Clinical Reasoning: A 67-Year-Old Woman With Abdominal Pain, Constipation, and Urinary Retention

Sebastian S. Hanna, BS, BA, Ryan Jewell, MD, Christopher J. Anker, MD, John C. DeWitt, MD, PhD, Bruce Tranmer, MD, and Alissa A. Thomas, MD

Neurology® 2022;99:117-122. doi:10.1212/WNL.0000000000200748

Correspondence
Sebastian Hanna
sebastian.hanna@med.uvm.edu

Abstract

Meningeal melanocytomas are extremely rare, pigmented tumors of the CNS. They generally carry a favorable prognosis, although recurrence and transformation into the more aggressive malignant melanoma have been reported. We present a case of a patient who reported constipation and abdominal pain around the umbilicus, which progressed into cord compression with lower extremity weakness and gait instability. Spinal MRI revealed a tumor at the level of T11, and she underwent gross total resection of the mass. Pathology demonstrated a meningeal melanocytoma with intermediate features. She received postoperative radiation therapy and had stable disease for 3 years, at which time she developed new weakness and drop metastases. This case represents a rare presentation of a rare disease, in which a spinal cord tumor presented with constipation and abdominal distress. Intradural extramedullary tumors of the thoracic spine are most commonly nerve sheath tumors or meningiomas, but rare entities such as melanocytomas can present in this location; even more rarely, these tumors can have an aggressive course with delayed recurrence.

From the University of Vermont Larner College of Medicine (S.S.H., R.J., C.J.A., J.C.D., B.T., A.A.T.), Burlington; Department of Surgery, Division of Neurosurgery (R.J., B.T.); Department of Radiology, Division of Radiation Oncology (C.J.A.); Department of Pathology and Laboratory Medicine (J.C.D.); and Department of Neurological Sciences (A.A.T.).

Go to Neurology.org/N for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.

Section 1

A 67-year-old woman presented with severe pain just below her umbilicus radiating to her back. This initially felt like gas pain, and an abdominal CT scan was unrevealing. Over the next few weeks, the pain increased in severity, and the patient developed constipation. She underwent a colonoscopy that did not show any abnormalities, and she subsequently was seen in the emergency department. She was given a working diagnosis of a functional bowel problem and was treated with antispasmodics, peppermint oil, dietary modifications, and a bowel regimen. Despite these treatments, she had a second emergency evaluation for an acute episode of severe pain with nausea and vomiting. On discharge, she developed rapidly progressive bilateral lower extremity weakness and was unable to walk. She crawled into her house and returned to the emergency department through ambulance presenting with urinary retention, inability to walk, and lower extremity numbness and weakness. Examination was notable for full strength in the bilateral upper extremities with weakness in the lower extremities as follows: hip flexor: 4/5 right, 4+/5 left; hamstring: 4+/5 right, 5/5 left, and 5/5 strength in her quadriceps, anterior tibialis, extensor hallucis longus, and gastrocnemius bilaterally. There was an intact sensation in the bilateral upper extremities, with diminished sensation on the medial aspect of her right leg. She reported pain at the level of the umbilicus. She also had markedly diminished rectal tone and hyperreflexia in the lower extremities.

Questions for Consideration:

1. What is the localization of the patient's symptoms?
2. What kind of imaging is warranted?

GO TO SECTION 2

Section 2

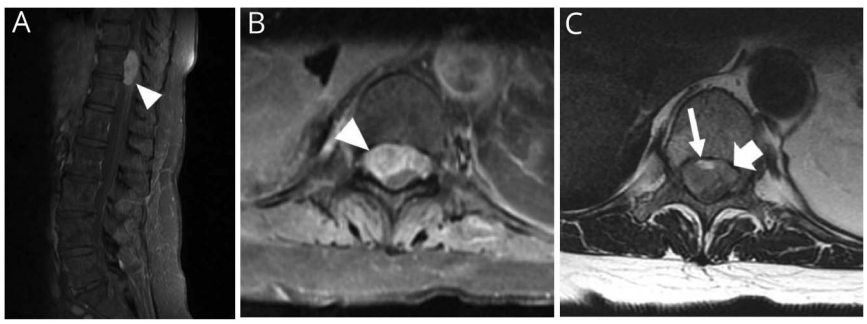
The combination of bilateral lower extremity hyperreflexia and weakness, bowel and bladder symptoms, and loss of the ability to walk should be recognized as cord compression, which is a neurologic emergency. Bilateral lower limb weakness can be observed following lesions anywhere along the descending lateral corticospinal tracts. Starting at the brain, midline parasagittal masses or vasospasm after subarachnoid hemorrhage leads to ischemia of both anterior cerebral arteries, resulting in bilateral upper motor neuron (UMN) lesions in the corticospinal tracts. Most cases of bilateral lower limb weakness are a result of spinal cord lesions, such as demyelinating disease or compression by a tumor. These pathologies can affect UMNs in the spinal cord or lower motor neurons through damage to the ventral horns or roots. Cervical spine lesions often present with both upper and lower extremity weakness. Our patient did not demonstrate any cortical signs, nor did she have upper extremity deficits, which localized her symptoms to the thoracic or lumbosacral spine. Hyperreflexia in the lower extremities further points to UMN signs, suggesting a lesion above the conus medullaris. UMN lesions are also associated with spastic segmental colonic contractions and decreased propulsive peristalsis, which might explain the constipation. Abdominal pain, in the context of neurologic deficits, may result from irritation of the thoracic nerve root and spinothalamic tract injury.

