Issacs' Syndrome Successfully Treated With Phenytoin At Low Doses

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Citation

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Abstract

We report two patients with Isaacs' syndrome (acquired neuromyotonia) who responded remarkably well clinical and electromyografically to low doses of phenytoin orally. Patients presented with associated common diseases in the former Transkei (South Africa) such as neurocysticercosis, shistosomiasis, tuberculosis and HIV seropositive and we have hypothesized about neuro-immunologic mechanism, and peripheral nerve membrane disorders in these patients and the phenytoin response.

INTRODUCTION

Isaacs' syndrome (IS) is characterized by spontaneously occurring muscle activity of the peripheral nerve origin, which can be triggered by induced muscle contraction or voluntary muscular activity. This uncommon disorder described in 1961 [1] in which hyper excitability of peripheral motor nerves resulting in continuous muscle fiber activity leading to incapacitating muscle twitching, cramps, and weakness. Although IS (also known as acquired neuromyotonia) may sometimes accompany hereditary neuropathies or other diseases. IS has been long recognized by several physicians 1 [2,3] however its rarity and the variability of its clinical manifestation and ways of presentation is probable the most important reason why its frequently misdiagnosed or wrongly treated [4]

Autoimmune etiology had been proposed [5,6] Clinical evidence suggesting a possible autoimmune etiology included the presence of oligoclonal bands in the spinal fluid of some patients and clinical improvement following plasma exchange 6 [7] In the first group of 40 patients reported in the past thirty years, thymomas, myasthenia gravis, raised anti-acetylcholine receptor antibody titers among other immunological disorders were indentified 6 and antibodies against potassium channel of peripheral nerves were also found [8,9,10]

Phenytoin and cabamazepine have been reported to be efficacious 1 [11] Modulation of neuronal sodium channels decreases cellular excitability and diminishes the axonal propagation of nerve impulses, this is a clinically useful mechanism and has been demonstrated to be integral to the activity of major antiepileptic drugs such as carbamazepine and phenytoin [12]

Here we report two patients diagnosed as IS and treated with dosage of 100 mg or less of phenytoin orally and observed a remarkable improvement clinical and electromyografically.

CASE REPORT 1

XhM a 49 year old lady came to special medical clinic complaining, painful inability to open her hands and to extends her toes which were in flexed position 24 hours a day for the past six months after a complete recovery of acute renal failure due to herbal medicine intoxication and defaulted antiepileptic (figure 1). Past medical history a family history of pulmonary tuberculosis, hematuria is mentioned. Apart from cramps and muscle stiffness on the distal region of the limbs she denied any other clinical manifestation currently. On examination mild weakness on the distal regions in the four limbs, bilateral and symmetrical pseudomyotonia in the hands and feet, were observed. EMG before treatment showed doublet, triplet and multiplet single unit discharges with high an irregular intraburst frequency apart from fibrillation potentials. No laboratory tests abnormalities were seen. After a regular oral course of 50 mg of phenyotin twice daily all neuromuscular manifestation disappeared (figure 2) and EMG only showed a few isolated fibrillation potentials

Figure 1

Figure 1: Painful inability to open her hands and to extends her toes which were in flexed position

