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Intraoperative Anatomical Findings in Pediatric Clear Cell Meningioma of the Lumbar Spine: Case Report and Literature Review

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Abstract

Clear cell meningioma (CCM) is a WHO classification Grade II meningioma. It is a very rare disease, of which only 41 cases of spinal cord CCM in children have been reported to date. CCMs sometimes do not have the "dural attachment" that is usually found in meningiomas, and our understanding of the origin of CCMs is therefore controversial. We hereby present a case of pediatric CCM of the lumbar spine, in which we examined intraoperatively, the detailed anatomical location of the tumor. The case is a 10-year-old boy, who presented to our hospital with a 2-month history of lower back and bilateral lower extremity pain upon waking, which gradually worsened. Lumbar spine CT and MRI revealed an intradural extramedullary tumor at the L3 vertebral level, and surgery was performed to remove it. The tumor was in close contact with the dura mater, and also in contact with the cauda equina via the arachnoid. The tumor was likely located primarily between the dura mater and arachnoid. The pathological diagnosis was CCM, with an MIB-1 index of less than 1%. His back pain and bilateral lower extremity pain improved after surgery, and he was discharged from our hospital. Postoperative radiation therapy was not performed. Based on this case, we suggest that intraoperative examination of the anatomical location of these tumors and accumulation of relevant experience are important to elucidate the embryological mechanisms of this rare disease.

Keywords: clear cell meningioma, cauda equina, pediatric

Introduction

Clear cell meningioma (CCM) is a subtype of meningioma, with WHO classification of Grade II. It was first reported by Manivel and Sung as a glycogen-rich meningioma in 1990,[1)] and then reported by Scheithauer as CCM.[2)] The incidence is reported to be rare, ranging from 0.2% to 0.39% of all meningiomas. It occurs at a younger age than other meningiomas, is known to be more common in females, and is with a higher likelihood of recurrence in the angular part of the cerebellum and the cauda equina.[3,4)] Spinal cord CCMs in children are very rare, and to the best of our knowledge, there have been 41 cases of pediatric spinal CCM cases reported.[3,5–32)] Meningiomas, as a rule, adhere to the dura mater,[33,34)] but one of the characteristics of CCMs is that 15 cases have been reported at the moment in which there

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was no dural attachment.[3,5,6,10–14,16–18,25,29,30] There is therefore currently no settled opinion on the origin of these tumors,[13,33,35] and no report has ever reviewed the intraoperative findings in detail. In this study, we intraoperatively examined the detailed anatomical location of this tumor.

Case Report

Two months prior to coming to our hospital, a 10-year-old boy presented with low back and bilateral lower extremity pain on waking up, which gradually worsened. He was unable to bend forward or backward at the waist and the pain was noted to increase, especially at night and in the morning. At the first visit to our department, there was no obvious sensorimotor impairment and no bladder or rectal dysfunction. Lumbar spine CT showed high absorption at the L3 vertebral level (Fig. 1A), and lumbar MRI T1-weighted images showed faint high-signal (Fig. 1B) with low-signal on T2-weighted images with a clear hard border (Fig. 1C, 1E, and 1F), suggesting an intramembranous extramedullary tumor occupying the spinal canal and excluding the cauda equina ventrally (Fig. 1E and 1F). Contrast-enhanced MRI showed a uniform contrast effect within the tumor (Fig. 1D). There was no dural tail sign, and continuity between the dura mater and the tumor could not be determined from the images. Intracranial as well as cervical and thoracic spine MRI revealed no obvious lesions. The preoperative diagnosis was considered to be meningioma including CCM based on the CT and MRI features.

