

## Case Report

## Stiff Man Syndrome with Invasive Thymic Carcinoma

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Stiff man syndrome is a rare disease characterized by painful chronic spasms in the muscle and skeletal system. This syndrome is an autoimmune neurologic disorder which is associated with thymoma. We treated a 32-year-old male patient with a type C thymoma (based on the World Health Organization classification) who had stiff man syndrome. The patient underwent an extended thymectomy which brought about alleviation of his symptoms.

**Keywords:** Autoimmune disease, stiff man syndrome, thymic tumor, thymoma

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**Introduction**

Stiff man syndrome (SMS) is a rare neurologic condition characterized by muscle rigidity and cramps, which are caused by immune-mediated inhibition of catecholamine excitatory and  $\alpha$ -aminobutyric acidergic neuron function.<sup>1</sup> Symptoms of this rare condition may include muscular tightness, stiffness in axial muscles of the neck, paraspinal and abdominal muscles, and proximal limb muscles. Paraspinal rigidity may lead to low-back pain and a prominent lordosis. Shortness of breath may also occur as chest muscles get involved. Smiling, swallowing, and speaking are other symptoms caused by cranial muscles stiffness in SMS.<sup>2-4</sup> This report presents the diagnosis and management of a patient with type C thymoma and SMS.

**Case Report**

A 32-year-old male was admitted to our hospital in February 2009 with symptoms of continuous muscle stiffness and painful muscle spasms, which began as tightness in the lower limbs and deteriorated into muscle stiffness of the trunk and upper limbs five months after the onset. He had no history of diabetes, injuries, or epilepsy. A laboratory examination and tumor markers also revealed nothing abnormal. No abnormality was noticed using thoracic and cervical spinal magnetic resonance imaging (MRI). A computed tomography (CT) of the chest was conducted, which revealed an anterior mediastinal tumor that was considered to be a thymoma (Figure 1). It was proposed that his symptoms may have been caused by a paraneoplastic neurologic syndrome associated with a thymoma. A laboratory measurement of the anti-GAD antibody in serum was 230 (normal range, < 1.5). High titer of anti-GAD antibody and mediastinal mass can lead to diagnosis of SMS. Despite of taking baclofen and diazepam, his symptoms of having continuous muscle stiffness and painful muscle spasms were continued. The patient, using opium as a pain killer, gradu-

ally became addicted to opium. We performed a median sternotomy and extended thymectomy with segmental resection of the left upper lobe of the lung and a partial pericardectomy. A histology examination revealed the type C thymoma (thymic carcinoma), poorly differentiated thymic carcinoma according to the World Health Organization (WHO) classification<sup>5</sup> with invasion of the lung and the pericardium. The postoperative course was uneventful and the patient was able to recover muscle strength enabling him to maintain a standing or sitting position. Ten days after the operation he was discharged from the hospital and was referred to an oncologist. In a six-month follow-up the patient was in a good condition.

**Discussion**

Stiff man syndrome is a rare neurologic syndrome. In some cases, this syndrome is seen to be frequently in association with other autoimmune diseases, such as insulin-dependent diabetes mellitus, Graves disease, Hashimoto thyroiditis, and pernicious anemia, while in others, the disorder reveals a paraneoplastic feature associating with breast cancer, mediastinal tumors, thymoma, small cell lung cancer, Hodgkin disease, and colon cancer.<sup>2-4</sup>

According to previous studies, anti-GAD antibody, associated with autoimmune disease, was positive in 60% of cases with SMS.<sup>2-4</sup> Also in anti-amphiphysin antibody was often detected in paraneoplastic syndrome of thymoma.<sup>2-4</sup> Further, the anti-GAD antibody was positive in two out of four cases presented with thymoma, but anti-amphiphysin was negative<sup>1</sup>. Thymectomy was conducted, and the histologic subtypes of the three resected thymomas included one cortical and two predominantly lymphocytic types.<sup>2</sup>

These histologic thymomas were considered B<sub>1</sub> or B<sub>2</sub> tumors based on WHO histologic classification. In two out of four patients, myasthenia gravis was also found and in one case, the anti-AChR antibody was positive.

According to Nicolas and colleagues,<sup>6</sup> the case presented with serologically negative MG with positive EMG findings. These patients responded effectively to diazepam as it promotes the effect of endogenously released GABA on cell receptors.

