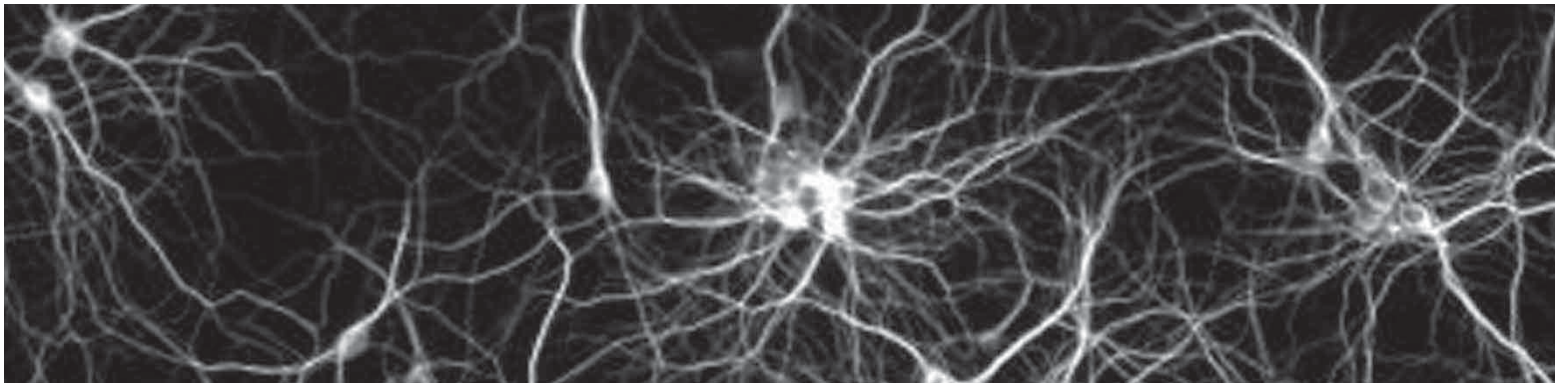

Third ventricular chordoid meningioma or chordoma: a diagnostic dilemma based on a single case

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ABSTRACT - We report a case and literature review of a rare third ventricular tumor in a child with histologic characteristics of chordoma and chordoid meningioma (CM). *Case*: A 13-year-old boy was diagnosed with a recurrent intraventricular tumor 22 months after complete surgical removal. Reoperation was indicated; treatment consisted of total microsurgical removal, histologic and immunohistochemical classification, and follow up. Literature review on Pub Med was performed using the Mesh key words: "Cerebral Ventricle Neoplasms" AND "Pediatrics". Histologic and immunohistochemical analysis after the first operation had shown chordoma, and second histologic and extended immunohistochemical analysis showed positivity for D2-40 marker, which is negative in chordoma but can be positive in CM. It was concluded to be a case of CM. Fourteen months after reoperation there were no signs of tumor recurrence. Literature review showed two cases of intraventricular CM, one situated in lateral ventricle and the other in third ventricle. *Conclusion*: This is the second reported case of CM situated in the third ventricle in a pediatric patient. In this case, follow up was performed regularly for 22 months after the first complete resection, when the tumor recurred. First histologic and immunohistochemical analysis showed chordoma, whereas second analysis showed CM. Fourteen months after reoperation there were no signs of tumor relapse. The boy returned to his everyday activities, with some hormone misbalance treated with hormone substitutes.

Key words: intraventricular meningioma, chordoid meningioma, pediatrics, chordoma, immunohistochemistry

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INTRODUCTION

Chordoid meningioma (CM) tumor was first described by Kapes *et al*. in 1988 (13). It is estimated that CM account for less than 0.5%-1% of all meningiomas (4, 5). In the latest World Health Organization (WHO) tumor classification system, CM is graded as atypical (GII grade) meningioma because of a high rate of recurrence after surgical resection (14, 18).

Morphologically, CM is composed of epithelioid or spindle cells that form cords or nests in a basophilic mucoid matrix resembling physaliferous cells of the chordoma. Diagnosis is made morphologically and immunohistochemically but in some cases the exact diagnosis can be difficult because the minority of CM are focally positive for S-100 protein (S-100) and pan-cytokeratin (pan-CK), markers typically associated with chordomas (6).

Chordomas account for less than 0.2% of primary intracranial tumors (23), typically arising along the midline of neuroaxis at the sacrococcigeal (50%-60%), skull base (25%-35%) and vertebral (15%) region (8). Peak incidences are reported in the sixth decade of life and are uncommon in patients below thirty years of age (11). It is believed that they originate from vestigial cell remnant of the primitive notochord (21) or from benign notochordial cell tumor (2). They are mainly extra-dural intraosseous lesions that are locally aggressive, posing a challenge to treat. Intradural intracranial location is rarely reported. Intradural, extraosseous localized chordomas tend to have good prognosis when compared to intraosseous classical chondromas (10). Intraventricular localization without dural involvement is described in only one case (1).

There are 19 cases of CM in pediatric population (16,17,22) reported in the literature. To the best of our knowledge, there are two described cases of intraventricular CM in pediatric population, situated in the left lateral ventricle and third ventricle one each (17,22).

In this article, we report a third ventricular CM in a child, diagnosed, treated and followed-up at our department.

