

INTERACTN CASE SUMMARY

The case of a 30-year-old man with subacute gait instability, weakness, and muscle spasms

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Case Summary

A 30-year-old healthy man presents after a fall with diffuse weakness and pain and recent onset left eye ptosis in the setting of three weeks of progressive bilateral leg weakness, gait instability, and difficulty washing his hair due to upper extremity weakness. He had also developed stiffness in his neck and shoulders and uncontrollable muscle spasms. Exam was notable for ptosis, fatiguing weakness in extremities, increased tone, hyperreflexia with clonus, and spastic gait. A mediastinal mass was found on chest CT (Fig. 1), and biopsy confirmed an invasive thymoma with positive nodes. Serum testing was positive for antibodies to acetylcholine receptors as well as glutamic acid decarboxylase.

Diagnosis: Myasthenia Gravis-Stiff Person Syndrome (MG-SPS) in the setting of metastatic thymoma

Discussion

Stiff Person Syndrome (SPS) was first described by Moersch and Woltman in 1956¹. It is a rare syndrome that progressively decreases inhibition of the central nervous system due to blockade of glutamic acid decarboxylase (GAD) causing increased muscle activity. This leads to characteristic symptoms like severe muscle stiffness, rigidity, and painful spasms in the trunk and extremities. Spasms can be provoked by sudden movements, emotional distress, or noise.

It affects twice as many women as men usually between the ages of 20 and 50 and is postulated to have an autoimmune component². Indeed, it is often associated with type 1 diabetes mellitus (T1DM), thyroiditis, vitiligo, and pernicious anemia. There are also paraneoplastic conditions of which it is associated, including breast cancer, small cell lung cancer, Hodgkin disease, and colon cancer³.

Prior to our case, five cases of SPS associated with a thymoma have been reported in the literature⁴. Three patients had MG-SPS with histologically proven thymoma, and two of these patients had positive anti-GAD and anti-AChR antibodies^{4–6}.

The diagnosis of SPS requires a high index of suspicion as there is no formal diagnostic criteria; however, the following are features generally considered necessary to make the diagnosis: Stiffness in the axial and limb muscles resulting in impairment of ambulation; presence of superimposed episodic spasms that are precipitated by sudden movement, noise, or emotional upset; a positive therapeutic response to oral diazepam or findings of continuous motor-unit activity on electromyography (EMG) that are abolished by intravenous diazepam; and an absence of other neurologic disorders that may explain the clinical features^{7–8}. Anti-GAD antibody testing is positive in approximately two-thirds of SPS patients, but it is usually negative when a patient has paraneoplastic SPS⁹. Antibodies against amphiphysin, an intracellular protein promoting cleavage of intracellular vesicles, have been present in paraneoplastic SPS especially with breast cancer¹⁰. SPS patients often have oligoclonal bands targeting different GAD epitopes in their CSF¹¹. SPS patients with bulbar symptoms or eye abnormalities should be suspected to have comorbid MG and should be investigated for thymoma usually with CT chest⁴.

All patients with SPS should be assessed for T1DM and have routine cancer tests performed that are appropriate for their age. Studies include CBC, CMP (including tests of renal function, liver chemistries, CK or aldolase), CRP/ESR, TSH, thyroid peroxidase antibodies, and hemoglobin A1c.

Treatment of SPS is directed at symptomatic improvement, increasing mobility and function. The optimal initial therapy is utilizing benzodiazepines with gradual upward titration until symptoms are adequately controlled. If symptoms

