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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 to date. Presenting symptoms may include insidious onset of back pain, slowly progressive neurological deficits such as weakness and sensory changes, in addition to 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 three patients with non-traumatic spinal cord injuries secondary to primary CNS 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 pre-operative counseling setting, immediately post-operatively and in follow up care. A comprehensive multidisciplinary approach including physical and occupational therapists, rehabilitation nurses, rehabilitation neuropsychologists and physiatrists is important for recovery of these patients.

Keywords: Central nervous system • Primary melanocytomas • Rehabilitation

Introduction

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 5th decade and are more common in females [11]. Presenting symptoms may include insidious onset of back pain and slowly progressive neurological 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 [12]. Although primary melanocytic tumors of the CNS are typically benign, malignant variants have been reported and local recurrence is possible [1,2]. Genetic studies have demonstrated frequent Guanine-nucleotide binding protein G(q) subunit alpha (GNAQ) and G-protein subunit alpha-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 raised the question of an association between GNA11 mutations and more aggressive tumor behavior, as this mutation has been observed to occur more commonly in intermediate grade CNS melanocytomas [14,15]. In this case series, we present three patients with non-traumatic spinal cord injuries secondary to primary CNS malignant melanocytoma, who were admitted to a single Inpatient Rehabilitation Facility (IRF) at a tertiary care center within a 12-month timeframe. In two of these cases, the tumor was intramedullary, and in the third case, the tumor was primarily extramedullary with intramedullary extension.

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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 six 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. Magnetic Resonance Imaging (MRI) of the 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. Postoperatively, the patient was noted to have new left hemiparesis, diminished sensation to light touch of the bilateral upper extremities and left lower extremity, left-sided proprioceptive impairments, left-sided spasticity, neurogenic bladder requiring straight catheterization, and neurogenic bowel. She was admitted to acute inpatient rehabilitation and achieved significant functional gains. She was discharged to a wheelchair accessible apartment, requiring power wheelchair for household mobility. She was independent to contact guard assist for transfers and was independent to modified independent with self-cares. One-month post-discharge, she developed new onset diplopia and dysphagia. MRI of the cervical spine demonstrated recurrence of tumor at the operative site as well as leptomeningeal enhancement throughout the cervical cord and visualized upper thoracic cord consistent with metastatic disease. Positron emission tomography scan did not demonstrate other primary lesions. Neuro Oncology, Medical Oncology, and Radiation Oncology recommended that she begin chemotherapy, mitogen-activated protein kinase inhibitor, and palliative craniospinal radiation, respectively. Unfortunately, the

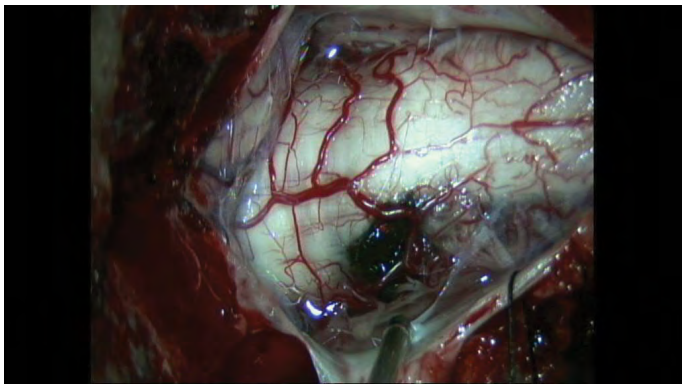

Figure 1. Intraoperative images of and upper cervical primary melanocytoma resection.

patient passed away from sudden cardiac arrest before these interventions could occur, two months post-discharge from inpatient rehabilitation.

