Spinal intradural clear cell meningioma following resection of a suprasellar clear cell meningioma

Case report and recommendations for management

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The authors report on a 32-year-old woman with a history of a previously resected suprasellar clear cell meningioma (CCM), who returned to their institution after 3 years suffering from progressively worsening leg and back pain associated with leg weakness and bowel and bladder dysfunction. A magnetic resonance imaging of the thoracic and lumbar spine demonstrated a homogeneously enhancing intradural mass that filled and expanded the thecal sac. The patient underwent multiple-level laminectomies for resection of the lesion. Results of pathological studies confirmed distant recurrence of a CCM.

Since its initial recognition as a rare but aggressive histological variant of meningothelial tumors, the body of literature on CCMs has grown to include more than 40 cases. Nevertheless, the natural history of this neoplastic entity remains ill defined, as are the recommendations for management. Of particular concern is the treatment of patients who have undergone subtotal resection or present with recurrence. To the authors’ knowledge, the present case represents the sixth distant recurrence of CCM reported in the literature. The radiographic and histological studies are reviewed along with the current literature on this subtype of meningioma. Recommendations for surveillance and treatment are made.

KEY WORDS • spinal tumor • clear cell meningioma • intradural mass • recurrence • laminectomy • radiation

CLEAR cell meningiomas are one of the rarest and most aggressive neoplasms among the tumors of meningothelial origin recognized by the WHO. Initially classified as a Grade I lesion by the WHO because of its innocuously bland histological appearance, the high rates of local recurrence (42–80%) and inordinately aggressive clinical course have prompted a change in classification to Grade II. Despite the 48 cases reported in the literature, the full spectrum of clinical behavior in CCMs remains ill defined and the mechanisms underlying the higher rates of recurrence are not presently known. To the body of literature, which reveals an uncertain malignant potential in CCMs, we add the present case of a suprasellar CCM that recurred after 3 years as a large spinal tumor that filled and eroded the lumbar and sacral thecal sac. To our knowledge, this is the sixth reported case of a distant recurrence of CCM.

Case Report

History. This 32-year-old woman suffered headaches and blurred vision over the course of 3 months. Magnetic resonance imaging studies demonstrated a large, enhancing suprasellar mass with multiple cystic components. The tumor impinged on the optic chiasm superiorly and extended posteriorly and inferiorly into the posterior fossa, where it compressed the right side of the pons (Fig. 1). The patient underwent a right frontotemporal orbitozygomatic craniotomy for resection of this suprasellar mass in the cavernous sinus and posterior fossa. Subsequent histological diagnosis confirmed CCM. A postoperative MR image obtained 12 months later revealed no residual tumor. The entire neuraxis was not imaged at this time. The patient received no form of adjuvant therapy.

Examination. Three years after her initial operation, the patient experienced progressively worsening back and leg pain, lower-extremity weakness, and bowel and bladder dysfunction. She required a wheelchair and could not walk without assistance. Results of MR imaging of the thoracic and lumbar spine revealed a homogeneously enhancing in-
tradural mass that filled and expanded the thecal sac, extending from the T-12 to the S-1 level (Fig. 2).

**Operation.** The patient was taken to surgery and laminectomies from T-12 to S-1 were performed in the standard fashion. At the superior aspect of the wound, the dura mater was intact but markedly distended from the intradural lesion. Beginning from the midlumbar region, the tumor had actually eroded through the dura and, in fact, there was no competent dura along the dorsal aspect of the thecal sac from the midlumbar region to the sacrum. After initial dissection, the superior and inferior poles of the tumor were identified. The tumor was internally decompressed using an ultrasonic aspirator and bipolar coagulation. Using microsurgical techniques the tumor was freed from adjacent nerve roots. Once a gross-total resection was achieved, a duraplasty was performed using bovine pericardium and Tisseal. Based on a pathological examination, we established the diagnosis of CCM with histological features identical to the patient’s initial intracranial lesion. No histological evidence of malignant transformation was noted (Fig. 3).

**Postoperative Course.** The patient had an uneventful hospital stay and was discharged to a rehabilitation facility. She ambulates with the assistance of a walker and requires the use of ankle-foot orthotics for a significant weakness in her bilateral dorsiflexion. She has regained the use of her bowel and bladder. Her most recent MR imaging studies, obtained 11 months postoperatively, reveal no evidence of tumor recurrence (Fig. 4 left). Similarly, a contrast-enhanced MR image of the brain obtained approximately 4 years postoperatively demonstrates no evidence of tumor (Fig. 4 right).

