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Case Report

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A 75 Year-Old Man With Progressive Lower Extremity Weakness

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Section 1

A 75 year old man presented with progressive and painless lower extremity weakness. His past medical history included type 2 diabetes, myocardial infarction, bilateral carpal tunnel release, removal of a skin lesion, and abnormal arches and toes since young age. His mother had similar high arches and toes. In 2012 he developed sensory changes in his feet and a left foot drop. Based on these findings and an EMG, a local neurologist diagnosed him with Charcot-Marie-Tooth disease. His weakness progressed, requiring a cane in 2016, walker in 2018, and a wheelchair in July of 2019, a month prior to presentation. He thought his left leg was worse than his right. He also noted a year of fecal and urinary incontinence with decreased sensation during micturition. He reported decreased sensation below his knees but denied saddle anesthesia.

On exam, he had a normal mental status and cranial nerve function. In the upper extremities, he had 4/5 strength proximally and 4+/5 strength distally, with the left side being slightly worse than the right. In his right lower extremity he had 4/5 strength proximally and 4+/5 strength distally. In the left lower extremity he had 2/5 strength throughout. Reflexes were reduced in the upper extremities with a negative Hoffman's sign. In the lower extremities he had brisk reflexes proximally with crossed adductor signs but ankle reflexes were absent. Babinski sign was positive bilaterally. He had diminished sensation to light touch below the T4 level with absent vibration and joint position sense at the toes and ankle. Pinprick was more diminished on the right side compared to the left. Prominent high arches and hammertoes were noted.

Questions for Consideration:

1. What is the localization for his presentation?
2. What are the differential diagnoses?

Section 2

The patient's high arches, hammertoes, and long history of distal weakness and foot drop are consistent with Charcot-Marie-Tooth disease, the most common hereditary neuropathy[1]. However, his recent progressive asymmetric lower extremity weakness, along with reduced reflexes in the upper extremities and upper motor neuron signs in the lower extremities is concerning for cervical myelopathy. Given his sensory level at T4 with more impairment to light touch on the left and pinprick on the right, it may represent a partial Brown-Sequard syndrome with a lesion near the cervicothoracic junction.

The differential diagnosis for a progressive myelopathy in this clinical context includes multiple compressive and intrinsic etiologies, especially given the difficulty in understanding the timeline of myelopathy deficits concurrent with the severe neuropathy. A structural etiology (e.g. spondylosis) or tumor with cord compression should be considered with asymmetric features at the cervicothoracic junction and a prolonged clinical decline. Progressive multiple sclerosis is frequently characterized by an asymmetric progressive myelopathy evolving over years, but the more recent rapid decline and suspected onset > 70 years of age would argue against this. Sarcoidosis can cause a subacute to chronic progressive myelopathy in isolation at any age without additional systemic symptoms, and could eventually lead to a more rapid decline. A paraneoplastic etiology could be considered given the severe progressive nature and potential multifocal localization (nerve), but paraneoplastic myelopathy as a predominant clinical presentation is very rare and such focal findings with a sensory level and features of Brown-Sequard syndrome would be unusual. Other inflammatory etiologies would not be expected given the chronic progressive presentation. A spinal dural arteriovenous fistula could be considered, although clinical localization at the cervicothoracic junction is rare. Toxic and nutritional etiologies are unlikely with asymmetric findings and sensory level. The timeline of deficits and clinical features would be atypical for chronic infectious etiologies (e.g. human immunodeficiency virus, human T-lymphotrophic virus, syphilis). Although rare, an intrinsic neoplasm (e.g. glioma) should be considered given the chronic progressive decline that eventually became rapid.

Questions for Consideration:

1. What additional testing should be considered?

Section 3

MRI of the cervical and thoracic spine showed an unusual contrast enhancing intramedullary mass at T1-T2 that was eccentric to the left side with associated vasogenic edema extending from C7-T5 (Figure 1). Expanded lab work was performed given the challenging timeline with central and peripheral features, including screening for an inflammatory, infectious, and metabolic etiology with serum syphilis IgG antibody, human T-lymphotrophic virus antibody, vitamin E, zinc, copper, antinuclear antibodies, antineutrophil cytoplasmic antibodies, thyroid stimulating hormone, pernicious anemia cascade, aquaporin-4-IgG, coccidioides, cryptococcus, histoplasmosis, and HIV which were all unremarkable. EMG showed chronic, axonal, length-dependent, sensorimotor peripheral neuropathy, but the degree of abnormality was not severe enough to explain his weakness.