One week after admission, we performed surgery. After L3 laminectomy, median dural incision was performed, and the tumor was found to be in close contact with the left lateral side of the dura mater, with some areas encased by the arachnoid and others compressing and excluding the arachnoid (Fig. 2A and 2D). On the ventral side of the tumor, there was adhesion to one cauda equina, but through the arachnoid membrane and could therefore be bluntly dissected off (Fig. 2B and 2E). Although the site of origin could not be definitively determined, the tumor was most likely located primarily between the dura and arachnoid membrane. The tumor was slightly yellowish in color and hard, and was totally removed piece by piece (Fig. 2C). The tumor was fed from left lateral dural arteries. Dural coagulation was performed taking into consideration of the possibility of dural origin (Simpson Grade II).

Pathological analysis revealed substantial tumor cells with pale cytoplasm, classified as corded collagen fiber bundles (Supplementary Fig. 1A and 1B; Supplementary materials are available online). The mitotic findings of the tumor cells were unremarkable (0 cell/10 HPF) and there was no necrosis. Tumor cells were positive for PAS (Peridodic acid schiff) (Supplementary Fig. 1C) and negative for digestive PAS (Supplementary Fig. 1D), and immunostaining was positive for EMA (Supplementary Fig. 1E) and negative for GFAP (Glial fibrillary acidic protein). The patient was diagnosed with CCM, Grade II (WHO classification). The MIB-1 index was less than 1% (Supplementary Fig. 1F).

Postoperatively, his lumbar and bilateral leg pain improved, and he was discharged from our hospital 10 days after surgery, and MRI showed no residual disease. Since there is a high possibility of recurrence of the disease,[36] we plan to follow up with an outpatient MRI scan of the entire cerebrospinal axis. As the MIB-1 index was low, less than 1%, postoperative radiation therapy was not performed.

Discussion

Reported here is a case of pediatric CCM of the lumbar spine examined intraoperatively for the detailed anatomical location of the tumor. This revealed that the tumor was likely located primarily between the dura mater and arachnoid.

We summarized the pediatric spinal cord CCMs reported to date (Table 1). To the best of our knowledge, 42 pediatric (age <20 years) cases have been reported, including our case. The mean age was 9.3 years (Table 2). Thirty cases (71.4%) were female and 12 (28.6%) were male, with a male to female ratio of 2:5. With respect to the site of tumor occurrence, of the 45 tumors including two cases of multiple tumors,[5,14] 21 (46.7%) occurred in the lumbar spine. Lesions spanning more than three intervertebral spaces were found in 15 (33.3%) cases. Dural attachment was described in 29 cases, while 14 (48.3%) did not have dural attachment. Only one case was treated with adjuvant therapy after the first operation and radiation therapy was performed.[21] Postoperative follow-up was a median of 25 months (1–720 months). Of the 40 cases reporting the presence of recurrence, 13 (32.5%) had a postoperative recurrence. Although spinal CCMs, including adult cases, have been reviewed in recent years,[36] the results of the present case suggest that the trend was similar to the previous study, with respect to age, sex, and tumor location. The recurrence rate tended to be slightly higher in pediatric patients (32.5% vs. 23.8%). Some reports suggest that pediatric cases have shorter progression-free survival (PFS)[31] and are more likely to have high rates of recurrence. However, pediatric spinal cord CCM is extremely rare, with up to four cases reported so far in a single institution,[31,32] mostly accounted for

