



## Case Report



# Clear Cell Meningioma: A Rare Great Mimicker

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### Abstract

**Introduction:** Clear cell meningioma is an infrequent, aggressive variant of meningioma that shows proclivity to the spine. This study aimed to report a case of clear cell meningioma of the lumbar spine and discuss the differential diagnosis, and emphasize the necessity and usefulness of immunohistochemistry for definite diagnosis.

**Case report:** A 23-year-old man admitted to the Department of Neurosurgery with backache existed for about 4 years. Magnetic Resonance Imaging revealed a well-circumscribed intradural and extramedullary mass in the spinal canal at the 5th lumbar vertebra extending to the right neural foramen. The lesion was excised gross totally and diagnosed as “clear cell meningioma”. The patient has been doing well for a year without any sign of recurrence.

**Discussion:** Clear cell meningioma should be considered in the differential diagnosis of the masses located in the spine radiologically. In addition, the histopathological mimickers of it that are composed of clear cells, particularly renal cell carcinoma, should be ruled out by the aid of immunohistochemistry.

**Keywords:** Clear cell meningioma; Differential diagnosis; Immunohistochemistry; Spine tumor

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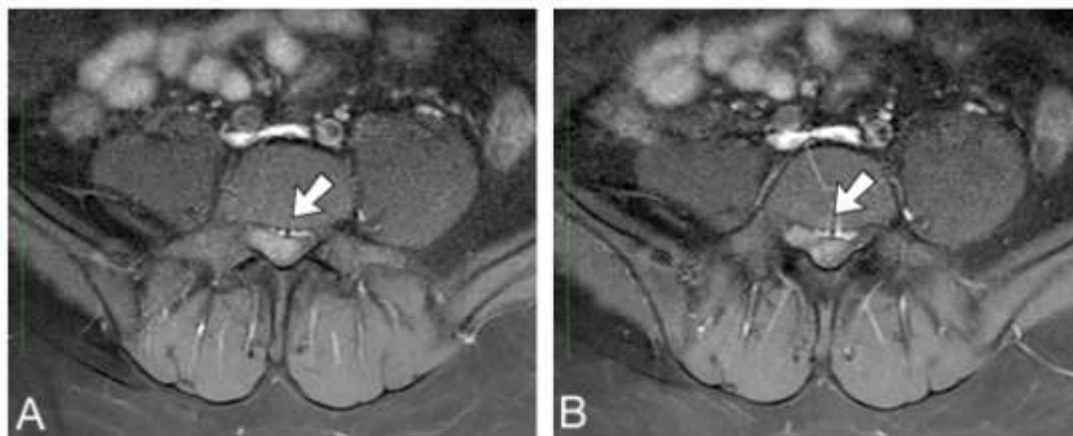
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## Introduction

Meningiomas are the neoplasms originated from meningotheial [arachnoidal] cells that account for only about 1-2% of all brain tumors [1-4]. Most of them are benign and correspond to grade I according to the current World Health Organization [WHO] grade II 2007 Classification [1]. However, a subset of meningiomas are designated as WHO grade II and III due to their increased risk of a recurrence and poor outcome [1]. Herein, we report a clear cell meningioma [CCM]-an infrequent variant of WHO grade II meningioma- of a 23-year-old male located in the spine at the level of 5th lumbar vertebra. Our goals are to emphasize the difficulty in the differential diagnosis of CCM histopathologically, including frozen section, and to underline the utility of immunohistochemistry for exact diagnosis. We suggest that this case report may contribute to a better understanding of this rare unique entity.