Cord compression necessitates urgent neuroimaging, and MRI of the spine is the modality of choice. Emergent imaging was obtained, and MRI of the thoracic spine with and without contrast showed an enhancing 1.2 × 1.3 × 1.5 cm intradural extramedullary mass at T11 (Figure 1). The patient was transferred to a neurosurgical center in which she underwent T10, T11, and partial T12 laminectomy and gross total resection of a pigmented mass.

Questions for Consideration:

1. What is the differential diagnosis for intradural extramedullary spinal cord masses?
2. What is the differential diagnosis for pigmented neoplasms of the CNS?

Figure 1 MRI of the Thoracic Spine



T1-weighted, postcontrast images from MRI of the thoracic spine in the (A) sagittal and (B) axial planes demonstrate a heterogeneously enhancing 1.2 × 1.3 × 1.5 cm intradural extramedullary mass (arrowhead) at the T11 level. (C) T2-weighted axial imaging shows the heterogeneously hyperintense tumor (long arrow) causing severe cord compression, completely displacing the CSF that typically surrounds the cord. Focus of T2 hyperintense signal thought to reflect myelomalacia secondary to the compression (short arrow).

GO TO SECTION 3

Section 3

Spinal tumors are divided into extradural, intradural extramedullary, and intradural intramedullary categories based on the location. Intradural extramedullary tumors account for 40% of all spinal tumors and are located within the subarachnoid space.[1] Nerve sheath tumors, such as neurofibromas and schwannomas, are the most common primary lesion in this area, whereas meningiomas are the second most common. Less common primary tumors include paragangliomas, lipomas, and meningeal melanocytomas, among many others. Metastatic disease involving the leptomeninges makes up a small percentage of intradural extramedullary lesions.[1] Non-neoplastic lesions to consider include sarcoidosis and arachnoiditis.

Gross pathology of our patient's lesion showed black lesions with seeding of the spinal cord and arachnoid surfaces, which were found to be melanin-filled macrophages, with an encapsulated brown-black soft-tissue mass (Figure 2). When considering pigmented neoplasms in the CNS, 4 main tumors should be on the differential, namely, meningeal melanocytosis, meningeal melanocytoma, malignant melanoma, and meningeal melanomatosis. In melanocytomas, staining is generally positive for HMB-45, Melan A, vimentin, and S-100, whereas staining for GFAP, NSE, EMA, and cytokeratin is usually negative.[2] After histopathologic and genomic analysis, it was concluded that our patient had pathology most consistent with a melanocytoma (Figure 2C).

Questions for Consideration:

1. What is the treatment for a melanocytoma?
2. What is the expected outcome associated with spinal melanocytomas?

Figure 2 Pathology Specimen

(A) Intraoperatively, black lesions covered the tumor and arachnoid surfaces. (B) On gross pathologic examination, the mass was an ovoid, centrally fragmented, but otherwise encapsulated soft-tissue nodule measuring 2.0 × 1.2 × 0.8 cm. Sections showed a dark brown/black cut surface. (C) On histologic examination, the cells exhibited extensive intracytoplasmic melanin pigment and scattered mitotic figures with a Ki67 of 5%–10%, diagnostic of a melanocytic neoplasm. The cells on the arachnoid surface were melanin-laden macrophages. S100 was positive on immunohistochemical staining.

GO TO SECTION 4

Section 4

The mainstay of treatment for primary CNS melanocytoma is complete surgical resection. Complete resection of spinal melanocytomas is associated with significantly better outcomes than incomplete resection, although overall survival after incomplete resection can be improved by postoperative radiotherapy.[3] As such, our patient underwent resection of her thoracic cord mass. Subsequent staging, including MRI of the brain, cervical, thoracic, and lumbar spine, as well as CT of the chest, abdomen, pelvis, and CSF cytology, showed no evidence of metastatic disease. After the resection, the patient underwent radiation to 5,040 cGy in 28 fractions to T10-T12.

