Multifocal meningeal melanocytoma: a new pathological entity or the result of leptomeningeal seeding?

Case report

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Meningeal melanocytoma is a rare benign CNS tumor derived from the leptomeningeal melanocytes. Although unusual, malignant transformation with leptomeningeal seeding into the brain or spinal cord may occur years after the initial diagnosis. The authors report a unique case of multifocal benign meningeal melanocytoma involving both cerebellopontine angles and the thoracic spinal cord, with associated diffuse leptomeningeal hyperpigmentation and a remarkably aggressive clinical course.

**Key Words** • melanocyte • meningeal melanocytoma • malignant melanoma • cerebellopontine angle • thoracic spine

MENINGEAL melanocytoma is a rare benign CNS tumor that arises from the leptomeningeal melanocytes and occurs almost exclusively in the posterior fossa and spinal cord.9,15 Although exceptional, leptomeningeal seeding secondary to malignant transformation has been reported to occur years after the initial diagnosis.10,19,24 We present a unique case of multifocal benign meningeal melanocytoma simultaneously affecting both CPAs and the thoracic spinal cord, with associated diffuse leptomeningeal hyperpigmentation and a remarkably aggressive clinical course.

### Case Report

**History and Examination.** This 31-year-old, previously healthy man presented with an 8-week history of early morning headache with vomiting and progressive hearing loss. Neurological examination showed severe bilateral sensorineural hearing loss, but was otherwise unremarkable. Results of the remainder of the physical examination were within normal limits; in particular, there was no evidence of cutaneous melanoma. Brain MR imaging revealed bilateral homogeneously enhancing CPA lesions with diffuse leptomeningeal enhancement and tetraventricular hydrocephalus. The lesions were hyperintense on T1-weighted and isointense on T2-weighted images (Fig. 1).

**First Operation and Postoperative Course.** Bilateral vestibular schwannomas associated with neurofibromatosis Type 2 were suspected, and ventriculoperitoneal shunt placement was initially performed. The CSF analysis showed a very high protein content (> 1 g/L), but a normal glucose level and cell count. Dark staining of the pia mater and arachnoid layers was noted intraoperatively. Therefore, leptomeningeal biopsy specimens were obtained at the site of shunt insertion, and these were consistent with a nonspecific inflammatory process with hyperpigmentation. The patient had an uneventful postoperative recovery and was discharged home a few days later. An MR imaging study of the entire spine was scheduled on an outpatient basis to screen for other neurofibromatosis Type 2 lesions.

However, 2 weeks after surgery the patient developed rapidly progressive lower-extremity weakness with urinary and fecal incontinence. Physical examination revealed marked paraparesis and an incomplete T-6 sensory level. Thoracic spine MR imaging was urgently performed and revealed an intradural, extramedullary, homogeneously enhancing lesion compressing the spinal cord at the T5–6 level (Fig. 2).

**Second Operation.** The patient underwent an emergency spinal cord decompression via a posterior approach. Intraoperatively, a dura-based dark brown lesion was found to be compressing the spinal cord and was adherent to its pial surface at several locations. However, a cleavage plane was easily developed between the lesion and underlying pia mater, which allowed gross-total resection.

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Abbreviations used in this paper: CPA = cerebellopontine angle; MM = meningeal melanocytoma.
Multifocal meningeal melanocytoma

Histopathological Findings. Pathological examination of the surgical specimen showed a melanocytic proliferation arranged in sheets of round epithelioid cells with rare spindle cell areas. Cells had round nuclei with occasionally enlarged nucleoli, but no evidence of nuclear pleomorphism or hyperchromicity. Mitotic figures were rare and pigmentation was irregular (Fig. 3). Immunohistochemical analysis showed positivity to Melan A and S100 protein and negativity to epithelial membrane antigen, neurofilament, and glial fibrillary acidic protein, with a low proliferative index (MIB-1). These features were consistent with the diagnosis of MM.

Postoperative Course. Postoperatively, lower-extremity strength was markedly improved and the patient was able to walk, although bladder and bowel control remained impaired. He was discharged home a few days later and arrangements were made for the treatment of his CPA lesions. Unfortunately, a few weeks later the patient developed a rapidly progressive coma, with signs of brainstem compression and hemodynamic instability. He was admitted to another local hospital, where his condition continued to deteriorate, ultimately leading to his death.

Discussion

Melanocytes derive from the neural crest during early embryonic development. These cells are present in the leptomeninges of healthy adults and may give rise to primary leptomeningeal pigmented tumors, a group of uncommon pathological entities that includes pigmentated meningioma, malignant melanoma, MM, melanotic schwannoma, and melanoblastosis.15

Meningeal melanocytoma is a rare CNS tumor that occurs almost exclusively in the posterior fossa and spinal cord.9,15 This lesion may present at any age and has also been reported in children.14 The appearance of MM on MR imaging is influenced by the effects of melanin.5 The lesion is typically isointense to hyperintense on T1-weighted images, hypointense on T2-weighted images, and tends to enhance strongly and homogeneously after contrast administration.5,23 On gross inspection, it usually presents as an encapsulated black or dark brown nodule that, like meningioma, tends to attach to the dura mater and may locally invade the neural structures.2,6,21 Microscopically, oval or fusiform cells with abundant cytoplasm, vesicular nuclei, and fine melanin granules are observed, whereas anaplastic features such as mitosis and pleomorphism are generally absent.13

Both macroscopic and microscopic features of MM resemble those of other melanotic tumors, such as melanotic meningioma and melanotic schwannoma.20 Immunohistochemical and electron microscopic studies can help differentiate between these entities, because MM demonstrates positivity for vimentin, S100 protein, and HMB-45, whereas immunoreaction to epithelial membrane antigen, cytokeratin, neuron-specific enolase, and Leu-7 is usually negative.13,23,25 The histological differentiation between malignant melanoma and melanocytoma is even more difficult. Lack of mitotic activity, nuclear pleomorphism, hyperchromicity, and indolent tumor growth spanning more than 4 years favor the diagnosis of melanocy-
original magnification × 100.

nucleoli, mitotic figures are rare, and pigmentation is irregular. H & E, anocytic proliferation arranged in sheets of round epithelioid cells with CNS melanoma has an extremely poor prognosis.12

outcome following partial resection. have been shown to control tumor growth and improve vant radiation therapy and Gamma Knife radiosurgery have 3 simultaneously occurring lesions: 2 in the pos-

5 months later.