CASE REPORT

An 11-year-old, previously healthy Caucasian boy underwent diagnostic examination for evaluation of occasional tremor of his left hand experienced for several months. Neurological examination showed no abnormalities. Brain computed tomography (CT) revealed a large mass located in the

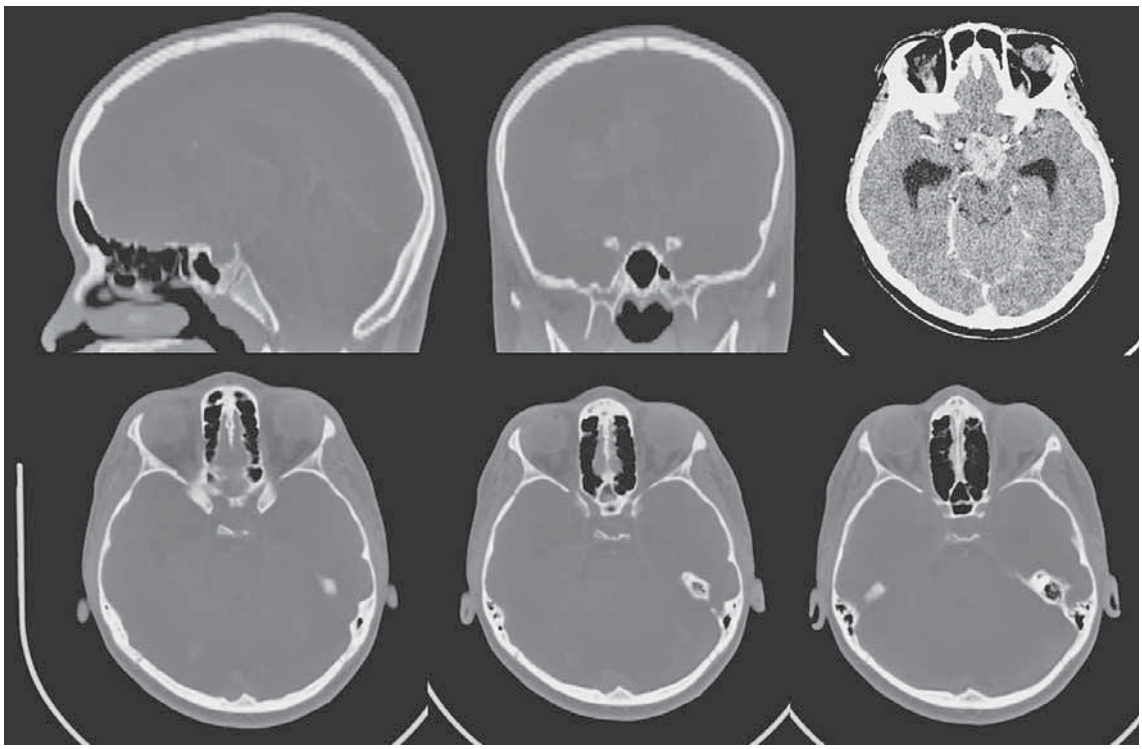

Fig. 1. *CT scan showing a large mass located in the third ventricle, measuring 6.3x5.0 cm, with supra- and retrosellar extension and no bone erosion.*

