

CASE REPORT

Remodeling Immune Response in A Celiac Disease Patient Using Herbal Supplementation: A Clinical Case-Study

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ABSTRACT

Background • Celiac disease (CD) is an autoimmune disorder characterized by abnormal serological response (autoimmune anti-tissue-Transglutaminase antibodies) triggered by gluten ingestion in genetically predisposed individuals. The only available effective management for those patients is a strict gluten-free diet.

Aim • To investigate the improvement of CD after completing a traditional herbal supplementation and alternative medicine treatment.

Case description, treatment, and results • A 23-year-old female presented with a confirmed CD diagnosis (positive anti-tissue Transglutaminase IgA with infiltration of

mixed inflammatory cell detected in small bowel biopsy). After 9 months of alternative treatment with traditional herbal supplementation (Taraxaf®, Ferrolina®, and Indomirol®), the clinical, laboratory, and endoscopy profile tests have shown an overall improvement with negative results for anti-tissue Transglutaminase IgA, and normal small bowel mucosal appearance. She was returned to an ordinary diet containing gluten.

Conclusion • A traditional herbal supplementation with specific doses followed by a physician's instruction led to obvious improvement in this CD patient. (*Altern Ther Health Med.* 2022;28(8):46-49).

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INTRODUCTION

Celiac disease (CD) is an autoimmune condition or immune-based enteropathy, characterized by a specific serological and histological profile triggered by gluten ingestion (a protein component of wheat, barley, and rye) in genetically predisposed individuals.¹ Studies have shown that most CD cases remain undetected in the absence of

serological screening due to heterogeneous symptoms and/or poor disease awareness.² The prevalence of CD has increased in Western countries 5-fold in the US between 1975 and 2000.³ Besides genetic predisposition and gluten exposure, many factors play a role in the CD pathophysiology including functional loss of intestinal barrier, gluten triggering of a pro-inflammatory innate immune response accompanied by the inappropriate adaptive immune response, and imbalanced gut microbiota.² The standard diagnosis for CD is confirmed by the combination of mucosal changes which is detected by duodenal biopsy and by positive serological tests (anti-TG antibodies, anti-endomysium antibodies (EmA), and deamidated gliadin peptide (DGP) antibodies).⁴ CD-related antibodies belong to IgA and IgG classes, but only those of the IgA class are highly sensitive and specific for CD.⁴

At present, the only effective treatment available for CD is lifelong adherence to a strict gluten-free diet, since it has been shown that this leads to the resolution of intestinal and extra-intestinal symptoms, negativity of autoantibodies, and the regrowth of the intestinal villi.² In addition, the diet offers a crucial protective effect against several complications. However, a gluten-free diet has some disadvantages, including a negative impact on life quality, psychological problems, fear of involuntary/inadvertent contamination with gluten,⁵ possible vitamin and mineral deficiencies, metabolic

Table 1. Serological, endoscopic, and histopathological results at the time of diagnosis