Case 2

A 70-year-old man presented with approximately 6 months of truncal and gait instability, confusion, and lethargy. MRI of the brain was consistent with communicating hydrocephalus. Imaging of the spine one week later revealed a ninth and twelfth thoracic vertebrae (T9-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 two weeks. Two days later, he underwent twelfth 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. Ophthalmology and dermatology were consulted and ruled out primary ocular and cutaneous melanoma, respectively. He was admitted to inpatient rehabilitation. Deficits included mild right hemiparesis, right upper limb incoordation, gait instability and neurogenic bowel and bladder. Fifteen days later he discharged in stable medical condition to home with his wife. At discharge, his functional independence had improved. He required a front-wheeled walker and standby assistance for ambulation and supervision for activities of daily living (ADLs). Following discharge, he received immunotherapy with nivolumab and ipilimumab and ten days of radiation therapy directed at T6 to the sacrum. Unfortunately, two weeks after discharge from inpatient rehabilitation, he developed subacute onset of paraplegia, bilateral lower extremity sensory loss, complete urinary retention and constipation. He was admitted to his local hospital. MRI at that time revealed leptomeningeal carcinomatosis throughout the thoracic and lumbar spine along with spinal cord compression. His physical and cognitive function rapidly declined and he discharged home with hospice. He passed away 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 non-diagnostic and resulted in right lower extremity weakness as well as neurogenic bladder that improved with self-cathing interventions. Eventually, his 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 dermatological and ophthalmological consultation to rule out primary ocular or cutaneous melanocytoma. The tumor was refractory to radiotherapy and neurosurgical intervention was recommended. He underwent a T10-L1 laminectomy and gross total resection of the spinal cord tumor. He was admitted to acute inpatient rehabilitation. His presenting deficits included pyramidal pattern weakness affecting the right lower limb with loss of antigravity strength in ankle dorsiflexion and toe extension, Modified Ashworth Scale 1+ tone in the left lower extremity and impaired proprioception at the great toe and ankle on the right lower extremity. He 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-cares. He has since continued to follow with regular neurological examinations and thoracic MRIs every 6 months without recurrence of disease.

Discussion

There are only 29 cases of primary spinal melanocytomas reported in the literature [5-9]. Our institution participated in the care of three separate cases confirmed by pathology within a 12-month timeframe. 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 non-specific 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 non-specific low back pain. Interestingly, one patient presented with symptoms of hydrocephalus, a condition associated with spinal melanocytomas which has been described in previously reported cases [19]. Post-surgical functional outcomes in spinal intramedullary tumors have been quoted as approximately 23% of patients showing neurological 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. Each of these impairments can be addressed in an inpatient rehabilitation setting. Teaching skin protective measures can help reduce skin breakdown due to sensory loss. Mobility and ADLs can be improved by skilled physical and occupational therapy teams. Spasticity management can include daily stretching, splinting, and titration of oral medications and even local injections of botulinum toxin. Equipment needs can be addressed including the use of orthoses, gait aids and wheel chairs. Neurogenic bladder can be managed with regular voiding trials, fluid schedules and self-catheterization versus indwelling catheter placement. Our patients presented with upper motor neuron pattern neurogenic bowel which was addressed with stool softening agents and teaching self-digital stimulation and extraction. All achieved clinically significant gains in their 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.

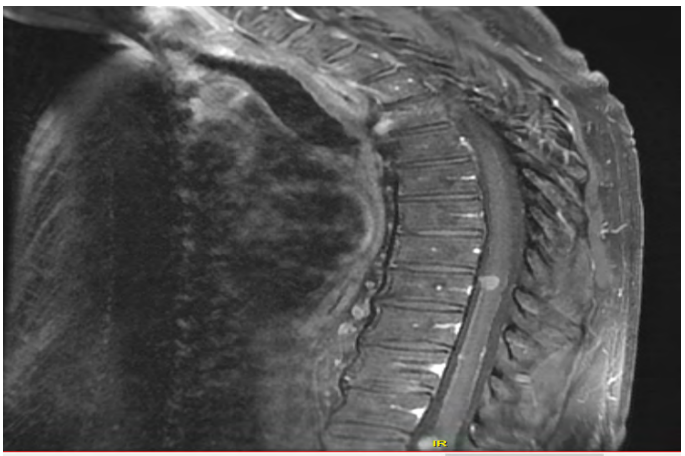

Figure 2. Sagittal T1 imaging of a primary lower-thoracic melanocytoma.

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 following gross total resection. Proposals to prevent recurrence have included high-dose radiotherapy, re-resection of 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 et al. observed that those with incompletely resected tumors had improved functional outcomes following 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. Pre-operative appointments can help establish baseline function and expectations following resection can be discussed. Immediately after surgery, a PM and R consultation service can be utilized to establish post-operative deficits and plan for acute care and inpatient rehabilitation. As the patients progress through post-surgical 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 two of our three cases. Thus, outpatient follow-up can serve as a point of contact to monitor neurological 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].

Conclusion

Primary melanocytomas of the spinal cord are rare occurring 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, GNAQ and GNA11 mutations. Consulting dermatology and ophthalmology is essential to rule out of primary ocular and cutaneous melanomas. Although unifying medical and surgical management has not been established, the rehabilitation team is essential. Rehabilitation specialists may encounter these patients in the outpatient pain, musculoskeletal, or spinal cord injury clinics prior to diagnosis as well as post-diagnosis following invasive interventions when acute inpatient rehabilitation services are needed. Post-surgical functional deficits can include weakness, primary sensory and proprioceptive impairments, gait instability, spasticity and neurogenic bowel and bladder as demonstrated by our three cases. The inclusion of the rehabilitation team such as 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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