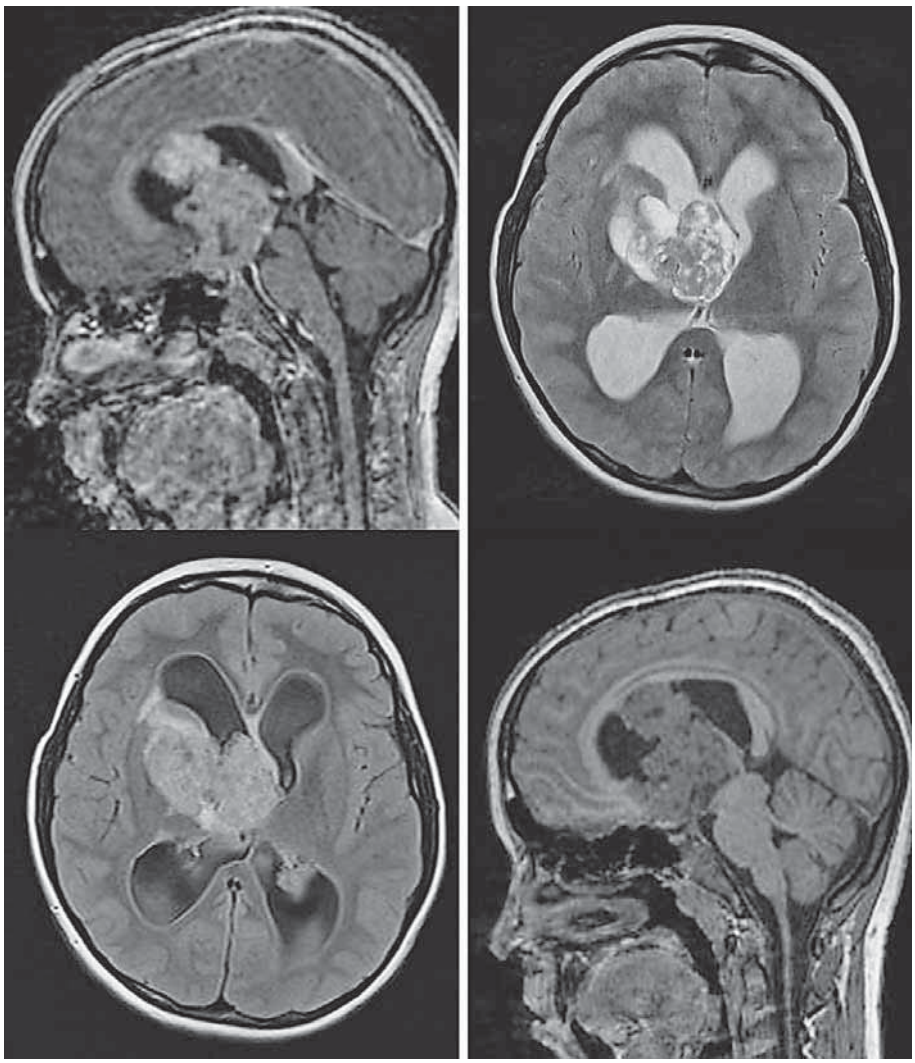

Fig. 2. *MRI scan showing a large, well-delineated mass measuring 6.3x4.2x5.0 cm, situated suprasellarly, involving the hypothalamic region with cranial extension at the third and right lateral ventricles. T2 sequence showed hypointense areas of calcifications. Post contrast sequence showed focal areas of enhancement. Internal cerebral veins are displaced by the tumor. Basal ganglia at the right side show perifocal edema. Dilated lateral ventricles and morphological loss of gyral and sulcal formations at the cortex are evident.*

third and right lateral ventricles, measuring 6.3x5.0 cm with supra- and retrosellar extension and no bone erosion (Fig. 1). Funduscopy showed papilledema. The patient was admitted to the hospital and magnetic resonance imaging (MRI) showed a large, well-delineated mass measuring 6.3x4.2x5.0 cm, situated suprasellarly and involving the hypothalamic region with cranial extension at the third and right lateral ventricles. MRI T2 sequence showed hypointense areas of calcification. Post contrast sequence showed focal areas of enhancement. Internal cerebral veins were displaced by the tumor. Basal ganglia at the right side showed perifocal edema. Dilated lateral ventricles and morphological loss of gyral and sulcal formations at the cortex were evident (Fig. 2).

SURGICAL PROCEDURE AND CLINICAL COURSE

The surgery was indicated soon after diagnosing the third ventricular tumor. The tumor was approached transcallosally interforniceally in general anesthesia and supine position, and completely removed using microsurgical technique with CT image guidance. No dural erosion was found intraoperatively. The tumor was completely removed (Fig.

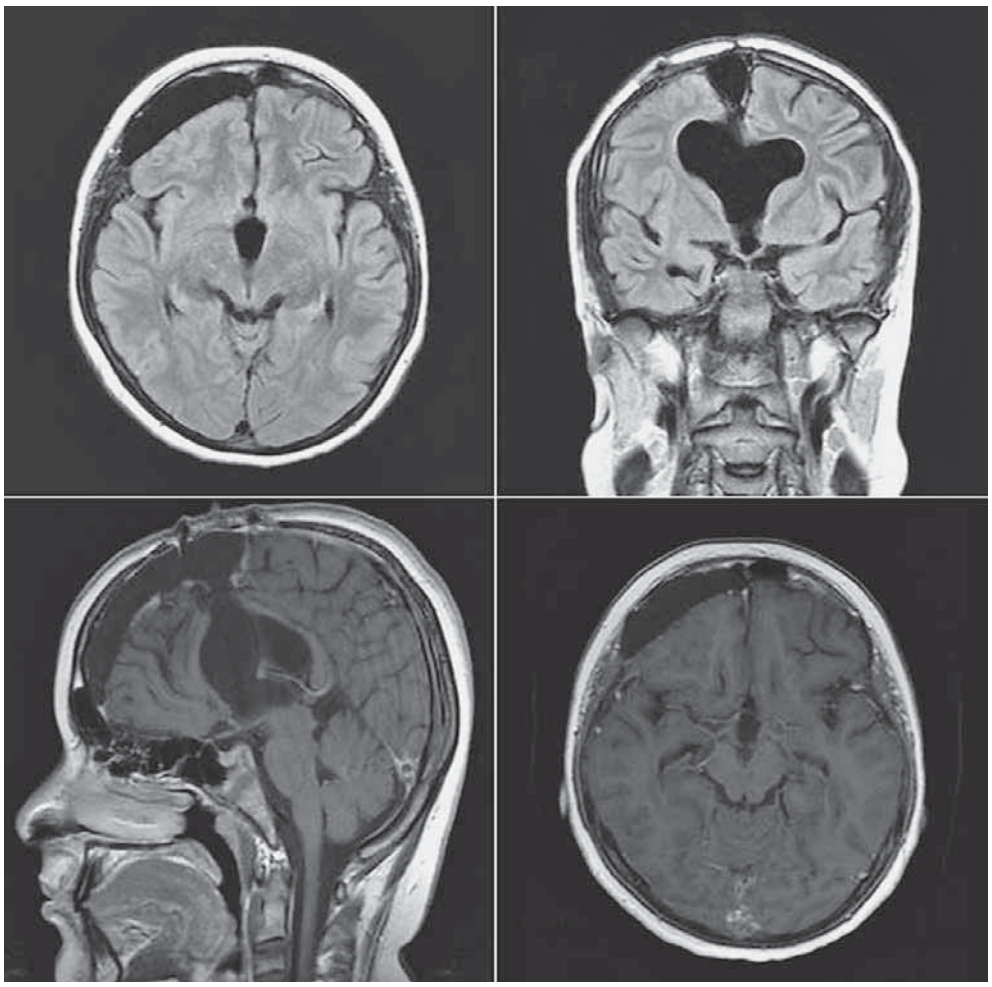

Fig. 3. *MRI acquired a month after the surgery showing complete tumor removal without new neurosurgical complications.*

3) and the tissue was sent for definite histologic examination. The postoperative course was complicated with short lasting polyuria and high potassium blood level on day 2, one episode of convulsions on day 5 and meningitis diagnosed on day 8 postoperatively. After the treatment of meningitis, the boy was transferred to the rehabilitation center with hydrocortisone as hormone replacement therapy. Periodic pediatric endocrinological follow up was performed regularly and hydrocortisone in low doses was continued as hormone replacement therapy. Follow up funduscopy showed no papilledema. The child resumed his everyday activities. Neurosurgical follow ups were performed regularly and 22 months after the surgery, tumor recurrence was evident on MRI (Fig. 4).

