Brief Communication

Ataxia due to isolated vitamin E deficiency in Turkey

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Vitamin E is the most important fat-soluble antioxidant substance. Vitamin E was discovered by Evans and Bishop in 1922.[1] Deficiencies in vitamin E may lead to structural and functional abnormalities in many human systems. Vitamin E deficiency generally presents with neurologic findings. Ataxia with vitamin E deficiency is an autosomal recessive condition associated with a defect in the α-tocopherol transfer protein.[2] The clinical presentation is similar to that of Friedreich's ataxia (FRDA), and patients may be misdiagnosed.

A 16-year-old girl, with normal prenatal, natal, and postnatal developmental milestones, was admitted to the Department of Neurology, Faculty of Medicine, Baskent University, Adana, Turkey with complaints of instability and tremor in her hands and feet. She had been diagnosed as having vertiginous epilepsy at the age of 4.5 years due to vertigo that lasted a few seconds. Then, at age 11, she began having tremors and sweating in her hands and feet. During the 2 years prior to her admission, instability was added, and her symptoms worsened. There was first-degree consanguinity between the parents (children of aunts). The father also had epilepsy and controlled his seizures with carbamazepine. A physical examination revealed a second-degree systolic murmur in the mesocardia region. A neurologic examination showed dysarthria, nystagmus with fast phase in the gaze direction, bilateral dysmetria, dysdiadochokinesia, and intentional tremor. Deep tendon reflexes were hypoactive in the upper limbs and absent in the lower limbs; vibration sensation was diminished in the lower limbs. Her gait was broad and ataxic. The results of other examinations were normal. Results of standard laboratory analyses including total blood count, and biochemical panel was normal. The results of tests for thyroid function, vitamin B12, alpha-fetoprotein, copper, ceruloplasmin, anti-gliadin antibody, and urine organic acid levels, as well as lipid electrophoresis, and stool were normal. Serum vitamin E level was 0.5 mg/dL (normal range: 0.8-1.5 mg/dL) and this was repeated 3 times. Cerebral MRI revealed a right frontal arachnoid cyst and minimal cerebral atrophy. Results of an echocardiography of the brainstem, and visual evoked potentials were normal. In a somato-sensorial evoked potentials study, by stimulating the median nerve, normal findings were obtained; however, by stimulating the posterior tibial nerve, the N39 latency was lengthened (to 47 milliseconds). On electroneurographic examination, median, ulnar, posterior tibial, and fibular nerve conduction velocities were normal; however, sural nerve conduction velocity was 38 meter/second (m/s) (normal: 46m/s). A guanine-adenine-adenine nucleotides (GAA) triplet study was conducted. Our patient's GAA triplet repeat number with regard to FRDA was normal (**Figure 1**).

Vitamin E is a fat-soluble vitamin manifesting 8 different forms. Alpha-tocopherol (α-tocopherol) is the name of the most active form of vitamin E in humans. It is also a powerful biological antioxidant.[1] Vitamin E deficiency may develop owing to primary or secondary causes. Isolated vitamin E deficiency syndrome occurs via a mutation on the alpha-tocopherol transfer protein gene (TTPA) localized on chromosome 8q with an autosomal recessive trait. This mutation was first reported by Quahchi and associates in 1995.[2] In isolated vitamin E deficiency, patients absorb dietary α-tocopherol and incorporate it into chylomicrons normally. Abnormal α-TTP function prevents the transfer of α-tocopherol to very low-density lipoproteins (VLDL) secreted by the liver, and therefore impairs delivery to peripheral tissues.[1] Secondary vitamin E deficiency (precipitated by abetalipoproteinemia or other fat malabsorptive states) is associated with neurologic manifestations including ataxia. In 1981, isolated vitamin E deficiency was described, and this was followed by other reports.[3,4] In these patients, without gastrointestinal disturbance, the onset of symptoms typically occurs between 4 and 18 years of age, with progressive ataxia, areflexia, sensory loss, and pyramidal signs, and sometimes with cardiomyopathy.[1] Cystic fibrosis, chronic cholecystis, liver disease, abetalipoproteinemia, short bowel syndrome, and other malabsorption syndromes may cause vitamin E deficiency to differing degrees. Patients found with a vitamin E deficiency should be examined to discern whether it is an isolated vitamin

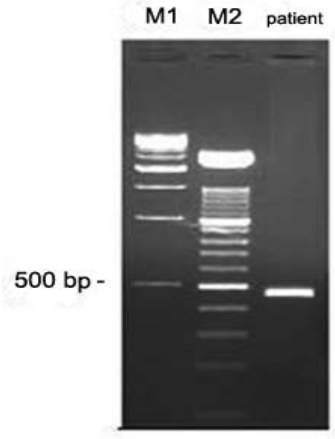

Figure 1 - Guanine-adenine-adenine nucleotides repeat expansion analysis in our case. M1 and M2: 500 and 1000 base pair (bp) ladders.

E deficiency or whether it is due to a secondary cause described above. In our patient, normal lipid profile (cholesterol, triglyceride, VLDL and LDL values) and lipid electrophoresis helped us to exclude abetalipoproteinemia. There were no findings of lung involvement or other exocrine gland disturbances, so cystic fibrosis was also excluded. Liver function tests, vitamin B12 level, alpha-fetoprotein, copper, ceruloplasmin, anti-gliadin antibody, and urine organic acid levels and stool examination were normal, so chronic cholecystis, liver disease, short bowel syndrome, celiac disease, and other malabsorption syndromes were also excluded. Thus, in our patient, secondary causes had been excluded by clinical and laboratory tests, and she was diagnosed as having isolated vitamin E deficiency.

Deficiency of vitamin E can affect the central and peripheral nervous systems, and it can cause ataxia and peripheral neuropathy. Neurologic findings of vitamin E deficiency develop generally in the first or second decade of life. However, there are also reports of patients developing this disorder in the fourth through sixth decades.[5] Neurologic findings in vitamin E deficiency follow a pattern of progression that can be divided into early and late stages. Early findings include hyporeflexia, truncal and limb ataxia, decreased proprioception, distal muscle weakness, night blindness, and abnormal gaze movements. Late manifestations are characterized by dysphagia and dysarthria, cardiac arrhythmias, ophthalmoplegia, and possible blindness. Cognition may be affected in later stages, and dementia can occur.[5] Clinical presentation may resemble FRDA. In our patient, a genetic study failed to show an increase in the GAA triplet. The diagnosis can be established by a serum vitamin E level lower than 0.8 mg/dL in the absence of fat malabsorption. Levels of plasma vitamin E are low and show abnormally rapid clearance of tocopherol from plasma.[1] In our patient, serum vitamin E level was below 0.8 mg/dL in the absence of malabsorption, and the test was repeated 3 times. During treatment, approximately 800 mg/day of α-tocopheryl acetate may return to normal plasma vitamin E concentrations. It has been reported that patients who undergo vitamin E replacement therapy show minimal or any neurologic improvement.[1] We started our patient on vitamin E (900 mg/day) and observed her as an outpatient.

We would like to emphasize that vitamin E deficiency should be included in the differential diagnosis of patients with autosomal recessive trait clinical findings similar to those of FRDA.

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