Tests	Results	Normal Range	Interpretation
Immunological tests			
Immunoglobulin A	1.04 g/L	0.7-4 g/L	Normal
Anti-tissue Transglutaminase IgG	26.6 U/mL	Negative: less than 20 U/ml	Positive
Anti-tissue Transglutaminase IgA	32.6 U/mL	Negative: less than 20 U/ml	Positive
Biochemistry tests			
Iron, serum level	35.61 g/dL	37-145 ug/dL	Decrease
Total iron-binding capacity	404 ug/dL	259-388 ug/dL	Increase
Ferritin, serum level	7.57 g/mL	4.63-204 ng/mL	Normal
Vitamin D	11 ng/mL	20-40 ng/mL	Decrease
Calcium, serum level	8.9 mg/dL	8.6-10.2 mg/dL	Normal
Hematology tests			
Hb	11.3 g/dL	12-16 g/dL	Decrease
Hct	34.4 g/dL	42±5 g/dL	Decrease
WBC	5.92 *10 ⁹ g/L	4-10 *10 ⁹ g/L	Normal
MCV	81.8 fL	80-100 fL	Normal
MCH	26.8 pg/cell	26-34 pg/cell	Normal
MCHC	32.8 g/dL	31-36 g/dL	Normal
RBC	4.57*10 ¹² Cell/L	3.8-5.8 *10 ¹² Cell/L	Normal
RDW	14.9%	4.6-13.5%	Increase
Neutrophil-segmented	60.5%	40-75%	Normal
Eosinophil	1.4%	1-6%	Normal
Basophil	0.3%	0-1%	Normal
Lymphocyte	30.3%	20-45%	Normal
Monocyte	6.4%	2-10%	Normal
Platelet count	354 * 10 ⁹ /L	140-440*10 ⁹ /L	Normal
Histopathology results			
A small bowel biopsy was randomly obtained from the duodenum. Then the specimen consisted of six fragments of grayish tissue measuring in aggregate 0.8x0.8 cm and was rapidly fixed in formalin. By microscopic examination, the sections show fragments of duodenal mucosal with blunting of villi, increased intraepithelial lymphocytes, as 40 lymphocytes per 100 enterocytes. The lamina propria shows mixed inflammatory cell infiltrate composed of neutrophils, lymphocytes, eosinophils, and plasma cells. There is no morphologic support for microorganisms, granulomas, or malignancy. This finding supports subtotal villous atrophy, Marsh IIIB.			

Abbreviations: Hb, Hemoglobin; Hct, Hematocrit; WBC, White blood cell; MCV, Mean Corpuscular Volume; MCH, Mean Corpuscular Hemoglobin; MCHC, Mean Corpuscular Hemoglobin Concentration; RBC, Red blood cell count.

syndrome, and often severe constipation.⁶ Recently, CD patients have been seeking therapies different from a gluten-free diet including larazotide acetate, gluten-specific proteases from a bacterial mix (ALV003), and vaccination (Nexvax2). The vaccine offers another possible therapeutic strategy aimed at desensitizing patients with CD to gliadin peptides, but it does have side effects.² Moreover, Aziz et al.⁷ identified that about 21.6% of CD patients in the UK take dietary supplements, especially probiotics. In the USA about 24% of patients with biopsy-proven CD use dietary supplements to treat CD-related

symptoms, although those using dietary supplements have more symptoms, but a higher quality of life compared with those who do not.⁸ There is not enough information on the use of alternative medicine and dietary supplementations such as probiotics in CD treatment. Therefore, the main aim of the treatment protocol for this case study was to investigate the effect of a newly proposed hypothesis about the role of active components and functional groups in herbs, and the role of alternative and complementary medicine in remodeling/adapting immune response in CD patients.

CASE DESCRIPTION, TREATMENT, AND RESULTS

A 23-year-old female with a history of celiac disease diagnosed 10 months prior was referred to The Herbal Dynasty Medical Center in Amman, Jordan (Feb 2020). She was diagnosed with iron deficiency anemia, multivitamin deficiency, female baldness, and normal body mass index (BMI 21.88; height 1.60 m, weight 56 kg). She has followed a gluten-free diet since the time of diagnosis (April 2019). The diagnosis of celiac disease was made based on endoscopy (Esophagogastroduodenoscopy (EGD)), histopathological and serological tests, additional biochemistry, and hematology results as shown in Table 1.

At the time of the first visit at The Herbal Dynasty Medical Center, physicians prescribed a group of traditional herbal supplementation of a specific dose as follows: Taraxaf[®] (consist of dandelion, olive leaves, nettle leaves, and turmeric; in equal quantities; each capsule is 1 g; two capsules each day; Bioenergy Company, Jordan). To deal with anemia Ferrolina[®] (consisting of 340 mg Spirulina micro-Algae and 27 mg Ferrous Bisglycinate; each capsule is 1 g; Biobalance Company, Jordan) was prescribed as two capsules/day. Also, to treat hair loss and female baldness, aloe vera shampoo and Aloe vera ampoules were prescribed for home use.

