

A man with weight loss, ataxia, and confusion for 3 months

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A 63-year-old white man who had known peripheral vascular disease, vitamin B12 deficiency (receiving replacement therapy for 2 years), and cataracts, and who smoked tobacco, presented to the Dartmouth-Hitchcock Medical Center emergency department on April 22, 1994. He had recently lost 5–10 kg and had developed progressive ataxia, difficulty with concentration, and confusion over the preceding 3 months. He also complained of constipation and anorexia. On examination, he was alert but unsure of the date or identity of the President. He demonstrated moderate generalised weakness, mild hyper-reflexia, distal loss of proprioception and vibration sensation, upgoing toes to plantar scratch, and truncal ataxia. He was admitted to the hospital (AR).

Laboratory testing revealed mild hypocalcaemia (2.02 mmol/L), hypoalbuminaemia (31 g/L), and normal B12 (248 ng/L) and prothrombin time. The vitamin E concentration was 4.4 mg/L (normal is more than 5.0). Cerebrospinal fluid (CSF) showed raised protein (1.81 g/L). Brain magnetic resonance imaging (MRI) demonstrated non-specific white-matter changes. Biopsies of the small intestine were consistent with coeliac disease (figure). His mental status and ataxia improved after he started a gluten-free diet with added water-miscible vitamin E (400 U three times a day). 3 months later, CSF protein had decreased (0.89 g/L). At 1 year, the patient had adhered strictly to his diet and vitamin therapy and had gained 3.2 kg. He remained clearer in mental status as evidenced by improvement in Folstein mini-mental status exam scores from a baseline of 21 to 26 points. Ataxia was absent, although his weakness and sensory loss had not significantly improved.

Neurological manifestations of adult coeliac disease include cerebellar ataxia, sensory neuropathy, myopathy, hyporeflexia, and seizures. Dementia has more recently been added to this symptom complex, but in all of these patients the dementia has been unresponsive to a gluten-free diet.^{1,2} A suggestion was subsequently made that the symptom complex, exclusive of dementia, resembled that of vitamin E deficiency (ataxia, sensory loss, areflexia, and gait disturbances) and that replacement therapy should be attempted.¹ Whereas diarrhoea, steatorrhoea, and weight loss are the most common (but not universal) clinical features of coeliac disease, the gluten-induced damage to intestinal villous epithelial cells results in malabsorption of

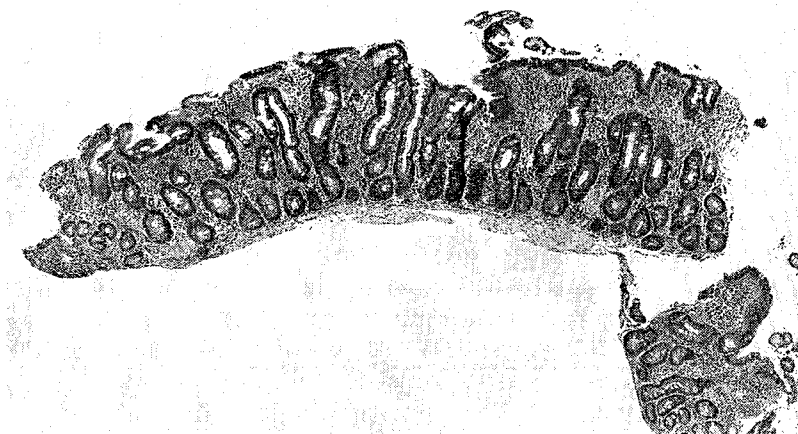


Figure: Duodenal biopsy (haematoxylin and eosin stain)

Villous flattening, focal crowding of surface enterocytes, increased mitotic activity in the crypts, and increased numbers of lymphocytes and plasma cells in the lamina propria.

fat-soluble vitamins, which can result in osteomalacia, hypocalcaemia, coagulopathy, and neurological abnormalities. Patients with abetalipoproteinaemia, who lack the lipoproteins necessary to carry fat-soluble vitamins, develop a similar neurological symptom complex. These patients do respond to water-miscible vitamin E supplementation.³ One case of coeliac disease (without dementia) showed neurological improvement after vitamin E supplements.⁴ Other features of our case have been previously reported. Coeliac disease with diminished vitamin E can present with subcortical hyperintense lesions on T2-weighted MRI and frank myoclonus on reflex testing,⁵ paralleling the MRI findings and hyper-reflexia of our case. Coeliac disease with dementia and a raised CSF protein has also been observed.¹ We believe this to be the first report of coeliac disease with dementia responding to a gluten-free diet and water-miscible vitamin E. The role of vitamin E deficiency in the dementia is unclear. No concurrent malabsorptive hypovitaminosis, infection, or metabolic disturbance was detected aside from mild hypocalcaemia. Vitamin B12 supplements had been adequate. However, given our patient's improvement, in evaluation of dementia, a malabsorptive syndrome (such as coeliac disease) with hypovitaminosis E should be considered whenever weight loss is a prominent feature. Furthermore, one should not be dissuaded from the possibility of this diagnosis by a lack of hyporeflexia, absence of diarrhoea, or the presence of non-specific CSF or MRI abnormalities. Such evaluation may benefit selected patients who present with cognitive decline.

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