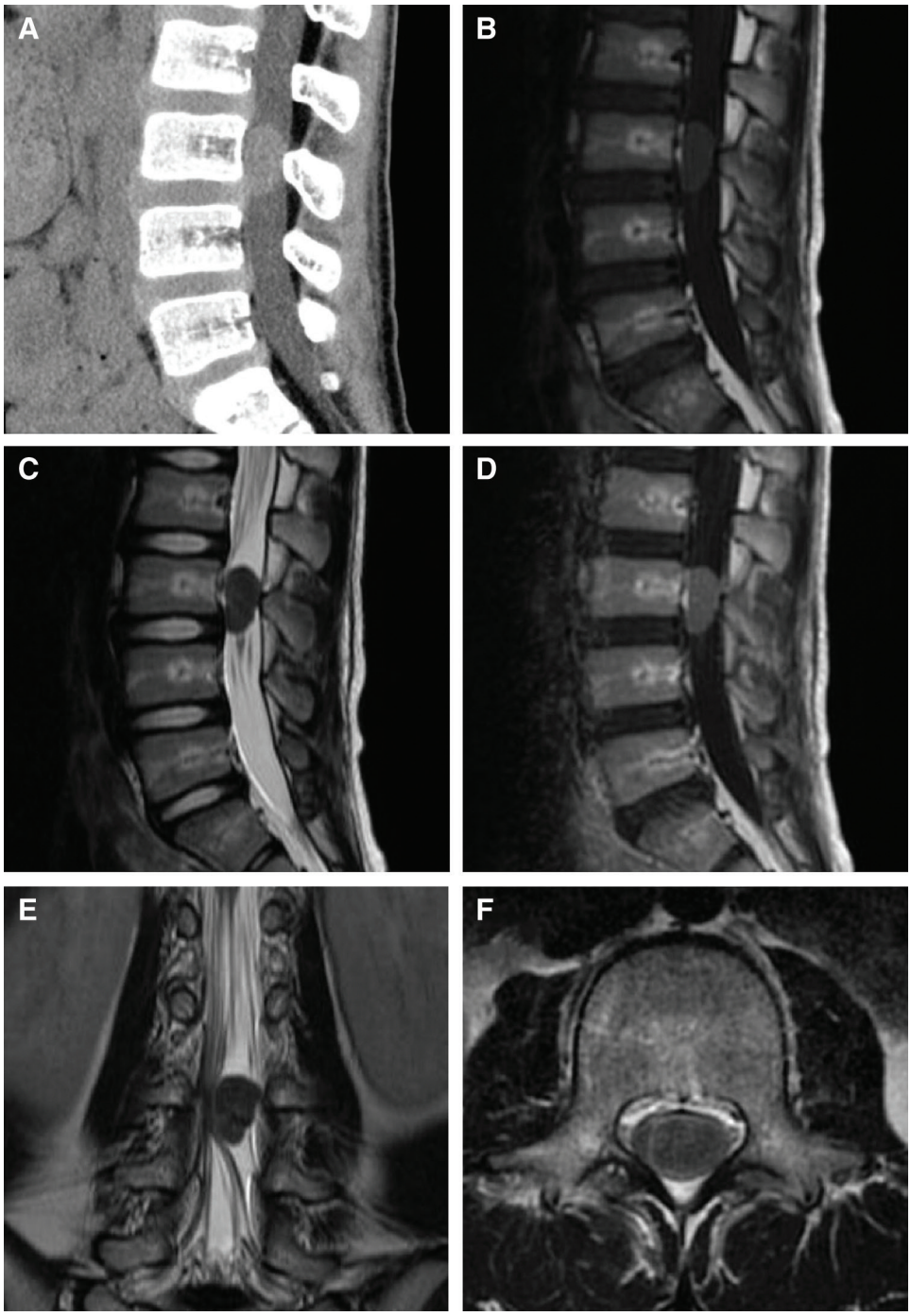

Fig. 1 Lumbar spine CT showed high absorption at the L3 vertebral level (A), and lumbar MRI T1-weighted images showed faint high signal (B) with low signal on T2-weighted images with a clear hard border (C, E, F), suggesting an intramembranous extramedullary tumor occupying the spinal canal and excluding the cauda equina ventrally (E, F). Contrast-enhanced MRI showed a uniform contrast effect within the tumor (D). There was no dural tail sign, and continuity between the dura mater and the tumor could not be determined from the images.

by single case reports, and its clinical characteristics and long-term outcome remain unknown.

