

Pediatric stiff-person syndrome with renal failure

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ABSTRACT

Stiff-person syndrome (SPS) is an autoimmune neuronitis with progressive myoclonus and stiffness. It is a rare but treatable disorder with few case reports in children. SPS is due to autoantibodies against the enzyme glutamic acid decarboxylase which is present in neuronal and nonneuronal tissues. This is the case report of an 8-year-old boy with clinical and investigational features suggestive of SPS with associated myoglobin-induced renal failure, who completely recovered with treatment.

Key words: Glutamic acid decarboxylase, myoclonus, rituximab, stiff-person syndrome

Introduction

Stiff-person syndrome (SPS) is an autoantibody-mediated disease against the GABAergic (Gamma-Amino Butyric Acid) neurons.^[1] Due to decreased GABA neuron function, which normally is inhibitory, there will be increased stiffness and spasm of muscles. Autoantibody against glutamic acid decarboxylase (GAD) in serum or cerebrospinal fluid (CSF) is supportive for the diagnosis.^[1,2] Pediatric case reports of this condition are less in number.^[3] Its true frequency has not been fully ascertained. The British Neurological Surveillance Unit identified 119 cases among the UK population over 5 years (2000–2005) implying a prevalence of 1–2 cases per million, of which 5% was seen in children.^[2]

Case Report

An 8-year-old male child born to nonconsanguineous parents came to us, with a 2 months history of progressively increasing jerky movements of body and limbs. This began on right leg, as sudden flexor spasms of the foot while walking, which led to frequent falling. In 2 weeks' time, it increased in frequency and spread to right thigh muscles

as flexion contractions of the hip. By 1½ months, trunk muscles and upper limbs were also affected. Extensor spasms predominated in trunk muscles which resulted in frequent prolonged arching back of the body. Due to these myoclonic contractions he could not sit or handle things. Spasms were painful, present during rest, increased by activity, touch, loud sound, and disappeared in sleep. His sensorium was normal. He had no difficulty in chewing or swallowing food. No bowel or bladder retention or incontinence. No sensory involvement. He developed oliguria and high colored urine in the last 1-week. No history of any serotonergic or antidopaminergic drug intake and no difficulty in opening mouth.

During examination, he had very frequent, violent myoclonic jerks of trunk and limbs. Due to severe lordosis he could not lie supine. He was in agonizing pain during the spasms and had visible severe wasting. Pulse rate 83/min, blood pressure 130/76 mmHg, respiratory rate 18/min, and had mild pedal edema. There were multiple pressure sores on areas where there was frequent rubbing of the skin. Higher mental functions and cranial nerves were within normal limits. Muscle tone was increased and passive movements were difficult.

Superficial reflexes were normal including flexor plantar. Deep tendon reflexes were brisk. All sensations were normally appreciated. No cerebellar signs. Skull and spine were normal. Fundus examination revealed no abnormality. We made a provisional diagnosis of subacute encephalomyelitis and myoglobin mediated acute tubular necrosis with differential diagnosis of SPS and progressive myoclonic epilepsy.

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His blood counts, serum calcium, thyroid function, blood sugar, glucose tolerance test, and tuberculosis screening, were within normal limits. Magnetic resonance imaging brain, spine, and electroencephalography (EEG) also were normal. Investigation results, which were abnormal, are given in the Table 1. X-ray chest, ultrasound sonography abdomen did not reveal lymphadenopathy or other neoplastic lesions. All investigations were sent in the first 2 days of admission based on the initial differential diagnosis.

He was treated with alkalinization and potassium lowering agents. Renal function started improving from next day. Methylprednisolone intravenous (IV) was given for 5 days along with clonazepam and valproate. Since there was no improvement, IV immunoglobulin (IVIG) was given for 5 days. There was no change in myoclonus. By then, the result of CSF autoantibody GAD65 came as positive. Hence, he was started on IV rituximab 375 mgm/m²/week. After the second dose of rituximab, myoclonus decreased significantly, he started sitting comfortably and began walking with little support in the next 7 days.

His renal function completely returned to normal. A total of 4 doses of rituximab was given at weekly intervals. He was discharged on oral tapering dose of prednisolone, clonazepam, and sodium valproate. He was doing well

at 1-month follow-up visit. His muscle spasms had completely subsided.

