CASE REPORT

STIFF PERSON SYNDROME WITH ATYPICAL FEATURES AND A FAVOURABLE OUTCOME WITH STEROIDS

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ABSTRACT
Stiff Person Syndrome (SPS) is a rare and disabling disorder characterised by continuous motor unit activity causing severe rigidity and episodic spasms in axial and limb muscles. It deteriorates the quality of life and causes a serious burden in the patient's life. Here we describe a male patient with stiff person syndrome having atypical features like pyramidal signs and generalised convulsions. Benzodiazepines, baclofen and IVIG did not alter the clinical status whereas oral methylprednisone had a dramatic effect and resulted in a favourable outcome.

Keywords: Stiff person syndrome, Stiff man syndrome, Stiff person syndrome and steroids

ATİPİK BULGULARI OLAN STIFF PERSON SENDROMLU BİR OLGUDA KORTİKOSTEROİDE DRAMATİK YANIT

ÖZET
Stiff Person Sendromu (SPS), seyrek rastlanan, gövde ve ekstremite kaslarında rijidite ve epizodik spazmlarla hastanın yaşam kalitesini oldukça bozan, devamlı motor ünite aktivitesi ile karakterli bir tablodur. Burada stiff person sendromunun tipik özellikleriyle birlikte jeneralize nöbetler ve piramidal bulgular gibi atipik öğelerin de rastlandığı 40 yaşındaki bir erkek olguda altı aylık izlem bildirilmektedir. Nörolojik muayenesinde bilateral biseps reflekslerinin aktivitesinde artış ve taban cildi refleksinin iki yanlı ekstansör oluşu gibi piramidal bulgular izlenen hastanın kranyal MR, servikal MR ve EEG'si normal bulunmuştur. Özellikle alt ekstremitelerindeki tonus artışı ön planda olan hastanın EMG'sinde, quadriseps femoris kas grubunda şiddetli, biceps femoris, gastrokinemus ve lomber paraspinal kas grubunda hafif ve bilateral trapez kas grubunda orta derecede devamlı motor ünite aktivitesi saptanmıştır. Baklofen, benzodiazepin ve IVIG tedavisine yanıt vermeyen hastada metil prednizolon tedavisine oldukça dramatik bir yanıt izlenmiş ve hasta kortikoterapi başlanmasını izleyerek bir hafta içinde mobilize hale gelmiştir. Elektrofizyolojik izlemde de yukarıda belirtilen kas gruplarında, devamlı motor ünite aktivitesinin belirgin ölçüde gerilediği izlenmiştir. Altı aylık izlemde oral steroide devam eden hastanın klinik tablosundaki iyilik hali devam etmiş, sürdürülen elektrofizyolojik izleminde sadece trapez ve biseps femoris kas gruplarında minimal düzeyde devamlı motor ünite aktivitesinin varlığı gösterilmiştir.

Anahtar kelimeler: Stiff person sendromu, Stiff-man sendromu, Stiff person sendromu ve steroidler

INTRODUCTION

Stiff person syndrome (SPS) was first described by Moersch and Woltman in 1956. The authors named the syndrome as '' Stiff-man syndrome'' and reported 14 patients with progressive muscular rigidity and spasms [1]. In 1967 Gordon, et al. described the clinical and electrophysiological diagnostic criteria of the disease[1,2]. There are several conditions with clinical features resembling SPS with demonstrable central nervous system pathology reported in the literature as atypical cases of this disorder[1]. Here we report a patient diagnosed as SPS with atypical features such as pyramidal signs in his neurological examination besides generalised tonic clonic seizures. Imaging studies and EEG were normal and the patient responded well to steroids both clinically and electrophysiologically.

CASE REPORT

A forty year old male patient with complaints of difficulty of swallowing, generalised muscle spasms and generalised seizures was admitted to our clinic. His complaints began 3 months before his admission. He had severe difficulty in swallowing both liquids and solid foods. The seizures were generalized and tonic and lasted for

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10 minutes. Apart from the seizures he also had episodic spasms that affected both his axial and limb muscles and they occurred very frequently. The patient reported that he could not walk because of his stiffness and had become bedridden with involuntary spasms lasting all day long. He also reported an aura like feeling preceding the spasmodic attacks. He had lost weight and realized that his limb muscles were wasting.

He reported a sequela of poliomyelitis affecting his left lower extremity. Cranial nerves were intact. Cervical, thoracal, abdominal and limb muscles had increased tonus. The tonus increase was especially very prominent in the lower extremities. Muscle strength in the left lower extremity was 3/5 both in the proximal and distal muscles (according to MCR scale). All other extremity muscle groups were normal in muscle strength. Deep tendon reflexes except biceps were normal. Biceps reflexes had increased activity bilaterally . Plantar reflexes were both extensor. Cerebellar tests and examination of sense were normal. There was not any syphincter disorder.

Electromyography (EMG) was performed and nerve conduction studies were normal while there was a continuous motor unit activity of both agonist and antagonist muscles at the same time. The clinical symptoms along with the continuous motor unit activity of both agonist and antagonist muscles were thought to be consistent with stiff person syndrome. Anti glutamic acid decarboxylase (anti GAD) antibodies were detected in serum but could not be found.

