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Progressive cerebellar syndrome in adult coeliac disease

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Summary. A case of slowly progressing cerebellar syndrome and pathologically confirmed adult coeliac disease is presented. Neurological symptoms progressed although the patient had no enteric complaints. This case seems to be identical with 18 previously reported cases of encephalopathy and adult coeliac disease. However, the aetiology and pathogenesis of the encephalopathy are still not known.

Key words: Coeliac disease – Cerebellar atrophy – Encephalopathy

Introduction

Degenerative disorders of the central nervous system in patients with confirmed adult coeliac disease have been described in detail by Cooke and Smith [4]. To our knowledge, there have been only three further reports on this topic [6, 9, 11]. The reason may either be that this multisystemic disorder occurs rarely or that symptoms of malabsorption are so subtle in some cases that they are not be recognized. In our patient, typical coeliac disease was diagnosed 3 years before cerebellar symptoms developed. Since she was not suffering from further enteric complaints during or even after stopping the gluten-free diet, a connection between her neurological disorder and coeliac disease was not recognized for 5 years.

Case report

This 52-year-old woman was first admitted to our hospital in September 1984. Since the age of 15 she had suffered from intermittent diarrhoea, which worsened after she had eaten or drunk dairy products. In 1946, she had had hypochromic anaemia, which was treated by iron medication. In 1976 she was hospitalized for intensive metrorrhagia, macrohaematuria, epistaxis, abdominal pain, and increasing bouts of diarrhoea. A severe malabsorption syndrome with vitamin K deficiency was found. The diagnosis of adult coeliac disease was made by peroral jejunal biopsy (Fig. 1). The patient made a steady improvement when treated with a gluten-free diet. Diarrhoea, abdominal pain and weakness did not recur even after she refused to continue with the diet from 1979 onwards. In the summer of 1979 the hitherto neurologically normal patient noticed marked gait difficulty and a tremor of her arms; this developed within 2 weeks. There was no history of chronic alcohol or drug abuse nor were neurological disorders known amongst her relatives. In November 1979 the patient was admitted to a neurological hospital for the first time. A pronounced cerebellar syndrome with gait ataxia, intention tremor, dysarthric speech and nystagmus was found. CT scan and cerebral angiography showed no abnormalities. CSF con-

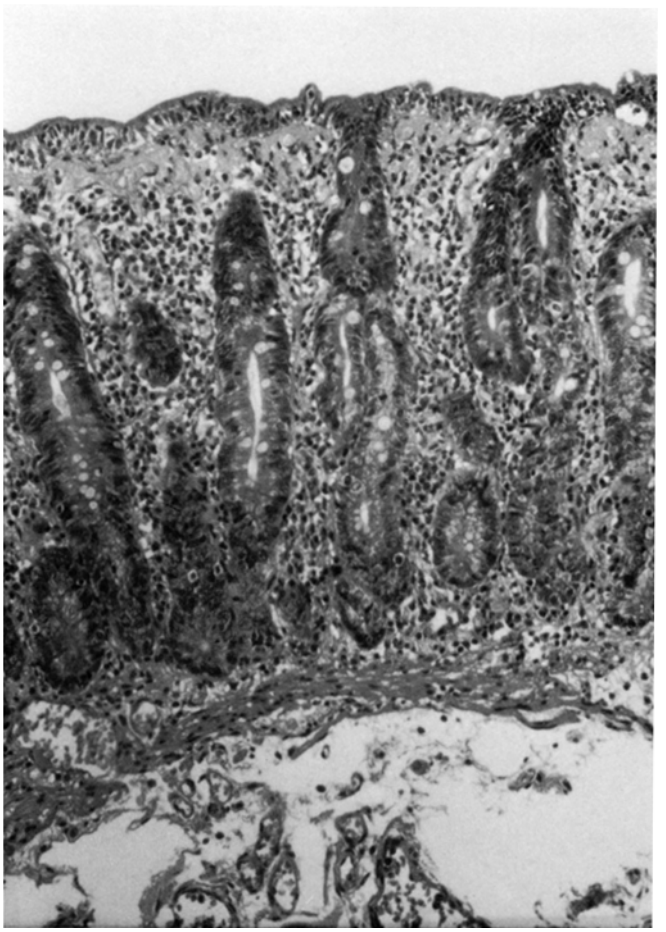

Fig. 1. Jejunal biopsy specimen from the first jejunal loop. Note the flat mucosal surface, the absence of villi, the hypertrophy of crypts and the infiltration of the lamina propria by chronic inflammatory cells

