

Isolated vitamin E deficiency and progressive ataxia

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Abstract

A case of progressive spinocerebellar syndrome due to isolated vitamin E deficiency is reported. Measurement of the vitamin E concentration in serum should be included when investigating all children with unexplained, progressive ataxia, even in the absence of malabsorption. Replacement treatment in patients with a vitamin E deficiency can arrest or improve the associated neurological disorder.

(*Arch Dis Child* 1993; 69: 602-603)

The differential diagnosis of progressive ataxia in childhood includes Friedreich's ataxia, ataxia telangiectasia, Refsum's disease, and spinocerebellar syndromes secondary to vitamin E deficiency, occurring in abetalipoproteinemia,¹ cystic fibrosis, cholestatic liver disease, coeliac disease, and short bowel syndrome.² Vitamin E deficiency in the absence of fat malabsorption (isolated vitamin E deficiency)³ can result in a characteristic progressive neurological syndrome resembling Friedreich's ataxia. It is probably inherited as an autosomal recessive trait.²⁻⁴

Case report

A 6 year old girl was referred to the Regional Child Development Centre with abnormal gait. She was the second of non-identical twins, the product of her mother's third pregnancy, born at 34 weeks' gestation by breech extraction, weighing 2200 g. She was well in the neonatal period. Her early development was normal, though her mother felt that she had always been clumsy. There was no history of jaundice, chronic diarrhoea, or lung disease and she ate a normal diet. There was no relevant family history or parental consanguinity.

Examination showed an intoeing gait and early pes cavus with bilateral tightness of the tendo Achillis. Her arms and legs were incoordinated, deep tendon reflexes were absent, plantar reflexes were equivocal, muscle power was normal, and Gower's manoeuvre negative.

Over the next two years her gait became ataxic. She developed a bilateral intention tremor and positive Romberg's test. At the age of 10 years her handwriting was deteriorating, her gait became more ataxic, and proprioception and vibration sensation were impaired in her legs. Widespread, discrete yellowish white spots were noted in the peripheral retina (fig 1). There was no 'bone-spicule' formation suggestive of retinitis pigmentosa. Visual acuity and eye movements remained normal.

INVESTIGATIONS

Electromyography and motor and sensory nerve conduction studies on three occasions were normal, apart from the absence of H waves. The visual evoked responses, electroretinography and electro-oculography, electrocardiography, echocardiography, computed tomography of the brain, and radiographs of the thoracic and lumbosacral spine were normal.

Plasma creatine phosphokinase, urea and electrolytes, calcium, phosphate, liver function tests, phytanic acid, serum immunoglobulins, and α -fetoprotein were normal. Fasting lactate concentration was 0.3 mmol/l (normal range 0.45-1.3). No acanthocytes were seen on a peripheral blood film and serum cholesterol was 5.5 mmol/l (normal range <5.2).

At 10 years, her fasting serum vitamin E concentration was only 0.2 μ mol/l (normal range 11.5-35.0), repeat cholesterol 4.7 mmol/l, and fasting triglycerides 0.51 mmol/l (normal range 0.3-1.7). There was no evidence of abetalipoproteinaemia. Plasma vitamin A was 1.14 μ mol/l (lower limit of normal range).

Microscopy and culture of stool specimens were normal. A three day faecal fat collection gave a fat excretion of 2.1 g/day (2.8% of dietary fat intake). Stool chymotrypsin was 181 μ g/g (normal >120). Tests for

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Accepted 21 July 1993

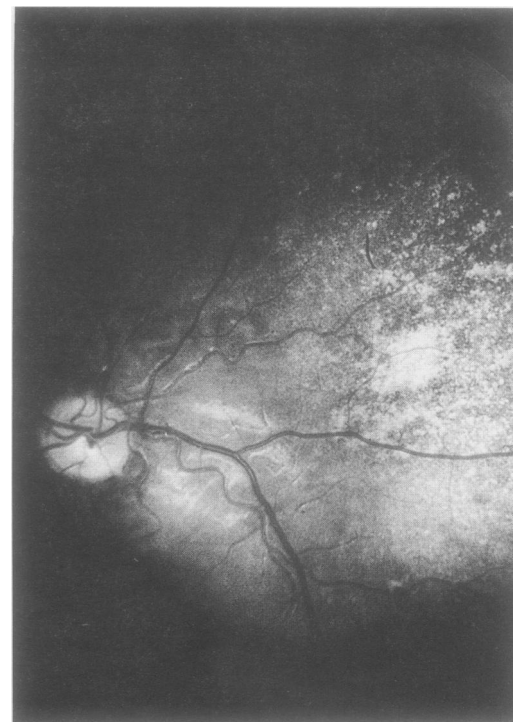


Figure 1 Photograph of the retina showing patches of atrophy in the peripheral retinal pigment epithelium.

antigliadin antibodies were negative. A small bowel barium meal examination was normal. Serum B-12 and folate, plasma ferritin, and clotting studies were normal.

