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Chordoid Meningioma: Clinical, Hsitopathological and Radiological Study

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Abstract

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Keywords

- Chordoid, meningioma
- apparent diffusion coefficient

The purpose of this study is to discuss the clinical, radiological and histopathological features of a rare grade 2 variant of meningioma. <u>Patients and methods</u>: A retrospective analysis of the data of 6 patients who underwent surgery for a histopathologically proven chodroid meningioma. <u>Results</u>: Six patients' pathology reports showed chordoid meningioma. On imaging, four lesions (67%) were isointense in T1 while the other two were hypointense. On T2 weighted images, four patients were hyperintense (67%) and displayed non-restricted diffusion pattern with elevated values on corresponding apparent diffusion coefficient maps. Pathologically, chordoid elements varied vastly among cases, radiological characters corresponded to choroid elements in all cases. <u>Conclusion</u>: choirdoid meningioma, as a rare meningioma entity, should be suspected pre-operatively in cases with high signal intensity in T2, homogenous enhancement and increased apparent diffusion coefficient, gross total surgical excision is curative.

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Introduction

Meningioma is the second most common primary intracranial tumor with an incidence of about 15 % of all intracranial neoplasms, the majority of meningiomas are benign with WHO grade I. According to WHO classification, chordoid meningioma (CM) as well as anaplastic and atypical meningiomas are classified as grade II.

Chordoid meningioma (CM) is a rare subset, representing about 0.5% of all meningiomas. These are graded as World Health Organization (WHO) Grade II tumors and are associated with a high likelihood of recurrence 1 . The subtype chordoid meningioma was first reported by Kepes et al ² in 1988 in a case series of seven patients with this pathology which was characterized by "chordoma-like histologic appearance with a clustering of tumor cells against a myxoid background", according to their histopathological description. In 2007 WHO classification, CM was first listed as grade II due to reports of its aggressive behavior and high tendency to rapid recurrence unless complete surgical resection is achieved 3 .

Histopathologically, CM is characterized by cords/nests composed of epithelioid or spindle cells, in the background of pale, basophilic mucoid matrix. Tumorous cells greatly resemble physalliferous cells of chordoma, which are characterized by vacuolated cytoplasm. Pure CM cases are rare, however, the majority of CM pathologies intermingled are by typical meningioma tissues, the CM characters are higher with recurrence. Chronic inflammatory infiltrates are often patchy when present, but may be prominent⁴.

Earlier publications linked CM to systemic manifestations, Castleman like syndrome, due to reports describing refractory microcytic hypochromic anemia in patients with CM ², this was explained by an assumed systemic reaction to peritumoral lymphoblastcellular infiltrate, this connection was ruled out later with case series whose patients showed no such manifestations.

The purpose of this study is to review and analyze clinical, radiological, laboratory and histopathological features of six cases of proven chordoid meningioma patients.

Patients and methods

Retrospective search in pathology archive using the term "chordoid meningioma" during the period 2015 through 2020 was executed, patients' medical reports were viewed for epidemiology, clinical presentation, radiology, histopathology and outcome.

Preoperative Magnetic Resonance Imaging (MRI) examinations were performed on 1.5 T MRI scanner (Inginia, Philips, Best, The Netherlands) equipped with a self-shielding gradient set. Dedicated multi-channel head coil has been used for all cases. MRI protocol was as follow; axial Fast Spin Echo (FSE) T1-weighted images, T2 weighted image, fluid attenuation inversion recovery (FLAIR), and susceptibility weighted images (SWI), sagittal and coronal fast spin echo T2 weighted images. Axial diffusion weighted images (DWI) (b values of 0, 500 and 1000 s/mm2) and apparent diffusion coefficient (ADC) were then obtained before contrast administration. Contrast-enhanced T1-weighted imaging were obtained after administration of an intravenous gadolinium-based contrast agent (0.1 mmol/kg). Images were analyzed for tumor location, size,

signal characteristics on T1, T2 and FLAIR images, enhancement, diffusion pattern, perifocal edema, calcification, cystic areas, nearby osseous changes and dural sinus involvement. Signal characteristics were classified as hypointense, isointense, or hyperintense as compared to normal gray matter. Enhancement was classified as homogeneous or inhomogeneous while diffusion pattern was classified into restricted and free patterns. The lesions had restricted diffusion when it showed bright signal on diffusion weighted images and corresponding low values on ADC maps. SWI was used to assess calcification within the tumor.

