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Case Report

Primary Melanocytomas of the Spinal Cord: Case Studies and Rehabilitation Perspectives

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Abstract Primary melanocytomas of the central nervous system are rare tumors arising from leptomeningeal melanocytes. Only 29 cases have been reported in the literature. Presenting symptoms may include insidious onset of back pain, slowly progressive neurologic deficits such as weakness and sensory changes, and bowel and bladder dysregulation. Advanced imaging including magnetic resonance imaging can be helpful in lesion localization but does not distinguish between primary and metastatic melanoma. In this case series, we present 3 patients with nontraumatic spinal cord injuries secondary to primary central nervous system malignant melanocytomas who were admitted to a single inpatient rehabilitation facility within a 12-month time frame. These cases highlight the importance of the rehabilitation team in the continuum of care for patients undergoing resection of primary melanocytomas of the spinal cord. The rehabilitation team should be involved in the preoperative counseling setting, immediately postoperatively, and in follow-up care to assess for signs of recurrence. A comprehensive multidisciplinary approach including physical and occupational therapists, rehabilitation nurses, rehabilitation neuropsychologists, and physiatrists is important for optimizing the function of these patients.

List of abbreviations: CNS, central nervous system; GNA11, G-protein subunit α-11; GNAQ, G(q) subunit α; MRI, magnetic resonance imaging; PM&R, physical medicine and rehabilitation.

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Primary melanocytomas of the central nervous system (CNS) are rare tumors arising from leptomeningeal melanocytes. They may occur anywhere within the CNS but are most commonly located intracranially. In the spinal canal, these tumors are typically intradural, extramedullary lesions.[1-3] Intramedullary primary melanocytomas are extremely rare tumors. The first case in the literature was described by Barth et al in 1993 and, in total, only 29 cases have been reported to date.[4-9] These intramedullary variants derive from melanocytes of the parenchymal perivascular spaces, also known as Virchow-Robin spaces, and occur most commonly in the lower thoracic spinal cord.[5,10]

Intramedullary melanocytomas typically present in the fifth decade and are more common in female individuals.[11] Presenting symptoms may include insidious onset of back pain and slowly progressive neurologic deficits such as weakness and sensory changes. Physical examination may reveal features of myelopathy, including motor weakness, spasticity, hyperactive deep tendon reflexes, and pathologic reflexes such as a positive Babinski sign. Advanced imaging is usually delayed several months after symptom onset. Magnetic resonance imaging (MRI) can be helpful in localizing the lesion but does not distinguish between primary and metastatic melanoma.[11,12] Although primary melanocytic tumors of the CNS are typically benign, malignant variants have been reported and local recurrence is possible. Close follow-up is important for early detection.[1,2] Genetic studies have demonstrated frequent guanine nucleotide-binding protein G(q) subunit α (GNAQ) and G-protein subunit α-11 (GNA11) mutations in cases of CNS melanocytomas, whereas other mutations common to cutaneous and uveal melanocytic tumors are typically absent.[13,14] Additionally, Kusters-Vandevelde et al raised the question of an association between GNA11 mutations and more aggressive tumor behavior, because this mutation has been observed to occur more commonly in intermediate-grade CNS melanocytomas.[14,15]

In this case series, we present 3 patients with nontraumatic spinal cord injuries secondary to primary CNS malignant melanocytoma who were admitted to a single inpatient rehabilitation facility at a tertiary care center within a 12-month time frame. In 2 of these cases, the tumor was intramedullary, and in the third case, the tumor was primarily extramedullary with intramedullary extension. The primary purpose of this article is to highlight the role of the rehabilitation physician in the continuum of care for patients with newly discovered melanocytomas. Rehabilitation physicians should be involved in preoperative care to educate patients on what functional changes they may experience after surgery and the role of the rehabilitation team in their postoperative care. Physiatrists are also intimately involved in the acute rehabilitation of these patients during inpatient rehabilitation. Lastly, rehabilitation physicians should be involved in follow-up and surveillance of recurrence of disease and addressing rehabilitative needs. Our aim is to increase awareness of nonrehabilitation professionals to include a rehabilitation specialist in the care of this patient population.

Case 1

A 58-year-old woman presented to the outpatient clinic for a second opinion regarding evaluation and management of a known cervical spinal cord tumor. Symptoms began several years prior with morning headaches. Four to 6 months prior to presentation, she developed neck pain with radiation into her left upper extremity. More recently, she experienced right hand weakness and a tendency to veer rightward during ambulation.

