

Stiff Person Syndrome in A Patient With Pancreatic Adenocarcinoma: An Unusual Paraneoplastic Syndrome

E. Nayır¹, M.B. Koyuncu², S.Erdogdu³, A.Ata⁴, İ. A.Yılmaz⁵, A. Arıcan⁶

¹ Department of Medical Oncology, Kahramanmaraş Necip Fazıl City Hospital, K.maraş, Turkey

² Department of Internal Medicine, Mersin University Faculty of Medicine, Mersin, Turkey

³ Department of Medical Oncology, Elazığ Education and Research Hospital, Elazığ, Turkey

⁴ Department of Medical Oncology, Medicalpark Tarsus Hospital, Mersin, Turkey

⁵ Department of Neurology, Mersin University Faculty of Medicine, Mersin, Turkey

⁶ Department of Medical Oncology, Mersin University Faculty of Medicine, Mersin, Turkey

Özet

Stiff person sendromu (SPS), progresif kas katılığı, rijiditesi ve kas spazmı ile giden, emosyonel stress ve bazı tetikleyici faktörlerle daha da kötüleşebilen nadir bir klinik durumdur. SPS'nin otoimmün, idiyopatik ve paraneoplastik olmak üzere üç varyantı vardır. Paraneoplastik tipi neoplaziler ile ilişkilidir. Paraneoplastik varyant, meme kanseri ve küçük hücreli akciğer kanserli hastalarda bildirilmiştir. Ancak literatürde pankreas kanseri ile ilişkisi bildirilmemiştir. Bu olgu sunumu ile pankreas kanserinin SPS ile ilişkisini ilk olarak gösterdiğimizi düşünmekteyiz.

Anahtar Kelimeler: Stiff person sendromu, paraneoplastik, pankreas kanseri

Abstract

Stiff person syndrome (SPS) is a rare clinical condition which is characterized by progressive muscle stiffness, rigidity and muscle spasms which are worsened by emotional stress and some triggers. SPS has three variants : autoimmune, idiopathic and paraneoplastic. Paraneoplastic variant is associated with neoplasms. There is non-organ-specific antibodies, but not anti-GAD or anti-islet cell antibodies in circulation. Paraneoplastic variant was reported in patients with breast cancer and small cell lung cancer before. However, there is no report with pancreatic cancer at literature. We think that this case is the first one showing the relation of SPS with pancreatic cancer.

Keywords: Stiff person syndrome, paraneoplastic, pancreatic cancer

Corr. Author:
Erdinc Nayır,
Kahramanmaraş
Necip Fazıl City Hospital
46050 Kahramanmaraş,
Turkey
P: +90344 228 28 00
F: +90344 251 51 05
drerdincnyr@gmail.com

Introduction

Stiff person syndrome (SPS) is a rare clinical condition which is characterized by progressive muscle stiffness, rigidity and muscle spasms which are worsened by emotional stress and some triggers. Muscle stiffness is seen especially at paravertebral and lower extremity muscles¹. SPS has three variants: autoimmune, idiopathic and paraneoplastic.

Autoimmune variant includes patients with Anti-GAD, anti islet cell and other organ specific autoantibodies. These patients usually have autoimmune diseases such as type 1 diabetes mellitus, thyroiditis, vitiligo and pernicious anemia².

At idiopathic variant, there is no evidence of autoantibody production or association with any other diseases.

Paraneoplastic variant is related with neoplasms. There is non-organ-specific antibodies, but without anti-gad or anti islet cell antibodies in circulation. Some of these patients have anti-amphiphysin autoantibodies³. Remission at neurological symptoms may be seen after tumor excision and corticosteroids.

Spinal deformities may develop by continuous rigidity and muscle stiffness at patients with SPS. Axial muscles are especially affected in this entity. Posture changes, walking difficulties, Some patients become wheelchair bound or even bedridden. Muscle spasms triggered by sudden movements, noise or emotional stress are sensitive and specific features of SPS. In these patients, paroxysmal autonomic dysfunction signs such as temporary hyperprexia, diaphoresis, tachypnea, tachycardia, pupillary dilatation and arterial hypertension can be observed⁴. Respiratory arrest may develop because of involvement of respiratory muscles.

EMG studies reveal a continuous motor unit activity which is diminished with intravenous diazepam administration, sleep and anesthesia. Myoclonic reflexes which are seen 1-3 times after nerve stimulation are termed as spasmodic reflex myoclonus. It is seen in all SPS patients. There is no defined specific neuroradiological finding for SPS⁵.

