CASE REPORT

Effect of Omega Qgel\textsubscript{T} (Coenzyme Q10 and Fish Oil) in a Patient with Tuberous Sclerosis

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Abstract

A 5-year-old male child presented with convulsive seizures, mental retardation and cutaneous angiofibroma of about 4 years’ duration. A physical examination revealed that he was unable to sit up, stand and walk. He had fine wart-like lesions on the cheek and forehead. A systemic examination showed no abnormality. A computerized axial tomography scan revealed calcification at the head of the right caudate nucleus without associated edema. Irregular calcification was also seen adjacent to the posterior part of the body of the left lateral ventricle. He showed improvement in mental deficiency and seizures on treatment with coenzyme Q10 (90 mg day\textsuperscript{-1}) and fish oil (Eicosapataenoic acid (EPA) \textsuperscript{1}1.08 g + Docosahexaenoic acid (DHA) 0.72 g day\textsuperscript{-1}) within 12 weeks of follow-up.

Keywords: fatty acids, ubiquinone, sclerosis, brain.

INTRODUCTION

Tuberous sclerosis complex is an autosomal dominant genetic disorder characterized by mental retardation, cutaneous angiofibromas and convulsive seizures. Family history is often unhelpful because half of the cases are due to mutation [1, 2]. It is usual to find patients with tuberous sclerosis presenting with average intelligence and seizures and a few skin lesions. Treatment is only symptomatic. Brain tissue is rich in n-3 fatty acids in the cell membranes and coenzyme Q10 in the mitochondria [3, 4]. It is possible that deficiency of these nutrients during fetal life and the perinatal period may predispose mutations resulting in this genetic disorder. Treatment with these fatty acids can enhance the secretion of acetylcholine in the hippocampus which may benefit memory deficits [4]. Fish oil and coenzyme Q10 can also prevent the excitation of brain tissue responsible for seizures and both agents have been used for the treatment of memory deficits, Huntington’s disease and tumors [5]. Both agents appear to have cytotoxic effects on abnormal cells [5,6]. The deficiency of these agents during fetal life may result in mental deficiency, seizures and tuberous growth during infancy. In the present study both agents were administered in a proven case of tuberous sclerosis for possible benefit, as there is no known treatment for this disease.

CASE HISTORY

The patient was examined at the Medical Hospital and Research Centre, Moradabad. He was a male child aged 5 years who presented with an inability to understand, an excess of
weeping, irritability and no response to commands. He had six to eight convulsive seizures per day and was pushing his head against hard objects without any feeling of getting hurt. He was able to respond to loudly repeated commands by looking up. He was not able to sit up, stand and walk. He was unable to master language, to call “papa” and “mammi” or any other common word to fulfil his requirements. He was not interacting with people around him and making known his needs for water and food. He was neither smiling nor playing. All these manifestations indicate mental retardation. These manifestations started in June 1999 before which his mental status was almost normal for his age. His mental deficiency was slowly progressive.

The history of his present illness revealed that he developed convulsive seizures about 4 years ago in July 1998 at the age of about 9 months. He was irritable and weeping but was able to walk and call “papa” and “mammi” as well as demand water and food. He was also playing and smiling indicating no significant mental deficiency. He was given dilantin sodium for the seizures to which he responded and the frequency of his seizures diminished. After 1 year, in June 1999, he was referred to a neurology centre, the Ram Manohar Lohia Hospital, New Delhi, due to an increase in generalized convulsions and the development of mental retardation. He also had fine wart-like lesions over the cheeks and forehead. He was diagnosed with tuberous sclerosis due to the presence of facial angiofibromas, mental retardation and convulsive seizures.

A physical examination in May 2002 revealed that he had poor growth (height 96 cm, weight 11 kg) and was lean and thin with marked weakness. He was unable to sit up, stand and walk, and was always lying on his bed. He was able to sit with support. He had fine wart-like, pinkish, elevated lesions over the cheeks and forehead which increased in size (1–6 mm). His skin appeared thick (Fig. 1).

His heart rate was 100 bpm, regular, and his blood pressure was 86/60 mm Hg, without any evidence of enlargement in the heart, lymph node, liver or kidney. A systemic examination revealed no abnormality in the cardiorespiratory system. A neurological examination showed plantar’s flexors, diminished knee and ankle jerks without any other abnormality.

His computerized axial tomography scan revealed a medium-sized dense calcification at the head of the right caudate nucleus without associated edema. Irregular calcification was also seen adjacent to the posterior part of the body of the left lateral ventricle. Laboratory data showed normal blood counts, hemoglobin 9 g dl⁻¹, serum creatinine 0.4 mg dl⁻¹, serum bilirubin 0.8 mg dl⁻¹, zinc 120 μg dl⁻¹, copper 110 μg dl⁻¹, vitamin E 0.62 μg dl⁻¹, vitamin C 0.12 μg dl⁻¹, beta-carotene 16 μg dl⁻¹, Thiobarbituric acid reactive substances (TBARS) 1.2 ng dl⁻¹, malondialdehyde 2.5 μg dl⁻¹.