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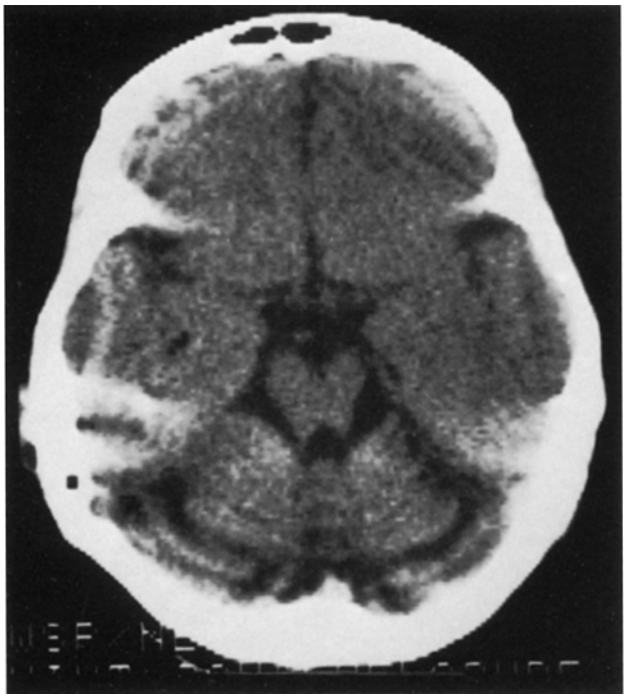

Fig. 2. CT scan demonstrating cortical cerebellar atrophy and dilatation of basal cisterns

tained a white cell count of less than 5/μl; total protein was elevated (65 mg/dl), IgG within the normal range (4.4 mg/dl). A connection between cerebellar symptoms and coeliac disease was not considered. In the autumn of 1980 the patient was admitted to a psychiatric hospital because of depression, which cleared after treatment with opipramol. Weight loss without diarrhoea had occurred throughout the 6 previous months. In January 1981 the patient was admitted to another neurological hospital because of progressing dysarthric speech. Now a CT scan showed marked cerebellar atrophy. The Schilling test revealed a "suspicion of malabsorption". Again there was no history of diarrhoea and no connection between cerebellar atrophy and coeliac disease was suspected.

When admitted to our hospital in October 1984, the patient mentioned that she had had no gastrointestinal tract problems since 1976 although she had not been on a diet since 1979. The neurological examination showed horizontal nystagmus on lateral gaze to either side. Speech was scanning. There was dysmetria, intention tremor and dysdiadochokinesia in all extremities. Tendon reflexes were not exaggerated and plantar reflexes were flexor. Impairment of sensation could not be detected. Gait was only possible with assistance and markedly atactic. There were signs of chronic organic brain syndrome with mild impairment of memory, comprehension and judgement. Findings on general examination were normal.

Laboratory findings showed normal red blood cell counts and a reduced haemoglobin level (10.5 g/dl). Serum calcium, phosphate, copper and zinc were within normal limits. Serum iron was reduced (25 μg/dl) and transferrin slightly elevated (413 mg/dl); ceruloplasmin was normal. Serum folate concentration, vitamin B_{12}, serum gastrin, folic acid and vitamin B_{12} absorption tests were within the normal range. 25-Hydroxyvitamin D was reduced (3.3 ng/ml) while the parathyroid hormone level was not elevated. Total serum protein and the immunoglobulins G, A and M were not decreased. Absorption of d-xylose was reduced (9.6% urine excretion in 5 h). Serum anti-gliadin antibodies were evaluated by red cell immunosorbent fluorescence test and showed elevated titres (1:16). ANA and LE cells could not be detected. Serum antibodies specific for cerebellar tissue could not be found by an indirect immunoperoxidase method and avidin-biotin amplification (kindly performed by H. Lassmann, Neurological Institute, Vienna University).

