Paraneoplastic Myelopathy

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KEYWORDS

• Paraneoplastic • Myelopathy • Autoimmune • Spinal cord

KEY POINTS

- Paraneoplastic myelopathies are an uncommon but important category of spinal cord disease to recognize because the neurologic presentation often precedes the detection of cancer.
- The hallmark MRI finding in paraneoplastic myelopathy is longitudinally extensive, symmetric, tract-specific signal changes within the spinal cord that often enhance after gadolinium administration.
- The two most common neural autoantibodies found are amphiphysin-IgG and colapsin-response-mediator-protein-5-IgG and the two most common oncological associations reported are breast and lung cancer.
- The initial treatment of paraneoplastic myelopathies involves detection and treatment of the underlying cancer, typically followed by consideration of a trial of immunotherapy.
- Despite treatment, only a minority of patients improves and, although treatment may confer some stability and delay time to wheelchair, most patients ultimately become wheelchair dependent.

INTRODUCTION

Paraneoplastic myelopathies are an uncommon but important category of spinal cord disease to recognize because the neurologic presentation often precedes the detection of cancer. Most patients present clinically with an insidiously progressive myelopathy with fewer patients presenting subacutely over a few weeks and even fewer with a relapsing remitting course. The recent discovery of novel neural specific autoantibodies, such as collapsin response-mediator protein-5 (CRMP-5) IgG,[1] has led to an increased recognition and improved understanding of the pathogenesis of paraneoplastic myelopathies. Autoimmune myelopathies may also occur in association with neural-specific antibodies, such as aquaporin-4 IgG,[2] without the presence of an underlying cancer and the myelopathic presentation is typically that of a transverse

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myelitis that is often recurrent. Neuromyelitis optica is discussed by Dr Sahraian in more detail elsewhere in this issue. Although myelopathies may occur in the context of a systemic autoimmune disease or with other inflammatory diseases of uncertain causes (eg, sarcoid), the focus of this article is paraneoplastic myelopathies.

CASE

A 54-year-old, previously healthy, right-handed woman developed lower extremity weakness. Three years before presentation, the patient had midthoracic pain followed by insidiously progressive gait impairment due to lower extremity weakness and spasticity with neurogenic bladder and bowel impairment. Her weakness progressed and she became wheelchair-dependent 18 months after symptom onset. She was initially diagnosed with primary progressive multiple sclerosis (MS) and treated with β-interferon. She reported some mild temporary improvement with corticosteroid treatments for presumed MS. She required a baclofen pump for severe spasticity. She was a lifelong nonsmoker without family history of autoimmunity. Her past medical history was notable only for remote pulmonary coccidiomycosis. Her neurologic examination revealed spastic-paraplegia with distal lower extremity pin and vibratory sensory loss. Spinal cord MRI spine revealed longitudinally extensive T2-signal hyperintensity with symmetric gadolinium enhancement in the lateral columns from T2 through T7, similar to that seen in **Fig. 1**. Brain MRI was normal. Cerebrospinal fluid (CSF) had revealed elevated white blood cells, but further results were not available.

Given the tract-specific findings on MRI (tractopathy), a paraneoplastic cause was suspected and a serum paraneoplastic autoantibody panel revealed elevated amphiphysin-IgG. CT of the chest, abdomen, and pelvis were normal. Mammogram results were equivocal but, considering the very high positive predictive value of amphiphysin-IgG positivity for cancer presence (~80%–90%), breast ultrasound and MRI were performed. These revealed a right breast lesion and subsequent breast biopsy confirmed an estrogen-receptor-positive adenocarcinoma. The patient underwent right mastectomy and sentinel lymph node biopsy revealed no metastatic disease. She received adjuvant hormonal therapy. The patient was placed on oral mycophenolate mofetil as maintenance immunotherapy without neurologic improvement.

The patient later developed cognitive impairment thought to be related to paraneoplastic syndrome, after other causes were excluded. The patient's neurologic condition remained stable; however, 4 years later she developed breast carcinoma in the left breast that was treated with surgery. Additional chemotherapy and radiation treatment were recommended; no further follow-up was available.

Discussion

Most commonly, paraneoplastic myelopathy presents with a progressive myelopathy manifesting before detection of underlying cancer. Additional multifocal neurologic symptoms, such as encephalopathy (as in this case), cranial neuropathies, and cerebellar ataxia are often present. Tract-specific spinal cord MRI signal abnormalities should raise suspicion for a paraneoplastic cause. The presence of neural specific autoantibodies confirms the autoimmune neurologic disease and guides the search for cancer. Some neural autoantibodies, such as amphiphysin-IgG, have a high positive predictive value for cancer and an aggressive search for malignancy is required. If initial cancer screening is negative, cancer surveillance screening every 6 to 12 months may be warranted because cancer may be detected long after the myelopathy occurred. Despite oncological and immunosuppressant treatments, morbidity is high and most patients remain wheelchair dependent.