Background: The purpose of this case report is to illustrate a case of mesenchymal chondrosarcoma arising in an unusual location in brain parenchyma, complicated by a rare complication of drop metastases to the spinal canal.

Mesenchymal chondrosarcoma is a rare skeletal tumor. Of the extraskeletal sites, the intracranial location is the most common, followed by the orbit and the soft tissues. First described by Lichtenstein and Bernstein in 1959, the histological feature is biphasic consisting of undifferentiated mesenchymal cells admixed with islands of cartilaginous tissue. Most intracranial tumors are meningeal-based, but several cases of tumors arising from cerebral parenchyma have been reported in the literature. This tumor has a tendency to be hypervascular, recur locally, and metastasize via cerebrospinal fluid (CSF). For these reasons, patients tend to do poorly.

Case Description: We present a 42 year-old man with a symptomatic tumor arising from parenchyma that was surgically removed. He underwent postoperative radiation. Ten and a half months later the tumor recurred and a partial resection followed by radiosurgery and chemotherapy was instituted. Eventually, the patient had drop metastases to the spinal canal and died 1 year after the initial diagnosis. Pertinent literature on the epidemiology, diagnosis and treatment is also discussed.

Conclusion: We report a case of primary intraparenchymal mesenchymal chondrosarcoma. It illustrates the distinctive radiological and histological features, as well as the unique clinical progression of the tumor leading to multiple spinal cord seeding. We also review the cases reported in the literature comparing the demographics, treatment options and prognoses.

Key words: Mesenchymal chondrosarcoma • Spinal metastasis

A 42 year-old male presented with sudden onset of headache, aphasia, right-sided hemiplegia, and facial droop. His initial CT scan and MRI are shown in Figure 1a, b.

He underwent a left pterional transylvian approach under General anesthesia. The insular cortex was entered and a grayish-purplish tumor was encountered, with areas of hemorrhage intermixed. Pathological examination was initially interpreted as “a poorly differentiated metastatic carcinoma with spindle cell features.” The morphology showed small hyperchromatic nuclei with numerous mitotic figures set into a “myxoid-type” background, which, upon closer examination, was cartilaginous (Figure
This biphasic morphology is commonly seen in mesenchymal chondrosarcomas. However, the keratin immunohistochemical stain was focally positive with a dotlike pattern, characteristic of small cell carcinomas, and the synaptophysin, an immunostain that is positive in cells of neuroendocrine origin, was also focally positive (Figure 3). Immunostains for GFAP, S-100, and desmin were negative.

The patient continued to improve neurologically. He received 6000cGy of fractionated radiation therapy to the brain and an extensive search for a primary tumor revealed no other lesion site in the body. The work-up included CT scan of the chest, abdomen and pelvis as well as nuclear bone scan with negative results. An MRI of the spinal axis and a lumbar puncture were not felt to be necessary during this initial work-up and were thus not performed then. Ten and a half months after surgery, he presented with generalized tonic-clonic seizures. Imaging studies of the brain at that time showed a lesion in the left sylvian fissure clearly distinct from the previous site of surgery but encircling the middle cerebral artery (Figure 4).
The patient was re-operated through the previous craniotomy. The tumor appeared as gray, amorphous and reminiscent of mucinous or cartilaginous tissue and was relatively avascular. It was clearly growing in the banks of the sylvian fissure, along the path of the prior transylvian dissection.

On pathological examination, the morphology was similar to that of the previous biopsy; however, in addition, the tumor showed compact cellular aggregates of spindle cells separated by numerous thin-walled vascular spaces and less dense cellular bands of collagenous and cartilaginous tissue. Additionally, the keratin immunostain was negative, raising the possibility that the previous keratin stain was a false positive. The synaptophysin was not repeated and the S-100 was then positive (Figure 5, 6). Immunostaining for desmin, HMB45, keratin, EMA, and myogenin was negative.