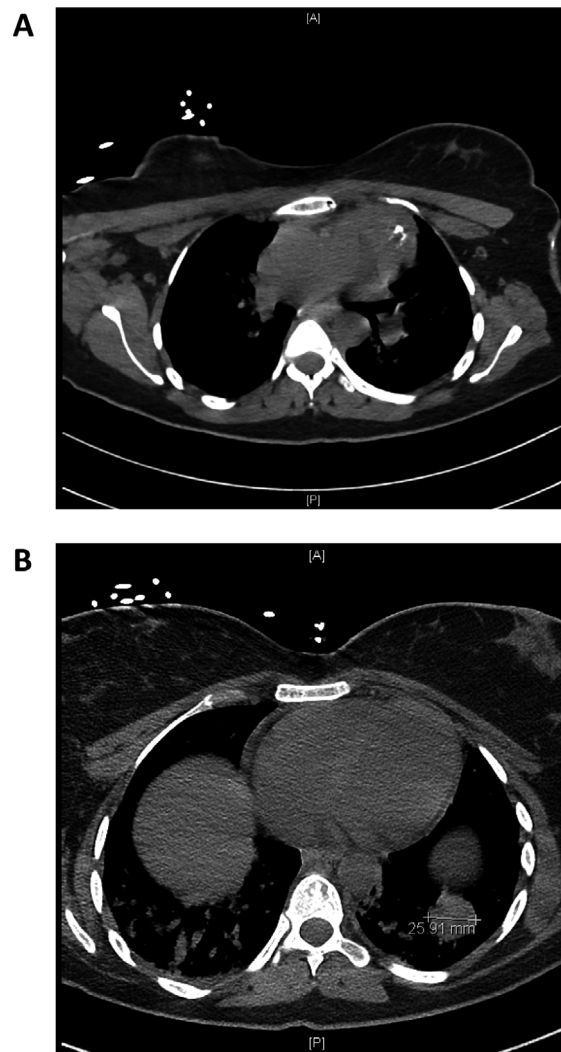


Figure 1. CT Chest without Contrast. (A) Patchy multifocal airspace opacity throughout the lungs likely represents multifocal pneumonia. Anterior mediastinal mass with central calcifications is concerning for thymic malignancy. (B) 2.5 cm left inferior pleural-based mass is nonspecific but metastatic lesion to the pleura is not excluded.

are refractory to benzodiazepines, either add or substitute baclofen, but be cautious to avoid sedation when using in combination. If disease is severe (symptoms significantly interfere with daily function and activities) or refractory to baclofen and benzodiazepines, IVIG is initiated. If SPS patients do not respond to IVIG, therapies like plasma exchange, rituximab, or other immunosuppressive agents may induce a response.

In the case of SPS associated with a thymoma, three cases that involved treatment with thymectomy showed positive outcomes with resolution of SPS symptoms^{6,12,13}. Therefore, a thymectomy is considered effective treatment of SPS with thymoma.

Outcome

The patient received one treatment course (five days) of plasma exchange for MG for stabilization. Because the patient was noted on imaging to have significant metastatic spread of the thymoma with potential invasion into the subclavian innominate junction as well as invasion into the left lung and hemidiaphragm in the setting of active antibodies, thoracic surgery elected to proceed with thymectomy involving mass resection, partial pleurectomy, left upper lung lobe wedge

resection, and diaphragm plication. The patient had evidence of increased spasms post-operatively and so received five days of IVIG treatment. He was then started on diazepam for SPS.

The patient's hospital course was complicated by a MICU transfer for pneumonia and potential spinal abscess formation following a diagnostic spinal tap. He continued to have recurrent aspiration events and was treated with antibiotics.

Following discharge, the patient was on a taper downward to discontinue diazepam. He continued using baclofen, gabapentin, and propranolol for SPS symptom management. The patient also had a flare of his MG causing difficulty swallowing and aspiration pneumonia. His MG symptoms slightly resolved with a dose of IVIG. He is due to continue plasma exchange. Overall, his symptoms of MG and SPS are improving.

Take-Home Points

- SPS is in itself uncommon; however, SPS associated with MG and a thymoma is extremely rare.
- If anti-GAD antibodies are negative, it does not rule out SPS.
- Investigate for thymoma using CT chest when a patient presents with ocular or bulbar symptoms of MG with SPS muscle spasms.
- If anti-amphiphysin antibodies are positive, consider paraneoplastic SPS.

See the discussion, including references, in the full case published here: <http://interactn.org/2020/06/03/276/>.

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