

Sensory ganglionopathy as a paraneoplastic manifestation of pulmonary carcinoid tumor

Ali Kuenzel APRN¹, Nathan K. McGraw MD¹,
Stephanie A. Kolakowsky-Hayner PhD¹

¹BJC Health, Saint Luke's Marion Bloch Neuroscience
Institute, Kansas City, Missouri

Introduction

Paraneoplastic neurological syndromes (PNS) represent a diverse group of immune-mediated disorders affecting the nervous system in patients with malignancy, occurring remote from the primary tumor site or its metastases.¹ These syndromes often precede the diagnosis of the underlying malignancy by weeks to months, with neurological symptoms frequently serving as the initial presenting complaint.¹ Among the various paraneoplastic neurological manifestations, sensory ganglionopathy—also termed sensory neuronopathy—is a distinctive syndrome characterized by selective damage to the dorsal root ganglia, resulting in progressive sensory ataxia, areflexia, and profound proprioceptive loss.²

Sensory ganglionopathy is most commonly associated with small-cell lung carcinoma, but has also been reported in association with breast, ovarian, prostate, and gastric cancers, lymphomas, and neuroendocrine tumors.² The pathophysiology involves an autoimmune attack on dorsal root ganglion neurons, mediated primarily by cytotoxic T lymphocytes and associated with antineuronal antibodies, particularly antineuronal nuclear autoantibody type 1 (anti-Hu), collapsin response mediator protein 5 (anti-CRMP5), and amphiphysin antibodies.^{2,3} The presence of these antibodies, while highly specific (99%), demonstrates only moderate sensitivity (82%), indicating that their absence does not exclude an underlying malignancy.³

Pulmonary carcinoid tumors, representing well-differentiated neuroendocrine neoplasms of the lung, account for approximately 1-2% of all lung malignancies. While these tumors are generally considered low-grade with favorable prognosis, they can rarely present with paraneoplastic neurological syndromes. The association between carcinoid tumors and classical antineuronal antibody-mediated paraneoplastic syndromes has been infrequently reported in the literature. Tschernatsch et al. documented four patients with carcinoid tumors presenting with various paraneoplastic neurological syndromes, including sensory neuropathy one of whom had detectable anti-Hu antibodies.⁴ This finding supports the hypothesis that carcinoid tumors, like small-cell lung carcinoma, can express neuronal antigens capable of triggering an autoimmune response against the nervous system.

The rarity of this clinical presentation poses significant diagnostic challenges. Sensory ganglionopathy may manifest

with insidious onset of sensory symptoms, including numbness, paresthesias, and progressive sensory ataxia, which can precede tumor diagnosis by months. The recognition of this association is clinically important, as it may prompt earlier detection of an otherwise occult malignancy and influence treatment decisions.

We present a case of pulmonary carcinoid tumor manifesting as sensory ganglionopathy, contributing to the limited literature on this rare association and highlighting the diagnostic approach, immunological findings, and clinical course of this challenging presentation.

Case Report

A 71-year-old female presented with bilateral axillary burning paresthesias which started abruptly 14 years prior. There was no evidence of dermatologic abnormality including rash or erythema. Symptoms were persistent although would worsen with light touch (such as with clothing) and with sweat production. Topical treatments were attempted, however without any relief in symptoms; she was previously placed on gabapentin for chronic cough which had a modest benefit on her paresthesias. Neuromuscular exam at time of initial presentation revealed diffusely absent pinprick sensation in all extremities and the trunk with preservation of pinprick sensation on the face; strength was largely preserved (except for mild weakness at the bilateral thumb abductors) and reflexes were generally diminished in the lower extremities. Mild ataxia was noted on finger-nose-finger testing.

Initial work up included mildly elevated vitamin B6 (47.9 ng/mL, range 2.1-21.7 ng/mL) and otherwise normal/negative complete blood count, metabolic panel, inflammatory markers, serum electrophoresis, copper, and vitamins B12, folate, B1, and E. An electromyography/nerve conduction study (EMG/NCS) was pursued and showed diffusely absent or very low amplitude sensory studies with normal motor studies and negative needle EMG consistent with sensory ganglionopathy (neuronopathy). Further serologic revealed improved vitamin B6 level (now 10.5 ng/mL) and normal/negative antinuclear antibody, anti-SSA/SSb antibodies, Smith antibodies, anti-DNA antibody, paraneoplastic panel, and HIV antigen/antibody. CT chest revealed a mass in the right middle lobe which was followed with a PET/CT which showed a 13 mm hypermetabolic nodule in the right middle lobe without any evidence of metastatic disease. Biopsy was pursued which revealed a grade 1 carcinoid/neuroendocrine tumor which was subsequently resected.

In follow-up she has reported an improvement in her paresthesias since resection of her carcinoid tumor. She was last seen in neuromuscular clinic about 16-17 months post resection. While her paresthesias had improved she continues to note intermittent symptoms of burning pain in the axilla and continues neuropathic pain medications to mitigate her symptoms. She continues to have mild sensory abnormalities in the extremities to pinprick and vibration, however ataxia was noted to be improved on follow up. Repeat electrodiagnostic testing was not pursued.

Discussion

As mentioned earlier, this case is unique in its presentation and has very little similarity to other cases presented in the literature.

This case contributes to the limited literature documenting the rare association between pulmonary carcinoid tumors and paraneoplastic sensory ganglionopathy. While sensory ganglionopathy is most commonly associated with small-cell lung carcinoma there this syndrome has been described in patients with well-differentiated neuroendocrine tumors.⁴

This patient presented with paresthesias in a non-length dependent manner which is often the phenotype of sensory ganglionopathy, helping to differentiate it from a length-dependent sensory neuropathy.² Neurodiagnostic testing (EMG) was consistent with the diagnosis, with absent/low amplitude sensory nerve responses diffusely and normal motor nerve conduction studies and needle EMG. Vitamin B6 levels were found to be elevated initially, however given the elevation was minimal a vitamin B6 sensory ganglionopathy is thought to be unlikely.

Sensory ganglionopathy typically evolves over days to weeks and can precede a cancer diagnosis by weeks to months. This is somewhat inconsistent with the clinical history in the present case as symptoms had reportedly been present for several years prior to presentation. Records were incomplete, and it is unknown if pulmonary imaging had been completed in the years leading to presentation. Given the well-differentiated nature of her neuroendocrine tumor it is entirely possible that this mass was slow growing for many years as these tumors have a well documented slow growth rate; one study estimated a median volume doubling time of up to 4.1 years for low-grade pulmonary carcinoid tumors with another study suggesting a mean of 40.5 years until these tumors reach their final volume.^{5,6}

Another challenge this case presented was the lack of a serologic positive paraneoplastic antibody. As noted above anti-Hu, anti-CRMP5, and anti-amphiphysin antibodies have been described as pathogenic in sensory ganglionopathy. There have been documented cases, however, of paraneoplastic neurologic syndromes related to neuroendocrine tumors without positive paraneoplastic antibodies.⁴ The current

patient's clinical course suggests an association between her neuroendocrine tumor with sensory ganglionopathy, given the partial clinical improvement seen with removal of the tumor.

Conclusion

This case underscores several important clinical points. First, sensory ganglionopathy should prompt evaluation for underlying malignancy, including neuroendocrine tumors beyond small-cell lung carcinoma. Second, early recognition and aggressive immunotherapy may offer the best chance for neurological stabilization, even if complete recovery is unlikely. Third, treatment of the underlying carcinoid tumor, while essential for oncological outcomes, may not lead to full neurologic recovery. Finally, long-term multidisciplinary follow-up is essential to address both oncological and neurological complications.

References

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