Spontaneous Latency in Adult Patients with Celiac Disease on a Normal Diet after Gluten-Free Diet: Case Series

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Abstract

Celiac disease (CeD) is an immune condition induced by the consumption of gluten-containing foods in genetically-predisposed persons. CeD, in addition to digestive disease, is a multisystem disorder. If untreated, it is potentially can be a dangerous disorder and lead to morbidity and even mortality. At present, the only treatment option is a lifelong gluten-free diet (GFD), and all authors recommended this regimen. To the best of our knowledge, there are rare reports of the complete remission of disorder on GFD and reintroduction of a normal diet in affected patients. In this report, we describe five patients with CeD who developed complete remission of clinical symptoms, histopathological changes, and serology on a gluten-containing diet. All patients had CeD based on a positive tissue transglutaminase antibody (TTG IgA) and typical histopathological changes in duodenal biopsy with the complete disappearance of symptoms on the GFD regimen. All patients followed GFD for a mean 4 (±0.54) years. In conclusion, this study has shown that some CeD patients diagnosed in adulthood can recover a normal mucosa after a long period of the gluten-containing diet without relapsing any clinical or biological symptoms of CeD.

Keywords:
Celiac disease; Gluten, Remission; Spontaneous latency

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Introduction

Celiac disease (CeD) is an autoimmune disorder related to permanent intolerance of gluten in genetically predisposed individuals. Precise diagnosis of CeD at an early stage and its treatment with a gluten-free diet (GFD) are essential for effective treatment and prognosis.[1] CeD causes small bowel mucosal inflammatory changes and alternation in architecture, often resulting in decreased nutrient absorption, diarrhea, and weight loss.[2] In addition, various extraintestinal manifestations may also occur,[3] or even subtle symptoms that represent the clinical pattern of sub-clinical/silent CeD.[4] Currently, the only effective treatment is permanent GFD so that mucosal remission can occur and complications are reduced.[5] Despite diet therapy is a challenge in adolescent and adult patients with CeD and compliance with GFD being relatively low,[6] the interest of the general population in GFD may have increased.[7]

Even with the introduction of GFD, some evidence suggests that the natural course of CeD is variable.[8] Non-responsive CeD is a failure to respond after 6 months of a strict GFD and is typically due to accidental

gluten ingestion.[9] Evidence showed that 1%-2% of patients with CeD have refractory CeD, characterized as permanent or recurrent mucosal damage despite a precise GFD for more than 6 months.[10] However, about 80% or more of adult patients with CeD present mucosal healing after up to 2 years or more on a GFD.[11,12]

Some data have shown that in some patients with CeD diagnosed in childhood who retained a normal diet after transient withdrawal of gluten, no biological or clinical relapse was observed.[13] However, it is still unclear if a precise GFD needs to be considered throughout the whole life in all patients with CeD or if tolerance may develop in some patients. In line with this uncertainly, herein, we report five cases of adult patients of different ages and varying degrees of mucosal damage at the time of CeD diagnosis who developed complete remission of serology, clinical symptom, and histopathological changes on a regular diet after a relatively long period of time on a gluten-free diet.

Case Report

We describe five patients (three females and two males) with CeD diagnoses. All five patients had CeD based on a positive tissue transglutaminase antibody (TTG IgA) and typical histopathological changes in duodenal biopsy with the complete disappearance of symptoms on the GFD regimen. The mean (±SD) age of the patients was 33.20 (±16.36) years.

The mean (±SD) of TTG Ab was 96 (±30.58) (reference value<18 U/dL), hemoglobin (Hb) level at the time of CeD diagnosis was 11.60 (±2.23) (reference value 12-16 mg/dL) as a biological marker of malabsorption, and body mass index (BMI) was 25.68 (±3.95) kg/m^2 as nutritional status. The characteristics of the studied subjects are presented in Table 1.

Following the diagnosis of CeD, all patients completely eliminated gluten intake from their diet, which resulted in good clinical and serological (anti-TTG) responses. The patients followed GFD for mean 3.4 (±0.89) years. Based on scientific instruction, we should not cut GFD. All of them had interrupted the GFD on their own decision and followed a normal diet. Because of the absence of symptoms in patients, we did not recommend the reintroduction of GFD. We did not calculate the amount of gluten consumed, but all patients had a regular diet. Serial patient follow-up

Table 1. Characteristics of the patients (n=5)

	Case 1	Case 2	Case 3	Case 4	Case 5
Gender	Female	Male	Female	Male	Female
Age at the time of diagnosis (year)	16	19	32	45	54
Initial presentation	Chronic diarrhea	Chronic diarrhea	Refractory dyspepsia	Refractory dyspepsia	Unexplained IDA
Comorbidity	Ulcerative colitis	Cryptogenic cirrhosis	-	-	Ulcerative colitis
TTG Ab at the time of diagnosis (U/dL)[a]	97	98	142	86	57
BMI (kg/m^2)	22.1	22.5	31.7	27.3	24.8
Hb (mg/dL)	10.6	8.7	11.7	14.8	12.2
EGD findings (D2)	Diffuse scalloping	Diffuse scalloping	Ultra short scalloping	Diffuse scalloping	Normal appearing mucosa
Histopathology	Marsh IIIB	Marsh IIIB	Marsh IIIA	Marsh IIIA	Marsh II
Duration of GFD (y)	5	3	3	3	3
Treatment	Mesalazine	Propranolol	Omeprazole, Domperidone	Omeprazole, Ranitidine, Nortriptyline	Mesalazine, Ferrous sulfate
Duration of normal diet (y)	4	5	4	4	5
TTG Ab after normal diet (U/dL) [a]	8	10	6	10	8