Surgical specimens were fixed in 10% neutral buffered formalin, routinely processed and paraffin embedded. Sections of 4 µm-thick were prepared for routine hematoxylin-eosin-stained (H&E) sections and immunohistochemistry.

Immunohistochemical stains were performed using Primary antibodies against Ki-67 (rabbit PAb, clone MIB-1, 1:20 dilution, Neo Markers, USA), and epithelial membrane antigen (EMA) (clone GP1.4, 1:400 dilution, Novo-castra) were used. The Envision flex /HRP labeled polymer was applied using diaminobenzidin and hematoxylin for counterstaining on Autostainer Link 48 system from DAKO.

Mitotic index, as well as MIB-1 anti-gen immunohistochemical staining, were used to assess cell proliferation. The MIB-1 labeling index (MI) was calculated in regions of maximal activity and expressed as percent nuclear area of staining. Diagnostic criteria, according to 2016 WHO classification of CNS tumors, included either: mitotic index more than 4/10 high-power fields (HPF) or the presence of three of the next findings: high cellularity, increased nuclear/cytoplasmic ratios in small cell, prominent nucleoli, sheet-like growth, and foci necrosis with spontaneous or geographic patterns. Malignancy was defined in this study as the presence of obviously malignant cytology or an exceptionally high mitotic index (>20/10 HPF).

Results

Six patients' pathology reports showed chordoid meningioma, 3 of them were males, mean age of 50.5 years which ranged from 35 to 66. One patient was presented with scalp swelling, one patient with seizures and all other patients (4 cases, 67%) were presented primarily with headache, two patients showed hemiparesis on neurological examination.

On imaging, four lesions (67%) were isointense in T1 while the other two were hypointense. On T2 weighted images, four patients were hyperintense (67%) and displayed nonrestricted diffusion pattern with elevated values on corresponding ADC maps. All lesions showed enhancement. Clinical homogenous and radiological criteria are summarized in Table 1, three patients (50%) showed calcification and one patient showed aggressive involving adjacent clavaria. Dimensions of the lesions ranged from 2.8 cm in the smallest tumor to 6 cm in the biggest one with mean volume of 67.7 cc which ranged from 16.5 cc to the biggest 60 cc. All lesions were supratentorial, most common site was frontal convexity in 2 patients, one occipital, two parietooccipital and one falcine. One patient showed double lesion, small posterior fossa meningioma in addition to the supratentorial one. Perifocal edema and subsequently midline shift was seen in four patients, in one patient the tumor invaded the superior sagittal sinus with full obliteration and collateral circulation.

Preoperative laboratory investigations were within normal ranges for all patients, mean hemoglobin concentration was 12.4 with range from 11.3 to 14.3. The histological criteria and percentage of chordoid morphology are summarized in Table 2. The patterns of chordoid morphology are illustrated in Figure 1. Microscopically, the tumorous cells were epithelioid cells in 50% of cases (3/6), while plump to spindle cells represented 50% (3/6), both categories were arranged in nests, chords or cribriforms in mucoid matrix.

The chordoid elements constituted 20– 95% of the tumorous volumes, with 3 of 6 (50%) over 70. Two specimens were characterized by sweeping and/or uninterrupted sheeting appearance, for these two cases, chordoid morphology was more than 90% of the examined areas; otherwise, they were alternating or intermixed with other subtypes; one transitional and five meningothelial. Via thorough examination typical meningothelial of the specimens, differentiation were identified and proven by whorl formation or intranuclear inclusions. Based on solo pathological examination, five tumors (83.3%) were classified as benign (grade I) and one tumor (16.7%) was classified as atypical (grade II), if based solely on histologic grading irrespective to chordoid parts. One recurrent tumor was classified as grade I. Lymphoplasmacytic infiltrate was present in three tumors (50%).

