An atypical spinal meningioma with CSF metastasis: fatal progression despite aggressive treatment

Case report

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The authors report the case of a 23-year-old man who presented with a C1–3 spinal mass. Following intraspinal decompression the tumor was histologically classified as an atypical meningioma (World Health Organization grade II). Two further surgical interventions resulted in almost total removal of the meningioma. In addition, radiotherapy was performed. During the 1.5-year follow-up period the diagnostic examinations identified a local tumor recurrence, an intraspinal C-6 metastasis, and a segmental instability with anterior C2–3 slippage and C3–4 kyphosis. The tumor was resected and occipitocervical stabilization was performed. Histological examination showed no change in malignancy. Despite additional hydroxyurea-based chemotherapy, the patient presented 4 months later with a hemiparesis and a massive recurrence of the tumor mass involving the posterior fossa and the upper thoracic spine. Because there were no further therapeutic options, the patient died. The authors discuss more aggressive therapeutic options in addition to surgery in patients with metastatic atypical meningiomas. The results in the reported case indicate that meningiomas associated with cerebrospinal fluid metastasis may represent a higher grade of malignancy.

KEY WORDS • cervical spine • atypical meningioma • hydroxyurea • spinal instability

Abbreviations used in this paper: CSF = cerebrospinal fluid; EMA = epithelial membrane antigen; MR = magnetic resonance; VA = vertebral artery; VB = vertebral body; WHO = World Health Organization.
10% (Fig. 2C). Histopathological investigation led to the diagnosis of an atypical meningioma according to the WHO criteria.11

Before the second surgery was scheduled, as early as 4 weeks after the first, progressive tetraparesis developed. On MR imaging the paravertebral tumor was invaginating through the neural foramen of C2–3 into the spinal canal and spinal cord compression was present (Fig. 3A). A lateral approach to the upper segments of the cervical spine was selected for extirpation of the lateral portion of the paravertebral tumor as well as its intraforaminal and spinal parts.

An additional tumor resection was performed 2 weeks later via a transoral approach to remove the retropharyngeal tumor. Because of the tumor's infiltration of the muscle, however, the resection could not be completed, although the postoperative MR images verified a gross tumor resection at C-3 (Fig. 3B). Following surgery fractionated external-beam radiotherapy (total of 50 Gy) was undertaken. The patient's clinical conditions had improved and the tetraparesis resolved within weeks. A mild paraparesis and a paresthesia affecting mainly the left arm remained. After rehabilitation, he was able to return to normal life.

During radiological control examinations in 2002, we observed C2–3 anterior vertebral slippage, C3–4 kyphosis, and increasing instability of the upper cervical spine (Fig. 4). An incomplete distraction of the cervical spine was achieved using a halo vest for a 4-week period. In January 2003 a posterior occipitocervical stabilization became necessary (Fig. 4C and D). In addition, a spinal drop metastasis, located at T1–3 segments, was observed (Fig. 5B). In this state only palliative therapy was undertaken. The patient died within 7 days. Final histological examination of the tumor was not possible because the patient's relatives refused a postmortem examination.

Discussion

We have presented the case of a young man with an WHO Grade II spinal meningioma. The patient's clinical course was complicated by different factors. A total excision of the meningioma was not possible because of diffuse soft-tissue infiltration and its complex location surrounding the craniovertebral junction and the left VA. Although histologically classified as atypical, the meningioma exhibited unusually aggressive behavior and clinical characteristics of malignancy such as early CSF metastases. This resulted in the patient's survival duration of only 21 months despite aggressive treatment. To our knowledge, this is the first reported case of a Grade II spinal meningioma associated with such fatal progression.

According to the WHO criteria, meningiomas are classified into three grades that intend to reflect the prognosis...
of the tumors. Most meningiomas are benign and classified as WHO Grade I, including some histopathological subtypes such as meningothelial, fibrous, and transitional lesions. Between 4.7 and 7.2% of meningiomas are classified as atypical, corresponding to WHO Grade II.