After two months (May 2020), there was a noticeable improvement in her hair growth and thickness with decreased hair loss. At this point the patient was prescribed use of Taraxaf[®], Indomirol (consisting of Italian broccoli flower 0.216 g, French Collie “Black Cauliflower” Leaves 0.108 g, plant roots stuck Shepherd “bistort” Japanese 0.04 g; each capsule is 360 mg; one capsule/day; Nutrimed Ltd, Ukraine), and home use derma roller (as massage equipment for activation of hair growth). After 7 months (September 2020), immunological, biochemical and hematological tests were performed to check the case prognosis, the results of which are shown in Table 2. There was an improvement in anti-tissue Transglutaminase IgG and Anti-tissue Transglutaminase IgA indicators (negative results). Also, Hb and Hct returned to normal values.

In November 2020, after 9 months of monitoring, the patient returned to gluten-containing foods as one loaf of wheat bread/per day, without any gastrointestinal complaints such as diarrhea or constipation. The hair improvement was 20% approximately, and the patient was

Table 2. Laboratory tests after 7 months of traditional herbal supplementation treatment

Tests	Result	Normal Range	Interpretation
Immunological tests			
Immunoglobulin A	1.13 g/L	0.7-4 g/L	Normal
Anti-tissue Transglutaminase IgG	Less than 0.1 U/mL ^a	Negative: less than 2.6 U/mL	Negative
Anti-tissue Transglutaminase IgA	2.2 U/ml	Negative: less than 2.6 U/mL	Negative
Biochemical tests			
Vitamin B 12	845 pg/mL	211-911 pg/mL	Normal
Vitamin D	20.4 ng/mL	Sufficiency: 30-150 g/mL	Insufficient
Ferritin, Serum level	11.3 ng/mL	10-291 ng/mL	Normal
Hematological test			
Hb	12.8 g/dL	12-16 g/dL	Normal
Hct	39.5 g/dL	42+/-5 g/dL	Normal
WBC	6.23 *10 ⁹ g/L	4-10 *10 ⁹ g/L	Normal
MCV	86.3 fL	80-100 fL	Normal
MCH	28.1 pg/cell	26-34 pg/cell	Normal
MCHC	32.5 g/dL	31-36 g/dL	Normal
RBC	4.57 *10 ¹² Cell/L	3.8-5.8 *10 ¹² Cell/L	Normal
RDW	15.2% ^b	4.6-13.5%	Increase
Neutrophil-segmented	58.1%	40-75%	Normal
Eosinophil	1.0%	1-6%	Normal
Basophil	0.4%	0-1%	Normal
Lymphocyte	34.0%	20-45%	Normal
Monocyte	7%	2-10%	Normal
Platelet count	262* 10 ⁹ /L	140-440*10 ⁹ /L	Normal
MPV	9.3 fL	7.2-11.1	Normal

^aThe high difference in the result reported during this period is due to the use of Indirect Enzyme-linked immunosorbent assay (ELISA), a method of detection, from a different company.

^bIncreased RDW indicates red blood cells of different sizes (microcytic: before ferrolina was used in this anemic patient, and Normocytic after ferrolina bid used)

Abbreviations: Hb, Hemoglobin; Hct, Hematocrit; WBC, White blood cell; MCV, Mean Corpuscular Volume; MCH, Mean Corpuscular Hemoglobin; MCHC, Mean Corpuscular Hemoglobin Concentration; RBC, Red blood cell count; MPV, Mean Platelet Volume.

very satisfied with the results. The patient was asked to continue using Indomirool (one capsule/day), ferrolina (two capsules/day), and the derma roller.

As part of the celiac disease follow-up, the EGD was repeated in July 2021. The EGD showed normal esophagus mucosa with a small 2 cm hiatal hernia, mild patchy erythema at the peripyloric region, patent and normal pylorus, mild bulbar duodenitis, and mild fissuring at D2. Specimens from random gastric biopsy and random duodenal biopsies were sent to the histopathology department as multiple fragments of

grayish tissue measuring in aggregate 0.3x0.4 cm. The final diagnosis of stomach biopsy was showed unremarkable gastric mucosa that was negative for *H. pylori* microorganisms, intestinal metaplasia, dysplasia, or malignancy. Microscopic examination of the small bowel biopsy showed unremarkable duodenal mucosa, and negative for increased intraepithelial lymphocytes, crypt hyperplasia, villous atrophy, granuloma, dysplasia, or malignancy.