	Age	Sex	site		Fallory				
				T1	T2	Enhancement	DWI	Midline shift	(months)
Case 1	66	f	Lt Sphenoid ridge	iso	hyper	Homogenous	Non	yes	36
Case 2	56	m	Lt Occipitoparietal	Iso	Mixed	Homogenous	Partial restricted	yes	14
Case 3	38	f	Rt Frontal	Iso	Iso to hypo	Homogenous	Restricted	no	48
Case 4	58	m	Rt falcine - middle 3rd	Нуро	Hyper	Homogenous	Non	no	34
Case 5	45	m	Lt frontal	Iso	Iso to hypo	Homogenous	Restricted	yes	44
Case 6	40	f	Rt occipital	Iso	Hyper	Homogenous	Non	yes	12

Table 1 : Pathological features

Table 2: Clinical and radiological features

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Increased cellularity	No	No	No	No	No	No
Small cell with high N/C ratio	No	No	No	No	No	No
Prominent nucleoli	Yes	No	Yes	Yes	No	No
Sheet-like growth	Yes	No	No	Yes	No	No
Geographic necrosis	Present	No	No	No No		No
Malignant cytology	Absent	Absent	Absent	Absent	Absent	Absent
Mitotic index (10 HPF)	3	0	3	0	2	0
MIB-1 labeling index (%)	25	1	10	15	1	2
Lymphocyte infiltration	Present	Absent	Present	Absent	Present	Absent
Additional morphology	meningothelial	meningothelial	Transitional	meningothelial	meningothelial	meningothelial
Percentage of chordoid	95	20	40	90	30	85
morphology						
Bone invasion	Absent	Absent	Present	Present	Absent	Absent

Illustrative cases

Case 1

Sixty six years old female patient, presented to neurosurgery clinic with history of long standing headache and recent right side hemiparesis, MRI brain with contrast examination (Fig 1, A-C) coronal T2, T1 and post contrast T1 images demonstrate high T2 and intermediate T1 signal intensity of a sphenoid ridge meningioma with avid homogenous enhancement after contrast administration. The lesion showed perifocal edema extending to adjacent motor area to which the hemiparesis could be attributed. Laboratory results were within normal values. Total microscopic excision was performed, follow up period lasted for 12 months with no recurrence.

Histopathological examination (Fig 2) showed epithelioid cells, to plump cells, forming cords, cribriforms or nests, in a mucoid matrix intermingled with classic meningothelial component evidenced by whorl formation or intranuclear inclusions. The chordoid elements 95% constituted of the tumor areas. Lymphoplasmacytic infiltrate as well as Geographic necrosis were present. No associated brain tissue after through sampling. MIB-1 labeling index was 25%

Fifty six years old male patient, presented to neurosurgical clinic with history of seizures which were controlled on medical anti-epileptic therapy. Neurological examination showed bilateral visual affection with visual acuity of 3/60 and 6/60. MRI brain showed (Fig 3) left parietooccipital meningioma. (A & B) axial T2WI and FLAIR images show extra-axial SOL with mixed low and high signal intensity. (C & D) axial DWI and ADC images show partial restriction pattern of the lesion corresponds to the T2 low signal intensity and non-chordoid component. (E & F) pre and post contrast T1 images show avid enhancement of the lesion.

Histopathological examination showed (Fig 4) showed а predominant classic meningothelial meningioma (WHO grade I) of average cellulariy with interspersed cords of physaliferous like tumor cells with frequent intracytoplasmic vacuolization characteristic of chordoid meningioma (WHO grade II). The chordoid component represents about 20% of tumor. No detected Lymphoplasmacytic infiltrate nor Geographic necrosis. No evidence of brain tissue invasion. MIB-1 labeling index was 1%.

Case 2



Figure 1: Case 1. A, Low-power view shows chordoid meningioma merging with areas of typical meningioma, (H&E,x40). B, a photomicrograph showing the cord-like arrangement of the tumor cells within the myxoid stroma; (H&E,x400).C, Lymphoplasmacytic cell infiltrate together with areas of necrosis D were also present (C & D, H&E,x40).



Figure 2: Case 1.Sphenoid ridge meningioma; (A-C) coronal T2, T1 and post contrast T1 images demonstrate high T2 and low signal intensity of the meningioma with avid homogenous enhancement after contrast administration.



Figure 3: Case 2. A, Low-power view illustrates typical meningothelial meningioma (WHO grade I) with interspersed cords of physaliferous like tumor cells with frequent intracytoplasmic vacuolization characteristic of chordoid meningioma (WHO grade II) and absent lymphocytic infiltrate (H&E,x40). B, high power showing the cord-like arrangement of the tumor cells (H&E,x400).



Figure 4: Case 2. Left parietal meningioma. (A & B) axial T2WI and FLAIR images show extra-axial SOL with mixed low and high signal intensity. (C & D) axial DWI and ADC images show partial restriction pattern of the lesion corresponds to the T2 low signal intensity and non-chordoid component. (E & F) pre and post contrast T1 images show avid enhancement of the lesion.