Paraneoplastic variant was reported at patients with breast

cancer and small cell lung cancer^{6,7}. However, there is no report with about SPS related with pancreatic cancer at literature. We think that this case is the first one showing the relation of SPS with pancreatic cancer.

Case Report

We report a 67-year-old male with no chronic disease other than hypertension. Whipple surgery was performed because of the 3.5x2.5 cm mass at head of the pancreas. Pathology revealed adenocarcinoma. Adjuvant 5-FU chemotherapy was given to the patient. After one year, he applied with weakness at both lower extremities, inability to walk and balance difficulties. A recurrent pancreatic mass was detected on abdominal CT. In nerve transmission studies, axonal polyneuropathy that predominantly affects lower extremity sensorial and motor fibers was seen. Continuous motor unit activity was detected at agonist and antagonist muscles at EMG studies. During follow up, initially stiffness of lower and upper extremities was observed. Later, stiffness of neck and facial muscles and irregular spasms of the axial muscles developed. Serum Anti-GAD was negative. Anti-amphiphysin antibody test couldn't be performed. SPS was diagnosed by characteristic symptoms and EMG findings. After diagnosis, benzodiazepin, steroid and plasmapheresis therapies were applied to the patient. However, neurological improvement was not observed. The patient died after second cycle of palliative gemcitabine+cisplatin chemotherapy because of septic shock.

Discussion

Paraneoplastic SPS is a rare clinical entity. Cases at literature are mostly related with small cell lung cancer and breast cancer^{6,7}. On the other hand, various neurological paraneoplastic syndromes such as polymyositis, dermatomyositis, peripheral neuropathy are defined at patients with pancreatic cancer. There is no report about relationship between pancreatic cancer and SPS which is a rare neurological syndrome in literature.

Although anti-GAD is generally negative at paraneoplastic variant of SPS, there is multiple anti-GAD positive paraneoplastic SPS cases in literature. So, If anti-GAD is positive, it doesn't prove that present neurological status is not paraneoplastic⁶. Being paraneoplastic or not affects treatment plan at SPS.

While response rate to treatment in idiopathic and autoimmune variant is low, response rate of paraneoplastic variant is higher after treatment strategies such as tumor excision.

Summary

In conclusion, screening for malignancy and to think rare causes in differential diagnosis is extremely important for both early diagnosis of primary disease and treatment of neurological symptoms in SPS cases.

Conflict of Interest Disclosures

The authors have declared that no competing interests exist.



References

1. Shaw PJ. Stiff-man syndrome and its variants. *Lancet*. 1999 Jan 9;353(9147):86-7.
2. Grimaldi LM, Martino G, Braghi S, Quattrini A, Furlan R, Bosi E, Comi G. Heterogeneity of autoantibodies in stiff-man syndrome. *Ann Neurol*. 1993 Jul;34(1):57-64.
3. De Camilli P, Thomas A, Cofield R, Folli F, Lichte B, Piccolo G, Meinck HM, Austoni M, Fassetta G, Bottazzo G, Bates D, Cartledge N, Solimena M, Kilimann MW, et al. The synaptic vesicle-associated protein amphiphysin is the 128-kD autoantigen of Stiff-Man syndrome with breast cancer. *J Exp Med*. 1993 Dec 1;178(6):2219-23.
4. Stayer C, Meinck HM. Stiff-man syndrome: an overview. *Neurologia*. 1998 Feb;13(2):83-8.
5. Kimura, J. *Electrodiagnosis in Diseases of Nerve and Muscle: Principles and Practice*, 2nd edition, FA Davis, Philadelphia, 1989.
6. Krishna VR, Kniewel K, Ladha S, Sivakumar K. Lower extremity predominant stiff-person syndrome and limbic encephalitis with amphiphysin antibodies in breast cancer. *J Clin Neuromuscul Dis*. 2012 Dec;14(2):72-4.
7. Nguyen-Huu BK1, Urban PP, Schreckenberger M, Dieterich M, Werhahn KJ. Anti-amphiphysin-positive stiff-person syndrome associated with small cell lung cancer. *Mov Disord*. 2006 Aug;21(8):1285-7.
8. Solimena M, Folli F, Aparisi R, Pozza G, De Camilli P. Autoantibodies to GABA-ergic neurons and pancreatic beta cells in stiff-man syndrome. *N Engl J Med*. 1990 May 31;322(22):1555-60.