



Stiff Person Syndrome Misdiagnosed as Oxaliplatin Induced Neurotoxicity

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ARTICLE INFORMATION

Received: January 21, 2021

Revised: March 26, 2021

Accepted: May 02, 2021

Published Online: May 07, 2021

Keywords:

Stiff-person syndrome (SPS), Autoimmune Disorder, Methylprednisolone, Bevacizumab, Oxaliplatin



DOI: [10.15415/jptrm.2021.91005](https://doi.org/10.15415/jptrm.2021.91005)

ABSTRACT

Introduction: Stiff person syndrome is characterized by muscle rigidity that waxes and wanes along with concurrent spasms. The symptoms of the stiff-person syndrome were identical to those of oxaliplatin side effects.

Methods: This was a case report of a 65-year-old man who was diagnosed with stiff-person syndrome. He experienced pain with bleeding from the rectum. Screening tests were used to check for amphiphysin antibodies and electromyography. FNAC was done from the government hospital which was conclusive of metastasis. He was initiated on Capecitabine and Oxaliplatin protocol.

Results: During the hospital stay, he was treated with 1gm Methylprednisolone for 5 days and sequentially with immunoglobulin 2gm per day for 5 days, concomitantly Benzodiazepam was given 10mg three times a day for 3 days but later withdrawn as the patient started experiencing dizziness. He achieved no clinical benefit in neurological status. Eventually developed aspiration pneumonia and succumbed to death after one month of diagnosis of SPS.

Conclusion: Further studies should carry out to develop an evidence-based approach to diagnosing and treating SPS patients.

1. Introduction

A rare acquired neurological disorder called Stiff Person Syndrome is characterized by progressive muscle stiffness and recurrent episodes of painful muscle spasms (Balint 2016). The muscular tension often gets worse and then gradually improves and usually occurs with muscle spasms. Spasms occur if events that act as triggers include a sudden noise or light physical contact. The seriousness and the progression of SPS vary from person to person. The cause of SPS is unknown (Corina et al., 2013); it can occur along with other autoimmune disorders. The prevalence and incidence of SPS are not known (Sasa 2013), although one estimate places the occurrence (Dekker et al., 2013; James et al., 2018) of about 1 in 1,00,000 people in the population. SPS usually becomes prevalent sometime between 30 - 60 years of age.

2. Methods

This was a case report of a 65-year-old man who was diagnosed with stiff-person syndrome. He experienced pain with bleeding from the rectum. Screening tests were used

to check for amphiphysin antibodies and electromyography. FNAC was done from the government hospital which was conclusive of metastasis. He was initiated on Capecitabine and Oxaliplatin protocol.

3. Results

A 65-year-old male presented with complaints of pain and PR bleeding in January 2019. He was evaluated with a CT scan abdomen, which was suggestive of Liver Limited cancer and rectal examination suggested ulcero-proliferative growth of around 4 cm from the anal verge (Joe et al., 2019). Colonoscopy was suggestive of circumferential growth with multiple sessile polyps, which was to document the metastatic nature of the disease. FNAC was done by the government hospital which was conclusive of metastasis. He was initiated on Capecitabine (Jonathan et al., 2016) and Oxaliplatin by protocol. At the time of presentation, his performance score was ECOG 1. However, the patient discontinued chemotherapy in view of severe loose motion after the first dose of the capecitabine and oxaliplatin regimen. He presented again in March 2019 after a gap of 2 months with worsening symptoms of weakness and bleeding