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phenomenon. Wang et al.24

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have accounted for the patient’s hydrocephalus, which is thought to develop due to reduced CSF absorption as a result of infiltration of the arachnoid villi by melanocytes or as a result of obstruction of CSF flow by the thickened leptomeninges.1

or intermediate-grade to a high-grade lesion is not pos-

ment of cutaneous lesions. Leptomeningeal melanosis may be considered a new entity, the multifocal MM, which simi-

larly appears to portend a poor prognosis, even when ma-

lignant pathological features are absent.

Finally, the diffuse leptomeningeal enhancement and hyperpigmentation in this case might represent melanocytic infiltration of the leptomeninges, a condition known as leptomeningeal melanosis and usually seen in the context of neurocutaneous melanosis.1,16 However, the latter diagnosis was ruled out in this patient, given the absence of cutaneous lesions. Leptomeningeal melanosis may have accounted for the patient’s hydrocephalus, which is thought to develop due to reduced CSF absorption as a result of infiltration of the arachnoid villi by melanocytes or as a result of obstruction of CSF flow by the thickened leptomeninges.1 Alternatively, hydrocephalus might have resulted from the associated hyperproteinorrachia, which may lead to reduced CSF resorption.3

Conclusions

Although rare, malignant transformation and lepto-

meningeal seeding may occur years after the initial diag-

nosis of MM, and are associated with an aggressive clinical course and a poor prognosis. In this paper, we introduce a new entity, the multifocal MM, which similarly appears to portend a poor prognosis, even when ma-

lignant pathological features are absent.

Disclaimer

The authors report no conflict of interest concerning the mate-

rials or methods used in this study or the findings specified in this paper.

References


2. Ahluwalia S, Ashkan K, Casey AT: Meningeal melanocyto-

ma: clinical features and review of the literature. Br J Neuro-

surg 17:347–351, 2003


5. Bydon A, Gutierrez JA, Mahmood A: Meningeal melanocy-
toma over that of malignant melanoma.15 Differentiating between these 2 conditions is crucial because primary CNS melanoma has an extremely poor prognosis.12

Gross-total tumor resection should be considered the goal of surgery, because incomplete resection has been shown to result in higher recurrence rates.5,7,17,20,22 Adjuvant radiation therapy and Gamma Knife radiosurgery have been shown to control tumor growth and improve outcome following partial resection.11,17,18

Brat et al.4 classified melanocytic lesions of the CNS into low-grade melanocytomas and high-grade melanomas. A minority of tumors in their study displayed moderately increased mitotic activity and cellularity, and these were classified as intermediate-grade lesions. According to these authors, the 3 groups represent separate histological entities, and transformation from a low-grade or intermediate-grade to a high-grade lesion is not possible. However, this theory has been challenged by Roser et al.,19 who reported a case of MM degenerating into ma-

lignant melanoma 12 years later. This resulted in rapid diffuse meningeal spread of the tumor throughout the en-

tire neuraxis. Despite whole-brain radiation therapy and chemotherapy, the patient died 4 months later. Koch et al.10 similarly reported on an MM of the CPA that presented with local recurrence and spinal meningeal seeding 6 years after diagnosis. This tumor did not respond to a combined radiation-chemotherapy regimen, and the patient died 5 months later. The possibility of malignant transformation was raised by those authors to explain this phenomenon. Wang et al.24 reported on a 57-year-old pa-

ient with a spinal MM that recurred locally with subcuta-

naneous seeding of tumor tissue 1 year after gross-total resection. Pathological examination of the recurrent le-

sion demonstrated transformation into a malignant mel-

noma. Despite subtotal resection and postoperative radio-

therapy, the patient developed liver and bone metastases 5 months later.

The patient described in this report was found to have 3 simultaneously occurring lesions: 2 in the pos-

terior fossa and 1 histopathologically confirmed MM in the thoracic spine. Although no tissue was obtained from the CPA lesions for diagnosis, their MR imaging signal characteristics were highly suggestive of MM. To the best of our knowledge, multifocal MM has not been reported previously. Although leptomeningeal seeding may be proposed to explain our findings, this rare phenomenon has been shown to occur late in the course of MM as a result of malignant transformation.10,19,24 Pathological examination of the spinal lesion in this case showed the absence of anaplastic features, which virtually eliminates the possibility of malignant transformation. We therefore believe that multifocal MM is a distinct pathological entity that seems to portend an aggressive clinical course and a poor prognosis, even when malignant pathological features are absent.

Fig. 3. Photomicrograph of a pathological specimen showing a melanocytic proliferation arranged in sheets of round epithelioid cells with rare spindle cell areas. Cells have round nuclei with some enlarged nucleoli, mitotic figures are rare, and pigmentation is irregular. H & E, original magnification × 100.
Multifocal meningeal melanocytoma is an aggressive course for a benign tumor. J Neurooncol 64:259–263, 2003