Postoperatively, the patient’s seizures were under control, and he was neurologically stable. In view of the aggressive recurrence, chemotherapy with methotrexate as well as Gamma knife radiosurgery treatment were instituted. Six weeks after his second operation he suddenly developed an inability to speak with increasing right side weakness. Studies revealed an increase in the size of the lesion. Dexamethasone dosing was increased with improvement to baseline.

Seven weeks after the second operation, he was admitted again with worsening neck and low back pain. Cytological analysis of CSF revealed malignant cells, and MRI of the spine was consistent with carcinomatous meningitis with extensive deposits around the cervical cord, thoracic cord, conus and among the nerve roots of the cauda equina (Figure 7).

Intrathecal chemotherapy with methotrexate and spinal irradiation were instituted, but his condition continued to deteriorate and he died 4 months after his second surgery.

Discussion

Cartilaginous tumors comprise 0.16% of all intracranial tumors [16]. They include chondroma and chondrosarcoma. Chondrosarcomas are further classified into classical or skeletal, mesenchymal and myxoid types based on histology. Classical chondrosarcoma are characterized by large cells with hyaline cartilage matrix and are graded according to their malignant potential. The rarest myxoid variant lacks hyaline cartilage but has a mucinous stroma among small cells. Mesenchymal chondrosarcoma has a biphasic pattern with islands of mature hyaline cartilage among undifferentiated mesenchymal cells.

The term “mesenchymal chondrosarcoma” was originally coined in 1959 by Lichtenstein and Bernstein. This tumor is much more common in the skeletal tissue (66%) than the soft tissue [31]. Among the extraskeletal sites, the intracranial location is the most common. The soft tissues of the lower extremities are another common site. Other sites reported in the literature are the orbit [1, 23], retroperitoneum [13], mediastinum [6], and paraspinal region [2, 4]. It was in 1962 that the first extraskeletal brain location was reported [11]. There have been several reported cases since (Table 1).

This tumor predominantly arises from the meninges although in a handful of cases the origin is parenchymal. There is a slightly higher preponderance in females than males (61%). There is a wide range of age at presentation (6 months to 61 years). The average is 22.5 years. Patients tend to be younger compared to those with soft tissue mesenchymal chondrosarcoma (44 years) [28]. Intracranially, these tumors occupy a supratentorial location and the frontoparietal convexity region seems to be a common site. In 4 patients the tumor was infratentorial. Although these
tumors tend to arise intracranially, several cases of intraspinal location have been described [19, 33, 39]. None of the radiological features are specific for mesenchymal chondrosarcoma. In our case the CT scan revealed a hemorrhagic lesion. MRI scanning usually reveals an enhancing heterogeneous lesion that can be intraparenchymal or dural-based. The latter feature explains the potential for confusion with meningiomas or hemangiopericytomas.

It has been theorized that the cell of origin is the pluripotent mesenchymal cell capable of differentiation into cartilage tissue [15, 27]. Mesenchymal cells give rise to meninges, connective tissue and soft tissues. Cases of mesenchymal chondrosarcoma with osteoid and rhabdomyosarcoma formation have been reported recently [26, 30]. This further supports a pluripotent cellular origin of the tumor that has the potential to differentiate into a variety of mesenchymal tissues.

Mesenchymal chondrosarcomas most commonly demonstrate an admixture of undifferentiated mesenchymal cells in cords and clusters and islands of poorly differentiated hyaline cartilage [39]. The nuclei of the undifferentiated cells are round to spindle-shaped with inconspicuous nucleoli and sparse eosinophilic cytoplasm. These cells are arranged in sheets containing scattered sinusoidal vascular channels lined by cytologically normal endothelium and can often be confused with hemangiopericytomas [39].