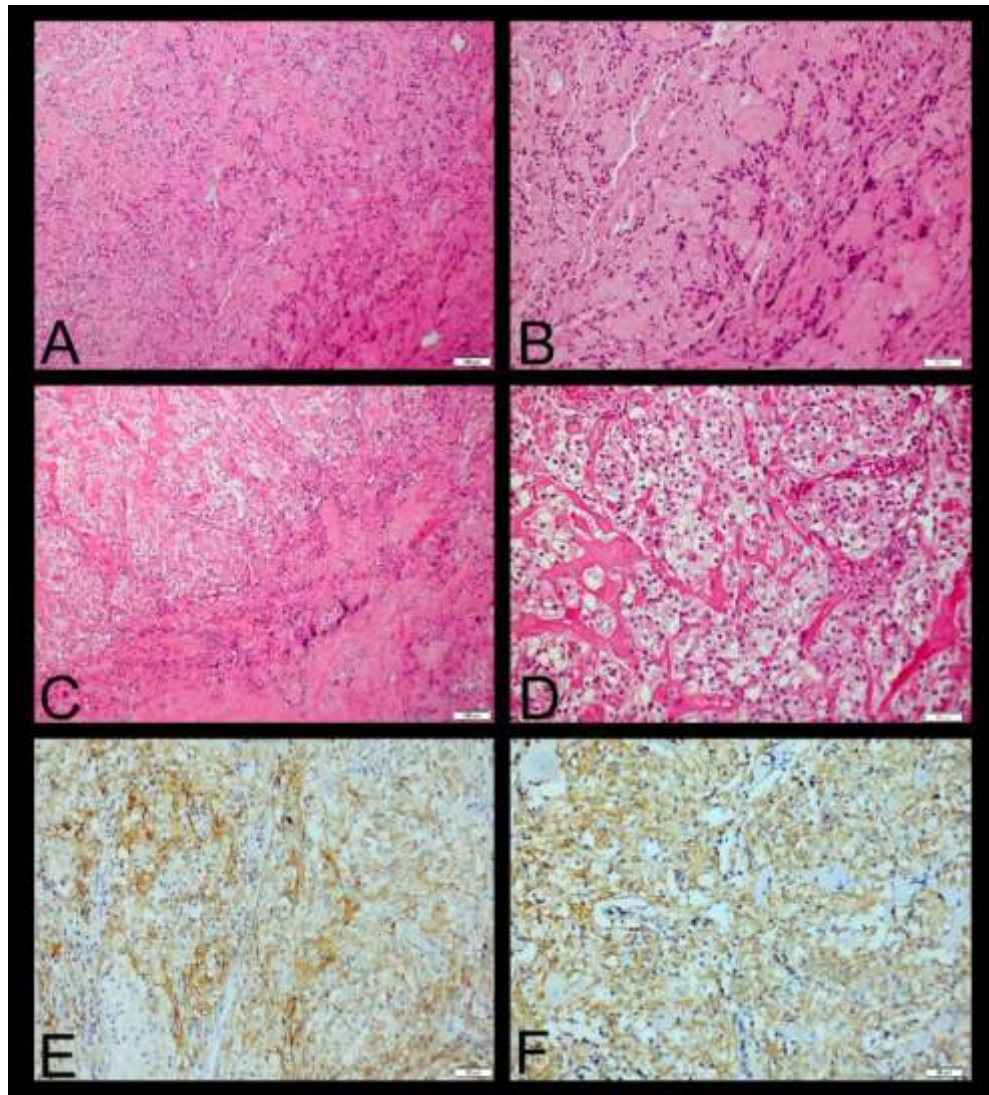
## Case Presentation



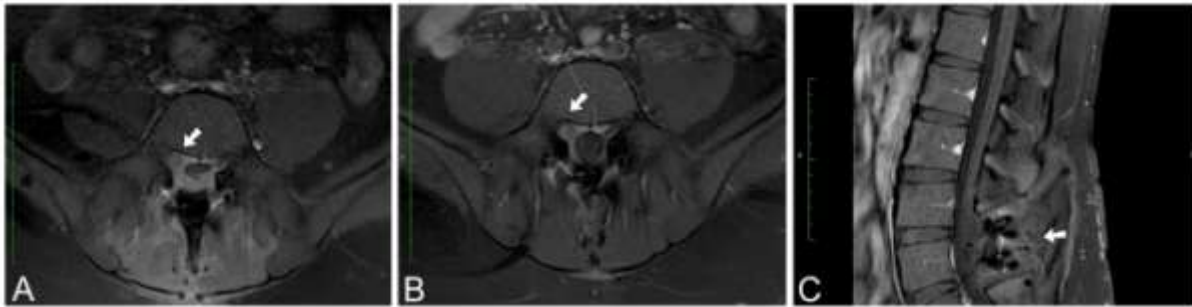
**Figure 1** Preoperative MRI images. **A-B.** Axial sections of the T1-weighted fat-suppression contrast-enhanced MRI showing bilobulated tumor extending to the neural foramen [arrows].

