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CASE REPORT **OPEN ACCESS**

A CASE REPORT ON NEUROMYOTONIA ASSOCIATED WITH MYASTHENIA GRAVIS: ISAACS SYNDROME

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A B S T R A C T

This case report details a 38-year-old male presenting with symptoms including muscle twitching, cramps, and bilateral ptosis. He was diagnosed with neuromyotonia (Isaacs syndrome) alongside myasthenia gravis (MG), indicated by the presence of serum acetylcholine receptor (AChR) antibodies. The patient showed significant improvement after a 5-day course of intravenous methylprednisolone and phenytoin administration. This case suggests overlapping pathophysiological mechanisms between neuromyotonia and autoimmune myasthenia gravis, warranting further research.

Keywords: Neuromyotonia, Isaacs syndrome, Myasthenia gravis, Acetylcholine receptor antibodies, Autoimmune disorders, Peripheral nerve hyperexcitability.

INTRODUCTION

Acquired neuromyotonia (Isaacs' syndrome) is a rare disorder where hyperexcitability of peripheral motor nerves leads to incapacitating muscle twitching, cramps, myokymia, pseudomyotoniaand mild weakness[1,2]. This syndrome may also be related to other autoimmune diseases such as chronic inflammatory demyelinating polyneuropathy[3], myasthenia gravis or the presence of Acetylcholine receptor antibodies[4]. According to Orphanet, only 100-200 total cases of IS have been recorded across the 41 countries[5]. Exertional weakness is unusual without coexistence of autoimmune myasthenia gravis (MG). A patient with NMT who developed exertional weakness with coexisting seropositive MG is reported herein.

CASE PRESENTATION

A 38-year-old male presented with the primary complaint of a decrease in his routine activities and ambulation difficulties associated with heaviness and cramping in both lower limb for last 20 days. He is also complained of drooping of upper eyelid in both eyes and trouble in sleep at night time for last 12 days . He denied any tobacco and alcohol had used in the past.There was no history of exposure to toxic substances or medications.

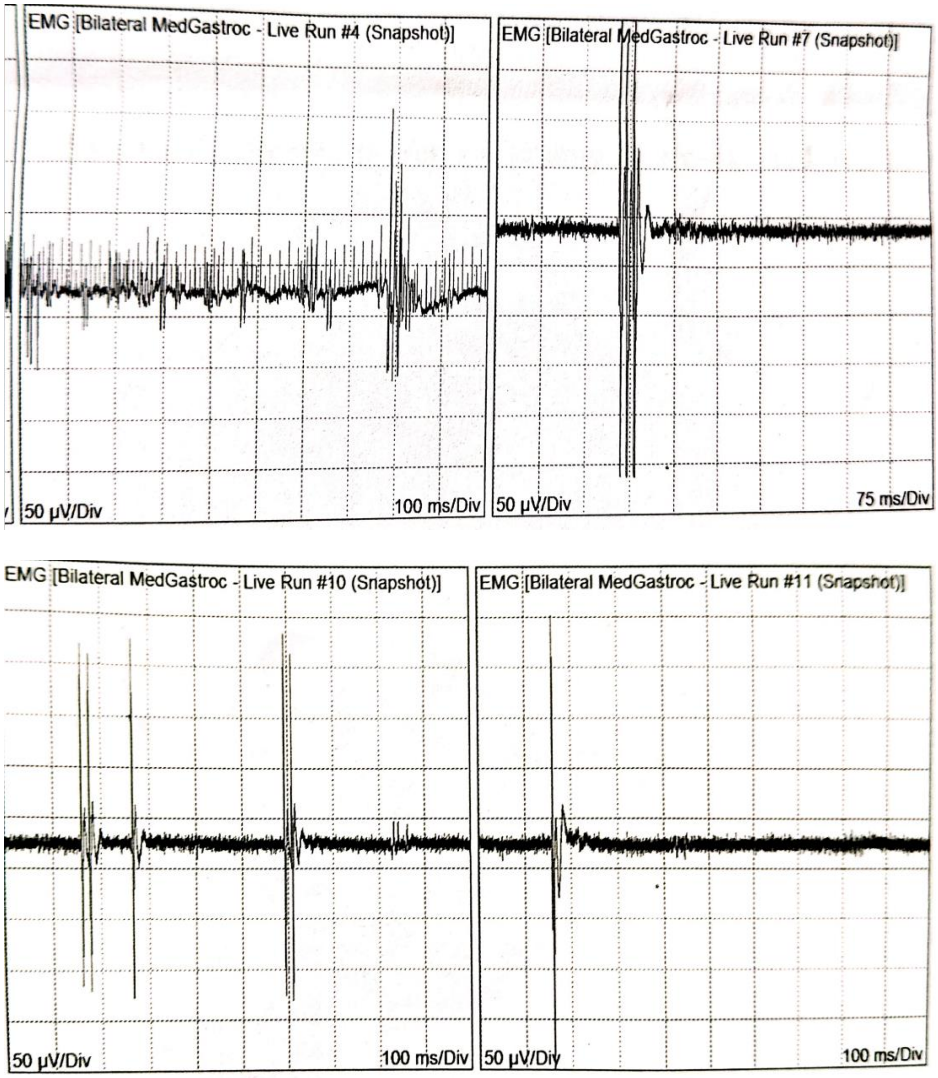
GCS E4V5M6, P- 90/MIN, BP- 124/78, no pallor, cyanosis, icterus and oedema. He was intellectually and emotionally normal. Neurological examination revealed normal cranial nerves except b/l ptosis present(Fig. 1). His posture was also stiff and all muscles were in a state of persistent contraction. The degree of stiffness was more remarkable in the distal than proximal muscles. The most striking physical findings were myokymia (constant undulating movement of the muscles) especially on his arms and calf. However, percussion myotonia was absent. Muscle strength was normal but tone was generally increased. Sensory examination was intact. Deep tendon reflexes were not elicitable. Lymph nodes

