Serial Monitoring of Basal Metabolic Rate for Therapeutic Evaluation in an Isaacs’ Syndrome Patient with Chronic Fluctuating Symptoms

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Abstract

A 52-year-old man presented with hyperhydrosis, painful pseudomyotonia and gait disturbance. The condition was diagnosed as Isaacs’ syndrome on the basis of characteristic findings noted on an electromyogram. Carbamazepine treatment was only partially and transiently effective. Intravenous immunoglobulin therapy was effective. The basal metabolic rate (BMR) was serially monitored using an automatic integrated system for breath analysis. Serial monitoring of the BMR facilitates therapeutic evaluation in an Isaacs’ syndrome patient with chronic fluctuating symptoms.

Key words: Isaacs’ syndrome, intravenous immunoglobulin, basal metabolic rate, automatic integrated system for breath analysis, carbamazepine

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Introduction

Isaacs’ syndrome (IS) is characterized by spontaneous and continuous activity of muscle fibers (1). Most cases of IS occur sporadically, and only 38% of all patients with IS test positive for anti-voltage-gated potassium channel (VGKC) antibodies (2).

Isaacs reported that the basal metabolic rate (BMR) is elevated in patients with acute-phase IS, but is normalized with treatment (1). Studies involving the serial monitoring of the BMR of these patients have not been performed because of the complicated procedures involved. We present the case of a patient with sporadic IS without anti-VGKC antibodies over a chronic fluctuating course. We serially monitored the patient’s BMR for therapeutic evaluation using an automatic integrated system for breath analysis.

Case Report

A 52-year-old man presented with gait disturbance, painful muscle cramps and hyperhydrosis and was admitted to our hospital in February 2008. He had no specific familial history of disease. He began to suffer from hyperhydrosis when he was in his 30s and from gait disturbance in May 2007. He occasionally experienced dysphagia but recovered from it naturally. His clinical course had fluctuated over several months.

Physical examination revealed that the patient was well nourished. He suffered from mild mental retardation. His blood pressure, heart rate and body temperature were all found to be normal. Neurological examination revealed myokimia, hyperhydrosis, and hypertrophy of the leg muscles. Furthermore, the patient experienced muscle cramps at various times during the day and night. Grip myotonia was not detected; however, the patient’s fingers spontaneously flexed after they were extended. His reflexes were slightly exaggerated but the Babinski sign was absent. A photograph of the patient showed flexed upper-limbs, forward-bend posture, standing with legs bending outwards, and hypertrophy of the calf muscles (Fig. 1). He walked with such posture. Painful cramps often occurred during walking. His cranial nerves and sensory perception were normal. He had experienced no epilepsy, hallucination, or insomnia.
Figure 1. A photograph of the patient.

Laboratory tests revealed that all the parameters, including the serum creatine kinase (CK) level and the thyroid hormone levels, were within the normal limits. Antibodies against VGKC and glutamic acid decarboxylase antibody were not detected in the serum.

An electromyogram (EMG) of the right biceps brachii, quadriceps and tibialis anterior muscles did not show myotonic discharge. Randomized doublet or triplet muscle waves were observed in the myokimic muscles of the left calf. A surface EMG study showed spontaneous and continuous motor-unit activity in the right biceps and the rectal abdominal muscles and the presence of M-wave afterdischarges in the upper extremities. Nerve conduction study was normal in the upper extremities, but it could not be assessed in the tibial nerves because of muscle cramps. Brain MRI and electroencephalography (EEG) showed no obvious abnormal findings. CT of the muscles showed hypertrophy of the calf muscles.

The BMR was measured at 9 a.m. while the patient was at rest and before breakfast, using an automatic integrated system for breath analysis (FUDAC-77, Fukuda Denshi, Tokyo, Japan). The BMR was 27.9% higher than the upper limit of the normal range for men in their 50s.

IS was diagnosed on the basis of the characteristic findings noted on the EMG, and the patient was administered oral carbamazepine (CBZ: 400 mg/d). The frequency of muscle cramps was reduced with the treatment. Furthermore, the BMR was reduced to 9.0% higher than the upper limit of the normal range. However, the gait disturbance did not improve. Shortly thereafter, the patient’s symptoms deteriorated once again, and despite CBZ treatment, he frequently experienced muscle cramps all over his body, both during the day and at night. As was expected with the exacerbation of the symptoms, the BMR was increased to 28.2% higher than the upper limit of the normal range.

We initiated intravenous immunoglobulin (IVIG) therapy (0.4 g/kg/d for 5 d). The patient’s symptoms improved with IVIG, and the BMR was normalized and maintained for at least 6 months (Fig. 2).

Discussion

We present the case of a patient with chronic fluctuating symptoms of IS, not accompanied by any hormonal disease. The BMR was serially assessed, and it was found that the patient’s clinical symptoms fluctuated in tandem with the BMR (Fig. 2).

The BMR is associated with many factors: age, sex, race, and thyroid hormone level (3). The major factors causing an increase in the BMR are hormonal disease and physiological factors: pregnancy, diet, a high environmental temperature, exercise, or a state of excitement (3). When we measure the BMR, the observed value reflects the result of total oxygen consumption of the whole body. The oxygen consumption of the brain and muscles at rest is estimated to be 23 and 20% of that of the whole body, respectively. The oxygen consumption of muscles at exercise reaches maximally 60 times that at rest (4). In general, the BMR test is not used as an indicator of chronic muscle activity; however, secondary chronic muscle activity due to an underlying disease may cause fluctuation in the BMR.

It is reported that IS is sometimes accompanied with dis-
turbance of the central nervous system (CNS), such as Mor-
van syndrome (5) or limbic encephalitis (6). However, the
findings of brain MRI and EEG in the present case sug-
gested no accompaniment of such a CNS disease. The in-
creasing value of BMR in our case mainly reflected the oxy-
gen consumption of muscles, not that of the brain.

In 1961, Isaacs first reported the cases of patients with
acute-phase IS, whose BMR was elevated because of con-
tinuous or spontaneous muscle fiber activity, but was nor-
malized with treatment (1). However, at that time, serial
monitoring of the BMR was not performed because the
methods available were complicated.

A closed-circuit respiratory device has been used to calcu-
late the BMR (3). In the method that has traditionally been
used to determine the BMR, the patient is required to
breathe through the mouth into the analyzer for 6 minutes
while at rest and before breakfast, and a skilled medical
technologist analyzes the resting end-respiratory volumes for
6 minutes and manually draws a straight line to calculate
the BMR.

Recently, an automatic integrated system for breath analy-
sis (FUDAC-77) has been developed; this device automati-
cally calculates the correct BMR by application of the
method of least squares (a straight line experiment) (7), and
remarkably facilitates its monitoring.

Anti-convulsion drug treatment (1), IVIG therapy (8), and
plasma exchange (9) are reported to be effective modalities
for IS patients; however, no study thus far has performed an
objective therapeutic evaluation of the parameters that reflect
the symptoms, such as the BMR. The condition of IS pa-
ients is reflected in real time in the BMR.

In the present case, CBZ treatment reduced spontaneous
muscle activities, i.e., painful cramps. The BMR was re-
duced in tandem. However, the gait disturbance and posture
did not improve because of completely uncontrolled con-
tinuous muscle fiber activities. Spontaneous and continuous
muscle fiber activities were finally controlled by IVIG treat-
ment.

Improvement shown by patients treated with immuno-
modulatory treatments is observed neurophysiologically, but
quantitative assessment is also necessary. Serial BMR moni-
toring is a well-tolerated, quantitative assessment for IS pa-
patients with such a fluctuating course.

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