Discussion

Chordoid meningioma is a rare variant of meningioma, though CM was first described by Kepes in 1988, two earlier reports used the terms "vacuolated" and "myxomatous" to describe a special type of meningioma in 1977⁵ and 1979⁶ as well as Connors et al⁷ case report in 1980 which was the initiator to Kepes' concerns. So far, only around 150 cases of CM have been published in English language literature.

All our patients were adults with mean age of 45.3 years old, with no gender preference, in contrary to Kepes' original article which included 7 patients, all of them were below 20 years. Similar to our results, Linn's ⁴ series also included 12 patients of adult population while Couce ⁸ and Epari ⁹ showed 95% and 75% adults respectively, which could be attributed to their bigger number of cases.

Laboratory tests of our patients showed no iron deficiency anemia, as well as Couce, Epari, Linn and numerous case reports, which confirms that systemic manifestations of CM as Castleman syndrome is limited to pediatric group.

Numerous studies correlated consistency of meningioma to preoperative MRI, softer lesions

associated with increased preoperative are imaging 10 hyperintensity in T2 weighted specifically for chordoid meningioma Pond et al¹¹ proved increased apparent diffusion coefficient in a series of chordoid meningioma patients. In our study, increased chordoid content percentage is associated with hyperintense signal in T2 weighted images, while lesions with fewer chordoid element showed isointensity. These specific radiological findings can be attributed to the unique tumoral architecture and histopathological characteristics of the chordoid subtype. Diffusivity of water detected in MRI depends on extracellular matrix, cell density and cytoplasm/nucleus ratio ¹², ¹³. Hyperintensity of CM on T2 weighted MRI noted and elevated ADC are hypothetically explained by characteristic histopathological features of CM which allows free water motion; the mucoid extracellular matrix and increased cytoplasm/nucleus ratio due to vacuolized cytoplasm. This gives a clinical importance to preoperative radiological assessment, as when suspected, total excision including meningeal coverings should be the aim.

One patient (16.8 %) showed recurrence within 2 years after total resection in our series,

while none of the other patients showed recurrence after microscopic total excision, although Couce et al reported 61% recurrence rate in 10 years after subtotal excision, this ratio is still higher than recurrence rate for grade I meningioma after the same procedure, the follow up period for our study is not sufficient to judge recurrence.

According to 2016 newest CNS tumors classification, CM is classified as grade II meningioma, due to a high rate of recurrence, particularly following subtotal resection. Morphologically, CM consists of cords or trabeculae of round to flattened cells with eosinophilic or vacuolated cytoplasm and an abundant mucoid matrix background. Such chordoid areas are often interspersed with more typical meningothelial or transitional areas. The pure chordoid morphology is uncommon but can lead to a diagnostic dilemma when present exclusively. The differential diagnosis in this scenario includes tumors within or near the CNS exhibiting chondroid/myxoid appearance. These chordoid are chordoma, glioma, myxoid chondrosarcoma (skeletal and extra-skeletal), low-grade chondrosarcoma, myxopapillary ependymoma, mucinous and metastatic carcinomas¹⁴,¹⁵.

A panel of immunohistochemical stains is required for accurate diagnosis. Chordoma is very important because of its striking histological resemblance to CM. EMA positivity in CM cannot alone differentiate it from chordoma as the latter is typically EMA/CK/S-100 positive. Strong GFAP reactivity is present in chordoid gliomas and Myxopapillary ependymomas which are also positive for S-100 as well as Chondrosarcomas¹⁶.

Metastatic lesions can mimic CM particularly renal cell carcinoma and mucinous carcinomas of the gastrointestinal tract. However, clinical and radiological correlation along with immunohistochemical panel for the primary tumor are often adequate for the correct diagnosis. Recent studies have shown that D2-40, a monoclonal antibody initially developed against podoplanin is a selective marker of lymphatic endothelium and aids in identification of various benign and malignant tissues. Immunoreactivity with D2-40 antibody in CM is useful in the differentiation from both extraskeletal myxoid chondrosarcoma and chordoma¹⁴.

Although some authors ¹⁷ have implicated the mucin rich, chordoid morphology for rapid enlargement and aggressiveness of CM, it has not been established as an independent prognostic feature. The most important prognostic factor in patients with meningiomas is the extent of resection. The recurrence rate after subtotal resection of CM is high ¹. However, complete resection may not be possible in large tumors, which are present near important functional areas of the brain or major blood vessels. Postoperative radiotherapy is recommended in such cases ¹⁸.