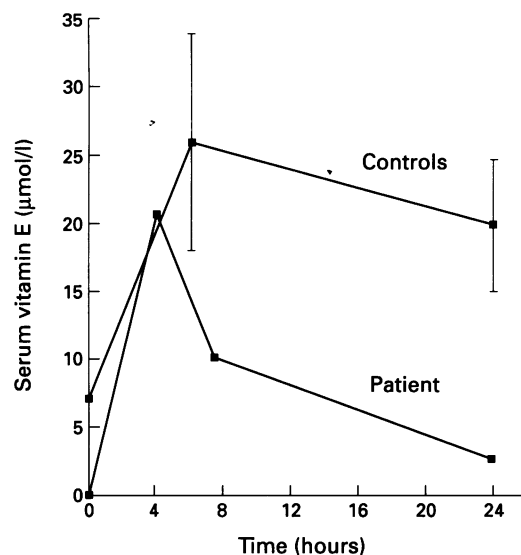


Figure 2 Response to 2 g α tocopheryl acetate by mouth given at time 0 hours, compared with the mean (SD) response of 11 healthy adult controls (the control figures are from Yokata *et al*¹).

A vitamin E absorption test (fig 2) indicated that she could absorb vitamin E in pharmacological doses, and the rapid decrease in serum vitamin E concentrations after loading was consistent with the diagnosis of isolated vitamin E deficiency.³ Her three siblings had normal fasting serum vitamin E concentrations and normal ratios of serum vitamin E to total lipids.

TREATMENT

The patient was treated with tocopheryl acetate 500 mg daily, gradually increased to 800 mg daily. After four months fasting serum vitamin E concentrations were in the normal range (26 μ mol/l). Plasma vitamin A concentrations had increased to 1.78 μ mol/l. Adequate serum vitamin E concentrations are now maintained on 500 mg daily.

Discussion

This case is important because neurological deterioration due to vitamin E deficiency is treatable. In cases associated with malabsorption, a good response can be expected if

vitamin E replacement treatment is started in infancy^{1,2} but useful responses can still be obtained in adults.² Several cases of isolated vitamin E deficiency have improved with treatment and in the remainder neurological deterioration has been stopped.^{2,4,5}

The vitamin E tolerance test in our patient shows rapid absorption of vitamin E from the bowel in pharmacological doses, but then a rapid decrease from the peak. This is a similar pattern to that described by Sokol *et al*³ and suggests increased utilisation or abnormal degradation of the vitamin. In contrast, the vitamin E tolerance test in the patient described by Harding *et al* showed that the decrease from peak concentration to that at 24 hours was normal,⁴ and it was suggested that intestinal absorption of vitamin E was selectively impaired. The exact cause of this disorder remains unclear, though deficiency of a hepatic vitamin E binding protein has been proposed.²

Our patient has many features in common with previously reported cases of isolated vitamin E deficiency, such as progressive ataxia (although for several years ataxia appeared to be non-progressive), areflexia, and decreased proprioception and vibration sensation.² The development of a retinopathy has not been reported previously. The retinal abnormalities are striking and probably attributable to long term vitamin E deficiency.⁶ There has been no further deterioration in her neurological condition since starting treatment 12 months ago, compared with the previous year in which there was a steady deterioration in gait and handwriting.

Review of the clinical features of previously reported cases (table) shows occasional atypical presentation with retention of deep tendon reflexes³ or pronounced muscle weakness.⁵

The diagnosis of isolated vitamin E deficiency relies on the demonstration of low circulating concentrations of vitamin E. It is important that paediatricians are aware of this potentially curable degenerative disorder. Estimation of serum vitamin E should therefore be included in the investigation of all children with unexplained, progressive ataxia, and considered in unexplained non-progressive ataxia.

We acknowledge the help of Professor A Harding and Dr D P R Muller in the investigation of this patient.

Clinical features of isolated vitamin E deficiency. Values are number of patients with this abnormal finding

	Areflexia	Ataxia	Loss of position sense	Loss of vibration sense	Dysarthria	Muscle weakness	Retinal changes
Other reported patients (n=9)	6	7	7	9	3	1	0
Our patient	+	+	+	+	-	-	+

+ = Abnormal finding present; - = Abnormal finding absent.

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