

Marked reduction in CSF lactate and pyruvate levels after CoQ therapy in a patient with mitochondrial myopathy, encephalopathy, lactic acidosis and stroke-like episodes (MELAS)

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Many CoQ trials for mitochondrial encephalomyopathy are reported, however, the action of CoQ in the central nervous system is unknown. We administered CoQ to a patient with MELAS, and decreasing CSF lactate and pyruvate levels were revealed. This reduction in CSF lactate and pyruvate may be evidence that CoQ acts directly on the CNS. There have been no other descriptions of evidence of CoQ effective action in the central nervous system, a finding unique to this report.

Mitochondrial myopathy, encephalopathy, lactic acidosis and stroke-like episodes (MELAS) is classified into "mitochondrial encephalomyopathy" (1-3). No effective treatment for this syndrome has been established, however, recent therapeutic trials of coenzyme Q10(CoQ) administration to patients with Kerns-Sayre syndrome have demonstrated clinical and biochemical improvement (4-8). We experienced a MELAS patient who developed marked reduction in CSF lactate and pyruvate levels with clinical improvement.

Case report

A thirty-one-year-old male was admitted to our hospital with untreatable seizures. Prenatal and perinatal histories were normal. He experienced the first seizure at the age of twenty-one, as a college student. He was then given an anticonvulsant drug. In spite of regular medication, he continued to suffer two or three seizures every year. In early 1989, as status epilepticus he was transferred to hospital. Right hemianopia and auditory agnosia were discovered. MR imaging revealed abnormal intensity lesions in the left parietal and the left operculum, but they diminished in two months. Cerebral angiography was also performed, although there were no abnormal findings. He was referred to our hospital for further examination.

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The patient was 159 cm in height, and had been prescribed a major tranquilizer to prevent occasional delirium. He seemed dull for his educational history. On neurological examination, he presented right hemianopia, auditory agnosia and slightly weak muscle strength. Deep tendon reflexes were slightly brisk, coordinative movements were normal. Laboratory data were in the normal range, except for an abnormal elevation in CSF lactate (32 mg/dl, normal control 4-16 mg./dl) and pyruvate (2.2 mg/dl, normal control 0.3-0.9 mg/dl) levels, but serum lactate and pyruvate levels were normal. No acidosis was demonstrated. The process of measurement of these lactate and pyruvate levels was as follows: immediately after sampling, 2 ml CSF was added to the same amount of 10% perchloric acid to move protein, and the supernatant was deep frozen until needed. After neutralization with 3N potassium, the CSF hydroxide lactate and pyruvate were analysed using the standard enzymatic methods (4, 17).

Our patient had the following clinical features: 1) short stature, 2) normal prenatal and perinatal histories, 3) seizures with hemianopia and auditory agnosia, 4) muscle weakness, 5) headache with nausea, and 6) increased CSF lactate and pyruvate levels. These clinical features are compatible with the criteria MELAS as described by Palvaskis (9). To confirm the diagnosis, a biopsy was performed in the right quadriceps muscle; no ragged red fibers were

