Case report

Underlying coeliac disease in a case of cerebellar ataxia with unknown etiology

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Abstract

Celiac disease is an immune mediated enteropathy in susceptible individuals as a response to gluten containing diets based on wheat, oat, rye and maize. It clinically presents with malabsorption syndrome along with a myriad of extraintestinal manifestations such as anemia, osteoporosis, dermatitis herpetiformis, peripheral neuropathies, ataxia and cognitive impairment. Although the prevalence of these extraintestinal features range from 1 to 15% in these patients, their presence in the absence of intestinal manifestations is very rare. Here we report the case of a middle aged female diagnosed with celiac disease with coexisting gluten sensitive ataxia in the absence of gastrointestinal symptoms.

Keywords: *coeliac disease; ataxia; malabsorption; gluten*

Introduction

Celiac disease is an autoimmune disease triggered by environmental agents, having positive association with genetic loci in HLADQ*2 and HLADQ*5 alleles [1]. As per Genome Wise Association Studies (GWAS) non-HLA alleles like chromosome 15q26 also have a significant contribution [2]. The serological markers of the disease are IgA antitissue trans glutaminase antibody (IgATTG), anti-gliadin antibody IgA and IgG, anti-endomysial antibodies [3, 4]. However, a definite diagnosis rests on biopsy. Celiac disease usually presents with steatorrhea and flatulence, followed by malabsorption heralded by growth failure, delayed puberty, weight loss, and severe anemia, neurological symptoms secondary to vitamins B1, B12 and E deficiency. The patients may often present with atypical features like arthritis, bone pain, infertility, neurological symptoms like peripheral neuropathy, ataxia, seizures and psychiatric complaints [5]. This intriguing spectrum of diseases befools clinicians and leads to misdiagnosis, where underlying celiac disease is overlooked. In fact, celiac disease with extra-intestinal manifestations only is a rare entity.

Case report

A 45 year-old female, presented with difficulty in walking and speech impairment for 2 years and both these symptoms exacerbated over last 2-3 months. The patient had two episodes of syncope, with clumsiness of movements and was not able to stand without support. Initially, the patient spoke in syllables and later her speech became incomprehensible to attendants.

She had no history of weakness, difficulty in swallowing, headaches and blurring of

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vision or bladder and bowel involvement. She had no history of chronic diseases, gastrointestinal symptoms like diarrhea or intake of any indigenous medication.

On examination she was conscious and oriented to time, place and person. Her vitals were stable. She had pallor but her respiratory, cardiovascular and abdominal examinations were within normal limits. On neurological examination, higher mental functions were intact. Cranial nerve examinations revealed no abnormality. Sensations pertaining to lateral columns and dorsal columns were intact throughout, with no dissociation. Motor testing showed normal muscle tone and power with preserved deep tendon reflexes and bilateral plantar flexor response. The patient had bilateral cerebellar signs, with nystagmus, dysdiadochokinesia, scanning speech, inability to complete point-to-point movement evaluation tests (finger-nose-finger test, heel to shin coordination test). Her biochemical investigations profile is summarized in Table 1.

Table 1. Biochemical investigations of the patient

Parameters	Reports	Parameters	Reports
Hb	**6.8 gm%**	T3	2.75 pg/ml (1.71-3.71pg/ml)
TLC	14000/mm3	T4	1.10 ng/dl (0.61-1.12ng/dl)
PBF	**Microcytic Hypochromic**	TSH	3.15 mIU/ml (0.35-4.94mIU/ml)
AST	22 U/L	Vitamin B12	87pg/ml (75-807pg/ml)
ALT	17 U/L	Vitamin B1	81nmol/l (70-180nmol/l)
Triglycerides	62 mg%	Vitamin E	7.8ug/ml (5.5-17ug/ml)
Cholesterol	116 mg%	Vitamin D3	45 IU/ml (>20 IU/ml)
LDL	81 mg%	ANA by IFA	Negative
VLDL	12 mg%	Serum Creatinine	1.0 mg%
HDL	23 mg%	Random Blood Sugar	98 mg%
Apo A1	1.12g/l	Serum Sodium	146 meq/L
Apo B	0.82g/l	Serum Potassium	4.3 meq/L
Apo B: Apo A1	0.73	Ig ATTG	**53.81U/ml(<12U/ml)**
Lipoprotein A	24.60 mg%	Anti gliadin Ab	**156mIU/ml(<32mIU/ml)**