The second surgery was performed and the tumor was approached as previously described and completely removed. The postoperative course was uneventful and after brief rehabilitation, the child returned to his everyday activities. He attends regular school but has slightly lower grades. Fourteen months after the second surgery, follow up MRI showed no tumor (Fig. 5). Periodic pediatric endocrinological follow ups are performed regularly. Hydrocortisone in low doses is continued as hormone replacement therapy.

HISTOLOGIC FINDINGS

First histopathology analysis

The tumor was composed of moderately polymorph cells in diffuse or lobular pattern, separated by fibrous septa of varying thickness. The cells were embedded in abundant basophilic alcian blue positive mucinous matrix. The cells had oval eccentric nuclei with a dense chromatin pattern. Some cytoplasm contained vacuoles of various size and other cells had a more solid eosinophilic (periodic acid Schiff, PAS) positive cytoplasm. The tumor had areas of pleomorphic cells. Mitoses were absent. The

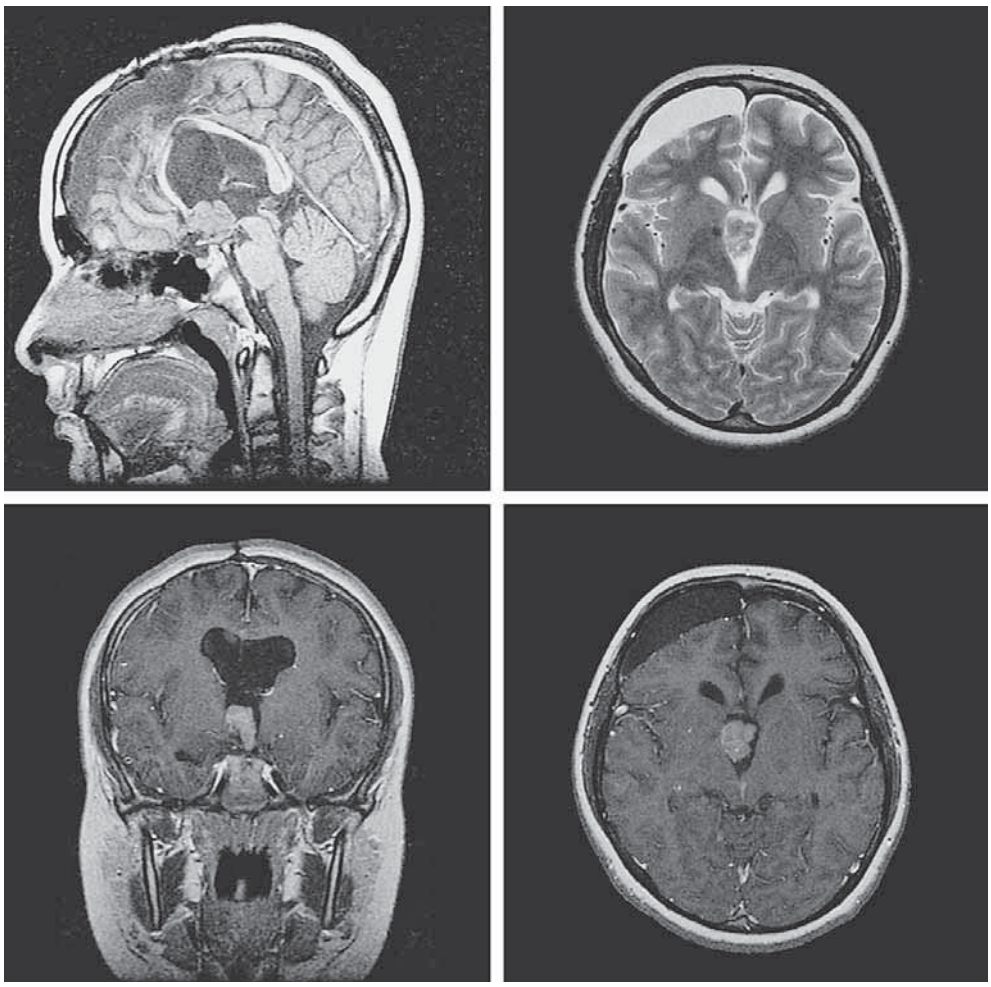

Fig. 4. *MRI acquired 22 months after the surgery showing tumor recurrence situated in the third ventricle.*

calcification and hemorrhage were uncommon. All tumor cells were strongly positive for epithelial membrane antigen (EMA) and vimentin (VIM). S-100 protein marker (S-100) was positive in most of the cells with a medium intensity and pan-cytokeratin (AE1/AE3) was partially positive in tumor cells. Immunostaining for glial fibrillary acidic protein (GFAP), actin (AC), chromogranin (Chg) and melanoma marker (HMB45) were negative. Ki-67 was 3%. The tumor was well demarcated from the surrounding brain tissue. The diagnosis was chordoma (Fig. 6).

Second histopathology analysis

The second histopathology analysis showed the same histologic characteristic except for the presence of one mitosis. Extended immunohistochemical staining showed positivity for D2-40 marker and sporadic and very weak S-100 positivity. In addition, D2-40 was performed on paraffin blocks from the first operation and it was positive in tumor cells. Ki-67 was 3%. Based on the morphology and immunohistochemical results, the diagnosis of CM was established (Fig. 6).