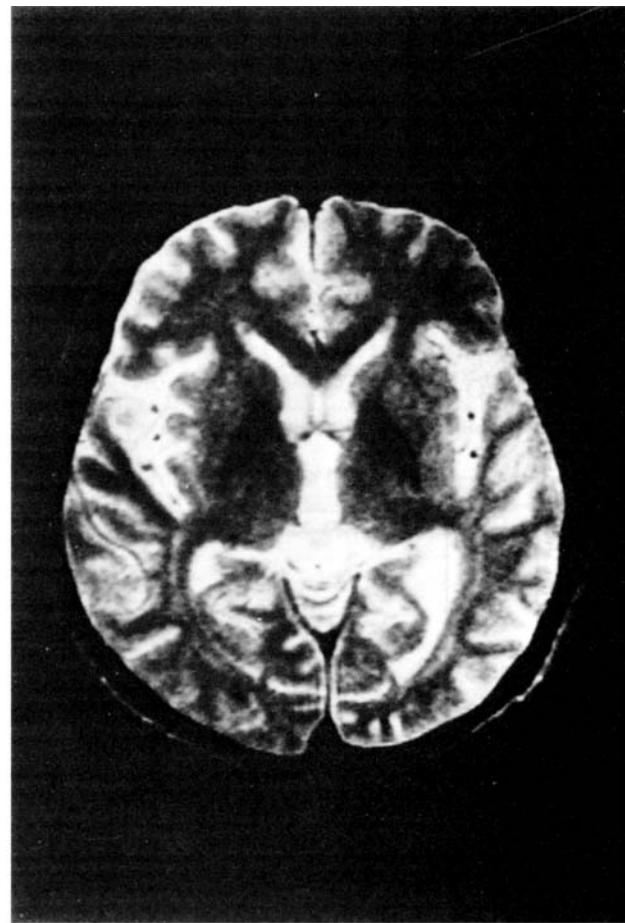
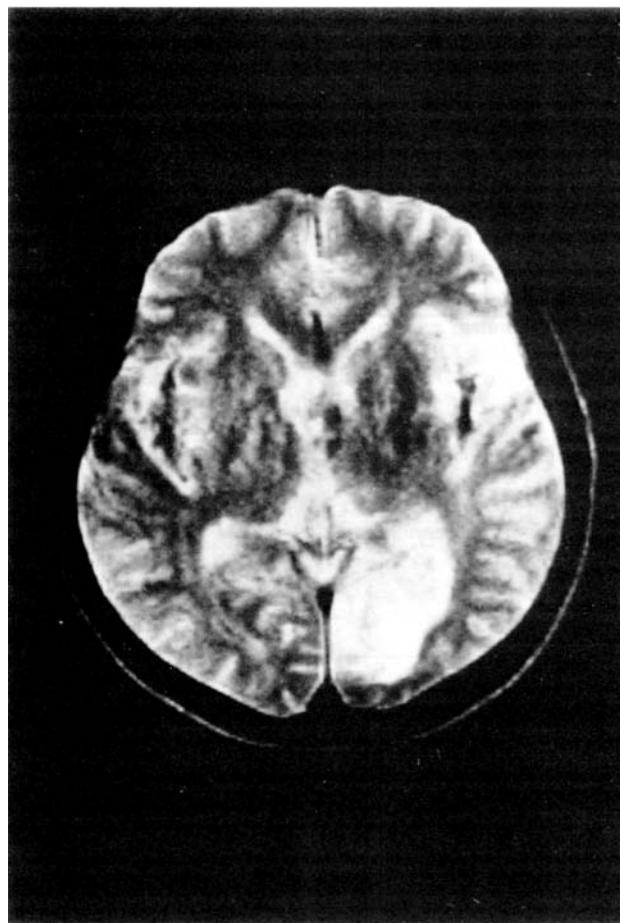


Fig. 1.a,b MR imaging (Shimazu 1.5 Tesla superconducting system, TR/TE = 2500/120) MR imaging reveals high intensity lesions in the left occipital, but these diminish on subsequent MR imaging.

observed. However, ragged red fibers are not always found in MELAS patients, and these histological findings are not contrary to the diagnosis of MELAS. We then began high dosage CoQ administration. After a week, his hemianopia and state of delirium began to improve. The doses of major tranquilizer were tapered. After three weeks, a lumbar puncture was performed, to reveal markedly decreased CSF levels of lactate and pyruvate. IMP-SPECT images demonstrated improved IMP-uptakes in the whole brain. Until now, no seizures have occurred and muscle weakness has gradually improved. Admission of high doses of CoQ is being continued. (Fig. 2).

Discussion

Our patient demonstrated elevated CSF lactate and pyruvate levels without lactic acidemia. CSF lactate and pyruvate levels do not parallel those in serum, and elevation of those levels has been considered to imply mitochondrial metabolic failure (9). Patients with such alternative diseases as diabetes mellitus or

inflammatory diseases not infrequently demonstrate elevation in CSF lactate and pyruvate levels, but our patient had no such disorders. Patients with cerebral infarction are also known to demonstrate elevated CSF lactate and pyruvate levels, but such change is transient (11-13). In our patient, impaired mitochondrial metabolism in the central nervous system is considered the possible cause for elevation in CSF lactate and pyruvate levels (14-16).

The most singular feature of our patient is a marked reduction in CSF lactate and pyruvate levels after CoQ administration. This reduction is unique, because CoQ therapy for mitochondrial encephalomyopathy has been tried previously, without, however, any reduction being reported. Ogasahara et al. (6) reported that cardiac conduction defect and abnormally elevated serum lactate and pyruvate levels were improved after daily administration of 60-120 mg of CoQ for three months. They postulated that exogenous CoQ is incorporated into the mitochondrial inner membrane and increases mitochondrial enzyme activities. Goda et al. (7) reported a MELAS patient who had normal enzyme activity

