported two adult cases. Case 1 showed a random admixture of meningothelial, atypical and anaplastic meningioma at presentation. The tumor recurred as pure anaplastic meningioma. Case 2 presented as a chordoid meningioma initially, but recurred as anaplastic meningioma with residual chordoid pattern.

The best treatment for clear cell or chordoid meningioma is still ill defined due to rarity of the tumors. Total resection of the neoplasm is most recommended as treatment of choice [12]. However, some tumors, particularly those involving the cavernous sinus, petroclival region, posterior aspect of the superior sagittal sinus or optic nerve sheath, cannot be completely removed due to their relationship to vital neural or vascular structures [27]. The patient should receive radiotherapy or chemotherapy if excision is subtotal. The list of treatment strategies in the article [27] shows that simple surgery has been gradually superseded by a combination of surgery and radiotherapy (including gamma-knife surgery and common radiotherapy), due to CCM's aggressive behavior. The recurrence rate is relatively low for the cases treated with total resection; however, it is still high for the cases treated with post-operative gamma-knife surgery and common radiotherapy after a subtotal surgery [14].

In the literature, there is only a single case report of CCM with chordoid features [9]. The tumor was located at the lumbo-sacral spine of a 42 year-old male. Although light microscopic appearance was characteristic of CCM, some of the ultrastructural findings were reminiscent of chordoma. The coexistence of clear cell and chordoid morphologies on light microscopic level in a meningioma has never been reported**.** Because both variants belong to grade II category, the combined clear cell-chordoid meningioma seems to carry similar prognostic significance to CCM or chordoid meningioma separately. Although the MIB-1 LI were higher in clear cell meningiomas with chordoid features than those without chordoid features, due to small number of our cases and relatively short follow-up period, it is too early to draw conclusion from the data.

Conclusion

Clear cell meningioma is capable of aggressive behavior and anaplastic change. This series is different from previous ones in that it highlights frequent chordoid features. The potential implication of combined clear cell-chordoid meningioma needs further investigation and long-term observation.

References

1. Louis DN, Scheithauer BW, Budka H, von Deimling A, Kepes JJ (2000) Meningiomas. In: Kleihues P, Cavenee WK (eds) Pathology and genetics of tumours of the nervous system. World Health Organization classification of tumors. IARC Press, Lyon, pp 176–184
2. Perry A, Louis DN, Scheithauer BW, Budka H, von Deimling A (2007) Meningiomas. In: Louis DN, Ohgaki H, Wiestler OD, Cavenee WK (eds) WHO classification of tumours of the central nervous system, 4th edn. IARC Press, Lyon, pp 164–172
3. Scheithauer BW (1990) Tumors of the meninges: proposed modification of the World Health Organization classification. Acta Neuropathol 80:343–354
4. Harkin JC, Leonard GL (1988) Abnormal amianthoid fibers in meningioma. Acta Neuropathol 76:638–639
5. Manivel JC, Sung JH (1990) Pathology of meningiomas. Pathol Annu 25(Pt 2):159–192
6. Shiraishi K (1991) Glycogen-rich meningioma: case report and short review. Neurosurg Rev 14:61–64
7. Kleihues P, Burger PC, Scheithauer BW (1993) Tumors of the meninges. In: Sobin LH (ed) Histological typing of tumors of the central nervous system, 2nd edn. Springer-Verlag, Berlin, pp 33–42
8. 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
9. Alameda F, Lloreta J, Ferrer MD, Corominas JM, Galitó E, Serrano S (1999) Clear cell meningioma of the lumbo-sacral spine with chordoid features. Ultrastruct Pathol 23:51–58
10. 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
11. Vural M, Arslantaş A, Ciftçi E, Artan S, Atasoy MA (2007) An unusual case of cervical clear-cell meningioma in pediatric age. Child's Nerv Syst 23:225–229
12. Tena-Suck ML, Salinas-Lara C, Gómez C, Bojórquez DR (2007) Frontotemporal clear cell meningioma. Report of 3 cases. Annals of Diagnostic Pathol 11:182–189
13. 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
14. Ma L, Liu WK, Wang K, Shrestha B, Zhang YK (2009) Intracranial clear-cell meningioma. Acta Neurochir 151:373–378 discussion 378
15. 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
16. 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
17. 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. doi: 10.1097/PAI.0b013e3181dd35d2
18. Bailey D, Baumal R, Law J, Sheldon K, Kannampuzha P, Stratis M, Kahn H, Marks A (1986) Production of a monoclonal antibody specific for seminomas and dysgerminomas. Proc Natl Acad Sci USA 83:5291–5295
19. Breiteneder-Geleff S, Matsui K, Soleiman A, Meraner P, Poczewski H, Kalt R, Schaffner G, Kerjaschki D (1997) Podoplanin, novel 43-kd membrane protein of glomerular epithelial cells, is down-regulated in puromycin nephrosis. Am J Pathol 151: 1141–1152
20. Schacht V, Dadras SS, Johnson LA, Jackson DG, Hong YK, Detmar M (2005) Up-regulation of the lymphatic marker podoplanin, a mucin-type transmembrane glycoprotein, in human squamous cell carcinomas and germ cell tumors. Am J Pathol 166:913–921
21. Evangelou E, Kyzas PA, Trikalinos TA (2005) Comparison of the diagnostic accuracy of lymphatic endothelium markers: Bayesian approach. Mod Pathol 18:1490–1497
22. Ordóñez NG (2006) Podoplanin: a novel diagnostic immunohistochemical marker. Adv Anat Pathol 13:83–88
23. Roy S, Chu A, Trojanowski JQ, Zhang PJ (2005) D2-40, a novel monoclonal antibody against the M2A antigen as a marker to distinguish hemangioblastomas from renal cell carcinomas. Acta Neuropathol 109:497–502
24. Shibahara J, Kashima T, Kikuchi Y, Kunita A, Fukayama M (2006) Podoplanin is expressed in subsets of tumors of the central nervous system. Virchows Arch 448:493–499
25. Huse JT, Pasha TL, Zhang PJ (2007) D2-40 functions as an effective chondroid marker distinguishing true chondroid tumors from chordoma. Acta Neuropathol 113:87–94
26. Bollag RJ, Vender JR, Sharma S (2009) Anaplastic meningioma: progression from atypical and chordoid morphotype with morphologic spectral variation at recurrence. Neuropathology. doi: 10.1111/j.1440-1789.2009.01060.x
27. Whittle IR, Smith C, Navoo P, Collie D (2004) Meningiomas. Lancet 363(9420):1535–1543