

## Amyotrophic Lateral Sclerosis As A Paraneoplastic Manifestation in the Neuroendocrine Tumor of Stomach: A Case Report

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**Abstract-** Motor neuron diseases have been reported as a rare paraneoplastic syndrome (PNS) of a systemic neoplasm. We present a patient with amyotrophic lateral sclerosis (ALS) in association with neuroendocrine tumor (NET) of stomach, which is the first case of motor neuronopathy with underlying neuroendocrine tumor. A 79-year old woman presented with a two months history of progressive dysphagia, spastic dysarthria and marked fasciculation in her atrophic tongue. Gag reflexes were diminished bilaterally. Other cranial nerves were intact. In muscle testing there was significant atrophy in thenar and hypothenar areas of both hands compatible with diffuse motor neuronopathy with active denervation. Upper GI endoscopic study showed patchy erythematous mucosa with congestion in body of stomach, Histological biopsy of stomach confirmed the neuroendocrine tumor (NET). The importance of considering a paraneoplastic syndrome in a patient with presentation of ALS, which can leads to searching for underlying neoplasm before its apparent signs and symptoms, to initiate tumor treatment so much sooner. In addition even though paraneoplastic motor neuron disease is rare, treating the underlying neoplasm may resolve neurologic signs and symptoms.

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**Keywords:** Amyotrophic lateral sclerosis (ALS), Neuroendocrine tumors (NETs); Paraneoplastic syndromes (PNSs)

### Introduction

Motor neuron diseases have been reported as a rare paraneoplastic syndrome (PNS) of a systemic neoplasm (1). This rare phenomena has been commonly associated with small cell lung cancer (SCLC), breast cancer and lymphoproliferative disorders (2). We present a patient with amyotrophic lateral sclerosis (ALS) in association with neuroendocrine tumor (NET) of stomach, which is the first case of motor neuronopathy with underlying neuroendocrine tumor.

### Case Report

A 79-year old woman, presented with a 2-month history of progressive dysphagia first to solid, and then to both solid and liquid foods, accompanied with recurrent choking. She also had complaint of difficulty in speech and hoarseness in her voice. She had nor diplopia

neither respiratory symptoms or sensory complains or sphincter disturbance. She mentioned 10 kg weight loss during last 2 months. Her past medical history was remarkable for hypertension and hyperlipidemia and a history of falling one month before her admission, which caused fracture in her right hip, and she underwent a surgical hip replacement. She was under treatment with metoral and enoxaparin.

Results of a neurological examination showed spastic dysarthria and marked fasciculation in her atrophic tongue. Gag reflexes were diminished bilaterally. Other cranial nerves were intact. In muscle testing there was significant atrophy in thenar and hypothenar areas of both hands, without visible fasciculation in limbs or trunk. Muscle strength testing based on Medical Research Council (MRC) grades, showed moderate distal weakness(power of 3/5 in all limbs; however muscle strength was not reliable in her right lower limb due to prior history of hip fracture and

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pain. All tendon reflexes were exaggerated, and plantar reflexes were equivocal bilaterally. Sensory and cerebellar findings were normal. Chest, abdominal and cardiovascular examinations were unremarkable.

Hematologic tests showed mild anemia (Hb=9.5), with normal serum electrolytes, liver function test, renal function tests and CPK. She had +3 occult blood in her stool exam. Erythrocyte sedimentation rate (ESR) was slightly elevated at 31 mm/hour. Serum tumor markers including CA-125, CEA19-9, AFP and paraneoplastic panel tests including Anti-HU, Ant-Ri and Anti-Yo, were negative.

Brain MRI without gadolinium revealed age related cortical atrophy and cervical MRI without gadolinium showed mild cervical spondylosis with mild disc protrusion in C5-C6 level, nothing that would account for her clinical condition.

Nerve conduction study demonstrated low compound motor action potentials (CMAPs) in a bilateral median, ulnar and peroneal nerve and absent in right peroneal nerve, with normal conduction velocities. Sensory nerve action potentials (SNAPs), F wave and H reflex were normal. Needle examination revealed diffuse neurogenic pattern in all tested muscles in upper and lower limbs, including genioglossus, with spontaneous activity (fibrillations and positive sharp waves), compatible with diffuse motor neuronopathy with active denervation. Chest and abdominal CT scans with contrast were unremarkable. Upper GI endoscopic study showed patchy erythematous mucosa with congestion in body of stomach, esophagus and duodenum were normal. Histological biopsy of stomach confirmed the neuroendocrine tumor (NET).

## Discussion

Written informed consent was obtained from the patient for publication of this case report and accompanying images. Paraneoplastic syndromes (PNS) refer to ability of some tumors to produce signs and symptoms at a distance from the site of the primary tumor or metastases, and which may develop before underlying tumor have been apparent (7,8).

Neurological paraneoplastic syndrome was first described by Oppenheim in 1888 (2). Neurological PNSs are introduced as different neurological involvement includes Lambert-Eaton syndrome, paraneoplastic cerebellar degeneration, limbic encephalopathy, peripheral neuropathy and motor neuronopathy.

The mechanism of development of neurological PNS

is not fully understood, however different mechanisms have been suggested. Evidences show that the main mechanism is an autoimmune response (3), which means tumoral cells have the ability to synthesize and secrete biologically active substances, which leads to autoimmune responses to different types of nervous system cells. Autopsy demonstrates patchy loss of anterior horn cells (AHC) in spinal cord with variable inflammatory cells (2).

A more problematic issue is however, if ever, isolated motor neuron disease ALS is a paraneoplastic syndrome. So far, 196 several epidemiologic studies of ALS, from various parts of the world report an incidence of neoplasm ranging from zero to 7.8% (2).

ALS are associated commonly with small cell lung cancer (SCLC), breast carcinoma, lymphoproliferative diseases, plasma cell dyscrasias and renal cell carcinoma (RCC) (1,2,5,6). However one case report has been presented by Khealani *et al.*, in which motor neuronopathy was described with esophageal adenocarcinoma (4).

Neuroendocrine tumors (NETs), may be either benign or malignant tumors that can cause neurological PNS. Neurological paraneoplastic syndromes reported so far, in association with NETs are Lambert-Eaton syndrome, paraneoplastic cerebellar degeneration, limbic encephalitis, and peripheral neuropathy. We present a patient with motor neuronopathy in whom neoplasm survey, discovered neuroendocrine tumor (NET) of stomach.

Conclusion: This report presentation highlight the importance of considering a paraneoplastic syndrome in a patient with presentation of ALS, which can leads to searching for underlying neoplasm before its apparent signs and symptoms, to initiate tumor treatment so much sooner. In addition even though paraneoplastic motor neuron disease is rare, treating the underlying neoplasm may resolve neurologic signs and symptoms.

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## Paraneoplastic amyotrophic lateral sclerosis

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