Due to the rarity of cases, the diagnosis is not easy to perform. In general, the differential diagnosis of cauda equina tumors includes schwannoma, neurofibroma, myxopapillary ependymoma, metastatic medulloblastoma, neuroblastoma, and pineal tumors, in addition to other meningiomas.[8] Imaging

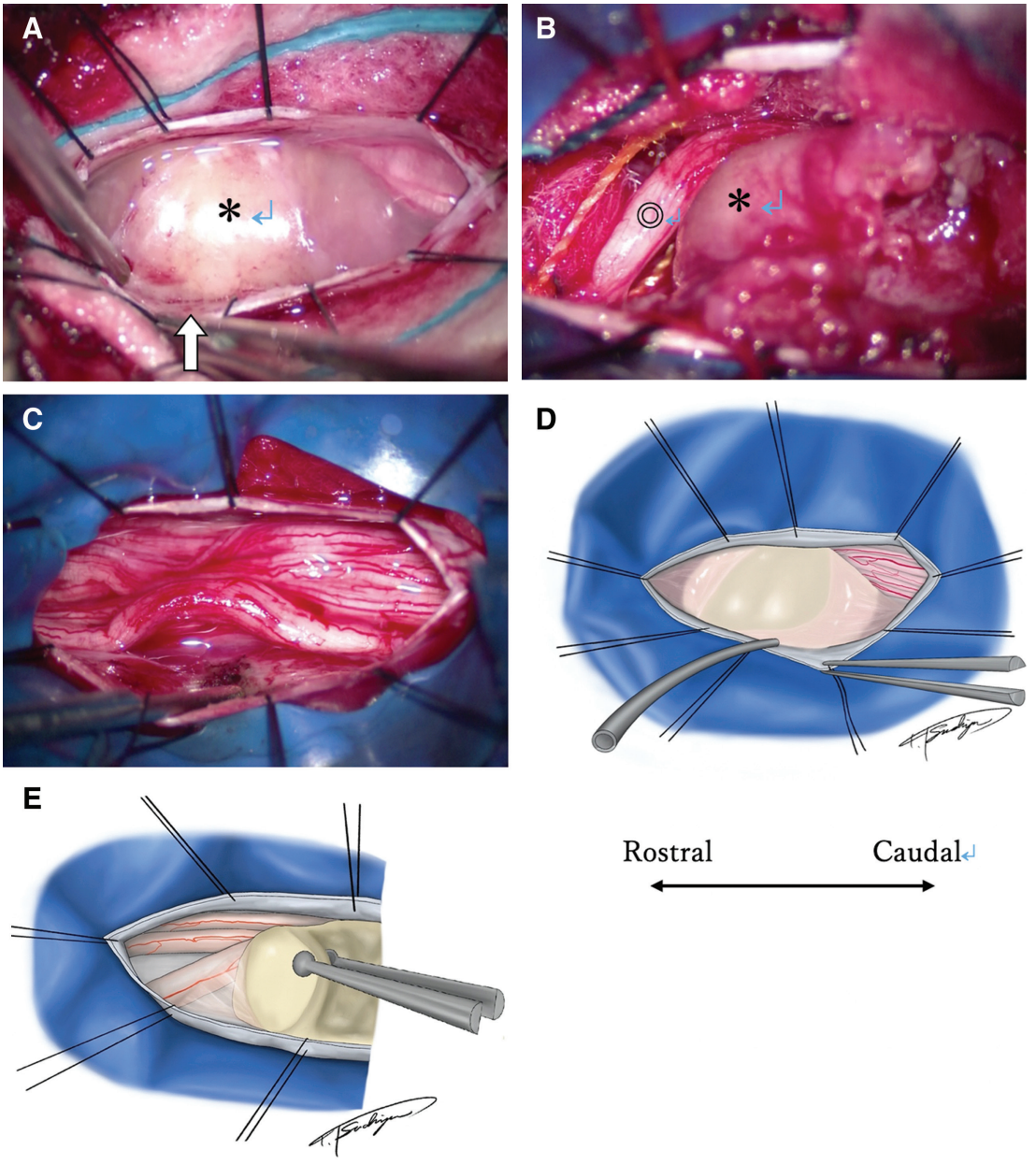

Fig. 2 After L3 laminectomy, median dural incision was performed, and the tumor was found to be in close contact with the left lateral side of the dura mater (arrow), with some areas encased by the arachnoid and others compressing and excluding the arachnoid (A, D). On the ventral side of the tumor, there was adhesion to one cauda equina, but through the arachnoid membrane and could therefore be bluntly dissected off (B, E). The tumor was slightly yellowish in color and hard, and was totally removed piece by piece (C). (*: tumor, ◎: nerve root).

findings for CCM include a signal that is grayish-white in both T1- and T2-weighted images. It is isotonic with respect to quality and is not different from conventional imaging features of meningiomas.[15,22,37] It also demonstrates a high absorption zone on CT.[23] Dural tail sign is not seen, in contrast to other meningiomas.[34,38] When a spinal cord tumor with these meningioma features is found, especially in young patients, the possibility of CCM should be kept in mind.[6,15]

CCMs have greater recurrences compared with other meningiomas and is a WHO classification Grade II.[3,36] The MIB-1 index for CCMs lies between Grades II and III meningiomas, and the high MIB-1 index may also explain the high recurrence rate of CCMs.[18] Although the MIB-1 index has been reported

Table 1 Clinical summary of 42 reported cases of pediatric spinal clear cell meningioma

