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A 72 YEAR OLD MAN WITH ISAACS' SYNDROME: A RARE ENTITY WITH DIFFERENT O

72 YAŞINDAKİ ISAAC SENDROM'LU ADAM: FARKLI SONUÇLARI OLAN NADİR BİR OLAY

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Abstract

Neuromyotonia is a neuromuscular hyperexcitability disorder characterized by muscle stiffness caused by continuous muscle fiber activity. It is an immune mediated disorder with elevated antibody level against presynaptic, voltage gated potassium channels, either as isolation or as a paraneoplastic process. Symptoms usually include muscle twitching during rest (myokymia), cramps, pseudomyotonia (delayed relaxation), increased sweating, and sometimes motor weakness. In this case report, we present a seventy two year old man who presented with pain in both thighs for one month. It gradually became worse to involve feet and chest. His brain CT scan showed features of brain atrophy. EMG showed fasciculation along neuromyotonic discharges with characteristic wave in frequency and amplitude typical of Isaacs syndrome. Potassium channel antibodies were very high. Diagnosis of Isaacs syndrome was made. He was followed up for two months with treatment by three day course of methyl prednisolone followed by oral steroid and methotrexate with much improvement. This is the first case of Isaacs syndrome in Kurdistan.

Keywords: Issacs, Syndrome, Myokymia, Neuromyotonia, Neurology, Motor, Disorders, Hyperexcitability

Özet

Nöromiyotoni, sürekli kas lifi hareketinden kaynaklı kas gerginliğiyle kendini belli eden nöromüsküler bir hipereksitilabite bozukluğudur. Bu rahatsızlık, voltaja duyarlı, presinaptik potasyum kanallarına karşı gerek izolasyon gerekse paraneoplastik bir süreç görevi üstlenen yüksek antikor seviyesine sahip immün aracılı bir bozukluktur. Belirtileri arasında kasların rahatlama hareketi esnasında kas çekilmesi (miyokimi), kramplar, psödomiyotoni (kas gevşemesinde gecikme), aşırı terleme ve bazen de kas güçsüzlüğü sayılabilir. Bu olgu sunumunda, bir ay boyunca her iki uyluğunda ağrı tespit edilen yetmiş iki yaşında bir erkek hastayı incelemekteyiz. Buna göre hastalık, ayaklara ve göğüs bölgesini de içine alacak şekilde git gide kötüleşmiş durumdaydı. Çekilen beyin tomografisinde, beyin atrofi olduğu ortaya çıkmıştı. EMG sonuçları, tipik Isaacs Sendromu belirtisi olan karakteristik dalga sıklığı ve genişliği tespitiyle bağlantılı olarak nöromiyotonik boşalım boyuncası fasikülasyon (kas seğirmesi) bulgusuna işaret etmekteydi. Ayrıca, potasyum kanalı antikor miktarı oldukça yüksek seviyede idi. Sonuç olarak hastaya Isaacs Sendromu teşhisi kondu. Hasta iki ay boyunca üç günlük süreyle önce metil prednizolon, sonrasında da oral steroid ve metotreksat tedavisi uygulanarak takip altına alındı ve bu süre zarfında hastanın durumunda önemli ölçüde iyileşme gözlemlendi. Bu klinik olay, Kürdistan'da kaydedilen ilk Isaacs Sendromu vakasıdır.

Anahtar Kelimeler: Issacs Sendromu, Miyokimi, Nöromiyotoni, Nöroloji, Kas Hareketi Bozuklukları, Hipereksitilabite.

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1. Introduction

Isaacs syndrome is a neuromuscular disorder characterized by muscle stiffness caused by continuous muscle fiber activity (Newsom-Davis & Mills, 1993a). Voltage-gated potassium channels (VGKCs) are the targets (Doi et al., 2011). Hyper excitability of the peripheral nerve can be induced by antibodies suppressing voltage-gated outward K(+) currents (Arimura & Watanabe, 2010). The first case of Isaacs' syndrome (also known as acquired neuromyotonia) was diagnosed in 1961 when two men presented with persistent, generalized muscle stiffness, in addition to electromyography which showed spontaneous, rapid discharges of motor-unit potentials (Gonzalez et al., 2008).

2. Case Report

A 72-year old man presented with pain in both thighs for 1 month. It started gradually within few days. It later became severe disturbing sleep, relieved only modestly by pain killers. After 3 weeks, the pain involved both feet and chest. Furthermore, he developed fever and rigor, cough, and sputum with radiological features consistent with chest infection. He is Ex-smoker; quit before 5 years. He was a sheep seller. No family history of similar condition. Moreover, he is a known case of Hypertension and Atrial fibrillation for 3 years for which he is on candesartan and amiodarone, respectively.