DISCUSSION

It is believed that chordomas originate from notochordial vestigial cell remnant that is demonstrated along the neuroaxial skeleton from sella turcica to the sacrum (6). They are situated intraosseously, which is the main radiological feature of these tumors. Intradural localization is exceptional (20).

The third ventricular chordoma has previously been described in only one case, as reported by Antigüedad *et al*. 1989 (1). The evidence available is suggesting that intradural chordomas have better prognosis if complete resection is achieved, in contrast to intraosseous classical chordomas (10,12,20). Further studies with longer follow ups are needed to support this clinical observation.

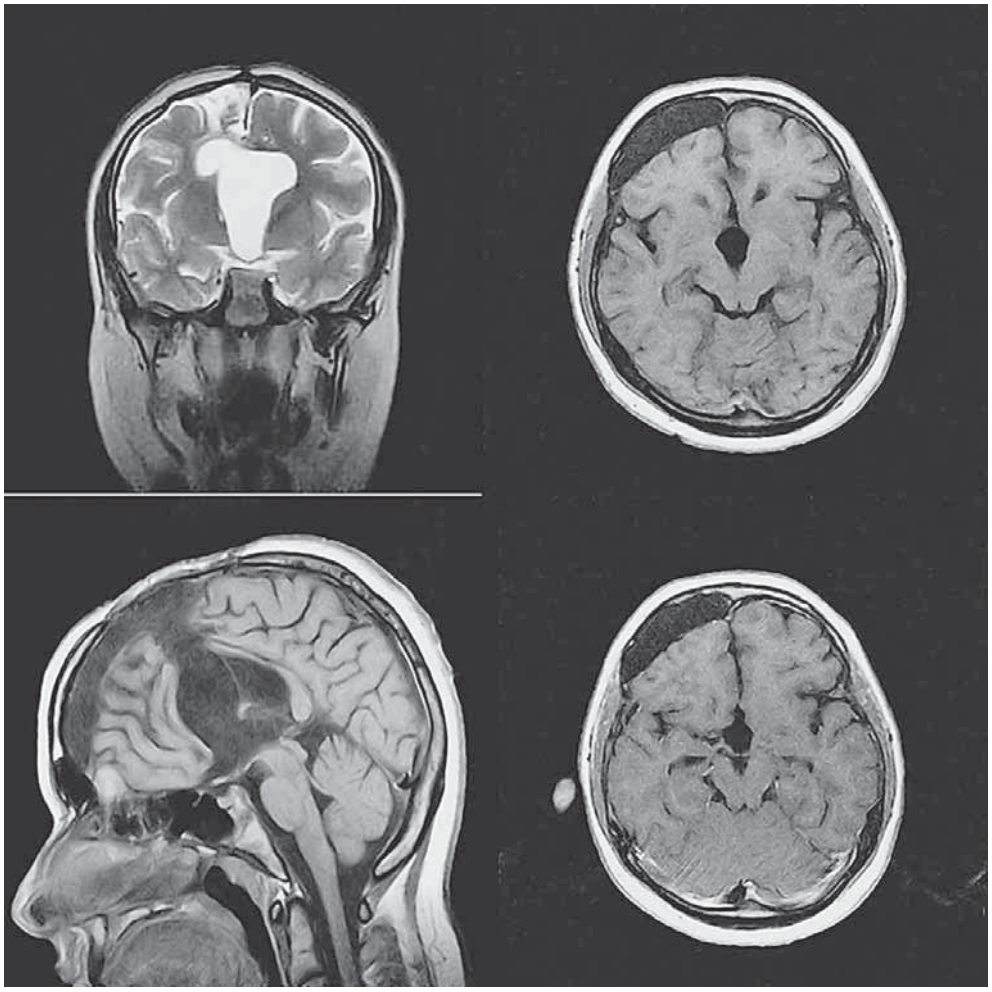

Fig. 5. *MRI acquired 14 months after the operation showing complete tumor removal and no signs of tumor recurrence.*

Intraventricular meningiomas arise from arachnoid cap cells trapped in the choroid plexus or velum interpositum during embryologic formation of the choroid fissure and plexus (7,15). It is estimated that 12% of reported meningiomas in pediatric population are situated within the ventricle. There are many series reporting a higher incidence of atypical and malignant variants of meningioma in children as compared with adults (19).

Chordoid meningiomas account for 0.5% to 1.0% of intracranial meningiomas (4,5). The tumor entity was first described by Kepes *et al*. in 1988; in 1993, it was classified separately as grade (G) I meningioma in the WHO classification (13,14). In the last WHO tumor classification revision from 2007, CM has been graded as atypical G II meningioma after the aggressive tumor behavior was described (18).

Histologically, CM is characterized by epithelioid cord-like tumor cells embedded in a myxoid stroma. Characteristic tumor cells with vacuolated cytoplasm strongly resemble physaliferous cells of chordoma. Morphologically, the diagnosis of CM is made when correct identification of the vacuolated trabeculae of neoplastic cells in a myxoid stroma is accompanied by co-existing areas typical of meningioma. The differential diagnosis includes chordoma, chordoid glioma, chondrosarcoma, myxopapillary ependymoma, metastatic mucinous and renal cell carcinoma. The accurate diagnosis is made on immunohistochemical profile but can be difficult because of overlapping in the morphological and immunohistochemical profiles (3) (Table 1).