First author, year [Ref.]	Age [years]	Sex	Tumor location	Operation	Dural attachment	Adjuvant therapy	MIB-1	Recurrence	Location	Treatment	Follow up (months)
Zorludemir, 1995 [3]	9	F	L3–5	GTR	Yes	No	NA	6 months	Same location	GTR	24
Zorludemir, 1995 [3]	17	F	L4–5	GTR	No	No	NA	No	–	–	36
Matsui, 1998 [5]	9	F	T11–12,L2,L4–5	PR	No	No	12%	4 months	T12, L5	Operation	16
Dubois, 1998 [6]	10	F	L1–4	GTR	No	No	NA	6 months	L1–2	Operation	6
Park, 2000 [7]	1 year 2 months	F	T12–L2	GTR	NA	No	3%–20%*	8 months	Cauda equina	GTR	8
Heth, 2000 [8]	7	F	L4–5	GTR	NA	No	NA	No	–	–	13
Shibayama, 2000 [9]	8	F	T10–12	GTR	Yes	NA	NA	NA	–	–	NA
Jallo, 2001 [10]	8	F	L3–4	GTR	No	No	NA	6 months	L3–5	GTR+RT	11
Jallo, 2001 [10]	1 year 10 months	F	C3–5	PR	No	No	NA	10 weeks, 5 months, 2 years	Same location, same location, CPA**	PR, GTR, GTR+RT+chemotherapy	38
Carra, 2001, 2003 [11,12]	1 year 10 months	M	T11–L4	GTR	No	No	NA	120 months	Vermis to C2	GTR	120
Douya, 2001 [13]	5	F	T11–L5	GTR	No	No	NA	No	–	–	72
Murakami, 2001 [14]	10	F	T12–L1,L2–3	GTR	No	No	NA	No	–	–	24
Yu, 2002 [15]	1 year 2 months	F	T12–L2	GTR	Yes	No	3%	8 months, 15 months	Same location	GTR, GTR+RT	15
Cho, 2003 [16]	17	F	S1	GTR	No	No	NA	NA	–	–	NA
Payano, 2004 [17]	19	F	L3	GTR	No	No	<1%	No	–	–	52
Oviedo, 2005 [18]	7	M	L2–3	GTR	No	No	10%	No	–	–	12
Liu, 2005 [19]	2	M	T10–11	GTR	Yes	No	NA	60 months	T12	NA	60
Vural, 2007 [20]	4	F	C1–2	GTR	NA	No	NA	No	–	–	6
Colen, 2009 [21]	13	F	L4–5	GTR	NA	Yes***	5%–7%	No	–	–	24
Balogun, 2013 [22]	3	M	L2–5	GTR	NA	No	5%–10%	9 months	L1–2	PR+RT	9
Wang, 2014 [23]	18	M	C6–T2	NA	NA	No	NA	19 months, 31 months, 40 months	NA	GTR, GTR, GTR+RT	NA
Evans, 2015 [24]	3	M	L1–2	GTR	NA	No	20%	No	–	–	18
Li, 2016 [25]	7	F	T11–L1	GTR	Yes	No	20%	No	–	–	9