Atypical meningiomas are diagnosed either when increased mitotic activity (defined as ≥ four mitosis/10 hpf) or three or more of the following features are encountered: increased cellularity, small cells with high nuclei, cytoplasm ratio, prominent nucleoli, uninterrupted patternless or sheetlike growth, and necrosis. The variants of chordoid and clear-cell meningiomas are also classified as WHO Grade II. Anaplastic meningiomas (WHO Grade III) exhibit histological features with frank malignancy including either obviously malignant cytology (for example, an appearance similar to sarcoma, carcinoma, or melanoma) or a high mitotic index (≥ 20 mitoses/10 hpf). Rhabdoid and papillary meningiomas are also classified as WHO Grade III; however, there is no consensus on the differential diagnosis criteria between atypical and anaplastic meningiomas. The prognosis in meningiomas worsens from Grade I to Grade III. The tumors meeting the aforementioned criteria, corresponding to WHO Grade III, are usually fatal, and the median survival duration is less than 2 years. Nevertheless, the prognosis in our patient was poor, as in the case of anaplastic meningioma. Both the first and the second tumors resected in our patient displayed no histological features corresponding to WHO criteria for anaplastic meningiomas; the mitotic indices were lower than 20 mitoses within 10 hpf, and no carcinomatous or sarcomatous appearances with frank malignancy were observed. Additionally, neither tumor exhibited rhabdoid or papillary features. Invasion, metastasis, and high proliferation indices have not been incorporated into the current WHO grading criteria and may occur in all histological types and grades. Metastasis in meningioma is very rare and can arise from various types of cell dissemination, such as hematogenic, lymphogenic, or through the CSF. Even extracranial metastases of benign meningiomas have previously been reported. It is generally stated that invasion as well as high mitotic and proliferation indices are associated with high recurrence rates and aggressive behavior. In our case, the increased proliferation and mitotic indices in the secondary tumor can be regarded as progression with an increased tumor doubling time, which may also be responsible for early recurrence together with invasion. A higher proliferation and mitotic indices in recurrences com-
pared with their primary counterparts have been reported.\textsuperscript{5,6} Additionally, we suggest that the absence of EMA expression in the secondary tumor is associated with the dedifferentiation and progression of the primary tumor.

Meinsma-vdTuin, et al.,\textsuperscript{14} reported a case of a spinal papillary meningioma in a 19-year-old man. The tumor was located between the C2–4 VBs and extended to the left foramen at C3–4. Six months after complete resection, MR imaging revealed metastases through the CSF pathway to L3–4 and to the posterior fossa. A recurrence developed at the cervical spinal level, and the patient died 15 months after the first operation.\textsuperscript{14} The case reported by Meinsma-vdTuin, et al., shows several similarities to our case; however, it is the case of a spinal papillary meningioma. These tumors are considered to be aggressive variants of meningiomas with frequent local recurrence, CSF dissemination, and metastases to remote sites.\textsuperscript{16} They are classified as malignant.\textsuperscript{7} A comparison of both cases underscores the unusual clinical behavior of the nonmalignant, Grade II spinal meningioma in the present case.

The tumor, initially located between the C1–3 VBs, metastasized to the C-6 segment and then to the upper thoracic spine. In the literature the phenomenon characterized by spinal metastases disseminated through the CSF pathway is mainly associated with malignant intracranial meningiomas.\textsuperscript{2,10} Ramakrishnamurthy, et al.,\textsuperscript{17} reported the

![Figures](image1.png)

**FIG. 3.** A: Axial MR image revealing the remaining paravertebral tumor mass after resection of its intraspinal part (September 2001). B: Axial MR image after two additional operations via a lateral and a transoral approach verifying a gross tumor resection (November 2001).

![Figures](image2.png)

**FIG. 4.** A: In January 2003 an intraspinal metastasis of the primary tumor was found at C-6 (arrow). B: In addition a segmental instability of the cervical spine with forward slippage was observed at C2–3 and C3–4. In consequence of a tumor infiltration into the osseous structures of the upper cervical spine with destruction of the atlantoaxial joints, a C1–2 transarticular fixation was not possible. C and D: Therefore, an occipitocervical stabilization was performed using a clamp/rod system.
case of a benign intracranial meningioma seeding through the CSF pathway. This way of metastasizing, however, is regarded as extremely rare.3 The role of surgery as a possible cause for dissemination of tumor cells along the CSF pathway remains unclear.

Our patient’s short survival duration confirms reports of other authors who found that complete excision is crucial for long-term control of nonbenign meningiomas.4-21 The standard treatment regimen for meningiomas with atypical histological characteristics, consisting of surgery and adjuvant external-beam radiotherapy, achieved a stabilization of tumor growth for a certain period. The patient did not respond to hydroxyurea-based chemotherapy, which had been started at a relatively late time point (~ 14 months after the first diagnosis). Various authors have reported that hydroxyurea is capable of causing a delay in disease progression, which seems to be more likely in benign than in nonbenign meningiomas.13,15,19 In our case the Grade II spinal meningioma exhibited an unusual aggressive behavior. Retrospectively, we speculate that meningiomas presenting with CSF metastasis may be considered malignant despite their histological grading according to the classification of pituitary adenomas. That, in conclusion, may lead to higher radiation doses and more aggressive chemotherapy.

Conclusions

In our opinion the findings observed in the present case indicate that the definition of Grade II meningiomas, if additional CSF metastases are present, should be reconsidered for more aggressive treatment with a higher-dose radiation and specific chemotherapy or even intrathecal chemotherapy corresponding to medulloblastomas.

References


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