Abbreviations: TTG Ab, tissue transglutaminase IgA; EGD, esophagogastroduodenoscopy; BMI, body mass index; D2, the second part of the duodenum; Hb, hemoglobin; GFD, gluten-free diet.
[a] Reference value<18 U/dL.

visits were maintained with all patients and have been continued for mean 4.4 (±0.54) years, and all patients showed complete remission in serology and clinical and para-clinical symptoms. Indeed, in three patients, endoscopy findings and duodenal biopsy were normal, and two of them (case 2 and case 3) did not allow to perform an endoscopic evaluation. Interestingly, all patients are still alive and completely symptom-free on a regular gluten-containing diet.

Discussion

It is still undetermined whether a patient with CeD needs for whole life (permanent) GFD or not and if tolerance may develop in certain patients. To our knowledge, this is the first report from Iran to describe adult patients with CeD who developed complete remission in serology, clinical symptom, and histopathological changes of mucosal damage on a gluten-containing diet (regular diet) after the introduction of a period of GFD. This is in agreement with some previous studies from the medical literature showing that symptoms were latent over time in children and adults with CeD. For instance, the first study in 1984 reported spontaneous histological remission on a gluten-containing diet in three patients with CeD with diagnosed CeD in childhood.[14] In another similar finding, Maki and others observed that among 29 patients with CeD who returned to a normal diet, four retained a normal mucosa for 2 years.[15] Shmerling and colleagues also found that 6 out of 91 patients with CeD with interruptions of GFD remained symptom-free after 2-6 years.[16] Also, another study showed that of 34 children with CeD after reintroduction of a gluten-containing diet, four had reported complete recovery, and six had a relatively normal mucosa 5-13 years later. More recently, Matysiak-Budnik and colleagues, in their prospective cohort study, found that 13 out of 61 children with CeD had spontaneous remission on a long-term normal diet.[17] Almost all of the mentioned reports are the CeD scenario in childhood, and the spontaneous remission of clinical and paraclinical symptoms in the present series of adult patients with CeD is inconsistent with the previous research.

The important factor in some studies was an early CeD diagnosis and, as a result, the early elimination of gluten from the diet. Ciacci et al studied the clinical and psychological status of adults with a childhood diagnosis of CeD who were reintroduced to a gluten-containing diet after a few years, and they follow a normal diet now, compared with adults with recently diagnosed CeD, and concluded transient gluten withdrawal in childhood partly minimized clinical and behavioral effects of gluten sensitivity in adults with CeD.[18] Evidence has shown that delayed introduction of gluten into infant's diet decreases the incidence of childhood CeD, and this hypothesis is not in line with our studied patients who were diagnosed in adulthood and spontaneously remained symptom-free.

Regarding BMI, three patients had a normal BMI (18.5-24.9), and two patients had a BMI of more than 25 (overweight). Traditionally underweight is a classic symptom of CeD. However, evidence indicates measuring BMI in patients with CeD at the time of diagnosis has shown inconsistent findings.[19-22] Therefore, patients with clinical manifestations in favor of CeD should be evaluated for CeD without considering their BMI.

Many studies indicated CeD is significantly associated with various extraintestinal presentations. The prevalence of CeD in cryptogenic cirrhosis was 10%-13%. Screening for CeD was suggested in cryptogenic cirrhosis. Moreover, liver functions recovered after GFD in patients with CeD and cirrhosis.[23,24] In addition, two patients had ulcerative colitis. There are already multiple studies that have reported an association between CeD and inflammatory bowel disease, ulcerative colitis more frequent than Crohn's disease. Impacts of underlying disease treatment on the course of the CeD need to be assessed with more cases.

This study had some limitations. First, given the clinical and biological remission, the patients refused HLA typing for DQ2/DQ8. Second, because of the lack of regular histological follow-up for patients, we could not determine the exact time of histological recovery. Future research should investigate the natural course of patients with CeD who had remission on GFD and then a regular diet introduced for them.

In conclusion, this study has shown that some patients with CeD diagnosed in adulthood can recover after a long period (3-5 years) of GFD without relapsing any serological, clinical, or histopathological problem of

CeD after normal diet introduction. It is important to know that this remission state may not provide ultimate healing, and because of the autoimmune nature of the disorder, the clinical problems may occur again.

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Ethical Approval

This study was designed based on the ethical principles of the Declaration of Helsinki (2008) for medical studies involving humans. The written consent forms were signed by all the participants. The Ethics Committee, affiliated with Mazandaran University of Medical Sciences, has approved this study (Registration No.IR.MAZUMS.REC.1400.432).

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Conflict of Interest

The authors declare no conflict of interest related to this work.

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