During his stay in the hospital the patient did not have any convulsions. His EEG was normal. In order to investigate neoplasia that can be seen with stiff person syndrome, tumor markers were studied and the tests were negative. Abdominal ultrasound and thorax CT were also normal. As there were signs of pyramidal involvement in the neurological examination, cranial and cervical MRI were performed. The cranial MRI showed nonspesific gliotic lesions and the cervical MRI was normal.

In EMG the degree of continuous muscle activity in both of the trapezius muscles was moderate. Left biceps femoris, right rectus abdominis, right lumbar paraspinals, left gastrocinemius, left tibialis anterior and right rectus femoris muscles showed a milder degree of continuous motor unit activity while the activity was very prominent in the right vastus medialis muscle (Fig 1 and Fig 2).

Baclofen and benzodiazepines did not alter the clinical status so IVIG (Intravenous immune globulin) therapy (0.4/g/kg/day for 5 days) was initiated. IVIG therapy was not sucsessful, either.

It was decided to begin methyl prednisone therapy and the patient gave a favourable response to a therapy of 40mg/day oral methyl prednisone. EMG was performed again after the first week of the therapy and the continuous motor unit activity of the muscle groups that was recorded before, had decreased significantly (Fig 1).

The patient became mobilised in about a week's time and the hypertonicity of the muscles decreased. It was decided to continue the therapy with 50 mg oral methyl prednisone per day and the patient was discharged to continue the follow up in the outpatient program. After a month the neurological examination and EMG were reviewed. Most of the patient's complaints ceased and he could walk without help. The EMG recordings showed that the continuous motor unit activity had disappeared in most muscle groups, but there was still some activity in both of the trapezius muscles.

DISCUSSION

According to the criteria of diagnosis of stiff person syndrome established by Gordon, et al., normal motor and sensory examinations are the rule[2]. Our patient had pyramidal signs in both lower extremities. In order to investigate the origin of the pyramidal signs, we performed MRI but both cranial and cervical MRI were normal. Another atypical feature was his generalised seizures. Although we had not witnessed them, we had to take the information seriously because doctors had observed his fits and had put down notes in his file during his stay in the previous hospital he had visited.

The presence of anti GAD antibodies is well reported in stiff person syndrome but most reports say that the level of the enzyme does not correlate directly with the severity of the disease or the outcome. The techal synthesis of antiGAD antibodies is specific for SPS[3]. We could only investigate serum antiGAD Ab in our patient and we could not perform the test for techal antibodies. It is not a must for every SPS patient to have antibodies and Rakocevic,. et al. reported that anti GAD antibody titers in serum and CSF do not correlate with disease severity or duration[4].