MRI of the brain and cervical spine demonstrated a gadolinium-enhancing expansile intradural, intramedullary mass extending from the level of the foramen magnum to second cervical vertebrae (C2). The patient was referred to a tertiary care center for suboccipital craniotomy with C1-C2 laminectomies and gross total resection of the C1-C2 spinal cord tumor as shown in figure 1. Surgical pathology was consistent with primary CNS melanocytoma. Gene analysis was notable for a GNAQ mutation. Dermatology and ophthalmology were consulted and ruled out primary skin and primary ocular melanomas, respectively.

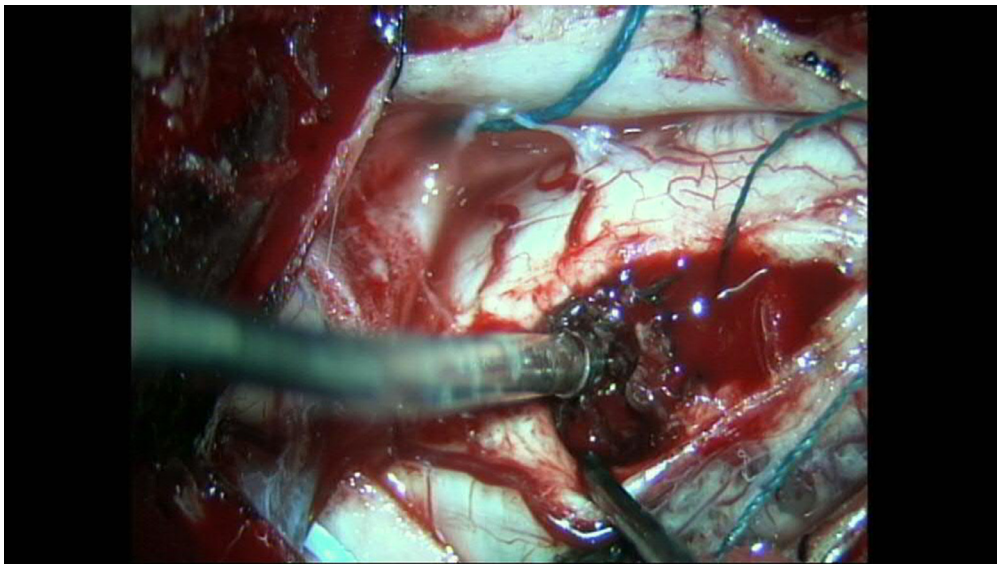

Fig 1 Intraoperative images of an upper cervical primary melanocytoma resection.

Postoperatively, the patient was noted to have new left hemiparesis with 2/5 strength in the proximal left upper extremity, 1/5 strength in the distal left upper extremity, 1/5 strength in the left hip flexors, 2/5 strength in the left knee extensors, 0/5 strength in the ankle dorsiflexors and great toe extensors, and 3/5 strength in the plantar flexors (manual muscle testing on a 0-5 scale). The patient had diminished but present sensation to light touch of the left upper extremity starting at C2 extending distally and right upper extremity on the palm of the hand extending distally to the fingers and absent sensation to light touch of the right lower extremity. Proprioception was absent distally and impaired proximally in the left upper and lower extremities. Spasticity was present with Modified Ashworth Scale 2 in the left triceps, wrist extensors, and quadriceps. The patient had neurogenic bladder requiring straight catheterization and neurogenic bowel requiring bowel medications.

She was admitted to acute inpatient rehabilitation and participated in intensive therapies focusing on range of motion, strengthening, coordination, gait training, neuromuscular re-education, use of adaptive equipment and compensatory strategies for completion of activities of daily living, and use of a power wheelchair. The patient achieved significant functional gains. At discharge, her left-sided strength had improved to 4/5 in the proximal left upper extremity, 3/5 distal left upper extremity, 4/5 in the left quadriceps, 3/5 in the left ankle dorsiflexors, and 5/5 in the left plantar flexors. Sensation testing to light touch was similar to that on admission. The patient was independent to contact guard assist for transfers and was independent to modified independent with self-care. Because of her continued severe left-sided proprioceptive impairments, the patient was unable to ambulate without assistance or propel a manual wheelchair. Additionally, the patient did not have full-time caregiver support; therefore, she required a power wheelchair and was discharged to a wheelchair accessible apartment.