Questions for Consideration:

1. What is the most likely diagnosis?
2. What are the next best steps?

Section 4

The spinal cord lesion demonstrated characteristics most consistent with an intramedullary neoplasm, likely representative of an astrocytoma or ependymoma as these are the most common intramedullary neoplasms [2]. Both tumors are often contrast enhancing, T2-hyperintense lesions. Ependymomas are usually better demarcated on MRI and show more homogenous enhancement than astrocytomas, which corresponds to less invasion into the spinal cord and a higher survival rate [2]. Given the recent rapid progression of symptoms, a high-grade astrocytoma may be a possibility although the lack of associated pain would be unusual for a rapidly expanding infiltrative mass, as the most common presenting symptom for an intramedullary spinal cord tumor is back pain [3]. This could represent an intramedullary metastasis, although that is less likely as the outside pathology showed the removed skin lesion was negative for tumor cells, the patient does not have a known cancer history, and intramedullary metastasis is extremely rar [4].

A PET scan showed moderate fluorodeoxyglucose (FDG) uptake in the known thoracic spinal cord mass but did not demonstrate other sites suspicious for malignancy or sarcoidosis. A lumbar puncture showed: 6 total nucleated cells, 0 erythrocytes, protein elevated at 142 mg/dL, and glucose 122 mg/dL. The CSF was negative for cryptococcus antigen, fungal smear and culture, paraneoplastic autoantibody evaluation, oligoclonal bands, and cytology with flow cytometry. He was started on 6mg of dexamethasone every 6 hours for 7 days without clinical improvement, despite improved edema on MRI (Figure 1). No clear early improvement was seen with the contrast-enhancing mass itself however, as might be seen with sarcoidosis, although a more prolonged duration of treatment is typically required for an accurate assessment of this when clinical suspicion is high [5]. We opted not to trial a long course of steroids (typically over a few months for suspected sarcoidosis) given the patient's severe declining functional status, diabetes, and the relatively low clinical suspicion for sarcoidosis.