In our case, the tumor showed morphologically chordoid and meningiomatous structure. Immunohistochemically, there was strong positivity for VIM, EMA and pan-CK as markers typically associated with chordomas. Tumor cells were negative for GFAP and well-delineated from GFAP positive brain tissue, the findings that were consistent on both analyses. At the time of the first histopathologic diagnosis, the pathology laboratory did not have D2-40 staining. Back then, based on the mor-

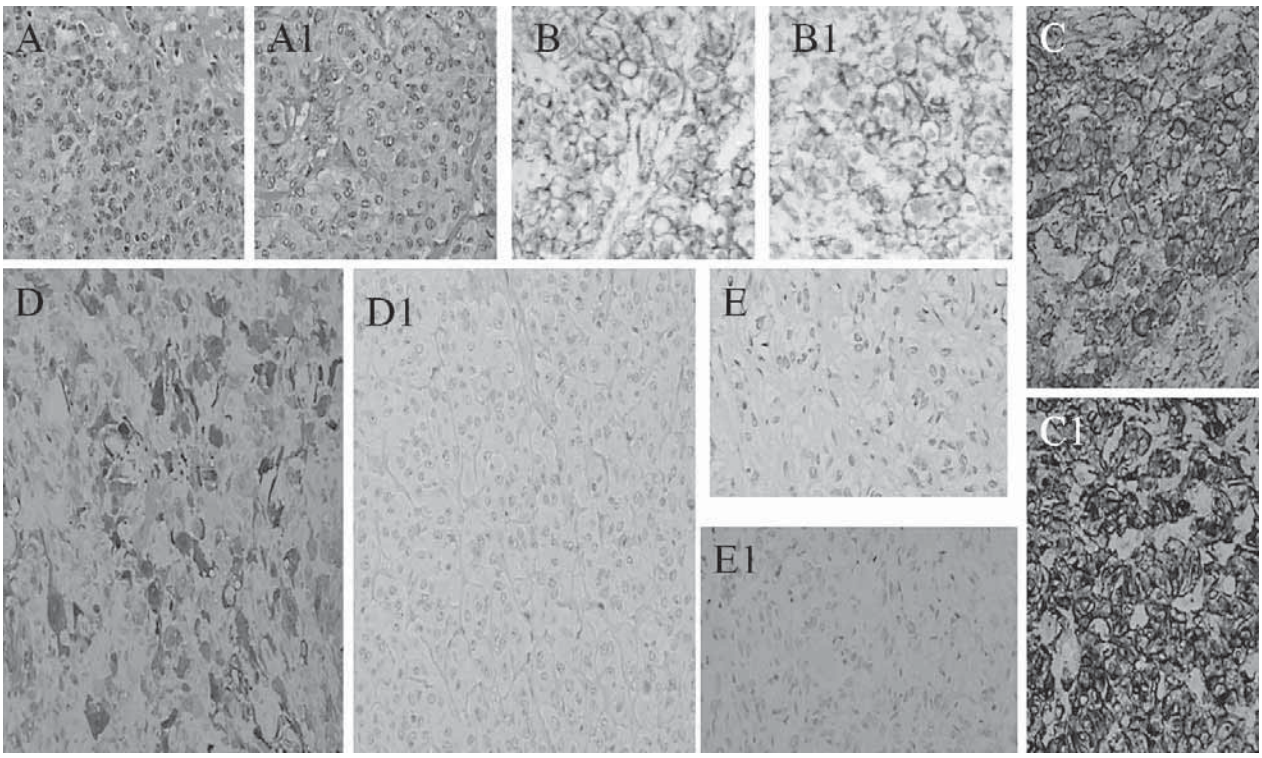

Fig. 6. *The morphological and immunohistochemical study of the tumor tissue acquired at first (A (hematoxylin and eosin stain), B (D2-40), C (epithelial membrane antigen marker), D (S100 protein marker), E (glial fibrillary acidic protein) and second (A1,B1,C1, D1, E1) surgery show a tumor composed of moderately polymorph cells in diffuse or lobular pattern separated by fibrous septa of varying thickness. The cells are embedded in abundant basophilic alcian blue positive mucinous matrix. The cells have oval eccentric nuclei with a dense chromatin pattern. Some cytoplasm contains vacuoles of various size and other cells have a more solid eosinophilic PAS positive cytoplasm. The tumor has areas of pleomorphic cells. The calcification and hemorrhage are uncommon. Tumor cells were positive for epithelial membrane antigen EMA, cytokeratin, VIM and D2-40. Immunostaining for GFAP was negative. Ki-67 in both tumors was 3%. The tumor was well-demarcated from the surrounding brain tissue. Described morphological and immunohistochemical features were found at first and second analysis. The final diagnosis of chordoid meningioma was established based on immunohistochemical positivity for D2-40 and loss of S-100.*

Table 1. *Immunohistochemical profiles of morphologically similar tumors*

	EMA	VIM	pan-CK	GFAP	S-100	D2-40
Chordoma	+	+	+	-	+/-	-
Chondrosarcoma	-	+	-	-	+	+
Myxopapillary ependymoma	-	+	-/+	+	+/-	+/-
Chordoid meningioma	+	+	-/+	-	-	+/-
Our case, first analysis	+	+	+/-	-	+	+
Our case, second analysis	+	+	+/-	-	-	+

phological and immunohistochemical findings, the diagnosis of chordoma was established. The second analysis showed sporadic and very weak S-100 positivity together with positivity for D2-40 staining. Based on the morphological and new immunohistochemical results, a conclusion that it was not a chordoma but a CM was made (Fig. 6 and Table 1).

