Isaacs syndrome

Introduction

Isaacs syndrome is a rare neuromuscular disorder first described by Isaacs in 1961. Also commonly referred to as Isaacs–Mertens syndrome, continuous muscle fibre activity syndrome or quantal squander syndrome, this disorder is associated with point mutations of the KCNA1 gene and is predominantly characterized by chronic painful muscle stiffness, fasciculations and myokymia, often with associated muscle atrophy, weakness, excessive perspiration and increased basal metabolic rate (Ramseyer, 1975; Gutmann and Gutmann, 2004). This article highlights a case and discusses the specifics of pathogenesis as well as management.

Table 1. Differential diagnosis of Isaacs syndrome

Differential diagnosis	Key clinical features
Amyotrophic lateral sclerosis	Insidious weakness, atrophy or fasciculations of one or more limbs
Schwartz–Jampel syndrome	Muscle stiffness and hypertrophy most severe in the thighs. Associated with a high rate of mental retardation, skeletal and joint deformities
Stiff person syndrome	Insidious onset affecting axial muscles. Initially presents with an exaggerated upward posture and back discomfort. Eventual involvement of proximal limb muscles
Striatonigral degeneration	Primarily parkinsonian-like features of bradykinesia, rigidity and postural instability

Discussion

The age of onset of Isaacs syndrome ranges from the newborn period to the sixth decade, with the peak incidence in the second and third decades (Ramseyer, 1975). Clinical evidence suggests a primarily autoimmune pathogenesis. A study of three patients found oligoclonal bands in the spinal fluid of all three (Davis and Mills, 1993). Other supporting evidence from a study of 40 patients includes the presence of an associated thymoma in five cases, myasthenia gravis in two cases and raised anti-acetylcholine receptor antibody titres in two cases (Davis and Mills, 1993).

Further insight into the pathogenesis of the condition has brought to light evidence of potassium channel blockade via a humoral factor being responsible for nervous hyperexcitability. Using patch-clamp techniques, Sonoda and colleagues (1996) investigated the effects on K+ current of serum taken from two patients with Isaacs syndrome using the clonal cell line PC-12. K+ current was reduced by 25–80% when cells were cultured for 3–6 days with 2% serum as compared to control serum values.

The differential diagnoses of Isaacs syndrome are numerous and include amyotrophic lateral sclerosis, Schwartz–Jampel syndrome, stiff person syndrome and striatonigral degeneration to name but a few (*Table 1*).

The management of Isaacs syndrome is primarily aimed at symptom relief. Anticonvulsants such as phenytoin, carbamazepine and sodium valproate are all highly beneficial (Vasilescu et al, 1987). The autoimmune nature of the condition has meant individuals suffering from the disease may benefit from immunomodulating therapies in the form of plasmapheresis, in which antibodies to potassium channels are filtered out from the individual's serum. Nakatsuji et al (2000) demonstrated a marked improvement in symptoms following immunoadsorption plasmapheresis in a 70-year-old woman diagnosed with the disorder. However, the effect was only temporary unless combined with immunosuppressive therapies.

There is currently no cure for Isaacs syndrome. Research is ongoing and further insight into the genetic basic, symptomatology and progression of the condition is needed before clinicians are ultimately able to offer a cure. BJHM

Case Report

A 57-year-old retired factory worker was admitted to the accident and emergency department complaining of a 3-month history of painful stiffness of his hands and toes. In addition he complained of generalized weakness, numbness and a tingling sensation of both his upper and lower limbs as well as weight loss. He was keen to mention that his stiffness had been long lasting and was even present during sleep. There was no significant past medical history. On general examination a mild weakness affecting the distal region of all four limbs were noted in addition to myokymia. He was also remarkably unsteady on his feet. There was no evidence of excessive perspiration or muscle wasting. A routine full blood count, urea and electrolytes, liver function and creatinine kinase were unremarkable.

The patient was referred for electromyography testing which demonstrated evidence of neuromyotonia and myokymia. Antibody testing to voltage-gated potassium channels was not performed. The patient was prescribed phenytoin 50 mg twice daily. After 1 week his symptoms had improved substantially and at 1-month follow up the patient was practically asymptomatic.

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