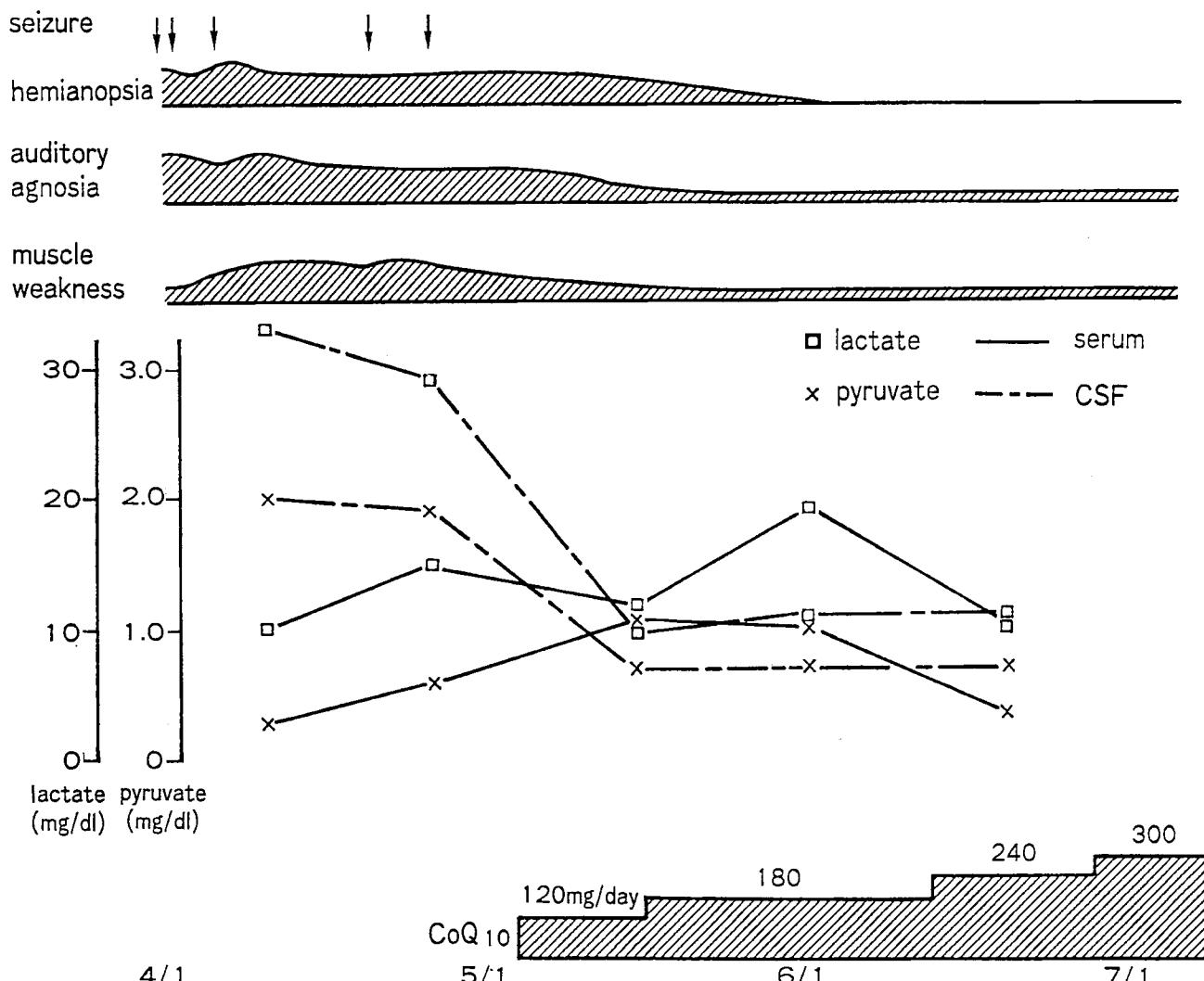


Fig. 2. Progress chart of this case. After CoQ administration, CSF lactate and pyruvate levels decrease and clinical symptoms are improved simultaneously.

in the electron transport system and normal lactic acidosis, and demonstrated a reduction in serum lactate and pyruvate levels, although, no changes in CSF levels. If CSF lactate and pyruvate levels reflect mitochondrial metabolism, reduction in those levels could be accompanied by clinical improvement. We believe the reduction in CSF lactate and pyruvate levels in our patient may indicate effective action of CoQ in the central nervous system. Although exogenous CoQ is known not to be able to pass the blood brain barrier, our patient had a broken blood brain barrier, so CoQ could pass relatively freely through it and into the brain tissue.

The mechanism of CoQ function in our patient is unknown, however, the reported reduction in CSF lactate and pyruvate levels is enough to rationalize CoQ administration.

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