The patient was admitted to the Department of Neurosurgery of our institute with backache existed for about 4 years. Magnetic Resonance Imaging [MRI] revealed a well-circumscribed intradural and extramedullary mass in the spinal canal at the 5th lumbar vertebra extending to the right neural foramen [Figure 1A-1B]. It was stated that the radiological findings were suggestive of meningioma according to the characteristics of the signal, whereas neural sheath tumors could not be discriminated due to the bilobulated contour and the presence of a part extending to the neural foramen of the lesion. The lesion was excised gross totally, sparing the part extending to the neural foramen in order to protect the neural tract. The residual lesion was cauterised. Peroperatively, the lesion was submitted for frozen section. Macroscopically, it was a nodular lesion of 1.4x1.1x0.8 cm with a fibrous capsule around. At frozen section, about 1.4x1.1x0.4 cm [nearly half of the lesion] of the biopsy was sampled and evaluated. A neoplasm composed of mostly spindle cells showing no sign of malignancy in a collagenous background containing rich vascular network was detected, microscopically [Figure 2A-2B]. It was diagnosed as “suggestive of schwannoma or fibrous meningioma” at frozen section. Then, the entire lesion was processed for the paraffin section. Surprisingly, extensive solid sheets of polygonal cells with clear cytoplasm accompanying spindle cell component were detected in permanent sections [Figure 2C-2D]. Prominent perivascular and interstitial hyalinization were present [Figure 2A-2D]. Whorl formation and psammoma bodies were absent.

Immunohistochemically, positivity for epithelial membrane antigen [EMA] [Figure 2E], vimentin [Figure 2F], and progesterone receptor [PR]; negativity for renal cell carcinoma [RCC], CD10, glial fibrillary acidic protein [GFAP], S100, pancytokeratin, chromogranin, synaptophysin, and monoclonal carcinoembryonic antigen [mCEA] were detected in the tumor cells. Ki-67 proliferation index was around 1-2%. Then, the permanent sections of the mass was diagnosed as “CCM, WHO grade II”. The patient was discharged uneventfully two-day after the operation. Postoperative MRI revealed a residual tumor of 0.82 cm [Figure 3A]. The patient has been under regular follow-up for a year. At the last consultation, he was asymptomatic. MRI showed the residual tumor was persistent without any increase in diameter [Figure 3B]. In addition, there was not any sign of recurrence [Figure 3C].



**Figure 2** The microscopic photos of the tumor. **A-B.** The frozen sections composed of spindle or ovoid cells in a collagenous background, [Hematoxylin&eosin stain, x100, x200, respectively]. **C-D.** The permanent sections of the tumor illustrating extensive solid sheets of polygonal cells with clear cytoplasm accompanying spindle cell component in a hyalinized stroma, [Hematoxylin&eosin stain, x100, x200, respectively]. **E-F.** Positivity for EMA and vimentin of the tumor cells by immunohistochemistry, respectively, [Streptavidin-Biotin-Peroxidase method, x200, each].



**Figure 3** Postoperative T1-weighted fat-suppression contrast-enhanced MRI images. **A-B.** Axial sections of the persistent residual tumor [*arrows*] at 40th postoperative day and one-year after the surgery, respectively, without any discernible increase in size. **C.** Sagittal section of the spine at postoperative one year showing no sign of intradural or intramedullary recurrence.

## Discussion

CCM is a rare subtype of meningioma, constituting 0.2% of all intracranial meningiomas [5]. In the literature, lesser than 100 CCMs have been reported, to the best of our knowledge [2-3, 5-11]. It usually shows propensity for the cerebellopontine angle and spinal cord [48%, intradural], particularly cauda equina region [6]. The radiological findings of CCM are mostly similar to those of conventional meningiomas [7]. However, it should be considered that nondural-based or paraneural tumors may not be infrequent [7]. CCM tends to affect younger patients [usually in 1st to 3rd decades] [5-6], similar to our case. CCM has been reported to arise in female patients predominantly, in opposite to our patient [5-6].

