TOXIN INDUCED CONTINUOUS MUSCLE FIBER ACTIVITY SYNDROME

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(Date received: 25.09.2008)

Abstract

Continuous Muscle Fiber Activity Syndrome describes rare heterogeneous group of conditions that exhibit sustained, diffuse motor unit activity due to hyperactivity of peripheral nerve motor axons. The disorder, which has both inherited and acquired forms, is characterized by muscular stiffness, cramps, fasciculation and weakness particularly in the limbs. We report a case 42 year old male who presented with easy fatigability and insidious onset gradually progressive difficulty in walking due to muscle stiffness in both lower limbs along with continuous twitching of muscles of all 4 limbs and chin. EMG study showed spontaneous, continuous, irregular rapid discharges of motor-unit potentials

Key Words: Continuous muscle fiber activity syndrome, Isaacs' syndrome, Neuromyotonia, Toxin, Voltage-gated potassium channel.

Introduction

Continuous muscle fiber activity and the eponym Isaacs' syndrome describes a heterogeneous group of conditions that exhibit sustained, diffuse motor unit activity due to hyperexcitability of peripheral nerve motor axons. First described in 1961 by Isaacs in two men (1-3). However presently "neuromyotonia" is the preferred term (4). Most cases are idiopathic. Voltage-gated potassium channels may be the target of an autoantibody attack in idiopathic generalized neuromyotonia (Isaacs' syndrome). The entity manifests with varying combinations of diffuse pain, undulating twitching and muscle stiffness. Central features with behavioral changes like anxiety, restlessness, hallucinations and sleep disturbances have been reported (5). Electromyography documents continuous spontaneous activity in the form of discharges in doublets, triplets or multiplets with high intraburst frequency now known as "neuromyotonic discharges" (6). Few patients with acquired neuromyotonia will have detectable voltage-gated potassium-channel antibodies .In various reports it was found to be between 5-33% (5,7).

Case Report

A fourty year old male, worker in a smelting factory, presented with history of abnormal undulating muscle movements with crampy pain in all 4 limbs for last 1 month. Along with this he also developed gradually progressive difficulty in walking due to muscle stiffness in both lower limbs without weakness or wasting. After two weeks he started feeling palpitation and restlessness most of the time and excessive sweating all over body. He had difficulty in falling and maintaining sleep. His duration of sleep decreased markedly for last ten days. He started feeling burning dysaesthesiae & hyperesthesia in both hands and feet without any complain of numbness.

On examination, there was resting tachycardia (Pulse rate=112/min) & supine blood pressure of 128/80 mm of Hg without any postural fall. There was profuse sweating all over the body, including hands and feet. The Respiratory, cardiovascular, & abdominal examination revealed no abnormality.

On Neurological examination, his higher mental and cranial nerves were within normal limit. Motor examination revealed continuous generalized fasciculation in all 4 limbs including chin and there was muscles stiffness present in all 4 limbs but more marked in lower limbs.

The Ankle reflex was lost bilaterally. The remaining of the neurological examination was normal.

Nerve conduction studies showed segmental demyelination of motor nerve in lower limbs. The function of the motor end plates was normal Needle EMG showed continuous spontaneous motor unit activity with neuromyotonic discharges in deltoids, biceps brachii, quadriceps and gastrocnemii (Fig. 1). Routine blood biochemical analysis including thyroid function, liver function, renal function, ELISA for HIV and protein and immune

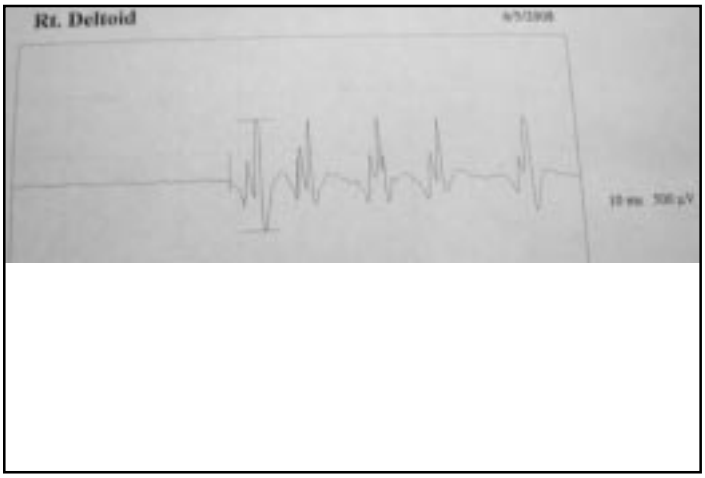

Fig.1 : Spontaneous activity in right deltoid

electrophoresis were in the normal range. CSF study was normal. Ultrasonography of abdominal and pelvic and CT thorax revealed no abnormality. In toxicological study (From IITR Lucknow) level of Lead and Silver in blood were increased {Pb=10.96, Ag=0.75 μg/dl ((N=<10 & 0.3 respectively)}, and Gold level was not detectable.

Patient left job for last one month. He treated with phenytoin, but he developed drug induced rash all over body then he put on oxcarbamazine and he responded to this but not complete

response. In between intravenous methylprednisolone was tried but response was not satisfactory.

Discussion

The diagnosis of Isaacs' syndrome is based on the clinical features and classic electromyographic findings. Repititive high frequency discharge and their site of origin (from any part of peripheral nerve) also has been reported from india (8-9). Abnormal muscle activities was continuous, gross, often rhythmic, relatively slow undulating movements visible from surface of skin and persisting during sleep . Generated force may lead to movements of small joints of hands (7). Movements was generalised in our case but focal form has been described (10-11). some reports described muscle stiffness. Muscle stiffness was present due to continuous active muscle contraction but there was no difficulty in muscle relaxation. Due to muscle stiffness he had difficulty in walking. Bilateral ankle reflex was absent in our patient and nerve conduction study revealed segmental demyelination in lower limb. Accordingly Patient had marked sensory symptoms in form of cramps, paresthesia and crawling sensation over skin that were intensified by nervousness and cold (11-12). In 1890 French physician Augustine Marie Morvan described a syndrome characterized by peripheral nerve hyperexcitability, Dysautonomia, insomnia and fluctuating delirium. This syndrome might be regarded as a form of neuromyotonia having prominent central features (5,11,13). Our patient also had some central features in form of excessive sweating, insomnia, anxiety and irritability. It has been hypothesized that the basic mechanism of the peripheral and central manifestations remains the same that is VGKC abnormality, occurring at different levels of neuraxis. The acquired form has been associated with neoplasm, thymoma, myasthenia gravis, lymphomas, and a variety of autoimmune nervous system disorders (14). Generalized form also can be seen in patients with systemic illnesses (eg, thyrotoxicosis, uremia) and following binge consumption of alcohol, exposure to toxins, timber rattlesnake bite. Case has been reported due to gold therapy for rheumatoid arthritis (15). Perhaps the only study from Indian subcontinent which has shown temporal association with toxins exposure in form of herbs and heavy metals in "Ayurvedic drug", but failed to demonstrate the blood level (11). As far as my knowledge, till date this is the first case, where the level of toxins (both lead & silver), is being documented from Indian subcontinent. The Exact mechanism by which these toxins leading to hyperactivity of the peripheral nerves in continuous muscle fiber activity is not clear and is yet to be determined. This is a rare but preventable and treatable condition, so keep high index of suspicion to make early diagnosis so that appropriate preventive and therapeutic measures with immune modulators and membrane stabilizers can be applied.

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