The second distinctive features of mesenchymal chondrosarcomas are the islands of hyaline cartilage. The transition to cartilage formation is usually abrupt, however, in our case, the cartilage was intermixed with the cellular component and was less prominent. Diagnostic difficulty may occur when the cartilaginous differentiation in mesenchymal chondrosarcomas is irregular or focally absent [41]. In such cases, the tumor may appear to be entirely composed of undifferentiated cells and, when accompanied by a sinusoidal vascular pattern, may be indistinguishable from a hemangiopericytoma [22]. While the histologic distinction between mesenchymal chondrosarcomas and meningiomas is usually straightforward, meningiomas may demonstrate focal cartilaginous metaplasia, adding further difficulty in making a correct diagnosis.

There is no definitive immunohistochemical staining pattern for mesenchymal chondrosarcomas, making the diagnosis difficult in cases where the morphology alone is not characteristic. Our case showed an unusual staining pattern, atypical for mesenchymal chondrosarcomas, which are usually keratin and synaptophysin negative. This may explain the discrepancy between the diagnoses of the first and second biopsy specimens.

There is very strong agreement in the literature that the first line of treatment should be an attempt at a radical resection of the tumor when feasible. Some authors have advocated preoperative embolization given the vascularity of the tumor [3, 19, 21]. The reduction in the vascularity of the tumor preoperatively may aid in the resection as well as keep the blood loss to a minimum. Another factor leading to limited resection is the attachment of the tumor to the dura, especially at the venous sinuses.

The type of adjuvant treatment has not been uniform across all cases. The optimal adjuvant therapy is unclear because of lack of systematic study due to the rarity of the disease. A closer look at the cases in Table 1 shows that almost all patients (6 out of 7) with parenchymal tumor had recurrence in spite of “gross total resection.” It has to be borne in mind that “gross
"total resection" almost never equates to microscopic eradication of all tumor cells.

Mesenchymal chondrosarcoma has a strong tendency for local recurrence. We found a 65% rate of recurrence in the reported cases. This was higher with documented subtotal resection. In our case, the