One month postdischarge, the patient developed new-onset diplopia and dysphagia. MRI of the cervical spine demonstrated recurrence of tumor from the cervical medullary junction to the C4-C5 vertebral body level as well as leptomeningeal enhancement throughout the cervical cord and visualized upper thoracic cord consistent with metastatic disease. A whole-body positron emission tomography scan did not demonstrate other primary or metastatic disease. Neuro oncology, medical oncology, and radiation oncology recommended that the patient begin chemotherapy, mitogen-activated protein kinase inhibitor, and palliative craniospinal radiation, respectively. Unfortunately, the patient died from sudden cardiac arrest before these interventions could occur, 2 months postdischarge from inpatient rehabilitation.

Case 2

A 70-year-old man presented with approximately 6 months of truncal and gait instability, urinary incontinence, confusion, and lethargy. MRI of the brain was consistent with communicating hydrocephalus, which was initially thought to explain his symptoms. A chronic right cerebellar infarct was also noted on that MRI. Placement of a ventriculoperitoneal shunt was planned. The patient was evaluated by physical medicine and rehabilitation (PM&R) in the outpatient setting at this stage regarding rehabilitation needs for hydrocephalus-related impairments. The patient was counseled on injury prevention given his gait instability, fall risk, and confusion. The physiatrist also recommended obtaining a home health assessment because of his limited mobility and need for assistance with self-care and provided education on disinhibited bladder management.

The patient underwent a diagnostic and therapeutic lumbar puncture as management for hydrocephalus. This led to a modest improvement in symptoms, and subsequent cerebrospinal fluid analysis revealed an elevated protein count. An MRI of the spine was obtained 1 week after initial presentation to further evaluate this finding. The MRI revealed 9th and 12th thoracic vertebrae (T9 and T12) intradural gadolinium-enhancing lesions with suspected intramedullary expansion of the lesion at T9.

The patient underwent external ventricular drain placement with eventual transition to ventriculoperitoneal shunt over the next 2 weeks for treatment of his hydrocephalus. Two days later, the patient underwent 12th thoracic through first lumbar (T12-L1) laminoplasty and subtotal resection of an intradural lesion located primarily extramedullary but with intramedullary extension into the conus medullaris. Final pathology demonstrated a primary melanocytic tumor of intermediate grade. Gene analysis identified a GNA11 mutation. Dermatology and ophthalmology were consulted and ruled out primary ocular and cutaneous melanoma, respectively.

The patient was admitted to inpatient rehabilitation. Impairments noted on admission included lower limb weakness with strength graded as 4/5 for bilateral hip flexion, right knee flexion, and right ankle plantarflexion; right upper limb dysmetria with finger-to-nose testing; impaired toe-walking; positive Romberg sign; and neurogenic bowel and bladder. Deep tendon reflexes were symmetrical and severely reduced at the biceps and were absent at the bilateral triceps, patella, and Achilles' tendons. Speech, language, light touch sensation, proprioception, and muscle tone were normal. The patient's right upper limb deficit was attributed to the chronic right cerebellar infarct seen on MRI.

The patient received physical and occupational therapy. Physical therapy consisted of gait training, transfer training, stair training, therapeutic exercise, neuromuscular re-education, and establishment of a home exercise program. Occupational therapy consisted of therapeutic exercise, therapeutic functional activity, self-care/home management, cognitive skills training, and neuromuscular re-education. Fifteen days later the patient was discharged in stable medical condition to home with his wife. At discharge, his functional independence had improved. The patient required a front-wheeled walker and standby assistance for ambulation and supervision for activities of daily living. After discharge, the patient received immunotherapy with nivolumab and ipilimumab and 10 days of radiation therapy directed at T6 to the sacrum.

Unfortunately, 2 weeks after discharge from inpatient rehabilitation, the patient developed subacute onset of paraplegia, bilateral lower extremity sensory loss, complete urinary retention, and constipation. The patient was

admitted to a local hospital. MRI at that time revealed leptomeningeal carcinomatosis throughout the thoracic and lumbar spine along with spinal cord compression. The patient's physical and cognitive function rapidly declined and he was discharged home with hospice. The patient died days later.

Case 3

A 66-year-old man presented with insidious onset of low back pain without weakness or disruption in sensation. After failing conservative rehabilitation strategies, a lumbar spine MRI revealed a well-circumscribed, 9-mm intramedullary uniformly enhancing lesion at T12 as shown in figure 2. An attempted biopsy was nondiagnostic and resulted in right lower extremity weakness as well as neurogenic bladder that improved with self-cathing interventions. Eventually, the patient's bladder function fully recovered without the need for continued intermittent catheterization.