**TREATMENT**

This patient was administered carbamazepine (200 mg day⁻¹), sodium valproate (100 mg day⁻¹) and phenobarbitone (60 mg day⁻¹) for the generalized convulsive seizures. He was also given coenzyme Q10 (90 mg day⁻¹) and fish oil (EPA 1.08g + DHA 0.72 g day⁻¹), vitamin E 78IU day⁻¹ and vitamin C 30mg day⁻¹ (Omega Qgel, Tishcon Corporation, Westbury, NY, USA). After 2 weeks of the above treatment, his convulsions were completely controlled. After 4 weeks, the child started responding to commands and was able to sit up, stand and walk as well as take care of himself by asking for water and food. He also started playing and smiling (Fig. 2). His anticonvulsant drugs were reduced as there were no seizures. His body weight increased from 11 to 12 kg after 4 weeks of treatment. After 12 weeks he showed further improvement in various parameters of mental deficiency and physical growth. Finally after 12 weeks he was lost to follow-up and stopped the treatment. After about 1 month, his clinical manifestations reappeared which characterized features of mental retardation and occurrence of the seizures which made his relatives return.
FIG. 1. The boy before treatment.

for treatment. He was readministered the above treatment again, to which he responded within the next 2 weeks.

COMMENTS

In India tuberous sclerosis is rare; this case is the second one referred in the last 25 years. In view of the presence of convulsive seizures, mental retardation, cutaneous angiofibroma and calcification in the brain, it is clear that this patient had been suffering from tuberous sclerosis for the last 4 years. The interesting points are that the treatment with coenzyme Q10 and fish oil was associated with a marked improvement in the mental deficiency and physical growth of the patient. The cessation of treatment was associated with the reappearance of clinical manifestations of mental deficiency and seizures, which disappeared on restarting the treatment, indicating that the response to treatment was most likely due to n-3 fatty acids and coenzyme Q10. Mental retardation is the most important manifestation of tuberous sclerosis; therefore, many patients with this problem are found in institutions for mentally retarded patients. However, in general hospital clinics, it is not unusual to see patients with average intelligence and only seizures and a few skin lesions.

The brain lesions consist of areas of malformed cortex with extensive astrogliosis and a peculiar mixture of glioblasts and monster nerve cells [1, 2]. Masses of subependymal glial tissue account for the nodules which project into and form “candle guttering” on the walls
of the ventricles that are often seen in pneumograms [1, 2]. Most cases of rhabdomyoma of the heart muscle are also associated with tuberous sclerosis. Tuberous sclerosis is also combined with tuberous malformations of the kidneys, liver, adrenal glands and pancreas.

Recent molecular, biological analysis has revealed that tuberous growths are clonal processes and true neoplastic growths [1, 2]. The TSC1 and TSC2 genes behave as tumor suppressor genes [1] and encode for the protein product tuberin. If a somatic mutation of the second allele occurs, abnormal cell growth and differentiation occur.

It is possible that mental deficiency may be due to cortical damage which may have developed because of malformation and maldevelopment of the cerebral cortex [1, 2]. It seems that treatment with n-3 fatty acids (EPA; DHA) may have increased their availability in the neurons causing repair and stabilization of their cell membranes. There is experimental evidence that DHA administration is associated with increased secretion of acetylcholine in the hippocampus and increased parasympathetic activity, which are responsible for memory function [4]. Coenzyme Q10 is rich in the mitochondria of neurons and enhances ATP production and energy generation in the cells, as well as antioxidant activity [3]. There is evidence that coenzyme Q10 administration may cause a significant reduction in lactate concentrations in the occipital cortex indicating a therapeutic effect of this agent [3]. It is possible that treatment with n-3 fatty acids and coenzyme Q10 improves the structure and function of neurons and inhibits the process of neurode generation and malformation resulting in regression of tuberous growths [3–6]. These beneficial effects may be translated
into improved memory function, better motor function and result in increased physical growth of the patient. Both agents also have antitumor effects due to their cytotoxic effects on abnormal cells of tuberous sclerosis [5, 6].

There was also a significant improvement in convulsive seizures which may be similar to the anti-arrhythmic activity of n-3 fatty acids [4]. It is possible that n-3 fatty acids decrease the excitation of neurons by their incorporation into neuronal cell membrane phospholipids, resulting in improvement in the electrical waves of electroencephalograms and decrease in seizure activity [4].

In brief, this case of tuberous sclerosis shows improvement in mental retardation and convulsive seizures on treatment with coenzyme Q10 and fish oil within 12 weeks of administration. A randomized, double-blind, controlled trial in a large number of patients would be necessary to confirm our observation. The reduction in seizures may be due to anti-epileptic drug treatment, whereas the improvement in behavior and memory, we suggest, may be mainly due to the nutritional supplements.

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REFERENCES
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