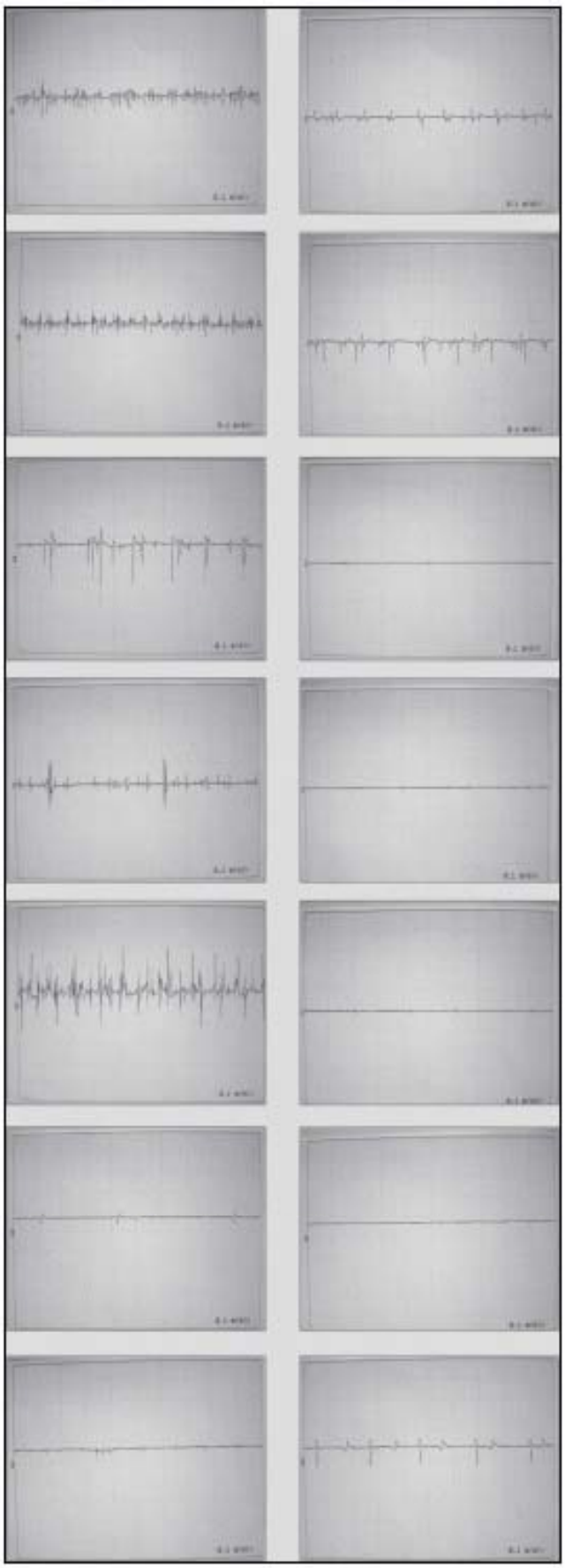

Fig. 1: Recordings of continuous motor unit activity from various muscle groups before and after one week of steroid therapy, from left to right:
First raw:
Left: Left tapezius recording before steroid therapy
Right: Left tapezius recording after steroid therapy
Second raw:
Left: Right tapezius recording before steroid therapy
Right: Right tapezius recording after steroid therapy
Third raw:
Left: Right biceps femoris recording before steroid therapy
Right: Right biceps femoris recording after steroid therapy
Fourth raw:
Left: Left gastrocinemus recording before steroid therapy
Right: Left gastrocinemus recording after steroid therapy
Fifth raw:
Left: Right vastus medialis recording before steroid therapy
Right: Right vastus medialis recording after steroid therapy
Sixth raw:
Left: Left tibialis anterior recording before steroid therapy
Right: Left tibialis anterior recording after steroid therapy
Seventh raw:
Left: Right rectus femoris recording after steroid therapy
Right: Right rectus femoris recording before steroid therapy

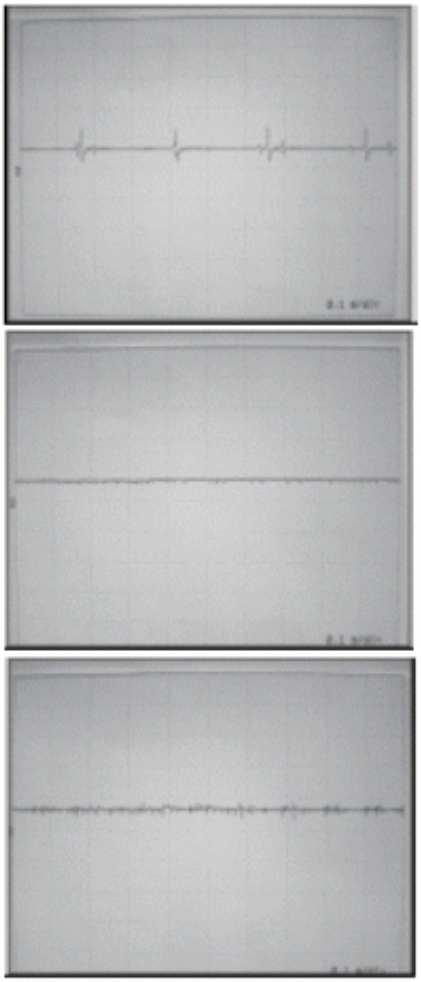

Fig. 2: Recordings of left biceps femoris, left rectus abdominis and right lumbar paraspinal muscles (from left to right) after one week of steroid treatment. The continuous motor unit activity is very mild After a month it was not seen any more.

Stiff person syndrome is reported to be associated with type 1 diabetes mellitus, autoimmune diseases and some types of cancer. Our patient had epilepsy besides SPS but not type 1 DM or malignancy. Epilepsy is less reported when compared with the other diseases appearing with SPS. Martinelli et al. reported a case of SPS associated with nocturnal myoclonus and epilepsy[5]. Another case of SPS reported with epilepsy had also type 1 diabetes mellitus[6].

According to Barker, et al., the response to diazepam and baclofen is only partial with half of the patients becoming wheelchair bound. The role of immunosupressive therapy is currently unknown. The disease lasts many years and may be due to a spinal interneuronitis although this remains speculative [7]. There are case reports expressing favourable outcome with IVIG[8-12] but studies with large numbers of patients are still lacking. In a recent review by Murinson BB, it was stated that IVIG is effective in the treatment of SPS while diazepam remains useful in managing the symptoms[13].There are also a few reports in the literature referring to therapy with plasma exchange (PE) and steroids. In a report of two patients with SPS it was concluded that autoantibody negative cases were less likely to respond to PE[14]. In another report of two patients with SPS, by Piccolo, et al., ACTH infusion produced an immediate clinical relief of muscle contracture and cramps, with parallel marked reduction of the EMG pattern of continuous motor unit activity in agonist and antagonist muscles. Apart from this effect, a more delayed response to oral prednisone was observed in both cases. These data lead the authors to consider a possible dysimmune pathogenesis of some cases with the stiff-man syndrome[15].

Our patient produced a good response to steroids and the clinical and neurophysiological findings improved quite rapidly. Our report therefore bares similarity to the report of Piccolo et al. We believe that studies of large numbers of patients are needed to find out the role of immune mediated therapies in SPS which can also enlighten the pathogenesis of this rare syndrome.

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