Vitals were within normal. Consciousness, mental state, tone, power, reflexes, sensory, cerebellar signs and cranial nerve exam. were all normal. He had muscle fasciculation (myokimia) in both thighs (see video 1a) with severe tenderness. A full blood count revealed an erythrocyte sedimentation rate of 24 and Hematocrit 47% and negative CRP. Creatine kinase was normal. EEG was normal. Brain CT and MRI scan showed exaggerated periventricular white matter hypodensity, with normal CT scan of chest, abdomen and neck. LP was normal. Muscle biopsy was normal. Liver, renal, and thyroid function tests were also within reference limits. Potassium gated channel antibodies were very high. Nerve conduction studies were normal. EMG showed fasciculation along with neuromyotonic discharges with characteristic wave in frequency and amplitude typical of Isaacs' syndrome (look at video 2). Serum calcium, vitamin D, iron and ferritine, and phosphate levels were normal. ECG showed only left axis deviation. Moreover, antinuclear antibodies (ANA), anti double strand antibody, anti cytoplasmic antibodies (ANCA), CEA and CA 19-9, anti-SSA (Ro) Ab and anti-SSB (La) ab were all negative. Additionally, Hepatitis screen, HIV, VDRL, anti brucella and toxoplasma antibodies were negative. Protein electrophoresis showed a slight increase in gamma globulin. Bone marrow aspiration showed hypercellular state. OGD and colonoscopy were normal. The patient received methylprednisolone vial 500mg for 3 days, followed by oral steroid (prednisolone) 60mg daily for a month, then tapered weekly and meanwhile methotrexate started 7.5 mg once a week with folic acid, vitamin D and carbamazepine. The patient became free of symptoms in two months.

3. Discussion

Radioimmunoassay of radioisotope labeled alpha-dendrotoxin-VGKCs solubilized from rabbit brain was first method to identify antibodies to voltage-gated potassium channels (VGKC). Only a proportion of patients with acquired neuromyotonia (Isaacs' syndrome) were found to have detectable antibodies (Watanabe, 2013a).

From the electrophysiological results it was seen that antibodies may decrease channel density rather than directly blocking the kinetics of VGKCs. The site of origin of spontaneous discharges, from electrophysiological, pharmacologic and immunologic studies, is located principally in the distal portion of the motor nerve (Watanabe, 2013b).

Demonstration of antibodies against voltage-gated potassium channels suggest the autoimmune basis of this disorder, from any cause, paraneoplastic or acquired (Newsom-Davis & Mills 1993; Newsom-Davis et al., 2003). The most commonly associated neoplasms are thymoma, small cell lung cancer, and Hodgkins lymphoma (Walsh, 1976).

Muscle cramp, slow relaxation following muscle contraction, and excessive sweating (hyperhidrosis) are the main symptoms of Isaacs' syndrome (Arimura & Watanabe, 2010; Watanabe, 2013; Kim et al., 2013). Patients almost always, develop persistent muscle contraction, which is often worse following exercise myokimia, generalized, and fasciculations are also common (Béquet et al., 1997; Maddison, 2006). Voltage-gated potassium-channel antibodies are detected in around 40% of patients with Isaacs' syndrome (Maddison, 2006).

Electromyography shows features of spontaneous, continuous, irregularly occurring doublet, or multiplet single motor unit (or partial motor unit) discharges, firing at a high intraburst frequency as well as myokymic and neuromyotonic discharges. Fasciculations and fibrillation potentials are also frequent (Newsom-Davis & Mills, 1993b).

Myokymia, pseudomyotonia and contracture of hands and feet are the main features of Isaacs' syndrome... Clinical features and classic electromyographic findings establish the diagnosis of Isaacs' syndrome. Moreover, a proportion of cases have positive serum antibodies against Voltage-Gated Potassium Channels (VGKCs) (Sukajintanakarn et al., 2006).

The main lines of treatment are plasma exchange and intravenous immune globulin; other potentially effective treatments include phenytoin, carbamazepine, acetazolamide and diazepam (Newsom-Davis & Mills, 1993a; Issa et al., 2011). Remission usually occurs after 13 months (8-18 months) at which treatment can be stopped (Newsom-Davis & Mills, 1993b). Treatment by immunoadsorption plasmapheresis also reported (Nakatsuji et al., 2000).

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