Table 1 Continued

First author, year [Ref.]	Age [years]	Sex	Tumor location	Operation	Dural attachment	Adjuvant therapy	MIB-1	Recurrence	Location	Treatment	Follow up (months)
Li, 2016 [25]	7	F	L2–4	GTR	No	No	10%	No	–	–	24
Li, 2016 [25]	4	M	T11–12	GTR	Yes	No	NA	No	–	–	24
Smith, 2017 [26]	19	F	T12	GTR	NA	No	NA	No	–	–	25
Smith, 2017 [26]	10	F	L1–2	GTR	NA	No	NA	No	–	–	16
Wu, 2017 [27]	14	M	C1–2	GTR	NA	No	NA	No	–	–	144
Wu, 2017 [27]	7	F	L2–4	GTR	NA	No	NA	No	–	–	48
Wu, 2017 [27]	16	F	T6–7	GTR	NA	No	NA	No	–	–	54
Tauziede-Espariat, 2018 [28]	13	F	C4–5	GTR	NA	No	NA	No	–	–	720
Kawasaki, 2020 [29]	8	F	L3	GTR	No	No	26%	No	–	–	26
Inoue, 2018 [30]	5	M	L5–S1	GTR	No	No	3%	No	–	–	96
Li, 2019 [31]	15	F	L3	GTR	Yes	No	NA	No	–	–	16
Li, 2019 [31]	16	M	L5–S1	GTR	Yes	No	NA	No	–	–	93
Li, 2019 [31]	16	F	T12–L1	PR	Yes	No	NA	120 months	NA	Operation	192
Li, 2019 [31]	14	F	L4	PR	Yes	No	NA	24 months	NA	Operation	56
Wu, 2019 [32]	7	F	T11–L1	GTR	Yes	No	NA	No	–	–	46
Wu, 2019 [32]	7	F	L2–4	GTR	Yes	No	NA	No	–	–	36
Wu, 2019 [32]	4	M	T11–12	GTR	Yes	No	NA	No	–	–	70
Wu, 2019 [32]	16	F	T12–L1	GTR	Yes	No	NA	No	–	–	126
Present report	10	M	L3	GTR	Yes	No	<1%	No	–	–	1

*MIB-1 index at first and recurrence.
**The third recurrence occurred in the left cerebellopontine angle.
***Radiotherapy was performed after the initial surgery.

Table 2 Summary of characteristics in 42 patients with pediatric spinal clear cell meningioma

Total number of patients	42
Age (years), mean (range)	9.3 (1.2–19)
Sex	
Female	30 (71.4%)
Male	12 (28.6%)
Tumor location	
Cervical	4 (8.9%)
Cervicothoracic	1 (2.2%)
Thoracic	7 (15.6%)
Thoracolumbar	9 (20.0%)
Lumbar	21 (46.7%)
Lumbosacral	2 (4.4%)
Sacral	1 (2.2%)
Number of involved segments	
1–2	30 (66.7%)
≥3	15 (33.3%)
Dural attachment	
Yes	15 (35.7%)
No	14 (31.1%)
NA	13 (28.9%)
Extent of resection	
GTR	37 (88.1%)
PR	4 (9.5%)
NA	1 (2.4%)
Adjuvant therapy	
Yes	1 (2.4%)
No	40 (95.2)
NA	1 (2.4%)
Follow-up (months), median (range)	25 (1–720)
Recurrence	
Yes	13
No	27
NA	2