from the rectum. Reevaluation with CT scan abdomen again showed suggestive of Liver Limited disease. His mutational status of KRAS and BRAF was not done because of financial constraints. Bevacizumab was not added in view of financial constraints. He was initiated with dose reduction of the CAPOX regimen. However, the patient again defaulted for 2 months because of personal issues. He did not develop severe enteropathy this time. He presented again in May 2019 and was re-initiated with the CAPOX regimen on 2 weekly bases, which he completed to 4 cycles till August 2019. From July 2019 the patient started to develop hypoalbuminemia and generalized weakness. In August 2019 patient developed generalized weakness, on clinical examination, he was found to have a severe stiffness of muscles. Based on clinical examination there was no neurological weakness attributable to the sensory neural deficit or cerebellar involvement. MRI brain was negative for any brain metastasis or leptomeningeal involvement. CSF analysis showed a mild rise in CSF protein. CSF was also sent for an anti GAD antibody which showed negative. His clinical examination was suggestive of generalized muscle involvement with laryngeal involvement. He was planned for tracheostomy, but no tracheostomy status was decided at a familial consensus. He underwent NCV studies, which were mild to moderate sensory deficits. During the hospital stay, he was treated with a high dose of Methylprednisolone 1gm for 5 days and sequentially with immunoglobulin 2gm per day for 5 days, concomitantly Benzodiazepam was given 10mg three times a day for 3 days but later withdrawn as the patient started experiencing dizziness. He achieved no clinical benefit in neurological status. Eventually developed aspiration pneumonia and succumbed to death after one month of diagnosis of SPS.

4. Discussion

The diagnosis of SPS is done upon identification of symptoms, detailed patient history, and a close clinical evaluation. The tests include screening tests to detect the presence of amphiphysin antibodies and electromyography. The characteristic feature of SPS is muscle motor rigidity or unit firing in stiff muscles which can be seen via electromyography.

The main aim of SPS is to give symptomatic relief and improve the patient's quality of life. Due to the rarity of the disease, there are limitations in the quality of treatment options that are available. Over the years, treatment modalities for SPS included Benzodiazepines and Baclofen as the first line of drugs followed by IVIG, plasmapheresis, immune modulators and Rituximab. IVIG and plasmapheresis are either used alone or in combination in refractory cases. Corticosteroids are used as monotherapy or as a combination with other drugs for SPS. However, their efficacy is not determined by

any clinical trial yet. In this case, the patient was treated with a high dose of Methylprednisolone, immunoglobulin, and Benzodiazepam.

In a para-neoplastic variant of SPS, the stiffness localizes to the arms and legs, making up only 5% of SPS cases. Generally, classical SPS patients respond well to treatment, but in about 10% of cases, sudden deaths occur due to autonomic dysfunction. Repeated spasms or sudden withdrawal of medicine may lead to autonomic dysfunction and may lead to sudden death.

Conclusion

A recent review was conducted by Balint et al regarding the stiff-person syndrome. The study highlighted the prevalence of immune-mediated movement disorders and the underlying pathophysiology of those Stiff person syndrome. The study concluded the importance of dipeptidyl peptidases like protein and glycine transporter 2 for the treatment of this disorder and physicians should update their knowledge regarding these new antibodies (Balint et al., 2016).

There is a paucity of evidence articles relating to Oxaliplatin induced neurotoxicity and Stiff person syndrome and how they are best treated. Recent studies reported the link between SPS and myasthenia gravis. Patients with SPS were prescribed muscle relaxants and anticonvulsants. Further studies should carry out to develop an evidence-based approach to diagnosing and treating patients.

Abbreviations

SPS- Stiff Person Syndrome, CT- Computerized Tomography, Bleeding PR- Rectal Bleeding, FNAC- Fine Needle Aspiration Cytology, ECOG- Eastern Cooperative Oncology Group Performance Test, CAPOX- Capecitabine and Oxaliplatin Regimen, KRAS, BRAF- Tumor Driven Genes, MRI- Magnetic Resonance Imaging, CSF- Cerebrospinal Fluid, GAD antibodies- Diabetes Associated Antibodies, NCV- Nerve Conduction Study, EMG- Electromyography, IVIG- Intravenous Immunoglobulin.

Acknowledgements

The authors are thankful to Chitkara University, Punjab for providing the necessary facilities during this work.

Authorship Contribution

Shaima & Sarita: Conceptualization of the study, study design & overall analysis.

Rooha & Meghana: Data collection, manuscript writing.

Funding

This research received no external funding.

Conflict of Interest

The authors declare no conflict of interest, financial or otherwise.

Declaration

It is an original data and has neither been sent elsewhere nor published anywhere.

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Journal of Pharmaceutical Technology, Research and Management

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Volume 9, Issue 1

May 2021

ISSN 2321-2217

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