CCM have been described initially as a distinct variant of grade I meningioma in the WHO classification in 1993 due to its bland histological findings [5, 8]. However, CCM is considered as WHO grade II in the current classification because of its aggressive clinical course, including high propensity for recurrence and occasional cerebrospinal fluid [CSF] seeding [5, 8]. The histological subtype, tumor grade, mitotic-count, PR status, Ki-67 proliferation index, brain invasion, some cytogenetic features and the extent of surgical extension are the well-known prognostic parameters for meningioma [1, 6]. The mean value of 7.4% for Ki-67 was suggested in nonrecurring CCMs, and that of 13.3% was proposed in recurring CCMs, in the literature [2]. Zorludemir et al. reported high Ki-67 proliferation index [range: 3.3-25.7%, mean: 13.3%] with 61% overall recurrence, 7.1% CSF seeding, 15% local discontinuous spread, 8% widespread cranial to spinal metastasis and 23% mortality rate as in their series of 14 cases of CCM followed-up for more than 5 years [9]. Lee et al. detected that the recurrence rate of spinal CCMs was lower than the intracranial CCMs as 46% [6/13 cases], and 80% [8/10 cases], respectively [7]. The Ki-67 proliferation index was low [1-2%] in our case, implying lower risk of recurrence. Lee et al. observed extensive contrast enhancement of the entire cisternal spaces on MRI and found gelatinous material during lumbar surgery of their case of CCM [7]. Then, they claimed that those findings should be considered as indicative of extensive CSF dissemination [7]. Any signs about CSF seeding mentioned by them were not determined neither preoperatively nor intraoperatively/postoperatively in our case.

Histopathologically, CCMs are composed of indolent polygonal cells with clear cytoplasm due to PAS-positive, diastase-digestible glycogen accumulation [7-9]. There is no precise guideline that describe the required extent of clear cells in the tumor in order to diagnose it as CCM, in the literature. Therefore, it is reasonable that recording the proportion of clear cell component in the pathology report might be important for the data collection about it. Among the clear tumor cells, prominent interstitial and

perivascular hyalinization, thick brightly eosinophilic collagen bundles, even confluent collagenization are often detected in CCMs [9]. In addition, the characteristic findings of meningiomas, such as whorling of cells and psammoma bodies, are usually absent or obscure in the vast majority of CCMs that cause difficulty in the differential diagnosis, similar to our case [9]. We suggest that the evaluation of the tumor, especially the periphery of it, in order to find out the vague conventional meningioma pattern accompanying the striking clear cell component microscopically is crucial to render its diagnosis. On the other hand, it should be taken into account that CCMs might be misinterpreted as spindle cell tumors [fibrous meningioma, neurofibroma or schwannoma, etc.] due to the dominance of collagen-rich stroma, freezing artifact, collagenous spindle cells, and the absence of abundant clear cells, psammoma bodies and characteristic whorls, similar to our frozen sections. This result may be attributed to the limited facility of frozen section for exact diagnosis as well as the haphazard fashion of the histological characteristics of CCM. The permanent sections and immunohistochemical studies are useful to discriminate the diagnostic mimickers.

Meningiomas typically show diffuse and strong positivity for vimentin [1]. EMA is positive in many meningiomas and may be considered the most reliable marker for meningioma [1]. Whereas, it should be noted that the staining pattern is usually focal and weak [1]. Positivity for PR, S-100 and claudin-1 have been documented in some studies [1]. Meningiomas do not express CEA and cytokeratin except secretory meningiomas [1]. Prior to the description of CCM as a distinct subtype of meningioma and the widespread use of immunohistochemistry in pathology practice, CCM was traditionally misdiagnosed as renal cell carcinoma, hemangioblastoma, oligodendroglioma, and clear cell ependymoma histopathologically, due to their content of clear cells [6, 10]. Renal cell carcinoma might be distinguished from CCM by the immunoreactivity for cytokeratin, CD10, and RCC, and negativity for PR [9, 11]. Lack of GFAP positivity in meningiomas may aid to exclude glial tumor [12]. Immunoreactivity for neural markers and negativity for EMA in haemangioblastoma might differ it from CCM [1]. Thus, we suggest that the tumors with clear cell morphology both primary and metastatic tumors should be ruled out by characteristic immunohistochemical findings, as in our case.

