A diagnostic approach to a patient with ascending sensory loss

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Abstract

Objective and method. Ascending sensory loss is a common reason for neurologic consultation. In this case report, we describe a 75-year-old male who presented with new onset ascending bilateral lower extremity sensory deficits, which rapidly progressed to include urinary retention and weakness.

Outcome. In addition to blood work, neuroimaging and CSF analysis, the definitive diagnosis required serum protein electrophoresis and a bone marrow biopsy.

Conclusion. This case highlights the formulation and diagnostic approach to patients with ascending sensory loss, considering the onset of the symptoms and comorbidities in a stepwise approach.

INTRODUCTION

Ascending sensory loss can be seen in a plethora of neurological diseases, ranging from neuropathies to lesions of the spinal cord, brainstem or cortex. Therefore, the arrival at a diagnosis can be a lengthy process, requiring a thorough history and examination. Guillain-Barre syndrome (GBS), for example, is a disorder that may be considered. GBS is an acute process of ascending weakness with mild sensory loss, sometimes involving hyporeflexia or areflexia [1]. The key with this diagnosis is the presence of albumin in cerebrospinal fluid. Acute inflammatory demyelinating polyneuropathy (AIDP) and Miller-Fisher syndrome (MFS) are some variants of GBS. Other differential diagnoses to consider include radiculopathy secondary to a disc herniation or degenerative diseases of the spine, trauma or a tumor creating a compressive lesion of the spinal cord, spinal artery thrombosis, subacute combined degeneration secondary to a vitamin deficiency, or an infection even. Here we present a 75 years old male patient with ascending sensory loss and our diagnostic approach.

CASE STUDY

A 75 year old male patient with a past medical history of desmoid tumor of the left shoulder, coronary artery disease and hypertension presented to the emergency department with progressive changes in bilateral lower extremity sensation. He had bilateral knee replacements 3 months before the symptom onset. The patient started with ascending numbness to the waist level and urinary retention over the course of 2 months. He had no other neurological complaints such as weakness, headache, ptosis or swallowing difficulties. Physical exam revealed mildly decreased motor strength in both legs. Areflexia was observed in both legs, with a downgoing plantar reflex. Pinprick sensation below T10 level was decreased, and vibration sensation was decreased distally in the toes. Contrast enhanced MRI of the neuraxis was significant for diffuse enhancement along the cauda equina. Nerve conduction studies showed evidence of absent lower extremity sensory nerve action potentials (SNAPs) and low amplitude compound muscle action potential (CMAPs) without evidence of demyelination. Needle electromyography (EMG) showed diffuse spontaneous activity with fibrillations and positive sharp waves in a distal to proximal pattern, involving the tibialis anterior, tibialis posterior, quadriceps, gluteus medius and biceps femoris, which was concerning for an acute to subacute sensorimotor polyradiculoneuropathy. Cerebrospinal fluid (CSF) studies were significant for protein of 90 mg/dL. CT Abdomen/ pelvis/ thorax was negative for malignancy except for a known and stable desmoid tumor in the left scapula. He later developed black and blue spots to the medial aspect of his knees with swelling.

Due to these skin changes, serum vascular endothelial growth factor (VEGF), Serum Protein Electrophoresis and Immunofixation were ordered to investigate for POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin abnormalities) syndrome. VEGF level was elevated at 802 pg/mL (ref 62 – 707). Serum protein electrophoresis revealed elevated lambda-kappa ratio. Our patient's elevated lambda-kappa ratio suggested a possible underlying plasma cell dyscrasia.

In order to make a definitive diagnosis, a bone marrow biopsy was performed, which showed CD5-positive B-cell lymphoproliferative process and MYD-88 Mutation. Waldenström's Macroglobulinemia was diagnosed. In the light of these findings, the patient was diagnosed with POEMS syndrome, a rare plasma cell dyscrasia involving subacute neuropathy.

On initial presentation, the patient was treated with plasmapheresis and intravenous steroids for possible chronic inflammatory demyelinating neuropathy until the definitive diagnosis was reached. He did not improve with these treatments, but he noted that the symptoms 'stabilized'. After the POEMS syndrome diagnosis was reached, the patient was started on steroid treatment with taper (60 mg prednisone daily, 6 month taper) and ibrutinib (irreversible Bruton's tyrosine kinase inhibitor). Later, he was maintained on rituximab (an anti-CD-20 monoclonal antibody) and bendamustine (an alkylating agent) regimen.