Couce *et al*. showed that a small portion of CM can be focally positive for S-100 and cytokeratin markers; the majority of CM are lacking S-100 and all

Table 2. *Patients with chordoid meningioma under 18 years of age*

Case	Age (yrs), sex	Localization	Systemic disease	Author, year [reference]	Follow up (years (y), months (m)	Treatment, outcome	Recurrence
1	15, M	Left tentorial	Castelman's disease	Kepes *et al*. 1988	5 y	GTR	No
2	10, M	Right parietal	Castelman's disease	Kepes *et al*. 1988	3 y	GTR	No
3	18, F	Right parietal	Castelman's disease	Kepes *et al*. 1988	2 y	GTR	No
4	17, M	Falx and right parietal	Castelman's disease	Kepes *et al*. 1988	3 y	GTR	No
5	16, F	Falx left occipital	Castelman's disease	Kepes *et al*. 1988	20 m	GTR	Yes
6	8, F	Falx, left	Castleman's disease	Kepes *et al*. 1988	6 m	GTR	No
7	15, F	Tentorial	Previously treated for Wilms tumor	Glasier *et al*. 1993	Not described		
8	10, F	Supratentorial	No	Zuppan *et al*. 1994	Not described		
9	5, M	Bilateral frontal	No	Kumar *et al*. 1996	6 m	GTR	Yes
10	15, F	Right Falco-tentorial	No	Kobata *et al*. 1998	5 y	GTR	No
11	12, F	Fronto-parietal	No	Couce *et al*. 2000	Lost to follow up	GTR	Lost to follow up
12	15, M	Fronto-temporal	No	Couce *et al*. 2000	Lost to follow up	GTR	Lost to follow up
13	12, M	Cerebellum (midline)	No	Epari *et al*. 2006	3 m to 2 y	GTR	No
14	17, M	Cerebellum	No	Epari *et al*. 2006			
15	18, F	Left parietal	No	Epari *et al*. 2006			
16	12, F	Frontal with spinal dissemination	No	Mullassery *et al*. 2006	14 m	GTR, 2 mt follow up, GRT cranio-spinal RT, spinal dissemination after 14 months	Yes
17	3, M	Foramen magnum	No	Marhx-Bracho *et al*. 2007	10 m	GTR	No
18	12, M	3rd ventricle	No	Song *et al*. 2008	12 m	GTR	No
19	11, M	Lateral ventricle (trigonum)	No	Nambiar *et al*. 2012	6 m, 56 m	GTR, GTR and 3D RT	Yes
20	M, 11	3rd ventricle	No	Present case	22 m, 14 m	GTR 22 m, GTR 14 m	Yes

CM were positive for VIM (4). In their series, Cho *et al*. showed that neither one diagnosed chordoma nor all diagnosed CM were positive for S-100, whereas all CMs were negative for pan-CK (3). Huse *et al*. suggest D2-40 immunoreactivity as a useful marker when differentiating CM from chordoma (9). Later studies dealing with immunohistochemical differences between CM and chordoma

showed no significance in D2-40 positivity, and suggested further studies (3) (Table1).

To the best of our knowledge, 19 cases of CM in pediatric population are reported in the literature (Table 2) (16,17,22). The reported CMs were situated supratentorially. In two cases, tumors were reported intraventricularly, i.e. in the lateral ventricle (17) and third ventricle one each (22). The follow up ranged from 3 months to 5 years. There are four cases where tumors recurred after gross total resection. In twelve reported cases, tumors were not associated with systemic disease.

CONCLUSION

This is the second case of CM situated in the third ventricle, and 20th case of CM in the pediatric population. Presented symptoms were not specific and systemic disease was not diagnosed. The tumor was approached transcallosally and interforniceally, and completely removed. Twenty-two months after complete tumor resection, recurrence was confirmed (Fig. 4). Reoperation was performed in the same manner and the tumor was completely removed (Fig. 5).

Histologic and immunohistochemical results showed chordoid and meningeal formations that were GFAP, AC, CHG and HMB45 negative and positive for EMA, VIM, AE1/AE3 and D2-40. S-100 was positive on the first but negative on second analysis (Fig. 6). The first diagnosis was chordoma and the second one CM. Today, the patient attends regular school and is back to his everyday activities. Regular MRI and neurosurgical follow ups 14 months after the second surgery showed no signs of tumor recurrence.