Discussion

Myoclonus is a movement disorder, which presents itself with sudden, brief, shock-like jerks. Normal EEG is a pointer against progressive myoclonic epilepsy and degenerative disease associated myoclonic seizures.^[4] No detectable neoplastic lesions, is against paraneoplastic immunologic events, even though long-term follow-up is required to certainly rule out neoplasm. The absence of, altered sensorium, neuropsychiatric symptoms, and choreoathetoid movements were pointers against other autoimmune encephalitis.^[5] No history of any drug intake ruled out drug-induced dystonia. Absence of lock jaw pointed against tetanus. Normal imaging studies of brain and spine with absent CSF pleocytosis, prompted us to send the CSF for the most common neuro autoantibodies in children – N-methyl D-aspartate (NMDA) and GAD65.^[6]

We made the final diagnosis after investigations, as SPS with myoglobin-induced acute tubular necrosis. Barker *et al.* divided SPS into three categories: The classical SPS, the stiff limb syndrome (c/c spinal interneuronitis), and progressive encephalomyelitis with rigidity.^[2] Our child had classical SPS, since he had predominant axial involvement and auditory stimulus sensitivity of muscle spasms.^[4] The dalakas criteria are used worldwide to diagnose SPS.^[2] Following five are the components of the criteria.^[1] Stiffness in the axial muscles, prominently in the abdominal and thoracolumbar paraspinal muscles leading to a fixed deformity (hyperlordosis).^[2] Superimposed painful spasms precipitated by unexpected noises, emotional stress, tactile stimuli.^[3] Confirmation of the continuous motor unit activity in agonist and antagonist muscles by electromyography.^[4] Absence of neurological impairments that could explain the stiffness.^[5] Positive serology for GAD65 (or amphiphysin) autoantibodies, assessed by immunocytochemistry, western blot or radioimmunoassay. Reported child had 4 out of 5 parameters of the above criteria. We could not do electromyogram. Other autoantibodies and GAD65 epitope binding studies were not done due to financial constraints and lack of easy availability. GAD autoantibody titer in serum or CSF does not correlate with symptom severity, and so titer monitoring is unnecessary.^[2]

Autoantibody GAD is also found in non-neuronal tissues, such as beta cells of pancreatic islets, thyroid, thymus, testes, and oviducts. Thirty percent of patients with SPS have insulin-dependent diabetes and both diseases share

Table 1: Investigations results SPS

Investigation	Result
CSF	
Cells	02 lymph/cumm
Protein	16 mgm %
Sugar	95 mgm %
NMDA antibody	Negative
GAD 65 antibody ELISA	116.1 IU/ml (normal 0.05)
Virology	Negative for entero, herpes, west Nile and Japanese B viruses
RFT	
Urea	177 mgm %
Creatinine	3.9 mgm %
Serum potassium	6.9 meq/L
Serum sodium	129 meq/L
Urine myoglobin	Positive
Serum CPK	14680
LFT	
Bilirubin T/D	1.2/0.5 mgm%
AST	4240 IU/L
ALT	120 IU/L
AP	142 IU/L
Serum protein/albumin	5.8/3.9 Gm%
PT/INR	13 sec/1.2

SPS: Stiff-person syndrome, NMDA: N-methyl D-aspartate, GAD: Glutamic acid decarboxylase, RFT: Renal function test, LFT: Liver function test, ALT: Alanine transaminase, AST: Aspartate aminotransferase, PT: Prothrombin time, INR: International normalized ratio, CPK: Creatine phosphokinase

autoantibodies to the same GAD65 with the difference in epitope binding. Our child did not have nonneuronal involvement.

As it is an autoimmune disorder, steroids and IVIG, either alone or combined, is the first line immunotherapy.^[2] Since he did not show improvement after 10 days, we used the second line immunosuppressant, IV rituximab.^[2] After the second dose of rituximab, there was a significant decrease in spasms. Plasma exchange is another option but not well established in SPS.^[2]

We are reporting this case, to include SPS in the differential diagnosis of any child with myoclonic jerks, normal sensorium, and absent pyramidal signs with normal EEG.

In all children with frequent muscle spasms, renal function also needs to be tested, since myoglobin released from overacting muscles can cause acute tubular necrosis.

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