Research Article

Acquired Neuromyotonia (Isaac's Syndrome): A Rare Report of Treatment with Cortico-Steroids and Plasmapheresis in a 38 Year Old Male Patient with Strong Positive Anti-Caspr2 Antibodies

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Abstract

Acquired neuromyotonia (Isaacs' syndrome) is a rare disorder characterized by hyperexcitability of peripheral motor nerves. The cardinal features consist of myokymia, pseudomyotonia and contracture of hands and feet. The diagnosis of Isaacs' syndrome is based on the clinical features and classic electromyographic findings. Serum antibodies against Voltage-Gated Potassium Channels (VGKCs) are detected in some cases. The authors report a 38-year-old military man presented with twitching in muscles all over the body for 2 months, difficulty in writing, pain in the back for months and body aches for 2 months with severe pain in left hand for last 1.5 months.

His bodyweight had decreased from 67 kilograms to 60 kilograms during that period. Physical examination was remarkable. Muscles were in a state of contraction with fasciculation, action myotonia without percussion myotonia, myokymia and carpopedal spasm.

The patient also complained of profuse sweating. Electromyography showed classical neuromyotonic and myokymic discharges. The investigations for conditions associated with Isaacs' syndrome were unrevealing. VGKCs antibody was performed with weak positive Anti LGI1 (Leucine-Rich Glioma-Inactivated Protein 1) abs and Strong positive ANTI-CASPR2. Treatment with carbamazepine and plasmapheresis along with plasma transfusion resulted in substantial improvement of the symptoms within 5 days.

***Keywords**: Contactin-associated protein-2, Isaac, neuromuscular hyper-excitability, neuromyotonia, voltage-gated potassium channel, myokymic discharges, Leucine-Rich Glioma-Inactivated Protein 1.*

Introduction

Isaacs' syndrome ("acquired neuromyotonia") is a disease characterized by peripheral nerve hyper-excitability and spontaneous and continuous skeletal muscle overactivity presenting as twitching and painful cramps, often accompanied by stiffness, pseudomyotonia, pseudotetany and weakness [1]. The commonest acquired form is autoimmune, caused by antibodies against nerve voltage-gated potassium channels (VGKC). Patients are commonly treated with symptomatic therapies (carbamazepine, phenytoin, lamotrigine or valproate) and immunomodulatory approaches, but no clinical trial is available to date and the optimal treatment approach is unknown [1]. Here, we report the case of a patient with Isaacs' syndrome tested positive for anti-contactin-associated protein-2 (Caspr2) antibodies.

Case Report

A 38-year-old man presented with a complaint of twitching of various muscles of the body for 2 months. Followed by severe pain in the left hand for 1.5 months.

The patient also complained of profuse sweating for 2 weeks. The patient did not have any significant history also he did not have any relevant family history.

Neurological examination revealed continuous muscular twitches with tremors in upper and lower limbs. The muscles were in a state of contraction. Myokymia and carpopedal spasm were significant.

Routine laboratory investigations revealed increased creatinine kinase levels(CK) (337 U/L; normal <190), hemoglobin 13.0 g/dl, increased total leukocyte count (WBC) (18.90 thou/µL; normal (4-10 thou/µL), Absolute neutrophil count 14.74 thou/µL; normal (2-7 thou/µL). Serological studies were negative for HIV and syphilis. Serum calcium and inorganic phosphorus were within normal limits.

Liver function tests were within the normal range.

Serum ANTI-VGKC antibodies were done. ANTI LGI1 was weakly positive and ANTI-CASPR 2 was strong positive which confirmed the diagnosis of Isaac's syndrome.

Spine and brain magnetic resonance imaging were normal. Nerve conduction study of bilateral median (m+s+f), bilateral ulnar (m+s), bilateral peroneal (m), bilateral tibial (m+f) nerve was performed and all parameters of above-sampled nerves were within normal limit.

Electromyography of bilateral deltoid, bilateral vastus lateralis, bilateral tibialis anterior was performed and all parameters of the above sample nerves revealed spontaneous activity in form of fibrillation, fasciculations. Also, doublets and triplets were witnessed.