<table>
<thead>
<tr>
<th>Year</th>
<th>Authors</th>
<th>Age/Sex</th>
<th>Location/origin</th>
<th>Initial Treatment</th>
<th>Postop course</th>
<th>Survival after 1st surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>1962</td>
<td>Dahlin</td>
<td>44, F</td>
<td>Parietal, dura</td>
<td>GTR</td>
<td>9 Rec (2yr-9yrs)</td>
<td>D, 9yrs</td>
</tr>
<tr>
<td>1963</td>
<td>Flyger</td>
<td>11, M</td>
<td>Frontal, Parenchyma</td>
<td>GTR</td>
<td></td>
<td>A, 5mos</td>
</tr>
<tr>
<td>1966</td>
<td>Raskin</td>
<td>48, F</td>
<td>Frontal, Parenchyma</td>
<td>R</td>
<td></td>
<td>D, 3 days</td>
</tr>
<tr>
<td>1970</td>
<td>Wu</td>
<td>18, F</td>
<td>Frontoparietal, dura</td>
<td>STR</td>
<td>4 Rec</td>
<td>D, 16mos</td>
</tr>
<tr>
<td>1972</td>
<td>Waga</td>
<td>51, F</td>
<td>Parietal, dura</td>
<td>STR, XRT</td>
<td>Rec at 2 mos, Mets at 10mos</td>
<td>D, 11mos</td>
</tr>
<tr>
<td>1973</td>
<td>Guccion</td>
<td>19, M</td>
<td>Parietal, dura</td>
<td>R, XRT</td>
<td>Rec at 1 yr</td>
<td>A, 1yrs</td>
</tr>
<tr>
<td>1978</td>
<td>Cianfriglia</td>
<td>20, F</td>
<td>Temporal, dura</td>
<td>GTR</td>
<td>No Rec</td>
<td>A, 27mos</td>
</tr>
<tr>
<td>1978</td>
<td>Scheithauer</td>
<td>7, M</td>
<td>Temporal, dura</td>
<td>R</td>
<td>Rec at 3 yr</td>
<td>D, 7 yrs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>17, F</td>
<td>Frontal, dura</td>
<td>R</td>
<td>No Rec</td>
<td>D, 2 yrs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>40, M</td>
<td>Parietal, dura</td>
<td>R</td>
<td></td>
<td>D, 5days</td>
</tr>
<tr>
<td>1978</td>
<td>Zucker</td>
<td>19, M</td>
<td>Occipital, dura</td>
<td>GTR</td>
<td>No follow-up</td>
<td></td>
</tr>
<tr>
<td>1979</td>
<td>Rollo</td>
<td>11, M</td>
<td>Occipital, dura</td>
<td>STR</td>
<td>Rec at 6mos, Mets at 8yrs</td>
<td>A, 8yrs</td>
</tr>
<tr>
<td>1980</td>
<td>Heros</td>
<td>26, F</td>
<td>Frontoparietal, dura</td>
<td>GTR</td>
<td></td>
<td>D, 3days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>33, M</td>
<td>Frontal, dura</td>
<td>R</td>
<td>2 Rec</td>
<td>A, 3 yrs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>26, F</td>
<td>Cerebellar, dura</td>
<td>R</td>
<td>None</td>
<td>A, 2.5 yrs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>23, F</td>
<td>Parietal, dura</td>
<td>R, XRT</td>
<td>None</td>
<td>A</td>
</tr>
<tr>
<td>1981</td>
<td>Harwood</td>
<td>22, M</td>
<td>Cerebellar, Parenchyma</td>
<td>R</td>
<td>Rec at 4mos</td>
<td>D, 4mos</td>
</tr>
<tr>
<td>1982</td>
<td>Kubota</td>
<td>21, F</td>
<td>Frontal, dura</td>
<td>R</td>
<td>Mets at 4 yrs</td>
<td>D, 7 yrs</td>
</tr>
<tr>
<td>1984</td>
<td>Rodda</td>
<td>12, F</td>
<td>Frontal, dura</td>
<td>GTR</td>
<td>Rec at 2.5 mos</td>
<td>D, 7.5mos</td>
</tr>
<tr>
<td>1987</td>
<td>Nokes</td>
<td>61, F</td>
<td>Parietal, dura</td>
<td>R, XRT</td>
<td>Did well postop</td>
<td>No follow-up</td>
</tr>
<tr>
<td>1989</td>
<td>Schut</td>
<td>11mos,M</td>
<td>Frontal, dura</td>
<td>R, XRT</td>
<td>Rec</td>
<td>D</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12, F</td>
<td>Frontal, dura</td>
<td>R,XRT,C</td>
<td>Rec</td>
<td>D</td>
</tr>
</tbody>
</table>

A, Alive ; C, Chemotherapy ; D, Died; F, Female; GTR, Gross total resection; M, Male; Mets, Metastasis; MI, Myocardial infarction; R, Resection; Rec, Recurrence; STR, Subtotal resection; Wks, Weeks; XRT, Radiation therapy

Table 1. Reported cases of intracranial mesenchymal chondrosarcoma in the English literature

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recurrence was 10 months after initial surgery and, interestingly, at a site distinct from the original location, yet within the general vicinity. It is compelling to assume that the transylvian dissection during the first surgery allowed subsequent localized seeding of tumor cells from their original intraparenchymal insular location to their new subarachnoid location along the superficial banks of the sylvian fissure. We speculate that specific, poorly definable biological characteristics predisposed this specific tumor to have a tendency to seed via the CSF pathway to both intracranial and intraspinal locations.

There are case reports of extracranial spread of the tumor. Lung is the most common site of spread [24, 39]. Dissemination of the tumor via CSF is very rare. Our case illustrates this unusual mode of spread. We have encountered only one other case of spinal dissemination, and in that case the primary was in the cerebellum [29]. Both patients had total resection followed by radiation therapy and yet presented with spinal metastasis within a year.