The patient later developed recurrent back pain with progressive right lower extremity weakness and sensory changes. Repeat imaging revealed increased lesion size. Repeat biopsy suggested a melanocytic neoplasm. Pathology confirmed primary melanocytoma with GNAQ mutation. The patient had dermatologic and ophthalmologic consultation to rule out primary ocular or cutaneous melanocytoma. The tumor was refractory to radiotherapy and neurosurgical intervention was recommended. Physiatry was involved in preoperative evaluation to discuss gait retraining, spasticity treatment, and neurogenic bladder management after surgery. The patient underwent a T10-L1 laminectomy and gross total resection of the spinal cord tumor.

The patient was admitted to acute inpatient rehabilitation. The patient's presenting deficits included 4/5 hip flexor, 4/5 quadriceps, 2/5 ankle dorsiflexors, 2/5 long toe extensor, and 3/5 ankle plantar flexors. Tone included Modified Ashworth Scale 1+ in the left lower extremity and impaired proprioception at the great toe and ankle on the right lower extremity. Light touch and pinprick sensation were diminished or absent below the T12 level. Rehabilitation treatments included gait training, neuromuscular reeducation, therapeutic exercise, functional activity training, and safety education. The patient achieved significant functional gains and was discharged home with a right ankle-foot orthosis, a single point cane, and supervision level of assistance for mobility and self-care. The patients

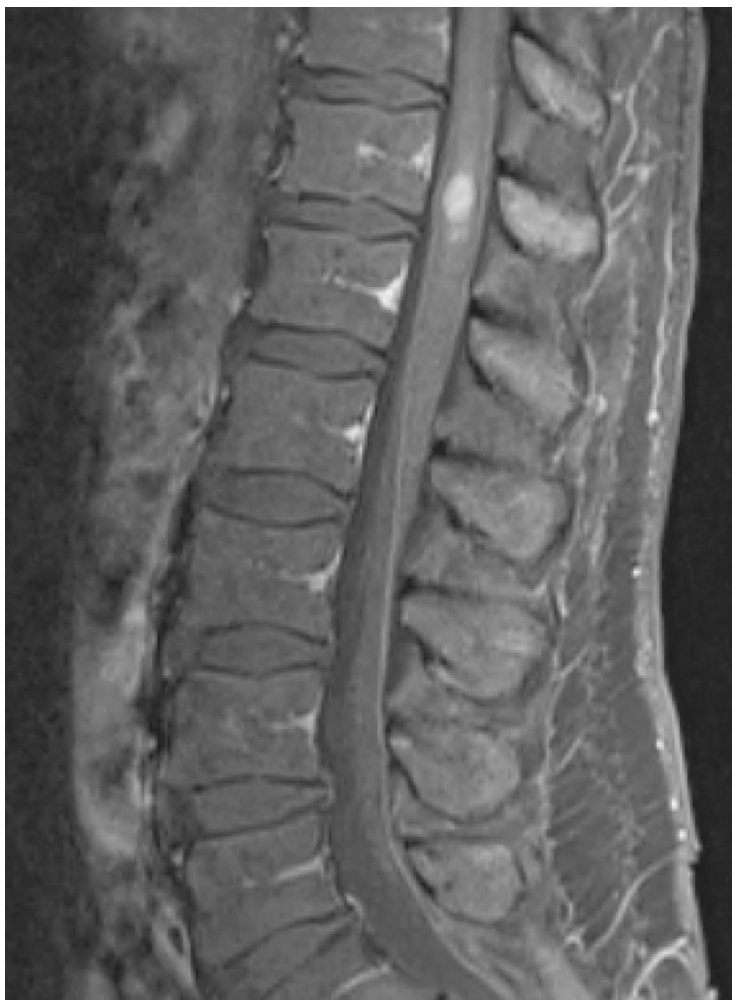

Fig 2 Sagittal T1 imaging of a primary lower thoracic melanocytoma.

has since continued to follow up with regular neurologic examinations and thoracic MRI every 6 months without recurrence of disease.

Discussion

Only 29 cases of primary spinal melanocytomas are reported in the literature.[5-9] Our institution participated in the care of 3 separate cases confirmed by pathology within a 12-month time frame. It is possible that cases of spinal melanocytomas are more common than previously reported due to the often-insidious nature of these tumors.[16] The slow-growing nature, initial nonspecific symptoms, and rarity of the disease may contribute to prolonged time to diagnosis or cases being missed altogether. The most common initial symptom for intramedullary tumors is pain, which may be described as radicular, dull, aching, midline, or with paravertebral tightness and stiffness.[17,18] The presenting symptoms in our cases included headache, confusion with gait instability, and nonspecific low back pain. Interestingly, 1 patient presented with symptoms of hydrocephalus, a condition associated with spinal melanocytomas that has been described in previously reported cases.[19] A recurrence of 1 patient's disease involved the brain stem and caused diplopia and dysphagia.