DISCUSSION

A gluten-free diet is the only solution prescribed for CD patients, and it is used as a precaution to prevent symptoms or disease deterioration, not as a treatment.⁴ Epidemiological studies have confirmed that CD patients resort to using nutritional supplements and probiotics to improve quality of life and to treat related symptoms compared to patients who did not use these supplements.⁸ To our knowledge, there is not enough information on the use of alternative medicine and dietary supplementations for CD treatment, not to mention relieving symptoms. Therefore, the main purpose of the treatment protocol in the current case study was to investigate the effect of alternative and complementary therapy in remodeling/adapting the immune response by introducing herbal supplementation in CD patients, as CD is an autoimmune disease.

After approximately 7 months of following the prescribed herbal supplementation protocols, the patient’s health improved with mitigation of the CD symptoms. The improvements were noticed along with a significant decline in the immunological results (anti-tissue transglutaminase IgG and anti-tissue transglutaminase IgA), improved results in hematological tests (Hb and Hct), and the normal appearance of EGD and the unremarkable gastric and duodenal mucosa detected by the gold standard diagnostic tools of EGD and duodenal biopsy.

A proteomic study done by KhalKhal et al⁹ showed that CD patients had dysregulation in the oxidative/antioxidant status favoring the overproduction of reactive radicals and hence a pronounced oxidative stress. The study also showed irregularities in carbohydrate, lipid, and protein metabolism and the increase of inflammatory biomarkers. Therefore, based on these above-mentioned key points, the hypothesis of restoring these imbalanced pathways to their normal status can be a possible approach to alleviating or even treating CD.

In the current study, the active ingredients of the herbal supplement used in this study, in particular dandelion, olive, and nettle leaves, and turmeric possess known antioxidant activities and therefore could have eliminated the excessive free radicals noticed in CD patients and consequently halted the progression of the disease.¹⁰ Furthermore, being an inflammatory mediated disease, CD’s symptoms can be further reduced via the introduction of compounds and extracts that have anti-inflammatory activities. Again, the active compounds used in this study have well-known anti-inflammatory activities and immune-modulating action that

may have lessened the innate inflammatory body response in such a way as to reduce the mucosal damage of the small intestine which in turn reduced the severity of CD's symptoms.¹⁰

The gastrointestinal tract health's distribution and the harsh diet of total gluten-free foods can result in additional health problems such as deficiencies of vital vitamins and minerals, anemia, loss of hair, tooth loss, weight loss, osteoporosis, dermatitis, and other malabsorption-related diseases.² Dandelion, olive and nettle leaves, and turmeric are given in this study and are recognized for their rich nutritional values containing many essential macro- and micronutrients that can replenish the deficiencies occurring in CD patients.¹¹ Indeed, the study patient showed improvements observed by the positive biochemistry results and the 20% hair improvement. Moreover, ferrolina, aloe vera shampoo, and derma roll may have further played an important role in the corrections of anemia and hair loss in the patient.

In summary, the herbal supplementations used in the current study showed a significant improvement in the CD patient's gastrointestinal tract health. These improvements were characterized by the absence of gastrointestinal discomfort, relief of allergy onset upon the consumption of small quantities of gluten-containing foods, corrections of certain micronutrient deficiencies, and the reduction of small intestine wall degeneration. Our results provide a possible alternative treatment that can reduce CD severity. Nevertheless, this study reported only one CD case within a short period and therefore warrants further studies on a larger scale and for a longer period duration.

CONFLICT OF INTEREST

The material of the manuscript under the title of "Remodeling Immune Response in A Celiac Disease Patient Using Herbal Supplementation: A Clinical Case-Study" is original research, has not been previously published and has not been submitted for publication elsewhere while under consideration. There are no conflicts of interest.

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AUTHOR CONTRIBUTION

Mahmoud, F.I.: writing draft and revision
Alhilo, I: diagnosis, following up patient, writing, revision
Alhilo, S: diagnosis, following up patient, writing, revision
Hasan, H: case description and case follow up with laboratory analysis
Alkhaleedy, A: lab tests and writing draft
Alkhatib, B: writing draft, data collection, analysis

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