The main therapeutic approach for CCM is maximal surgical excision [7]. Radiosurgery, radiotherapy, and chemotherapy are the other choices of treatment in residual or recurring cases [2, 6, 7]. Radiotherapy is the only alternative option when excision is impossible [6].

## Conclusion

In summary, CCM is a rare histological subtype of WHO grade II meningiomas. It shows a higher rate of recurrence than conventional meningiomas, despite its indolent histopathological features. Thus, close and long-term follow-up is mandatory to determine the natural outcome of the patients with this rare entity. In addition, it should be considered that CCM may cause some histopathological difficulties in discriminating some other tumors mentioned before that are composed of spindle cells and/or particularly clear cells due to their similar histopathological appearances. Therefore, performing immunohistochemistry is crucial in order to exclude the mimickers of CCM that have different biological behaviour, clinical course and treatment protocols.

## References

1. Louis DN, Ohgaki H, Wiestler OD, Cavenee WK, Burger PC, Jouvet A. The 2007 WHO classification of tumours of the central nervous system. *Acta Neuropathol.* 2007, 114(2):97-109

2. Ranjan R, Sethuraman S. Supratentorial clear cell meningioma in a child: A rare tumor at unusual location. *J Pediatr Neurosci.* 2010, 5:141-143
3. Colen CB, Rayes M, McClenden J, Rabah R, Ham SD. Pediatric spinal clear cell meningioma case report. *J Neurosurg Pediatr.* 2009, 3:57-60
4. Germano IM, Edwards MS, Davis RL, Schiffer D. Intracranial meningiomas of the first two decades of life. *J Neurosurg.* 1994, 80:447-453
5. Yin S, Zhou P, Li Q, Jiang S. Intrasellar clear cell meningioma mimicking invasive pituitary adenoma: Case Report and Review of the Literature. *Turk Neurosurg.* 2015, 25:976-979
6. Kumar R, Das KK, Jaiswal AK, Mehrotra A, Sahu RN, Srivastava AK, Jaiswal S, Behari S. Clear cell meningioma in a child: A case report and review of literature. *Asian J Neurosurg.* 2015, 10:53
7. Lee W, Chang KH, Choe G, Chi JG, Chung CK, Kim IH, Han MH, Park SW, Shin SJ, Koh YH. MR imaging features of clear-cell meningioma with diffuse leptomeningeal seeding. *Am J Neuroradiol.* 2000, 21:130-132
8. Ide M, Yamamoto M, Hagiwara S, Tanaka N, Kawamura H. Rapid regrowth of intracranial clear cell meningioma after craniotomy and gamma knife radiosurgery-case report. *Neurol Med Chir.* 2004, 44:321-325
9. Zorludemir S, Scheithauer BW, Hirose T, Van Houten C, Miller G, Meyer FB. Clear cell meningioma. A clinicopathologic study of a potentially aggressive variant of meningioma. *Am J Surg Pathol.* 1995, 19:493-505
10. Deb P, Datta SG. An unusual case of clear cell meningioma. *J Cancer Res Ther.* 2009, 5:324-327
11. Benchetritt M, Hofman V, Long E, Odin G, Basc E, Pasquier B, Pedeutour F, Hofman P. Primary clear cell meningioma of the orbit mimicking a metastatic carcinoma: usefulness of immunohistochemistry and cytogenetic analysis. *Virchows Arch.* 2008, 452:209-213
12. Meis JM, Ordóñez NG, Bruner JM. Meningiomas. An immunohistochemical study of 50 cases. *Arch Pathol Lab Med.* 1986, 110:934-937