Spinal meningeal melanocytomas include a spectrum of diseases with some tumors that have a benign course and a favorable prognosis, intermediate tumors that have a high risk of recurrence, and tumors with potential for transformation to malignant melanoma. In the benign variant, patients with localized disease and complete resection may be cured, with excellent disease-free survival.[4] Next-generation sequencing may identify mutations in *GNAQ* and *GNA11*, which are markers of more aggressive tumors.[5]

Next-generation sequencing on our patient's tumor tissue demonstrated a *GNA11* mutation. Owing to the high risk of recurrence, the patient agreed to proceed with radiation therapy. Six months after radiation, the patient had recovered nearly all motor function, and only residual neuropathic pain in her feet and constipation remained. Unfortunately, after 3 years of stability, the patient presented in the spring of 2021 with new right leg dysesthesias and foot drop. MRI revealed recurrent disease with a drop metastasis at L4 and progression at the site of prior resection at T10-T12. Leptomeningeal spread of disease was identified covering nerve roots at the time of subtotal resection of the L4 metastasis.

Discussion

Melanocytes are cells that arise from the neural crest, and in rare cases, melanocytes found in the leptomeninges can give rise to primary melanocytic neoplasms.[6] One such tumor is the meningeal melanocytoma, first described in the literature as a primary melanotic tumor of the leptomeninges with a benign histology and favorable clinical course.[7] The age at diagnosis ranges from 9 to 73 years with a peak incidence in the 5th decade and is most often seen in females.[6] Spinal melanocytomas are commonly seen in the cervical region and are most often found in the intradural extramedullary compartment.[8] On MRI, the signal intensity of melanocytomas correlates with the quantity of melanin. The clinician should look for a uniform mass displaying hyperintensity on T1-weighted imaging and hypointensity on T2-weighted imaging, with contrast enhancement being remarkable and homogenous.[4,9] The pathogenesis remains unclear but may involve mutations in *GNA11* and in exon 4 of *GNAQ*.[10]

The WHO revised classification of CNS tumors (2016) classifies primary melanocytic lesions into meningeal melanocytosis, meningeal melanocytoma, malignant melanoma, and meningeal melanomatosis (eTable 1, which is available in the supplement, links.lww.com/WNL/C18).[11] After incomplete resection of spinal meningeal melanocytomas, in a series of 49 patients with surviving patients followed for a median of 45 months, local recurrence occurred in 78% without radiation vs 0% with radiation if a dose of ≥5,000 cGy at standard fractionation (i.e., 1.8–2 Gy) was used.[3] At this dose, the risk of radiation myelopathy is exceedingly low. Although prognosis is improved with complete resection, with a 5-year local recurrence rate of 22% after surgery alone, the authors encourage the use of postoperative radiotherapy for all patients. On occasion, meningeal melanocytomas may recur and transform into malignant melanomas.[12] Even in the absence of malignant transformation, the clinician should be aware that meningeal melanocytomas may be associated with leptomeningeal spread and aggressive characteristics when deciding treatment.[13]

Our case highlights a rare presentation of a rare disease, in which an intradural extramedullary spinal cord tumor presented first with constipation that progressed to cord compression and was found to be a melanocytoma. This illustrates an unfortunate situation in which diagnosis of a spinal cord tumor was initially masked by prominent abdominal symptoms, including severe burning pain below the umbilicus with subsequent constipation. A key takeaway from this case is that the clinician should always consider cord compression when there is abdominal pain, especially when it is followed by lower extremity weakness and bladder and bowel dysfunction. Intradural extramedullary tumors of the spinal cord have a broad differential and require histopathology to diagnose a tumor as rare as a melanocytoma.

Study Funding

The authors report no targeted funding.

Disclosure

The authors report no disclosures relevant to the manuscript. Go to Neurology.org/N for full disclosures.

Publication History

Received by *Neurology* November 1, 2021. Accepted in final form April 4, 2022. Submitted and externally peer reviewed. The handling editor was Whitley Aamodt, MD, MPH.