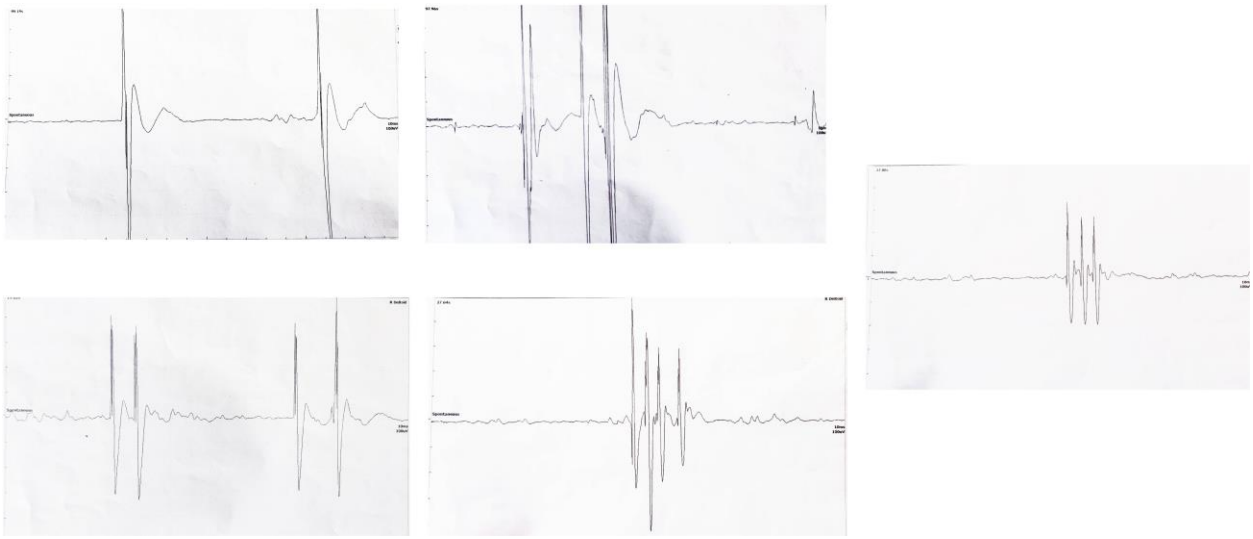

Figure-1

At last, the patient was treated with high dose corticosteroid (methylprednisolone 1 gm/day x 6 days) subsequently, tapering the corticosteroid to 25 mg per day.

Broad-spectrum empirical antibiotic therapy was given for 7 days. The treatment plan also consisted of seven sessions (about 4 hrs every alternate day) of plasmapheresis.

After the second session of plasmapheresis, there was a tremendous improvement in muscular twitches and tremors. The patient was discharged after 18 days. Total leukocyte counts and creatinine kinase levels were within normal limits.

Discussion

Neuromyotonia (NMT) is a form of peripheral nerve hyperexcitability that causes spontaneous muscular activity resulting from repetitive motor unit action potentials of peripheral origin. It can be triggered by voluntary or induced muscle contraction.

The abnormal activity is characterized electromyographically by doublet, triplet or multiplet single-unit discharges that have a high intraburst frequency, the frequency of the bursts themselves being irregular. Our patient had these EMG criteria.

The exact cause is still unknown. However, autoimmune antibodies can be detected in several peripheral (e.g. myasthenia gravis, Lambert-Eaton myasthenic syndrome) and central nervous system (e.g. paraneoplastic cerebellar degeneration, paraneoplastic limbic encephalitis) disorders. Autoimmune neuromyotonia is typically caused by antibodies that bind to potassium gated channels on the motor nerve resulting in hyperexcitability.

Anti-VGKC autoantibodies have been recognized in patients with acquired neuromyotonia. VGKC-antibodies define neurological conditions that are usually immunotherapy-responsive, but patients with anti-Caspr2 antibodies could have an increased risk of an underlying tumor and a poor prognosis.

Our case report suggests that Treatment with Methylprednisolone 1 gm/day x 6 days along with plasmapheresis proved to be very effective and well-tolerated by the patient diagnosed with Isaac's syndrome due to anti-caspr2 antibodies.

As this is a rare condition, controlled studies are not possible to be conducted.

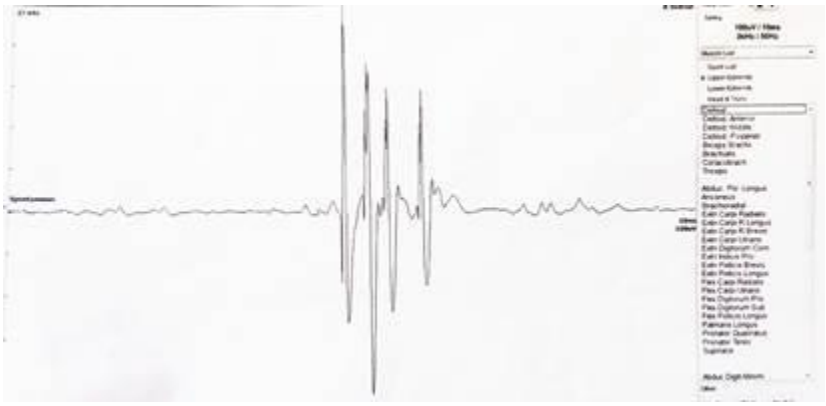

Figure-2

Figure-3

Declarations

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None.

Conflicts of Interest

There are no conflicts of interest.

Patient consent

Patient consent was duly taken before writing this manuscript.

Ethics approval

Not applicable.

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