and thyroid gland were not palpable. Abdominal wall was tense but there was no hepatosplenomegaly or palpable masses. There was no other evidence of systemic diseases.

Complete blood count, erythrocyte sedimentation rate and other blood chemistries including calcium, phosphate and magnesium levels were normal. Serum creatine kinase was normal. Computerized tomography of the chest and abdomen showed no mediastinal mass or other abnormalities. MRI BRAIN- No significant abnormality detected. Thyroid function tests were normal. Serum VGKC (voltage gated potassium channel) antibodies positive and ACHR (acetyl choline receptor antibody) positive in serum. Conventional physiologic studies were tested and revealed abnormal spontaneous activities particularly doublet triplet motor unit potential discharges. Motor unit action potential and continuous muscle fiber activities that fired at frequencies of 100 to 300 Hz were also presented with normal motor sensory nerve conduction study. Peripheral autonomic dysfunction was normal in sudomotor function by using Sympathetic Skin Response(SSR).

Test Report

Test Name	Results	Units	Bio. Ref. Interval
VGKC (VOLTAGE GATED POTASSIUM CHANNEL) ANTIBODIES, SERUM (Cell based assay, IFA)			
LG 1 antibody	**Positive**		Negative
CASPR 2 antibody	**Positive**		Negative
ACETYL CHOLINE RECEPTOR BINDING ANTIBODY, SERUM (EIA)	**0.53**	nmol/L	<0.40



EMG studies were tested and revealed abnormal spontaneous activities particularly doublet triplet motor unit potential discharges. Motor unit action potential and continuous muscle fiber activities that fired at frequencies of 100 to 300 Hz.

DISCUSSION

Isaacs syndrome, characterized by hyperexcitability of peripheral motor nervesleading to the clinical manifestations of muscle cramps, increased sweating, and occasionally muscle weakness. Isaacs syndrome is primarily associated with autoantibodies targeting voltage-gated potassium channels (VGKCs) such as CASPR2 and LGI1[1,4,6].The presence of these autoantibodies in about 45-50% of affected individuals underscores the autoimmune nature of the disorder, with potential associations with paraneoplastic conditions, notably thymoma in some cases[7,8].

Among patients diagnosed with neuromyotonia characterized by doublet, triplet, or multiplet EMG discharges, 20% were found to have thymoma, and 10% had lung cancer.Panagariya A et al showed Electromyographic evidence of spontaneous activity in the form of "neuromyotonic discharges" was seen in all patients[9] . Additionally, autoimmune diseases were observed at a higher frequency specifically, myasthenia gravis (MG) with antibodies against the acetylcholine receptor (AchR) emerged as the most commonly associated autoimmune condition. This suggests a potential immunological basis linking peripheral nerve hyperexcitability syndromes with autoimmune mechanisms, particularly involving AchR in MG[10].

Neuromyotonia is characterized by abnormal motor unit firing patterns, This hyperexcitability of peripheral nerves is hypothesized to reduce the amount of immediately releasable neurotransmitter quanta at nerve terminals, thereby decreasing quantal content [11]. Moreover, sustained exposure of acetylcholine receptors (AChR) to their agonist due to

continuous motor unit firing can lead to prolonged endplate currents, resulting in receptor desensitization and depolarization block [12].

The patient exhibited significant symptomatic improvement, particularly in ptosis, following a 5-day course of intravenous methylprednisolone pulse therapy. Additionally, fasciculations markedly improved with the administration of phenytoin at a dosage of 100 mg three times daily.

The discovery of AChR antibodies in this patient is notable, as these antibodies are primarily associated with MG, a neuromuscular autoimmune disorder characterized by muscle weakness and fatigability. The coexistence of NMT and AChR antibodies challenges the conventional classification of these conditions as distinct entities. Instead, it suggests a spectrum or overlapping pathophysiological mechanisms involving neuromuscular hyperexcitability and autoimmune dysregulation.

CONCLUSION

The co-occurrence of neuromyotonia and acetylcholine receptor antibodies in our patient suggests a potential overlap in pathophysiological mechanisms, highlighting the need for further studies are warranted to elucidate the prevalence and clinical implications of AChR antibodies in patients with NMT, as well as the optimal management strategies for such cases.

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