Radiological investigation of the vertebral spine, the pelvis, the hands and both femora showed no signs of osteomalacia. Conventional upper gastrointestinal series demonstrated a malabsorption pattern of the small intestine (thickening of folds, coarse mucosa, clumping and flocculation of the barium). The patient refused selective enteroclysis (Sellink's technique). Fundoscopic examination and visual-evoked potentials were normal. EEG showed a slightly abnormal record with left temporal slow activity (theta) and some anterior slowing on both hemispheres. Cranial CT scan showed marked cerebellar atrophy (Fig. 2). Regional blood flow studies by i.v. xenon clearance were normal. Motor nerve conduction velocity, distal latency and compound action potentials of the right peroneal nerve were within normal limits.

Discussion

Amongst neurological complications associated with adult coeliac disease, such as neuropathy, myelopathy, myositis and seizures [2–4, 7], to our knowledge encephalopathy has only been reported in 18 cases [4, 6, 9, 11]. Our patient suffered from a progressive, predominantly cerebellar syndrome and CT scanning showed diffuse cerebellar atrophy. The disease was not restricted to the cerebellum because signs of chronic organic brain syndrome showed that other cerebral regions were also affected. Thus late cerebellar atrophy seems not to be the cause of our patient's disorder. No evidence for hereditary, inflammatory, paraneoplastic, toxic or metabolic cerebellar disorder was found in the case history or investigations. All of the patients who had had neuropathological studies were found to have spinal cord involvement [4, 6, 9]. However, the lack of clinical evidence for spinal cord lesions in our patient does not exclude their morphological existence. Ataxia due to lesions of the dorsal column, which was affected in the majority of the cases [3], may have been masked by the predominant cerebellar ataxia and minor differences of vibration sense could not be evaluated because of the organic brain syndrome. On the other hand, profound Purkinje cell loss has been reported to be the most consistent neuropathological finding in patients with encephalopathy and adult coeliac disease [3, 4, 6, 9] and in 6 of the 18 reported cases cerebellar symptoms were the most prominent neurological findings [4, 6, 9, 11]. Therefore, our patient resembles reported cases with adult coeliac disease and predominant cerebellar symptoms [3, 6]. In our patient, coeliac disease was confirmed by jejunal biopsy and by the presence of anti-gliadin antibodies in the serum. Gastrointestinal symptoms ceased when she was treated with a gluten-free diet. On the basis of our laboratory investigations, however, we could still detect signs of malabsorption.

The aetiology of the encephalopathy in adult coeliac disease is still not known. Malabsorption, vitamin deficiency or

direct gliadin toxicity do not seem to be the principal cause of the neurological disease. A similar progressive cerebellar syndrome that follows chronic fat malabsorption has been linked to vitamin E deficiency [1, 10]. Yet Ward et al. [11] were not able to show vitamin E deficiency in their patient with adult coeliac disease and spinocerebellar degeneration. In most cases, encephalopathy progresses even when treated with a gluten-free diet and vitamins [3, 4, 6, 9]. An immunological mechanism involving both small bowel and brain tissue has been suggested to be a possible cause [5]. We were not able to detect serum antibodies reacting with cerebellar tissue. It has also been postulated that adults with coeliac disease may be at risk for superimposed neurological disease of the central nervous system due to a permanent or intermittent state of immunodeficiency [9]. One case of multifocal leucoencephalopathy has already been reported in an adult with celiac disease [8].

In retrospect, we cannot decide whether or not the cerebellar syndrome began while the patient was still on a gluten-free diet or shortly thereafter. However, we emphasize the fact that the patient had no complaints as regards coeliac disease while neurological symptoms were progressing. This is probably the explanation why connections between coeliac disease and the cerebellar syndrome were not suspected for 5 years. All patients with encephalopathy of unknown origin, including even those with no gastrointestinal symptoms, should be examined with respect to coeliac disease.

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