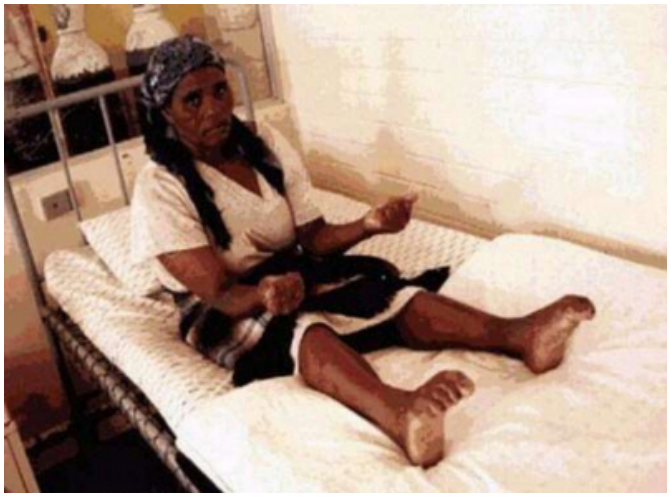
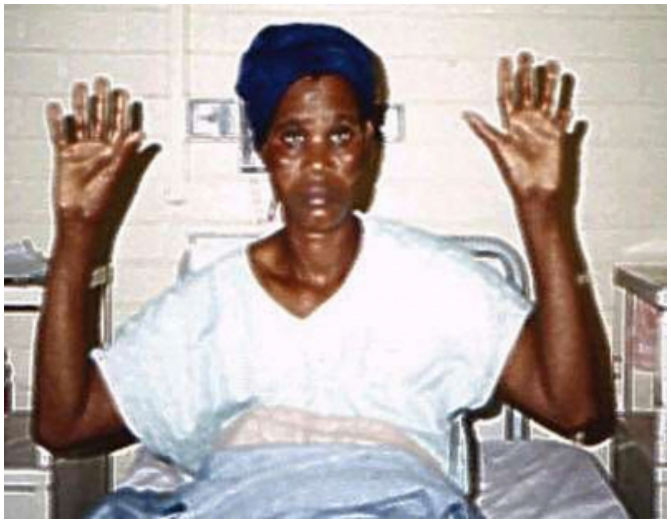


Figure 2

Figure 2: All neuromuscular manifestation disappeared after treatment



CASE REPORT 2

YK a 43 year old, taxi driver presented to outpatient clinic complained of inability to driving because of weakness, numbness, and tingling sensation of the limbs with permanent flexion of his finger and toes (even during the sleeping time), for the past eleven months that disorder of muscle relaxation after any voluntary contraction of the skeletal muscle in hands and feet was usually worse after a new attend of voluntary muscle contraction. General physical examination revealed unremarkably findings and neurological examination showed myokymia and pseudomyotonia on the four limbs, (absent of muscle relaxation was noted after strong hand grips without percussion myotonia) Routine laboratory tests and serum electrolytes, thyroid function test, liver function test, creatine kinase, were normal. CT Scan of the brain showed many calcified lesions of neurocysticercosis and HIV test was positive. EMG showed myokymic discharges. A single dose of 100mg of phenytoin at bed times is prescribed and the patient became practically symptomatic

COMMENTS

There is not doubt about benefits providing by phenytoin on IS from the pharmacological point of view is well known that phenytoin peak plasma level occur 3 to 12 hours after a single oral dose, and its half life after oral administration ranges from seven to 42 hours with a mean of 22 hours but is good to remain that phenytoin is metabolized by hepatic enzymes, and phenytoin levels are influenced by concomitant medications and by factors such as pregnancy, age, and liver and renal diseases.

We have hypothesized that phenytoin from low to high doses can be useful for differentiated IS from other conditions mimicking pseudomyotonia such as myotonic syndrome, stiff limb syndrome, stiff man syndrome, pyramidal syndromes, extra pyramidal syndromes, focal lesions of the spinal cord, and progressive encephalomyelitis with rigidity on simple clinical grounds, and whether such distinction has implications for etiology, treatment, and prognosis.

Patients coming from rural areas in the former Transkei are usually presenting combination of different forms of tuberculosis, neurocysticercosis, schistosomiasis and HIV/AIDS therefore their neuro-immunological status can not be compare with others from another regions [13], we know that patients with those combinations presented with immunological dysfunction on the CNS by accumulations of master cells containing immunoreactive tryptase and multifunctional effectors of the neuroimmune system; its can synthetisize and secrete endorphins, serotonine, histamine, heparin, kinins, leucotrienes, prostaglandins, cytokines, and phospholypases; theses factor can modify all functional mechanisms of the neuronal cell and peripheral nerves membranes then low dosages of phenytoin can work more efectivately therefore at low or high doses it is the medication of choice for Isaacs' syndrome.

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