Brain and spine MRI were normal. Cerebrospinal fluid examination was normal and nerve conduction studies were also normal. Thus, after ruling out the most probable etiologies and considering the patient's immunological background, celiac disease induced ataxia was thought of. Upper GI endoscopy revealed scalloping of mucosal folds in second part of duodenum (Figure 1).

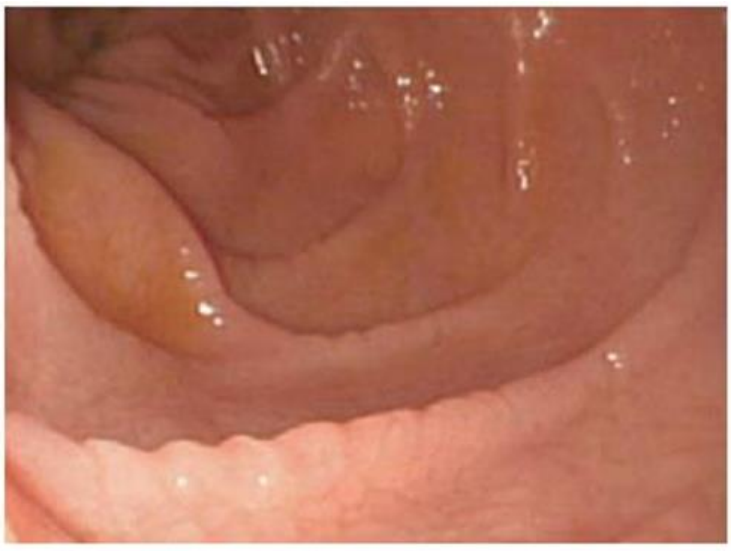

Fig. 1. UGI endoscopy showing scalloping of mucosal folds in D2

Biopsy was taken from the site and histopathological examination showed evidence of crypt hyperplasia, marked villous atrophy along with presence of >30 intraepithelial lymphocytes/100 enterocytes, consistent with celiac disease stage IIIC as per Modified Marsh Classification (Figure 2).

