

# Pediatric Patient with a Celiac Crisis (Rare Presentation of a Common Disease) Case Report and Literature Review

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## Abstract

Celiac disease (CD) is a systemic chronic immune-mediated disorder that is associated with weight loss, diarrhea, and laboratory abnormalities. Celiac disease (CD) is a disease in which the mucosal lining of the small intestine is damaged in response to the ingestion of gluten and similar proteins, which are found in wheat, oats, rye, barley and other grains. Children with CD are very common [1].

Celiac crisis is a life-threatening syndrome in which patients with celiac disease have profuse diarrhea and severe metabolic disturbances. Celiac crisis is rare among the pediatric age group and not well documented. To improve awareness of this condition and to facilitate diagnosis, we reviewed cases of celiac crisis to identify presenting features and treatment strategies [1].

We present a 3-year-old boy who presented with severe weight loss, severe diarrhea, vomiting, abdominal distension, and lower limb edema. There was persistent hypoalbuminemia, hypokalemia, hypophosphatemia, and hypomagnesemia. Celiac disease was confirmed by histopathology, and the patient's condition improved on a gluten-free diet with a short duration of steroids.

**Keywords:** Celiac crisis; Celiac disease

## Introduction

Celiac Disease (CD) is a systemic chronic immune-mediated disorder triggered after the ingestion of gluten protein in genetically susceptible individuals [1]. CD is manifested by a variety of clinical signs and symptoms [2]. There are four types of celiac disease: 1- typical (classical) CD is common in the pediatric age group with gastrointestinal symptoms, positive celiac antibodies and abnormal small intestine biopsy results; 2- silent CD manifests with no gastrointestinal symptoms but with positive celiac antibodies and abnormal small intestinal biopsy results; 3- latent (potential) CD manifests with no gastrointestinal symptoms or positive celiac antibodies but with normal small intestinal biopsy results; and 4- atypical (non-classical) CD is presented with fatigue, constipation, anemia, osteoporosis, dermatitis herpetiformis (rash), neuropathy, infertility, etc. Classical CD is common in children less than 2 years old and is manifested by symptoms of malabsorption such as chronic diarrhea, poor appetite, vomiting, weight loss and failure to thrive. On the other hand, non-classical CD is more common in older children and adolescents with extraintestinal symptoms such as iron deficiency anemia, decreased bone mineralization, neuropathy, and unexplained increases in liver enzymes [2].

Celiac crisis is a life-threatening syndrome in which celiac disease causes acute dramatic metabolic derangements. Celiac crisis includes severe diarrhea, hypoproteinemia, and metabolic and electrolyte disturbances significant enough to require hospitalization. 1, 2 The term 'Celiac crisis' was first discovered in literature from 1953 when Anderson and di Sant-Agnese reported the clinical course of 58 children with Celiac disease, 35 of whom presented with Celiac crisis. Children with Celiac crisis have a fatality rate of 90% and high morbidity and mortality. However, since this initial report, no individual publication has described more than three cases of Celiac crisis [2]. Celiac crisis is a life-threatening complication of CD rarely seen today [2,3].

## Case Presentation

A 3-year-old boy presented at our hospital with vomiting, diarrhea and weight loss for 1 month. His weight loss was significant,

and he lost 42% of his weight in the last month. He also complained of abdominal distention and upper and lower limb swelling. On physical examination, the patient's body weight and height were 9.3 kg and 90 cm, respectively (his weight-to-height percentile was less than a 3<sup>rd</sup>). His vital signs were stable. The patient was looking ill with a senile face, sunken eyes, dehydration, fair perfusion, muscle wasting, loss of subcutaneous fat, and bilateral pitting with lower limb edema. A soft distended abdomen was observed with no tenderness or hepatosplenomegaly (Figure 1,2 and 3).