DISCUSSION

POEMS syndrome is a rare plasma cell dyscrasia involving subacute neuropathy. As the name suggests, the multi-organ involvement results in a distinct syndrome. Other symptoms include organomegaly including lymphadenopathy, sclerotic bone lesions, skin changes such as hyperpigmentation, thrombocytosis, polycythemia, edema, and more [2].

Our patient's physical exam findings of numbness and areflexia suggested a peripheral nerve or root localization. Symptoms were more prominent distally which suggested length dependent polyneuropathy. Notably there was no pain, which is common in primary polyradiculopathies. The 2 month onset suggested an acute to subacute etiology, such as inflammatory, neoplastic or paraneoplastic disorders of the nerves and nerve roots. However CT scans and CSF analysis did not support this. Neurolymphomatosis was also ruled out due to the lack of cells for CSF cytology analysis. Neurosarcoidosis was also less likely since the patient had no sign of systemic granulomas or cranial nerve lesions. Enhancing roots seen in MRI and elevated CSF protein with normal cell count were in favor of an inflammatory polyradiculoneuropathy. There was no demyelination out of proportion to axonal loss to suggest Chronic Inflammatory Demyelinating Polyneuropathy (CIDP).

Due to the polyneuropathy and rare nature of the syndrome, POEMS can often be misdiagnosed as CIDP, also a rare neurological disorder [3]. CIDP involves gradual sensory and motor loss of the peripheral nerves, both proximally and distally, along with hyporeflexia. Symptoms are progressive and symmetric in nature. Nerve conduction studies and electromyography can be utilized for diagnosis, differentiating the two disorders [4,5]. Slowed conduction velocity is more prominent in the intermediate than distal nerve segments in POEMS syndrome, whereas demyelination in CIDP is distributed multifocally and involves both the distal and intermediate nerve segments. Conduction blocks are seen less frequently in POEMS syndrome.

In POEMS syndrome, the monoclonal gammopathy is characteristically lambda-specific [2,6]. Often seen are elevated levels of the serum VEGF in addition to the expected increases in inflammatory cytokines. The association with VEGF is rather specific for POEMS syndrome and can be utilized to monitor prognosis and treatment-response [7]. As a paraneoplastic disorder, treatment may involve radiotherapy for localized states, or autologous stem cell transplant (ASCT) and/ or chemotherapy for systemic states [6,8]. Unlike other neuroinflammatory pathologies immunoglobulin or steroid therapy are not effective in lasting treatment.

Lastly, lower extremity nerves are affected more severely in POEMS syndrome, contrary to CIDP, which can affect both upper and lower extremities. Additionally, disease modifying treatment for CIDP involves IV immunoglobulins or plasma exchange, which is not effective in POEMS syndrome [9]. This is because of the difference in pathophysiology. Endoneurial macrophages, multifocal myelinated nerve fiber loss and onion bulb formation are seen in CIDP, which is consistent with chronic inflammation and demyelination, caused by a primary immune response. Conversely, there are no findings of immune-mediated demyelination and remyelination in POEMS [3]. Nerve biopsy in POEMS syndrome reveals major signs of

demyelination with uncompact myelin on electron microscopy in the absence of macrophages [10]. Nerve also shows predominant axonal damage characterized by loss of myelinated nerve fibers, and the presence of myelin ovoids indicating acute axonal degeneration which is due to endothelial injury and microvascular ischemia. This explains why treatment must be targeted to the underlying plasma cell disorder, which causes increased VEGF [10]. Therefore, POEMS syndrome is an important and distinct diagnosis that needs to be considered in acute to subacute presentations of ascending sensory loss.

CONCLUSION

Diagnostic approach to ascending sensory loss may be complicated and time consuming, potentially delaying the treatment. In this case, we highlighted our approach to one of the rare cases of sensory loss and emphasized the other signs to look for in these patients. As stated above, patient was treated for the most likely pathology firstly, in order to preserve the remaining function and stop the progression, while the definitive diagnostic workup was underway.

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