The role of postoperative radiation treatment is inconclusive. Radiation therapy has yielded varied results. In our case there was recurrent tumor after surgery and a complete cycle of radiation therapy. On the other hand, some patients have had no recurrences 1.5 years after combined therapy [3, 7-8, 40]. Salcman et al described one year tumor-free survival in a patient with implantation of I-125 radioactive seeds during re-operation for myxoid chondrosarcoma.

### Table 1 cont.

<table>
<thead>
<tr>
<th>Year</th>
<th>Authors</th>
<th>Age/Sex</th>
<th>Location/origin</th>
<th>Initial Treatment</th>
<th>Postop course</th>
<th>Survival after 1st surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>1992</td>
<td>Saleman[27]</td>
<td>28, F</td>
<td>Frontal, Parenchyma</td>
<td>GTR</td>
<td>Rec at 10mos</td>
<td>A, 22mos</td>
</tr>
<tr>
<td>1992</td>
<td>Chhem[7]</td>
<td>11, F</td>
<td>Parietal, Parenchyma</td>
<td>R, XRT</td>
<td>Rec at 1.5 yrs</td>
<td>D, 1.5yrs</td>
</tr>
<tr>
<td>1996</td>
<td>Malik[29]</td>
<td>8, M</td>
<td>Cerebellar, Parenchyma</td>
<td>GTR,XRT,C</td>
<td>Spinal Mets, 8mos</td>
<td>Unknown</td>
</tr>
<tr>
<td>2000</td>
<td>Crosswell[16]</td>
<td>6mos, M</td>
<td>Temporal, dura</td>
<td>GTR</td>
<td>Rec at 3 weeks (chemotherapy)</td>
<td>D, 2mos</td>
</tr>
<tr>
<td>2000</td>
<td>Bingaman[3]</td>
<td>24, F</td>
<td>Frontal, dura</td>
<td>GTR, XRT</td>
<td>No Rec</td>
<td>A, 1.5 yrs</td>
</tr>
<tr>
<td>2001</td>
<td>Marshman[30]</td>
<td>17, F</td>
<td>Temporoparietal, Parenchyma</td>
<td>GTR</td>
<td>2 Rec</td>
<td>D, within mos</td>
</tr>
<tr>
<td>2003</td>
<td>La Spina[26]</td>
<td>14, F</td>
<td>Tentorial</td>
<td>STR ,R, C</td>
<td>No Rec</td>
<td>A, 2 yrs</td>
</tr>
<tr>
<td>2004</td>
<td>Chen[5]</td>
<td>13, F</td>
<td>Frontal, falx</td>
<td>GTR</td>
<td>No Rec</td>
<td>A,30mos</td>
</tr>
<tr>
<td>2005</td>
<td>Salvati[38]</td>
<td>30, F</td>
<td>Frontoparietal, Falx</td>
<td>GTR</td>
<td>Rec 37mos (GTR,XRT)</td>
<td>A, 1mos</td>
</tr>
<tr>
<td></td>
<td></td>
<td>42F</td>
<td>Frontal, dura</td>
<td>GTR</td>
<td>No Rec</td>
<td>D, (MI,3 wks)</td>
</tr>
<tr>
<td>2007</td>
<td>De Cecio[12]</td>
<td>2mos, M</td>
<td>Parietal, Dura</td>
<td>GTR</td>
<td>Rec at 1mos</td>
<td>D,few wks</td>
</tr>
<tr>
<td>2008</td>
<td>Sheth (current report)</td>
<td>42, M</td>
<td>Insular and basal ganglia, Parenchyma</td>
<td>GTR, XRT</td>
<td>Rec at 10.5mos, Spinal Mets at 12mos</td>
<td>D, 15mos</td>
</tr>
</tbody>
</table>

A, Alive ; C, Chemotherapy ; D, Died; F, Female; GTR, Gross total resection; M, Male; Mets, Metastasis; MI, Myocardial infarction; R, Resection; Rec, Recurrence; STR, Subtotal resection; Wks, Weeks; XRT, Radiation therapy
of the falx [37]. Interstitial brachytherapy has been used for several recurrent skull-based tumors with variable results; the experience with mesenchymal chondrosarcoma is non-existent [18, 25]. The local delivery of high dose radiation for a protracted time period may spare the normal brain yet treats the surrounding tumor cells during the most vulnerable part of their cell cycle.

