Case Reports in Neurology

Case Rep Neurol 2019;11:217–221

DOI: 10.1159/000501793
Published online: July 16, 2019

Case Report

Stiff Person Syndrome Associated with Compartment Syndrome

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Keywords
Stiff person syndrome · Compartment syndrome · Glutamic acid decarboxylase antibody · Autoimmune disease

Abstract
Stiff person syndrome (SPS) is a rare and disabling neurological disorder of autoimmune origin, characterized by progressive stiffness and muscle spasms affecting the axial and limb muscles, most frequently associated with antibodies against glutamic acid decarboxylase. We describe a patient who presented initially with compartment syndrome and was later diagnosed with SPS. This is the first case report of SPS possibly presenting initially with compartment syndrome. This case illustrates the importance of recognizing that patients with SPS may present with varied manifestations, including compartment syndrome, which by itself is a medical emergency.

Introduction

Stiff person syndrome (SPS) is an extremely rare, neuroimmunological disorder characterized by insidious onset – progressive axial and limb stiffness with superimposed painful spasms – resulting in abnormal posture, gait difficulty, recurrent falls, and inability to perform activities of daily living independently [1]. We describe a patient who possibly presented initially with compartment syndrome and was later diagnosed with SPS.

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Case Report

A 66-year-old Chinese Singaporean man presented initially to the orthopaedic department with a 1-week history of left calf pain. On examination, the left calf was tender to palpation and visibly swollen with a larger circumferential diameter (measuring 20 cm above the upper border of the medial malleolus) compared to the right (40 vs. 37 cm). Otherwise, there was no neurovascular deficit detected over the left lower limb. Blood samples showed haemoglobin of 14.8 g/dL, total white blood cell count of 13,760/mm^3, and platelet count of 275,000/mm^3. Serum creatinine kinase was raised at 2,570 U/L with no acute kidney injury biochemically. C-reactive protein, procalcitonin, and D-dimer levels were all within normal limits. Plain radiography of the patient's left tibia and fibula showed no definite fracture or suggestion of acute osteomyelitis. He was subsequently treated as for left leg compartment syndrome and underwent left leg fasciotomy and tibialis anterior resection. It was noted intraoperatively that 80% of the patient's left tibialis anterior muscle was gangrenous while the rest of the anterior compartment muscles were less than 50% gangrenous. The remaining 3 compartments (deep and superficial posterior, lateral) muscles appeared healthy. Histological findings of the biopsied left tibialis anterior muscle eventually showed features suggestive of focal ischaemic change.

Postoperatively, the patient was transferred to another community hospital for a short course of rehabilitation. However, he developed acute bilateral hip pain about 2 weeks after his left leg fasciotomy, which was later attributed to bilateral undisplaced fracture of the acetabulum, seen on magnetic resonance imaging (MRI). On further questioning, he reported progressive, episodic, lower back and bilateral lower limb stiffness and spasms for the last 2 months, symptomatically similar to his left calf pain. There was no past history of diabetes mellitus or other autoimmune diseases. He denied having a family history of similar paroxysmal muscle spasms or stiffness as well as of connective tissue disease. On examination, the stiffness and spasms appeared to be precipitated by sudden movement but not by noise or emotional upset. The affected areas had a tight, hard, and board- like feel. Palpation, especially of the lower limbs, occasionally provoked more intense spasm. In addition, the patient was noted to have non-fatiguable, limited abduction of extraocular movement bilaterally, but he did not report any diplopia. There was no myoclonus and he was not encephalopathic. There were no signs of parkinsonism and the absence of history of traumatic injury or exposure of open wound to soil as well as trismus and facial spasms made tetanus less likely as the aetiology for the patient's muscle spasms. Bilateral hip flexion was limited due to pain. Otherwise, reflexes were normal in both the upper and lower limbs and examination showed cranial nerves and motor and sensory functions to be intact.

MRI of the brain and cervical and thoracolumbar spine were unremarkable except for findings suggestive of mild degenerative disc disease. Routine nerve conduction study of the upper and lower limbs was within normal limits. Electromyography of the lower limbs showed continuous motor unit activity at rest in spite of voluntary relaxation. There were no neuromyotonic discharges. In view of suspicion for SPS, serum was tested for anti-glutamic acid decarboxylase (GAD) antibody and eventually returned positive with a value of >300 U/mL (normal range is ≤0.9 U/mL). Antinuclear antibody and anti-double-stranded DNA antibodies were within normal limits. There were no paraneoplastic antineuronal antibodies (Hu, Yo, Ri, CV2, amphiphysin, PNMA2/TA) exhibited in our patient's serum sample. Biochemical screening tests for diabetes and thyroid disease were unremarkable. Contrast-enhanced computed tomography of the thorax, abdomen, and pelvis did not show any tumour.

The patient was treated for SPS initially with oral clonazepam and baclofen. Levetiracetam was subsequently added as it has been reported to be effective in ameliorating paroxysmal spasms via facilitating inhibitory GABAergic transmission. As the patient showed no significant symptomatic relief with clonazepam and/or baclofen, he was started on immunotherapy including prednisolone and two courses of intravenous immunoglobulin at a dose of 0.4 g/kg/day, each course lasting 5 days. He showed gradual improvement in his symptoms including stiffness and spasms as well as functional status. Prednisolone was tapered off successfully after 2 years. Currently, he takes clonazepam occasionally for symptomatic treatment.