REFERENCES

1. Antigüedad AR, Gómez M, Zarranz JJ. (Chordoma of the 3rd ventricle without extradural implantation.) Neurologia 1989; 4: 340-1. (Spa).
2. Chang SW, Gore PA, Nakaji P, Rekate HL. Juvenile intradural chordoma: case report. Neurosurgery 2008; 62: E525-6.
3. Cho HY, Lee M, Takei H, Dancer J, Ro JY, Zhai QJ. Immunohistochemical comparison of chordoma with chondrosarcoma, myxopapillary ependymoma, and chordoid meningioma. Appl Immunohistochem Mol Morphol 2009; 17: 131-8.
4. Couce ME, Aker FV, Scheithauer BW. Chordoid meningioma: a clinicopathologic study of 42 cases. Am J Surg Pathol 2000; 24: 899-905.
5. Epari S, Sharma MC, Sarkar C, Garg A, Gupta A, Mehta VS. Chordoid meningioma, an uncommon variant of meningioma: a clinicopathologic study of 12 cases. J Neurooncol 2006; 78: 263-9.
6. Fechner RE, Mills SE, ed. Atlas of Tumour Pathology Tumours of the Bones and Joints, 3rd series. Washington: Armed Forces Institute of Pathology, 1992.
7. Guidetti B, Delfini R, Gagliardi FM, Vagnozzi R. Meningiomas of the lateral ventricles. Clinical, neuroradiologic, and surgical considerations in 19 cases. Surg Neurol 1985; 24: 364-70.
8. Heffelfinger MJ, Dahlin DC, MacCarty CS, Beabout JW. Chordomas and cartilaginous tumors at the skull base. Cancer 1973; 32: 410-20.
9. Huse JT, Pasha TL, Zhang PJ. D2-40 functions as an effective chondroid marker distinguishing true chondroid tumors from chordoma. Acta Neuropathol 2007; 113: 87-96.
10. Ito E1, Saito K, Nagatani T. Intradural cranial chordoma. World Neurosurg 2010; 73: 194-7.
11. Jian BJ, Bloch OG, Yang I, Han SJ, Aranda D, Parsa AT. A comprehensive analysis of intracranial chordoma and survival: a systematic review. Br J Neurosurg 2011; 25: 446-53.
12. Katayama Y, Tsubokawa T, Hirasawa T, Takahata T, Nemoto N. Intradural extraosseous chordoma in the foramen magnum region. Case report. J Neurosurg 1991; 75: 976-9.
13. Kepes JJ, Chen WY, Connors MH, Vogel FS. "Chordoid" meningeal tumors in young individuals with peritumoral lymphoplasmacellular infiltrates causing systemic manifestations of the Castleman syndrome. A report of seven cases. Cancer 1988; 62: 391-406.
14. Kleihues P, Louis DN, Scheithauer BW. The WHO classification of tumors of the nervous system. J Neuropathol Exp Neurol 2002; 61: 215-25.
15. Koeller KK, Sandberg GD. From the archives of the AFIP. Cerebral intraventricular neoplasms: radiologic-pathologic correlation. Radiographics 2002; 22:1473-1505.
16, Marhx-Bracho A, Rueda-Franco F, Ibarra-de la Torre A *et al*. Chordoid meningioma of the foramen magnum in a child: a case report and review of the literature. Childs Nerv Syst 2008; 24: 623-7.
17. Nambiar A, Pillai A, Parmar C, Panikar D. Intraventricular chordoid meningioma in a child: fever of unknown origin, clinical course, and response to treatment. J Neurosurg Pediatr 2012; 10: 478-81.

18. Perry A, Louis DN, Scheithauer BW, Budka H, von Diemling A: Meningiomas. In: Louis DN, Ohgaki H, Wiestler OD, Cavenee WK, ed. World Health Organization Classification of Tumours of the Central Nervous System, 4th ed. Lyon: International Agency for Research on Cancer 2007, 164-172.

19. Ravindranath K, Vasudevan MC, Pande A, Symss N. Management of pediatric intracranial meningiomas: an analysis of 31 cases and review of literature. Childs Nerv Syst 2013; 29: 573-82.

20. Roberti F, Sekhar LN, Jones RV, Wright DC. Intradural cranial chordoma: a rare presentation of an uncommon tumor. Surgical experience and review of the literature. J Neurosurg 2007; 106: 270-4.

21. Rubinstein LJ. Tumors of the Central Nervous System. Atlas of Tumor Pathology, Series 2, Fascicle 6. Washington DC: Armed Forces Institute of Pathology, 1972.

22. Song KS, Park SH, Cho BK, Wang KC, Phi JH, Kim SK. Third ventricular chordoid meningioma in a child. J Neurosurg Pediatr 2008; 2: 269-72.

23. Zulck KJ. Brain Tumors: Their Biology and Pathology, ed 3. Berlin: Springer-Verlag, 1986.

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Hordoidni meningeom treće mozgovne klijetke ili hordom: dijagnostička dilema temeljena na jednom slučaju

SAŽETAK - Svrha ovoga rada je predstaviti slučaj i diferencijalnu dijagnostičku dilemu u djeteta s rijetkim tumorom histoloških karakteristika hordoma i hordoidnog meningeoma smještenog u trećoj mozgovnoj klijetki. *Opis slučaja:* Trinaestogodišnjem dječaku dijagnosiciran je recidivni intraventrikularni tumor 22 mjeseca nakon potpunog kirurškog uklanjanja. Indicirana je ponovna operacija te je učinjena ponovna histološka i imunohistokemijska analiza tumora, a bolesnik se nastavio redovno pratiti. Napravljen je pregled literature koristeći ključne riječi: MESH "Cerebral Ventricle Neoplasms" AND "Pediatrics". Histološka i imunohistokemijska analiza nakon prve operacije pokazala je hordom, a nakon druge histološke i dodatne imunohistokemijske analize koja je pokazala pozitivitet na D2-40 marker koji je negativan kod hordoma, a pozitivan kod hordoidnih meningeoma, zaključeno je da se radi o hordoidnom meningeomu. Četrnaest mjeseci nakon ponovljene operacije nije se pokazao recidiv tumora. Literaturni pregled pokazao je dva pedijatrijska slučaja intraventrikularnih hordoidnih meningeoma. Jedan od njih bio je smješten u lateralnoj, a drugi u trećoj mozgovnoj klijetki. *Zaključak:* Ovo je drugi prijavljeni slučaj hordoidnog meningeoma smještenog u trećoj mozgovnoj klijetki u pedijatrijskog bolesnika. U ovom slučaju bolesnik je redovito praćen 22 mjeseca nakon prve operacije i potpunog uklanjanja tumora kada je uočen recidiv tumora. Prva imunohistokemijska analiza pokazala je da se radi o hordomu, a druga je analiza pokazala da se radi o hordoidnom meningeomu. Četrnaest mjeseci nakon druge operacije nije došlo do recidiva. Dječak se vratio svojim svakodnevnim aktivnostima uz hormonsku nadomjesnu terapiju.

Ključne riječi: intraventrikularni meningeom, hordoidni meningeom, pedijatrija, hordom, imunohistokemija