

Isaacs' Syndrome (Acquired Neuromyotonia): A Case Report

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ABSTRACT

We report a case of a 24-year-old male, laborer by profession, who consulted neurology outpatient with chronic symptoms of gross muscle contractions, generalized weakness, and limitation in his routine activities since the age of eight. The examination was remarkable for pseudo hypertrophy in the calves muscles, pes cavus, and gross spontaneous muscle fasciculation with symmetrical involvement of the distal and proximal muscle groups in

lower and upper extremities. His creatinine phosphate kinase (CPK) levels in blood were high. Nerve conduction study (NCS) and electromyography (EMG) confirmed diagnosis of Issacs' disease showing neuromyotonic discharges associated with denervation and polyphasic units with fibrillation, positive sharp waves, and continuous repetitive discharges. He was started on carbamazepine, to which he responded well, and his symptoms improved.

Keywords: Neuromyotonia; Issacs' Syndrome; Pakistan

INTRODUCTION

Neuromyotonia is a combination of spontaneous and continuous muscular contractions along with increased excitation of peripheral nerves [1]. Evidence regarding association of this disease with various causes, including hereditary and acquired ones, have been discussed in the literature. Undulating myokymia, Isaacs' syndrome, and cramp-fasciculation syndrome are the various names suggested for this spectrum of manifestations [2].

CASE REPORT

We report a case of a 24-year-old married man, laborer by profession, from Peshawar, Pakistan. He presented to the neurology clinic with symptoms since eight years of age. He started noticing muscle contractions in his right calf muscle, which over a course of three months, also involved his left calf muscle. In one year, symptoms progressed and subsequently ascended involving both his thighs. Over the duration of the following three years, his symptoms progressed further, involving proximal and distal muscle groups of both upper limbs. He

experienced difficulty in walking long distances and weakness during prolonged standing. Similarly, he experienced difficulty holding heavy objects and weakness while lifting his arms above the shoulder level. He complained of mild paresthesia involving both legs, most prominently in the feet. Due to the nature of his symptoms, he was unable to continue his occupation. No constitutional manifestations, bulbar and sphincter disturbances, or cognitive decline were reported. His past medical and surgical histories were not significant. Family history was unremarkable for similar illness in the family. He took multi-vitamins and supplements few years prior to presentation prescribed by various general practitioners.

On examination, he was a young pleasant looking male of average built and height. He had normal vital signs. Higher mental functions and cognition were essentially normal. Cranial nerves assessment did not reveal any palsy. Spontaneous gross fasciculation were visible in muscle groups symmetrically involving his upper and lower limbs especially calves, anterior and posterior aspects of his thighs, hands, and forearms. Muscle contractions were described as continuous, rhythmic, and spontaneous, both on

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rest and during movement. An increased muscle bulk was noted in his legs involving calves. Pes cavus was present in his feet. Muscle tone was mildly decreased in lower limbs and normal in upper limbs. Power in upper limbs was 4+ in both proximal and distal muscle groups. He was not able to stand up from a squatting posture. Similarly, power in his legs was also 4+ in proximal and distal muscle groups. Deep tendon reflexes were reduced to 1+ in upper limbs and absent in lower limbs with flexor plantar response in both limbs. Gait was in short steps and tandem walking was difficult due to the leg weakness. Speech and articulation were both normal. Sensory and cerebellar examinations were unremarkable. Video link below shows the neuromyotonia evident in limbs of our patient. <https://www.youtube.com/watch?v=Puhj1ifTRUg&feature=youtu.be>

Laboratory investigation showed raised levels of serum CPK (Table 1). The EMG disclosed a permanent spontaneous activity normal in shape, amplitude and duration and more evident in the quadriceps. In addition, multiplets discharges and low motor units were also observed; in interferential pattern appeared at maximum contraction but the multiplets and low motor units potentials kept on showing even though voluntary muscular activity ceased. Autoimmune workup was positive for voltage-gated potassium channel antibodies (VGKC). Carbamazepine was started at a dose of 200mg BD and increased gradually every week to a target dose of 600mg BD. Follow up after three months showed mild improvement in his symptoms.

DISCUSSION

Neuromyotonia is a syndrome of spontaneously occurring muscle movements of peripheral nerve origin. It is an important cause of visible myokymia and most cases are acquired.

Table 1: Blood Investigation results

Tests	Patient's values	Normal Laboratory values
Serum CPK level*	1006 U/L	30-200 U/L
Serum TSH**	0.81 uIU/ml	0.35-4.94 uIU/ml
Serum Vitamin B12	25 pmol/L	25-165 pmol/L
ESR***	4 mm/h	4-14 mm in 1 hour

*CPK= Creatinine phosphokinase,

**TSH= Thyroid stimulating hormone,

***ESR= Erythrocyte sedimentation rate

Our patient showed polyphasic units with fibrillation, positive sharp waves, and continuous repetitive discharges, which are the hallmarks of Isaacs' disease [3]. Antibodies against voltage-gated potassium channel are observed in certain patients [4]. These antibodies are directed against Leucine-rich Glioma Inactivated 1 (LGI1), Contact in Associated Protein-like 2 (Caspr2), and some other unknown proteins that make a complex with voltage-gated potassium channels [5]. Symptomatic relief can be achieved with phenytoin, carbamazepine, or gabapentin treatment [6]. However, some patients may need treatment with intravenous immunoglobulins (IVIG), plasmapheresis, immuno-modulation or steroids [7].

CONCLUSION

Issacs' syndrome poses both a diagnostic and a therapeutic challenge. Carbamazepine can alleviate the symptoms to an extent and is not curative. Future studies can explore the potential for different immunotherapies in this rare disorder. Large-scale trials are not possible owing to a low prevalence of this rare condition.

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