**Figure 1:** Picture shows abdominal distension



**Figure 2:** Picture shows abdominal distension. Severe malnourishment can be seen in the muscle wasting



**Figure 3:** Severe malnourishment can be seen in the muscle wasting (Side way)

On laboratory investigation, the patient's complete blood count analysis was normal, except for mild anemia. Peripheral smear showed anisocytosis with mild microcytic hypochromic anemia. Erythrocyte sedimentation rate was 1 mm/L, and C-reactive protein was negative. Liver function tests were normal. Renal function tests were normal. There was hypokalemia, hypomagnesemia, hypophosphatemia and hypoalbumenia (re-feeding syndrome) (Table 1). A test of thyroid function was abnormal, as the patient's thyroid stimulating hormone was 8.3  $\mu$ IU/mL and free thyroxin was 10.65 pmol/L (normal values for this age are 0.27-4.2 and 12-22, respectively). The patient's lipid profile was within normal range. His albumin scan (isotope imaging to rule out primary intestinal protein losing enteropathy) was negative. Serological tests for hepatitis, salmonella, and Brucella were negative. IgG, IgM and IgE were within normal ranges. In addition, ferritin level and iron were normal, while iron binding capacity was low (7  $\mu$ mol/l). Vitamin B12 and folic acid were normal, but Vitamin D3 was low TTG 380. Urine and blood cultures were negative. Abdominal ultrasonic examination showed an increase in Liver size by 1 cm with a distended gall bladder and an increase in echogenicity in both kidneys. Chest X-ray, echocardiography, and abdominal CT-scan results were normal. The patient's albumin scan (99 m-Tc-human serum albumin performed) indicated that there was no detectable intestinal protein loss or enteropathy. Upper gastrointestinal endoscopy showed edematous mucosa with no ulceration in Duodenum1 and Duodenum. While performing endoscopy, a biopsy was taken and revealed complete villous atrophy, as well as the loss of villi with severe crypt hyperplasia and infiltrative inflammatory lesions (stain CD3 positive) –Marsh 3C in duodenal biopsy (Figure 1,2,3 and 4).

	Upon Admission	After GFD+ steroid in 3 days	After three months	After 6 months
<b>Weight</b>	9.3 KG	10.6 KG	14.4 KG	20.5 kg
<b>Height</b>	90 cm	90 cm	93.5 cm	98 cm
<b>Growth chart parameter (weight for height)</b>	Weight < 3 <sup>rd</sup> Hight < 3 <sup>rd</sup>	Weight 5 <sup>th</sup> Hight 5 <sup>th</sup>	Wight > 25 <sup>th</sup> Hight 25 <sup>th</sup>	Weight =75 <sup>th</sup> Height =75 <sup>th</sup>
<b>HB</b>	9 mg \dl	9.6 mg\dl	12 mg \dl	13 mg/dl
<b>MCV</b>	low	low	normal	normal
<b>Albumin</b>	13	Increased to 19 mg\dl (without albumin transfusion)	34.5 mg/dl	38 mg/dl
<b>K</b>	3.2		4.2	Normal
<b>Ph</b>	0.6 low	0.96 normal without phosphate given	1.86 normal	Normal
<b>Mg</b>	0.5 low	0.68 without magnesium given	0.84	Normal
<b>Ca</b>	2.3		2.22	Normal
<b>Vit D</b>	3		75	Normal
<b>Serum Iron</b>	9			Normal
<b>IBC</b>	7			Normal
<b>Ferritin</b>	50			Normal
<b>FT4</b>	10.6		normal	Normal
<b>TSH</b>	8.3		normal	Normal
<b>TTG</b>	380		57	