The experience with chemotherapy is further limited. La Spina demonstrated a marked reduction in tumor enhancement after using a “sarcoma-like” course of chemotherapy (carboplatin, etoposide, vincristine, ifosfamide, and Adriamycin) [26]. Crosswell et al treated recurrent tumors with vincristine, cisplatin, etoposide and cyclophosphamide but with eventual death in a month [10]. Harsh had no regrowth in a case of recurrent intraspinal tumor after total resection, radiation therapy and perioperative Adriamycin [19]. Another pediatric patient died shortly after resection, radiation therapy and chemotherapy (unknown agents) [40]. In the present case, the patient received chemotherapy with methotrexate, ifosfamide and MESNA, but the tumor continued to grow. We treated the intraspinal spread of the tumor with intrathecal methotrexate and spinal irradiation and there was interesting disappearance of malignant cells in a follow-up lumbar puncture. In the only other case of spinal dissemination, the patient received intrathecal chemotherapy (agent not specified), and the follow-up is unknown [29]. Given the propensity of this tumor for recurrence and metastasis, postoperative chemotherapy should be instituted, regardless of the extent of resection, with agents effective against sarcoma-like tumors. We feel that intrathecal treatment should be reserved for CSF seeding.

Conclusion

Mesenchymal chondrosarcoma is a rare tumor of bones, with brain being the most common extraskeletal organ affected. This tumor uncommonly arises in the parenchyma. Biphasic appearance is the histological hallmark of the tumor. Whenever possible, radical resection of the tumor followed by radiation therapy should be the initial goal of treatment because of its propensity for local recurrence. Because of the tendency of the tumor to metastasize, chemotherapy should be given postoperatively, and intrathecal therapy probably reserved for the highly unusual patients with CSF spread. Unfortunately, in spite of all modern management efforts, the prognosis remains extremely disappointing.

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We would like to thank Dr. Philip Robinson for his help in the review and interpretation of histological slides.

References


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Sheth RN et al. **Primary Mesenchymal Chondrosarcoma**


**Correspondence:**
Jacques J. Morcos, MD, FRCS
University of Miami-Department of Neurosurgery

**Annals of Neurosurgery, 2009; 9(7): 1-9**

**COMMENTS**

The authors describe a very unusual case of a primary intraparenchymal intracranial mesenchymal chondrosarcoma that has an aggressive course and eventually resulted in CSF dissemination. Despite all best attempts to treat this lesion, the patient died as a result of disseminated disease. I actually think this is a very interesting case report in that it describes a very unusual entity and points out the fact that these highly aggressive mesenchymal tumors can, indeed, disseminate and result in a drop metastasis.

**Mitch Berger MD**
San Francisco, USA

The authors report the rare occurrence of an intracerebral mesenchymal chondrosarcoma in a 42 year-old male patient. After initial successful surgery and radiotherapy, the tumor recurred intracranially as well as in the spinal canal. The authors present the epidemiology and clinical characteristics of intracranial mesenchymal chondrosarcoma and discuss the available treatment options for this aggressive and difficult tumor.

**Alain Barth MD**
Jura and Basel, Switzerland

The authors add an interesting case of a primary intracranial mesenchymal chondrosarcoma and secondary drop metastases to the spinal canal to our neurosurgical/neurooncological community. Both manifestation of CNS mesenchymal chondrosarcoma as well as primary and/or secondary drop metastases are rare. It is worthwhile to give summarized knowledge concerning diagnosis and treatment modalities (chemo – and radiotherapy) combined with own experience as best medical practice. This will help us to optimize treatment and improve outcome of such patients despite of lack of larger series.

**Jürgen Meixensberger MD**
Leipzig, Germany