Discussion

We describe a patient with SPS who possibly presented initially with compartment syndrome. Acute compartment syndrome (ACS) is a medical emergency requiring prompt recognition and appropriate decompressive treatment via fasciotomy. It is recognized that in ACS, there is raised intracompartmental pressure and resultant decline in tissue perfusion pressure within the compartment. Ischaemia ensues and eventually this leads to local tissue anoxia and necrosis. Multiple causes of ACS have been identified or reported including fracture of the tibial diaphysis, blunt soft tissue injury, crush syndrome, exercise, ischaemia-reperfusion injury, tetanus, snake venom, viral myositis, burns, casts, diabetes, and hypothyroidism [2]. Our patient did not sustain any fall or traumatic or burn injury prior to this presentation. The absence of underlying peripheral vascular disease with subsequent reperfusion therapy such as arterial grafting, stenting, or embolectomy excludes ischaemic-reperfusion injury as a cause for his ACS. His muscle spasms were less likely attributed to tetanus in the absence of exposed open wound to soil and clinical findings such as trismus and facial spasms. There was no painful, proximal weakness to suggest viral myositis, and this was supported by the absence of polyphasic, short-duration, low-amplitude motor unit action potentials on electromyography to suggest underlying myopathy.

He was eventually diagnosed with SPS based on the presence of muscle rigidity in the limb and axial muscles, episodic spasms which could be precipitated by tactile stimuli, continuous motor unit activity at rest in spite of voluntary relaxation as demonstrated on electromyography, and the presence of positive anti-GAD antibodies. Progressive encephalopathy with rigidity and reflex myoclonus (PERM) was considered in our patient with acquired limb and axial rigidity and spasms. However, he was not encephalopathic and myoclonus was absent. While intermittent spasms can be a manifestation of tetanus, this infectious disease caused by spores of the bacteria *Clostridium tetani* was deemed unlikely for reasons described earlier. Our patient's vertical eye movements were still intact and did not display autonomic dysfunction or cogwheel rigidity, which collectively could suggest an underlying extrapyramidal syndrome such as progressive supranuclear gaze palsy. A spinal cord lesion is unlikely to account for his stiffness, rigidity, and muscles spasms in the absence of brisk reflexes, a sensory level, and the presence of unremarkable MRI studies. Our patient was not tested for the presence of autoantibodies against voltage-gated potassium channels as clinical suspicion for Isaac's syndrome or peripheral nerve hyperexcitability was low. There was no myokymia, fasciculations, pseudomyotonia, or hyperhidrosis in our patient.

To our knowledge, this is the first report of an SPS patient possibly presenting with compartment syndrome. We hypothesize that the combination of recurrent episodes of muscle stiffness and spasms, as well as the continued use of the involved muscle groups (such as to

ambulate), may have resulted in repeated soft tissue injury and oedema. This may have contributed to the rise in intracompartmental pressure, eventually manifesting as compartment syndrome.

We acknowledged that our patient did not display the typical symptoms and signs expected of compartment syndrome such as pallor, pulselessness, paralysis, and paraesthesia. In addition, except for the episodic stiffness and spasms due to SPS, he regained normal limb function despite fasciotomy being performed about a week after symptom onset. This is much later than the widely accepted optimal timing (within 6 h), after which there is irreversible tissue ischaemia, major neurovascular complications potentially requiring amputation, and possible death [3].

It has been suggested that the extent of ischaemic damage is dependent on the degree of energy depletion during ischaemia. The atypical presentation and unexpected outcome of compartment syndrome of our patient could probably be due to recurrent short-lasting muscle stiffness and spasms, which resulted in shorter duration of ischaemia and, thus, less severe degree of injury [4].

Nevertheless, we find it of utmost importance to recognize that SPS could possibly present with compartment syndrome and it needs to be considered one of the possible aetiologies for this potentially limb- and life-threatening medical emergency.

Our patient's modified Rankin Scale (mRS) prior to symptom onset was 0, and progressively worsened to a peak of 4 prior to symptomatic treatment and immunotherapy for SPS. His mRS improved to 2 at the 6th month of follow-up and returned to 0 at 1 year of follow-up with long-term benzodiazepine, baclofen, corticosteroids, and levetiracetam. This is in contrast to a previous report by McKeon et al. [5] that there is no significant difference in mRS between time of treatment initiation and follow-up (range 2–23 years). In addition, a reduction in spasms and stiffness with symptomatic treatment and immunotherapy have improved the patient's social and occupational function as well as activities of daily living, an observation consistent with previous reports.

Conclusion

Our case report highlights the importance of recognizing that patients with SPS can present with varied manifestations, possibly including compartment syndrome, which by itself is a medical emergency and requires emergent fasciotomy to avoid significant complications.

Statement of Ethics

The patient gave informed consent for the publication of this case report.

Disclosure Statement

The authors have no conflicts of interest to declare.

Funding Sources

The authors received no financial support for the research, authorship, and publication of this article.

Author Contributions

K.P.Y. contributed to the clinical management of the patient and writing of the manuscript. Y.L.L. contributed to the clinical management of the patient and reviewing and editing of the manuscript. All authors read and approved the final paper.

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