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

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**Figure Count:**

2

**Table Count:**

0

**Search Terms:**

Acknowledgment:

Study Funding:

The authors report no targeted funding

Disclosures:

The authors report no disclosures relevant to the manuscript.

Preprint DOI:

Received Date:
2021-11-01

Accepted Date:
2022-04-04

Handling Editor Statement:

Submitted and externally peer reviewed. The handling editor was Whitley Aamodt, MD, MPH.

Abstract

Meningeal melanocytomas are an extremely rare, pigmented tumors of the central nervous system (CNS). They generally carry a favorable prognosis, although recurrence and
transformation into the more aggressive malignant melanoma has 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 magnetic resonance imaging (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 post-operative radiation therapy and had stable disease for three 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.

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 computed tomography (CT) scan was unrevealing. Over the next few weeks, the pain increased in severity, and the patient developed constipation. She underwent a colonoscopy which 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 anti-spasmodics, 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. Upon 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 via ambulance presenting with
urinary retention, inability to walk, and lower extremity numbness and weakness. Exam 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 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?

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 neurological 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 following subarachnoid hemorrhage leading to ischemia of both anterior cerebral arteries, resulting in bilateral upper motor neuron (UMN) lesions in the corticospinal tracks. 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 UMN in the spinal cord, or lower motor neurons via 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 neurological 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 the MRI of the thoracic spine with and without contrast showed an enhancing 1.2 x 1.3 x 1.5 cm intradural-extramedullary mass at T11 (Figure 1). The patient was transferred to a neurosurgical center where 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 central nervous system (CNS)?

Section 3:
Spinal tumors are divided into extradural, intradural-extramedullary, and intradural-intramedullary based on 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, while meningiomas are the second most common. Less common primary tumors include paragangliomas, lipomas and meningeal melanocytomas, amongst many others. Metastatic
disease involving the leptomeninges make up a small percentage of intradural-extradural lesions.\textsuperscript{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, four 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, while staining for GFAP, NSE, EMA, and cytokeratin is usually negative.\textsuperscript{2} After histopathologic and genomic analysis, it was concluded that our patient had pathology most consistent with a melanocytoma (Figure 2C).

\textbf{Questions for Consideration}:

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

\textbf{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 following incomplete resection can be improved by post-operative radiotherapy.\textsuperscript{3} As such, our patient underwent resection of her thoracic cord mass. Subsequent staging including MRI of the brain, cervical, thoracic, lumbar
spine, and CT of the chest, abdomen, pelvis, and CSF cytology showed no evidence of metastatic disease. After the resection, the patient underwent radiation to 5040 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. Next generation sequencing may identify mutations in GNAQ and GNA11, which are markers of more aggressive tumors.

Next generation sequencing on our patient’s tumor tissue demonstrated a GNA11 mutation. Due to the high risk of recurrence, the patient agreed to proceed with radiation therapy. Six months following radiation, the patient had recovered nearly all motor function, and only residual neuropathic pain in her feet and constipation remained. Unfortunately, after three 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 as well as 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. 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. The age of 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-extradural 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 homogeneous.6,9 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).11 Following 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 versus 0% with if a dose ≥5000 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% following surgery alone, the authors encouraged the use of post-operative 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-extradural 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.

eTable 1 - http://links.lww.com/WNL/C18

References

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Figure 1: MRI of the thoracic spine

T1-weighted, post-contrast images from the MRI of the thoracic spine in the (A) sagittal and (B) axial planes demonstrates a heterogeneously enhancing 1.2 x 1.3 x 1.5 cm intradural-extradural 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 cerebrospinal fluid that typically surrounds the cord. Focus of T2 hyperintense signal thought to reflect myelomalacia secondary to the compression (short arrow).
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 x 1.2 x 0.8 cm. Sections showed a dark brown/black cut surface. (C) On histological exam, 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.
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Neurology published online May 6, 2022
DOI 10.1212/WNL.0000000000200748

This information is current as of May 6, 2022

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