Postsurgical functional outcomes in spinal intramedullary tumors have been cited as approximately 23% of patients showing neurologic worsening in the immediate postoperative period with 14% developing permanent disability.[20] In our cases, deficits after surgical intervention included hemiparesis, proprioceptive impairment, spasticity, and neurogenic bowel and bladder. Proprioceptive deficits were the main functional impairments for 2 of our 3 cases. Each of these impairments can be addressed in an inpatient rehabilitation setting and are treated similarly to deficits that can be acquired from traumatic spinal cord injuries. Teaching skin protective measures can help reduce skin breakdown due to sensory loss. Mobility and activities of daily living can be improved by skilled physical and occupational therapy teams. Spasticity management can include daily stretching, splinting, titration of oral medications, and even local injections of botulinum toxin. Equipment needs can be addressed, including the use of orthoses, gait aids, and wheelchairs. Neurogenic bladder can be managed with regular voiding trials, fluid schedules, and self-catheterization vs indwelling catheter placement. Our patients presented with upper motor neuron pattern neurogenic bowel, which was addressed with stool softening agents and education on self-digital stimulation and extraction. All achieved clinically significant gains in functional independence by the time of discharge from inpatient rehabilitation. Herein lies the need for consideration of intensive inpatient rehabilitation after intramedullary spinal cord tumor resection to optimize quality of life, independence, and family training. During follow-up, surveillance should occur every 6 months, including serial neurologic examinations with cross-sectional imaging of the involved portion of the spine.

Currently, a unifying guideline for management of intramedullary melanocytomas does not exist. Our cases demonstrate the locally aggressive character of these tumors within the spinal cord and the challenges this presents in treatment of these patients after gross total resection. Proposals to prevent recurrence have included high-dose radiotherapy, re-resection of the tumor, and adjuvant radiotherapy in cases of subtotal resection.[16] Patients with total resection tend to have better outcomes than those with incomplete resection. Notably, Rades and Schild observed that those with incompletely resected tumors had improved functional outcomes after radiotherapy. With the high recurrence of spinal melanocytomas, most treatment recommendations include a combination of surgical and radiation therapy.[21]

The role of the physiatrist is important in the continuum of care for patients undergoing resection of primary melanocytomas of the spinal cord. Preoperative appointments can help establish baseline function, and expectations after resection can be discussed. Immediately after surgery, a PM&R consultation service can be used to establish postoperative deficits and plan for acute care and inpatient rehabilitation. As the patients progress through postsurgical cancer treatments including radiation, rehabilitation physicians can play an important role in monitoring for the development of radiation myelopathy.[21] Local recurrence is common and was demonstrated in 2 of our 3 cases and resulted in death. Thus, outpatient PM&R follow-up can serve as a point of contact to monitor neurologic function, assess equipment needs, and maintain functional status. Even when life-prolonging measures are no longer an option, a palliative rehabilitation approach can serve the patient during end-of-life care.[22]

Conclusions

Primary melanocytomas of the spinal cord are rare tumors. Presenting symptoms can be insidious in onset and mimic other disease states such as hydrocephalus, radiculopathy, or chronic musculoskeletal back pain. Although advanced imaging is helpful for localization of tumors, diagnosis is proven via biopsy demonstrating positive gene markers, including GNAQ and GNA11 mutations. Consulting dermatology and ophthalmology is essential to rule out primary ocular and cutaneous melanomas. Although unifying medical and surgical management guidelines have not been established, the rehabilitation team is essential. Rehabilitation specialists may encounter these patients in outpatient pain, musculoskeletal, or spinal cord injury clinics prior to diagnosis as well as postdiagnosis after invasive interventions when acute inpatient rehabilitation services are being considered. Postsurgical functional deficits can include weakness, primary sensory and proprioceptive impairments, gait instability, spasticity, and neurogenic bowel and bladder, as demonstrated by our 3 cases. The PM&R physician can serve to monitor neurologic function and immediately involve the oncology team if recurrence is suspected. The inclusion of the rehabilitation team composed of physical and occupational therapists, rehabilitation nurses, rehabilitation neuropsychologists, and physiatrists is important for a comprehensive multidisciplinary approach to the continuum of care in patients with primary spinal cord melanocytomas.

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