**Discussion**

In 1993 the WHO recognized CCM as one of the 13 histological subtypes of meningioma. Since its initial description, 49 cases, including this report, now make up the current body of literature on CCM. From these data, the epidemiological factors and natural history of this tumor are becoming evident. Obvious is the high rate of local recurrence in these lesions, but given that this report represents only the sixth case of a distant recurrence, the capacity of CCM to metastasize remains uncertain. In light of this circumstance, routine surveillance of the entire neuraxis is imperative. Also clearly established in the literature is the efficacy of gross-total resection, but less so is the role of radiotherapy in recurrence or subtotal resection. The collective experience in the treatment of recurrence and subtotal resection is reviewed to define this treatment modality further.

Clear cell meningioma is perhaps the rarest of the tumors of meningothelial origin. In the largest current series, the authors report that CCM accounts for 0.2% of all meningiomas. The mean age in the literature to date is 29 years, although both pediatric and elderly patients are represented among the reported cases (2–82 years). There appears to be a slight female predominance (female/male 1.25). Clear cell meningiomas have been reported at all levels of the neuraxis with almost equal frequency—that is, 25 within the cranial and 23 in the spinal column—which appears to dispute the previously reported predilection for the spinal column. In addition to the typical locations expected for meningiomas, CCMs have also been found in the brainstem parenchyma, fourth ventricle, cauda equina, and even sacrococcygeal tissues. The imaging features of CCM are no different from those of conventional meningiomas. They are most often extraaxial, isointense to brain parenchyma on both T1- and T2-weighted MR images, and demonstrate fairly homogeneous enhancement.Investigators have reviewed the radiographic aspects of reported primary CCM and found no unique identifying features when compared with conventional meningiomas. The absence of characteristic findings on imaging studies makes histological diagnosis imperative. Non-
Spinal intradural clear cell meningioma

operative management and observation have no role in the treatment of CCM.

From a histopathological perspective, CCMs have a unique and consistent appearance. They have moderate cellularity with a sheetlike or lobulated growth pattern. The heavy glycogen content within individual cells gives this tumor its defining characteristic, specifically the clear appearance of its cells on histological study (Fig. 3). Nuclei are round and bland, with inconspicuous nucleoli, and lack any appreciable mitotic activity. Separating tumor cell clusters is a distinctive hyalinized stroma that are often arranged in spherical configurations with central, punctate crystalline deposits. The appearance of the stroma together with inter-vining clear, bland tumor cells forms a histological picture that is memorable, yet not classically meningothelial (Fig. 3). Only occasionally will tumor cells show a tendency toward whorl formation, and psammoma bodies are not typical. Classic cytological features of meningiomas, including whorls, wispy cytoplasm, and dispersed, delicate chromatin within ovoid nuclei, appear more clearly on smear preparations. The high degree of tumor hyalinization, modest cellularity, bland cytological features, and lack of mitotic activity collectively make it surprising that CCMs are biologically aggressive compared with conventional Grade I meningiomas. Indeed, the WHO has recognized this tendency by modifying the classification of CCMs to WHO Grade II based on their histological appearance alone. Histopathological reasons for aggressive clinical behavior are not apparent.

Given that CCMs do not always have characteristic meningothelial features, additional studies can be supportive in reaching its diagnosis. First, due to the heavy content of cytoplasmic glycogen, tumor cells stain intensely with periodic acid–Schiff stains and are labile to diastase treatment. Like other meningiomas, almost all clear cell tumors show a membranous pattern of immunoreactivity for epithelial membrane antigen and are strongly reactive for vimentin. Nuclear progesterone receptor staining appears in 77% of these meningiomas, but estrogen receptor staining is usually absent. Stains for cell adhesion molecule 5.2 and S100 protein are negative. Ultrastructural features can be used if necessary to define these tumors as meningothelial: cytoplasmic intermediate filaments, some taking the form of whorls; interdigitating cell membranes; and intercellular junctions—mostly desmosomes are almost always present.