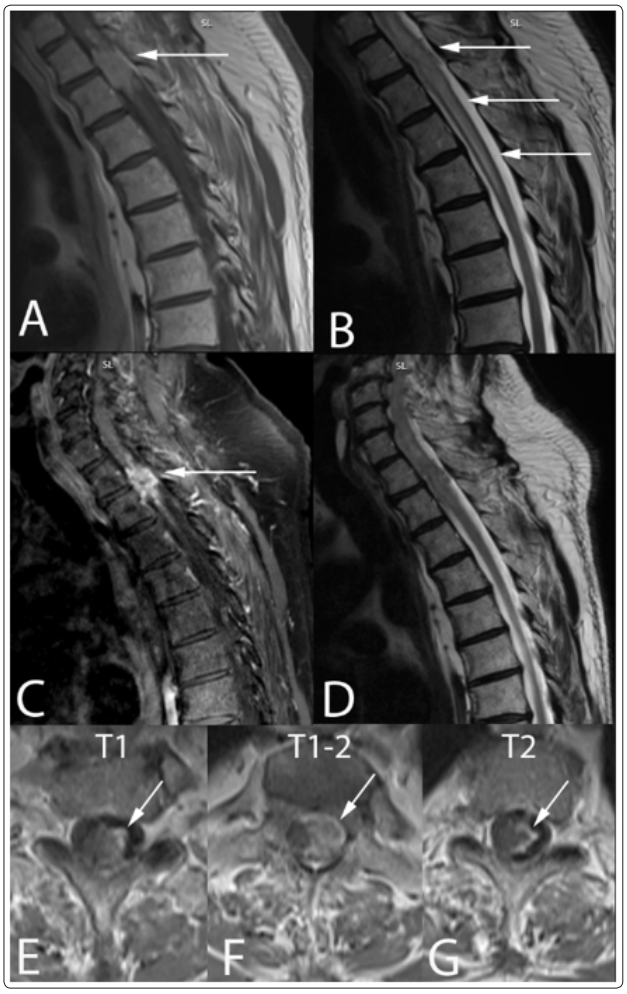

Figure 1: Sagittal T1 weighted MRI with contrast of the thoracic spine demonstrates a contrast enhancing intramedullary lesion at T1-2 (A) with T2-weighted sequences showing intramedullary vasogenic edema from C7-T5 (B). Sagittal T1-weighted and fat saturated MRI with contrast (C) and T2 sequences (D) following high dose steroids show significant improvement in the vasogenic edema without a change in the enhancement. Axial T1 weighted MRI with contrast shows an intramedullary lesion that is eccentric to the left side with possible extramedullary extension (E-G).

Given the lack of other potential biopsy sites, a C7-T3 laminectomy with biopsy and partial resection was performed. After a midline durotomy and opening the arachnoid, the exophytic portion of the tumor was easily identified arising from the spinal cord and not the arachnoid or dura (Figure 2). A portion of the vascular exophytic mass was removed, while sparing the traversing nerve roots. Additional tumor within the cord was not removed as there was no demarcation from the spinal cord and it was felt this could not be done safely. Expansile duraplasty was performed. No changes in neuromonitoring (SSEP/MEP) occurred. Final pathology showed a WHO grade IV glioblastoma (GBM), IDH-wildtype, and was negative for MGMT promotor methylation.

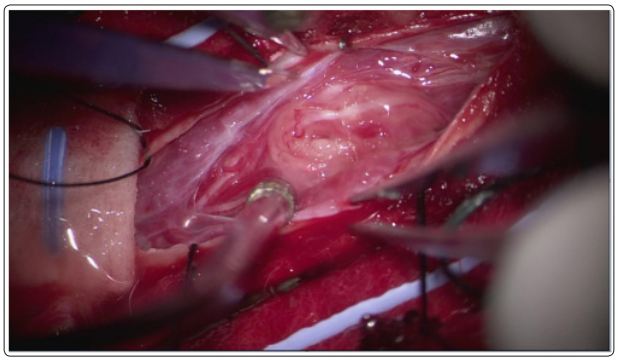

Figure 2: Intraoperative photograph after a midline durotomy and opening the arachnoid which demonstrates the exophytic portion of the intramedullary spinal cord tumor. Final pathology showed this to be a WHO grade IV glioblastoma, IDH-wildtype

Discussion

Spinal cord astrocytomas account for only 6-8% of spinal tumors and 25 to 30% of intramedullary tumors [6]. About 57% of astrocytomas are eccentric to the cord and cause displacement of the normal neural tissue, likely secondary to their origination within the parenchyma [7]. This is in contrast with ependymomas that are more commonly concentric as they arise from the intraspinal canal. Most spinal cord astrocytomas are either grade 1 or 2 with only 25% being grade 3 or 4 [2]. Prognosis for grade 4 astrocytomas is poor, with a study demonstrating mean survival of 14.3 months among 165 patients with grade 4 spinal cord astrocytomas [8]. In a cohort of 664 patients with spinal cord astrocytomas, five-year survival rate was only 14% for patients with grade 4 tumors [9]. Patients with spinal cord GBMs often tend to be younger, with a mean age of 26 years [8].

Aggressive resection of high grade spinal cord astrocytomas is often not feasible without unacceptable morbidity. A study reviewed all the reported cases of grade 4 spinal cord astrocytomas and found a gross total resection rate of only 12.7% and extent of resection did not influence overall survival [8]. Radiation therapy has been shown to be of benefit in patients with infiltrative astrocytomas, with one study demonstrating a median survival of 24 months in the patients who received radiation versus three months in those who did not [10]. Chemotherapy with similar agents that are used for intracranial astrocytomas, such as temozolomide, have shown some survival benefit in small case series [8].

Our patient had slight worsening of his left leg weakness post-operatively that was stable at discharge. He was offered radiation therapy but declined. If our patient had an MGMT promoter methylated tumor, we would have offered temozolomide as a chemotherapeutic treatment option. He was discharged to a skilled nursing facility two weeks after surgery and passed away two weeks later.

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