Appendix Authors

Name	Location	Contribution
Sebastian S. Hanna, BS, BA	University of Vermont Larner College of Medicine; Department of Surgery, Division of Neurosurgery	Drafting/revision of the manuscript for content, including medical writing for content; study concept or design; and other
Ryan Jewell, MD	University of Vermont Larner College of Medicine	Major role in the acquisition of data and other
Christopher J. Anker, MD	University of Vermont Larner College of Medicine; Department of Radiology, Division of Radiation Oncology	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; and other

Continued

Appendix *(continued)*

Name	Location	Contribution
John C. DeWitt, MD, PhD	University of Vermont Larner College of Medicine; Department of Pathology and Laboratory Medicine	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; and other
Bruce Tranmer, MD	University of Vermont Larner College of Medicine; Department of Surgery, Division of Neurosurgery	Major role in the acquisition of data and other
Alissa A. Thomas, MD	University of Vermont Larner College of Medicine; Department of Neurological Sciences	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; study concept or design; analysis or interpretation of data; and other

References

1. Beall DP, Googe DJ, Emery RL, et al. Extramedullary intradural spinal tumors: a pictorial review. *Curr Probl Diagn Radiol.* 2007;36(5):185-198.
2. Rades D, Schild SE, Tatagiba M, Molina HA, Alberti W. Therapy of meningeal melanocytomas. *Cancer.* 2004;100(11):2442-2447.
3. Rades D, Schild SE. Dose-response relationship for fractionated irradiation in the treatment of spinal meningeal melanocytomas: a review of the literature. *J Neurooncol.* 2006;77(3):311-314.
4. Yang C, Fang J, Li G, et al. Spinal meningeal melanocytomas: clinical manifestations, radiological and pathological characteristics, and surgical outcomes. *J Neurooncol.* 2016;127(2):279-286.
5. Urtatiz O, Cook C, Huang JL, Yeh I, Van Raamsdonk CD. GNAQ(Q209L) expression initiated in multipotent neural crest cells drives aggressive melanoma of the central nervous system. *Pigment Cel Melanoma Res.* 2020;33(1):96-111.
6. Liubinas SV, Maartens N, Drummond KJ. Primary melanocytic neoplasms of the central nervous system. *J Clin Neurosci.* 2010;17(10):1227-1232.
7. Limas C, Tio FO. Meningeal melanocytoma ("melanotic meningioma"). Its melanocytic origin as revealed by electron microscopy. *Cancer.* 1972;30(5):1286-1294.
8. Chacko G, Rajshekhar V. Thoracic intramedullary melanocytoma with long-term follow-up: case report. *J Neurosurg Spine.* 2008;9(6):589-592.
9. Xie S, Jiang Z. Primary spinal cord melanocytoma: a case report and review of literature. *Int J Clin Exp Pathol.* 2019;12(2):669-673.
10. Murali R, Wiesner T, Rosenblum MK, Bastian BC. GNAQ and GNA11 mutations in melanocytomas of the central nervous system. *Acta Neuropathologica.* 2012;123(3):457-459.
11. Louis DN, Perry A, Reifenberger G, et al. The 2016 World Health Organization classification of tumors of the central nervous system: a summary. *Acta Neuropathol.* 2016;131(6):803-820.
12. Wang F, Li X, Chen L, Pu X. Malignant transformation of spinal meningeal melanocytoma. Case report and review of the literature. *J Neurosurg Spine.* 2007;6(5):451-454.
13. Kim OH, Kim SJ, Choo HJ, et al. Spinal meningeal melanocytoma with benign histology showing leptomeningeal spread: case report. *Korean J Radiol.* 2013;14(3):470-476.
14. Küsters-Vandevelde HVN, Küsters B, van Engen-van Grunsven ACH, Groenen PJTA, Wesseling P, Blokx WAM. Primary melanocytic tumors of the central nervous system: a review with focus on molecular aspects. *Brain Pathol.* 2015;25(2):209-226.
15. Smith AB, Rushing EJ, Smirniotopoulos JG. Pigmented lesions of the central nervous system: Radiologic-pathologic correlation. *RadioGraphics.* 2009;29(5):1503-1524.

Call for Voices: Lived Experiences

The Editor of the *Neurology* specialty section Inclusion, Diversity, Equity, Anti-racism, & Social Justice (IDEAS) encourages you to submit short first-person accounts (1,000 words or less) of experiences lived within the realm of IDEAS with the goal of informing and enlightening our community on these critical issues. Some topics to consider include, but are not limited to:

- Descriptions of personal experiences that shaped your views of IDEAS.
- Reflections on the intersection between personal identity and career.
- Discussions at the intersection of IDEAS and neurology patient care, research, education, advocacy, or policy.

Submit your contributions to journal@neurology.org and include "Voices Submission" in the subject line.

Clinical Reasoning: A 67-Year-Old Woman With Abdominal Pain, Constipation, and Urinary Retention

Sebastian S. Hanna, Ryan Jewell, Christopher J. Anker, et al.

Neurology 2022;99;117-122 Published Online before print May 6, 2022
DOI 10.1212/WNL.0000000000200748