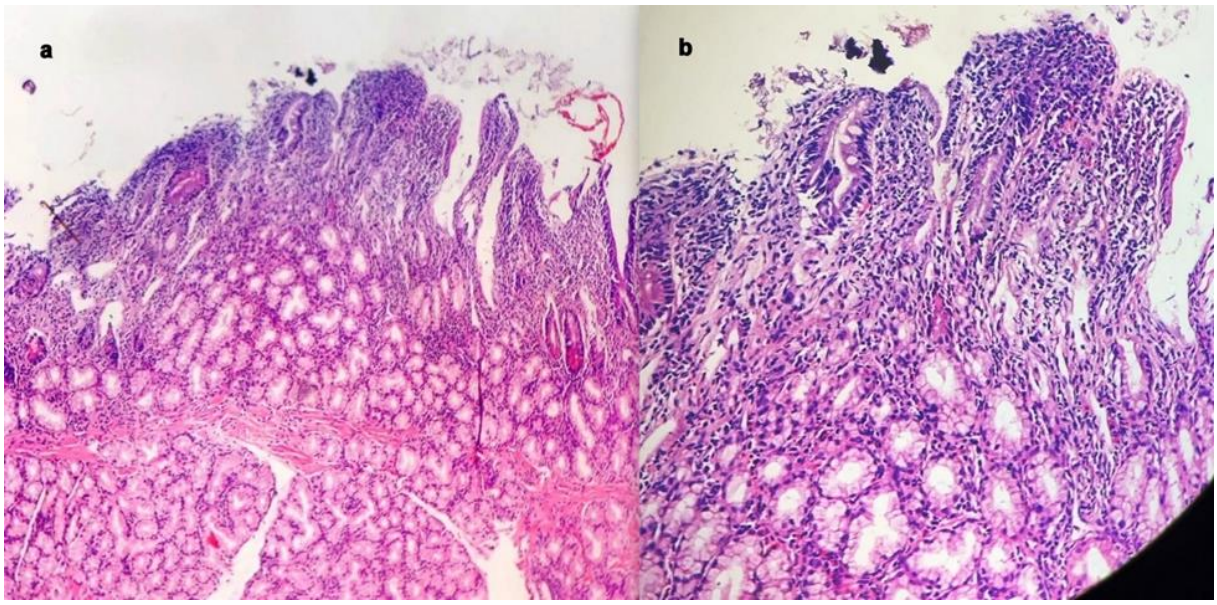

Fig. 2. Histopathological examination: increased intraepithelial lymphocytes, cryptal hyperplasia and loss of villi (a: HE, x50; b: HE, x100).

The patient was thereafter put on gluten-free diet along with iron supplementation. Follow-up examinations showed drastic improvement over 2-3 months. Her hemoglobin level rose to 9.2 gm%. Clinically, her speech improved and, to some extent, even her gait showed signs of improvement as she could walk few steps with support. Her cerebellar signs like nystagmus and dysdiadochokinesia also resolved.

Discussions

Neurological symptoms make up only 10% of celiac disease spectrum. Peripheral neuropathies are encountered at times in patients with silent celiac disease, but cerebellar ataxia is a rare entity. It may be secondary to neuropathy, demyelination of spinocerebellar tracts or direct damage to cerebellum. The pathogenic mechanism behind gluten sensitive ataxia remains unknown. It is suggested that a shared epitope between neural and mucosal tissues, catering to immune mediated neural tissue damage may be the link [6]. Retrospective analysis using karyotyping have further substantiated the hypothesis. HLA DQ2, HLA DQA1*0501 or DQB1*0201 are susceptible to celiac disease and have also been detected in ataxia of unknown etiology. Another subtle mechanism behind it may point to the coexisting malabsorption leading to vitamin deficiencies [7]. In a study by Burk et al., 11.5% of patients with sporadic ataxia had serum antibodies for celiac disease, while 70% of they were found to have the HLA DQB1*0201 haplotype, with only 10% showing histological findings consistent with celiac disease. Axonal neuropathy was demonstrable on electrophysiological testing in 50% of patients, while all of them had cerebellar atrophy. But all these patients had benefited from gluten-free diet [8]. In fact, celiac disease stands as a differential diagnosis for all patients with gait disturbance progressing over the course of time and having bilateral cerebellar signs, whereas unilateral signs direct towards vascular insults like ischemia and hemorrhage to the brainstem or cerebellum. So far, the few case reports available in this perspective have

highlighted peripheral neuropathy or cerebellar atrophy as the etiology behind celiac ataxia, much similar to the study made by Burk and colleagues [8]. The present scenario of celiac ataxia with only spinocerebellar tract involvement is quite rare in the literature.

Conclusions

Gluten sensitive ataxia patients pertain to a spectrum of atypical celiac disease and may be accompanied by other extraintestinal manifestation. Clinically, such patients are indistinguishable from patients with late onset ataxias of other etiology. However, it represents an easily reversible etiology of ataxia that is often overlooked. Celiac serology should always be assessed for ataxic symptoms after ruling out all other possible etiologies, as gluten-free diet serves as a cure from the ataxic symptoms.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests

The author(s) declare that they have no competing interests.

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