Conclusion

Chordoid meningioma is a rare variant which can't be clinically identified, but radiologically suspected. Pre-operative anticipation of such and aggressive pathology is important to plan radical excision.

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Conflict of interest:

The authors declare that there is no conflict and/or competing of interest regarding this paper.

Data availability statement:

The authors confirm that all data were analyzed to conclude these findings are deposited in the patients' medical records of pathology, neurosurgery and radiology departments.

References:

- Louis, D. N. et al. The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary. *Acta Neuropathologica* vol. 131 803–820 (2016).
- Kepes, J. J., Chen, W. Y., Connors, M. H. & Vogel, F. S. "Chordoid" meningeal tumors in young individuals with peritumoral lymphoplasmacellular infiltrates causing systemic manifestations of the castleman syndrome. A report of seven cases. *Cancer* 62, 391–406 (1988).
- Louis, D. N. et al. The 2007 WHO classification of tumours of the central nervous system. Acta Neuropathologica vol. 114 97–109 (2007).
- Lin, J. W., Ho, J. T., Lin, Y. J. & Wu, Y. T. Chordoid meningioma: A clinicopathologic study of 11 cases at a single institution. *J. Neurooncol.* 100, 465– 473 (2010).
- Eimoto, T. & Hashimoto, K. VACUOLATED MENINGIOMA: A Light and Electron Microscopic Study. *Pathol. Int.* 27, 557–566 (1977).
- Dahmen, H. G. Studies on mucous substances in myxomatous meningiomas. *Acta Neuropathol.* 48, 235–237 (1979).

- Connors, M. H. Growth and maturation arrest, hypochromic anemia and hyperglobulinemia associated with a brain tumor. *West. J. Med.* 133, 160–163 (1980).
- Telia, O., Borba, L. A., Machado, H. R., Claudio, J. & Da Nôbrega, M. Chordoid meningioma. Skull Base Surg. 7, 39 (1997).
- Epari, S. et al. Chordoid meningioma, an uncommon variant of meningioma: A clinicopathologic study of 12 cases. *Journal of Neuro-Oncology* vol. 78 263– 269 (2006).
- Yao, A., Pain, M., Balchandani, P. & Shrivastava, R. K. Can MRI predict meningioma consistency?: a correlation with tumor pathology and systematic review. *Neurosurgical Review* vol. 41 745– 753 (2018).
- Pond, X. J. B. et al. Chordoid meningioma: Differentiating a rare world health organization grade II tumor from other meningioma histologic subtypes using MRI. Am. J. Neuroradiol. 36, 1253–1258 (2015).
- Sugahara, T. et al. Usefulness of diffusion-weighted MRI with echo-planar technique in the evaluation of cellularity in gliomas. J. Magn. Reson. Imaging 9, 53–60 (1999).
- Ginat, D. T., Mangla, R., Yeaney, G., Johnson, M. & Ekholm, S. Diffusionweighted imaging for differentiating benign from malignant skull lesions and correlation with cell density. *Am. J. Roentgenol.* 198, (2012).
- Sangoi, A. R., Dulai, M. S., Beck, A. H.,
 Brat, D. J. & Vogel, H. Distinguishing

chordoid	meningion	nas	from	th	eir		
histologic	stologic mimics:						
immunohis	Am.	J.					
Surg. Pathol. 33, 669–681 (2009).							

- Cho, H. Y. *et al.* Immunohistochemical comparison of chordoma with chondrosarcoma, myxopapillary ependymoma, and chordoid meningioma. *Appl. Immunohistochem. Mol. Morphol.* 17, 131–138 (2009).
- Siraj, F., Ansari, M. K., Sharma, K. C. & Singh, A. Chordoid meningioma: A diagnostic dilemma. *J. Cancer Res. Ther.* 11, 663 (2015).
- Hasegawa, S., Yoshioka, S., Urabe, S. & Kuratsu, J. I. Rapidly enlarging chordoid meningioma with abundant mucin production. *Neuropathology* 26, 438–441 (2006).
- Zhu, H. Da *et al.* Chordoid meningioma: A retrospective study of 17 cases at a single institution. *Chin. Med. J. (Engl).* 126, 789–791 (2013).