Unlike the more typical meningioma, CCM’s propensity for local recurrence has been well-established in the literature. The capacity to present as a distant recurrence has been limited to five previous reports in the literature. Whether distant recurrences represent the capacity of CCM to metastasize or a multifocal characteristic remains uncertain. Multifocal manifestation of this disease is well-described and the distant recurrences may represent this. In contrast, Lee, et al., report on a patient with a left parietal convexity mass subsequently found to have leptomenineal seeding. Whether our patient had a distant recurrence because of a drop metastasis or a multifocal presentation is uncertain as the entire neuraxis was not imaged after her first surgery. It is evident that CCMs are an aggressive variant prone to recurrence after resection. Thus, MR imaging of the entire neuraxis at least every 6 months postoperatively is indicated.

In regard to adjuvant therapy, our careful review of the existing literature revealed that there is a clear role for fractionated local radiotherapy in the management of CCMs, particularly in cases of subtotal resection and recurrence. Of 49 known cases of CCM, 46 were treated with surgery alone, and the remaining three were treated with subtotal resection and adjuvant radiotherapy. Of the 46 treated with resection alone, 52.2% (24 patients) of these patients suffered from recurrences, five of which were distant. Of these 24 patients, 12 were treated with resection alone, seven with surgery and radiotherapy, and three with radiotherapy alone (the treatment and outcome in the remaining two patients were not reported). Among the group of 12 patients treated with surgery alone were a total of five subsequent recurrences. In comparison, among the seven patients treated with surgery and radiotherapy, only two recurrences were reported. Thus, the rate of subsequent recurrence after resection alone is significantly greater (41.7%) than that after surgery and radiotherapy (28.6%). Infrequently, recurrences were treated with radiation alone; of these three patients, only one suffered a distant recurrence, and the other two had no reported spread or growth of the tumors. Out of 49 reported cases of CCM, one case, specifically a recurrent tumor, was treated with surgery, radiation, and hydroxyurea chemotherapy. This patient had no reported subsequent recurrences.

Although reports of this rare but aggressive meningioma variant have accumulated in the literature, the most efficacious method of treatment remains ill-defined in the current...
literature. Given the earlier-referenced data collected by us and others, definitive recommendations for the management of CCMs can be made. The rarity of this neoplasm has precluded cohort or comparative clinical studies, thus the data reported are insufficient to support either treatment standards or guidelines.

Of the patients described in the literature who had no recurrences, all had undergone gross-total resection. Therefore, the treatment of choice for CCM is complete resection. Nevertheless, it appears that even gross-total resection is not sufficiently curative because of the inordinately high rate of recurrence (52.2%), both local and distant. In contrast, recurrent tumors have markedly lower rates of subsequent recurrence (28.6%) after surgery and radiation compared with the recurrence rate following surgery alone (41.7%; Fig. 5). The current literature does not adequately explain this dichotomy. In particular, it is uncertain why slightly less than half of the patients with CCM have no recurrence after an initial resection. Perhaps the group that suffers recurrence represents those with unrecognized subtotal resection. This hypothesis is supported by the unusual locations of CCMs that may limit gross-total resection. Another possibility is that among CCMs, there are variants that are more aggressive and thus recur. This hypothesis is supported by reported cases of repeated recurrences and, in some instances, eventual death from this disease.

Thus, we recommend

![Flowchart demonstrating pattern of recurrence after resection alone or combined with adjuvant therapy. Three of these patients had multiple recurrences. **These patients underwent initial subtotal resection. ***The management and outcome of two of these recurrences was not reported. XRT = radiotherapy.](image)

S. S. Dhall, et al.
Spinal intradural clear cell meningioma

treating cases of local recurrence or subtotal resection, CCMs with a combination of surgery and adjuvant radiotherapy to prevent recurrence. In the case of a distant recurrence, imaging the entire neuroaxis followed by gross-total resection is the treatment of choice. Frequent surveillance studies at regular intervals are also indicated. The role of immediate postoperative radiation for a distant recurrence has not been clearly established. The patient in this report remains disease-free 18 months after resection of the distant recurrence with no radiation. Although chemotherapy has not been adequately explored, it does not appear to have a significant role in the management of CCMs.

Conclusions

Clear cell meningiomas are rare and aggressive neoplasms with increased rates of local recurrence and an uncertain capacity to metastasize. The treatment of choice is complete resection. Because of the high rate of local recurrence and the still uncertain capacity of CCM to metastasize, the entire neuroaxis should be imaged after initial diagnosis and at regular intervals thereafter. Distant recurrences may be managed with gross-total resection and close surveillance with no need for immediate postoperative radiation. Note, however, that this specific recommendation is limited by the lack of more data in this exceedingly small patient population. Stereotactic radiation is indicated for residual tumor or following surgery for local recurrence.

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References


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