to be significantly higher in recurrent tumors,[3,39] some reports have found no significant effect on PFS time[25]; so the association between MIB-1 index and recurrence is currently unclear.[22] Some case reports did not mention MIB-1 index; so factors contributing to CCM recurrence are largely unclear, although partial resection has been reported to increase recurrence.[4,36] Therefore, total removal is recommended. En bloc resection seems to have low risk of recurrence, but for preventing nerve damage, piece by piece resection becomes an option. In our case, we totally removed tumor piece by piece, using gauzes to avoid local dissemination. Further, the presence of dural attachment has been suggested to have no relation to PFS.[36]

Recurrence after CCM surgery is known to cause not only local recurrence in the spinal cord, but also metastasis to the brain[3,10,11]; so postoperative MRI should include the brain as well as the entire spine.[6,11,19] There is also a need for imaging follow-up every 3–6 months long term.[11,19] Although there is no consensus on the pros and cons of radiotherapy after total tumor removal,[22] one case of adjunctive local radiotherapy has been reported to date after surgery for pediatric spinal CCM.[21] In children, the risk of radiation therapy is high, including radiation-induced myelopathy and vertebral radiation necrosis with spinal cord dislocation. Therefore, radiation therapy should only be considered if surgery fails to completely remove the tumor or after a recurrence.[6] The same is true for chemotherapy in terms of pediatric tolerability.[7] For local recurrent tumors, we support local radiation therapy after reoperation as in the previous reports.[10,22]

In general, meningiomas are tumors that arise from arachnoid superficial cells and are most commonly at the intracranial and spinal level, with those occurring in the cauda equina being rare.[3] Meningiomas generally adhere to the dura mater,[33,34] but cases of CCM not attached to the dura have been reported.[3,5,6,10–14,16–18,25,29,30] In such cases, the tumor is often attached to the nerve root. Lee et al. reported that 15 (83.3%) of 18 cases of spinal meningiomas did not have a dural attachment,[34] and lack of dural attachment is characteristic of this disease. A case of deep sylvian meningioma without dural attachment is also reported recently.[40] Theories regarding the origin of this tumor include the theory that it has a malignant nature,[13] a secondary tumor attached to the nerve root after loss of dural adhesions,[16] Schwann cells differentiation into spinal fluid histiocytes,[33] and the theory that it occurs from a pia matter[35]; but, there is no settled opinion. In our case, the tumor was found to have dural attachments, and the tumor was in contact with the roots through the arachnoid. Based on these intraoperative findings, the site of origin could not be determined, but the tumor was considered to be located mainly between the dura mater and arachnoid. Intraoperative images of pediatric spinal CCMs have been reported only in a limited number of cases,[16,20,29,30] and this is the first report to provide a detailed review of intraoperative findings. In order to identify the origin, dural incision and arachnoid incision should be performed separately; otherwise the

location of the tumor becomes ambiguous. It is also important to observe whether there are any adhesions to surrounding structures, like cauda equina. In our case, we could not identify the origin of the tumor; however, we believe that examining the anatomical location of tumors based on intraoperative findings as we have done, and accumulating experience, is important in elucidating the mechanism of development of this rare disease.

Conclusion

CCM in children is rare and have a characteristic high risk of recurrence, with frequent occurrence in cauda equina. Important aspects of management include total resection, as well as frequent follow-up postoperative spinal and brain MRIs. As the origin of these tumors is currently unclear, intraoperative anatomical findings are important and may contribute to better understanding of their developmental mechanisms.

Conflicts of Interest Disclosure

There are no conflicts of interest.

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