Other effective medications are clonazepam (Klonopin), oral and intrathecal baclofen, and sodium valproate (Depakene, De-

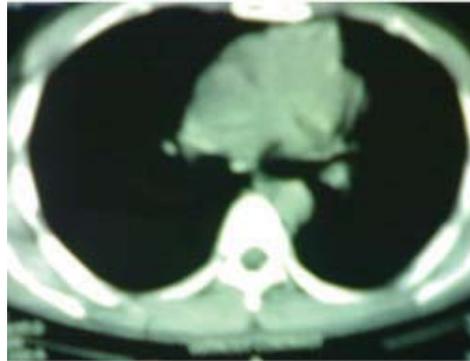
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**Table 1.** Review of Stiff Man Syndrome with a Thymoma

Year	First Author	GAD	MG	Thymoma Stage	Sex	Age
1989	Piccolo	ND	+	UK	Male	45
1997	Nicholus	ND	+	2B	Male	55
2001	Hagi Wara	High	-	1B	Male	40
2002	Murakawa	NP	-	UK	Male	UK
2002	Tanakawa	High	-	1B	Female	27
2006	Iwatal	High	-	AB	Female	79

**Figure 1.** Presents an anterior mediastinal mass

pakate); intravenous immunoglobulins have also been used successfully in this syndrome.<sup>2</sup>

Parathymic syndrome was found in 40% of cases with thymoma and two or more parathymic syndromes were also found in 1/3<sup>rd</sup> of this group.<sup>1</sup> Neurologic syndrome was infrequently observed in cases presented with thymoma.<sup>3,4,7</sup> Seven of these cases were identified in the article by Nicholas.<sup>6</sup>

According to previous studies, six cases have been reported with a thymoma.<sup>4</sup> Four patients out of these six cases were males and two were females with a mean age of 52 years. According to WHO histologic classification criteria, three patients were observed to have type B1 or B2, one was type AB and also type of thymoma was seen in the other two patients.<sup>5</sup> Five cases underwent thymectomy of whom, four responded positively to it and one failed. In case of positive respond to thymectomy the symptoms were resolved and serum titer of GAD returned to normal. If thymectomy was not effective Multiple plasmapheresis, baclofen, and clonidin can be useful for relieving the symptoms.<sup>4,8</sup>

Malignant thymoma may have association with paraneoplastic and neurologic syndromes including muscular rigidity and cramps. Further, SMS is considered to be associated with autoimmune disease. Literature shows that thymectomy can be an effective treatment for SMS with a thymoma.<sup>2,3,7</sup>

The patient in this report was examined thoroughly before treat-

ment of thymectomy. The results of thymectomy confirm with the previous reports.

## References

1. Iwata T. Thymectomy for paraneoplastic stiff man –person syndrome associated with invasive thymoma. *J Thorac Cardiovasc Surg.* 2006; **132**: 196 – 197.
2. Tanaka H, Matsumura A, Okumura M, Kitaguchi M, Yamamoto S, Iuchi K. Stiff Man Syndrome with Thymoma. *Ann Thorac Surg.* 2005; **80**: 739 – 741.
3. Venuta F, Anile M, Diso D, Vitolo D, Rendina EA, De Giacomo T, et al. Thymoma and thymic carcinoma. *Eur J Cardiothorac Surg.* 2010; **37**: 13 – 25.
4. Shield TW, Locicero J, Reed CE, Feins HR. Thymic Tumor, General Thoracic Surgery. *Lippincott.* 2007; **7**: 2323 – 2364.
5. Okumura M, Miyoshi S, Fujii Y, Takeuchi Y, Shiono H, Inoue M, et al. Clinical and functional significance of WHO classification on human thymic epithelial neoplasms: a study of 146 consecutive tumors. *Am J Surg Pathol.* 2001; **25**: 103 – 110.
6. Nicholas AP, Chatterjee A, Arnold MM, Claussen GC, Zorn Jr G, OH SJ. Stiff-persons' syndrome associated with thymoma and subsequent myasthenia gravis. *Muscle Nerve.* 1997; **20**: 493 – 498.
7. Hagiwara H, Enomoto-Nakatani S, Sakai K, Ugawa Y, Kusunoki S, Kanazawa I. Stiff-person syndrome associated with invasive thymoma: a case report. *J Neurol Sci.* 2001; **193**: 59 – 62.
8. Murakawa T, Nakajima J, Sato H, Tanaka M, Takamoto S, Fukayama M. Thymoma associated with pure red-cell aplasia: clinical features and prognosis. *Asian Cardiovasc Thorac Ann.* 2002; **10**: 150 – 154.