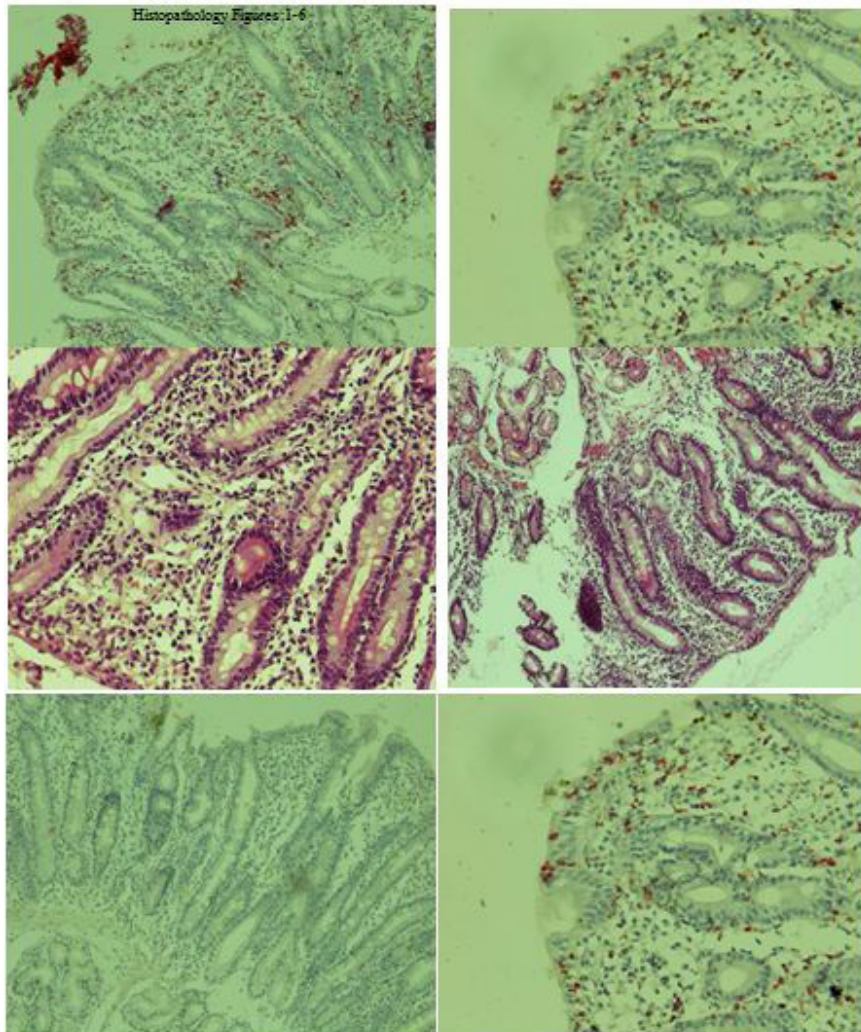
**Table 1:** Laboratory Summary



**Figure 4:** Picture shows post-treatment of celiac crisis



A gluten-free diet was introduced for the first 10 days, and the patient showed no significant clinical response (Figure 5). Apart of diarrhea and persistent edema, the metabolic disturbances were not corrected. Therefore, the patient was started on intravenous potassium chloride, potassium phosphate and magnesium sulphate, as well as albumin transfusion daily (1 gram per weight for 1 month). The patient was started on intravenous methylprednisolone for 3 days (2 mg/kg) once per day and continued on a gluten-free diet, as well, which resulted in improvement in the electrolyte abnormalities and serum albumin; in addition, the treatment rapidly decreased generalized edema. Steroids were discontinued, and the patient was to continue on a GFD indefinitely.



**Figure 5:** Histologic feature of celiac disease: increased intraepithelial lymphocytes (IELs) with villous atrophy of the duodenal mucosa

After a follow-up of three months, there was a significant improvement in the clinical condition, as well as normalization of the electrolyte disturbances, and the patient thrived well (Figure 4). A summary of the laboratory results is shown in (Table 1).

## Discussion

The most common symptoms in Celiac disease are diarrhea, vomiting, tetany, light headedness, and weight loss [4]. Additionally, afflicted children suffer from poor appetite, abdominal distention, abdominal pain, irritability, and failure to thrive. Some patients might not be aware that they have CD until they have a crisis episode, which is associated with metabolic abnormalities that require hospitalization. As Celiac disease is an immune-based reaction to dietary gluten, Immunoglobulin A (IgA TTG) is the preferred test for detecting Celiac disease in children over 2 years [4]. The classic form of the disease is diagnosed using serologic and histopathologic tests [5]. Anti-tissue transglutaminase antibody (anti-tTG), as the most sensitive and specific serology study, is used in suspected cases [1-4]. A positive serology study must be followed by endoscopy of the small intestine. Villous atrophy, crypt hyperplasia and increased intraepithelial lymphocytes (IELs, the threshold is > 25 lymphocytes in 100 enterocytes) are the main histopathologic findings for the confirmation of CD. Additionally, there are Marsh criteria for grading duodenal biopsies for potential Celiac disease [6], as follows [7]:

Marsh 0 = normal mucosa and villous architectures

Marsh 1 = normal mucosa and villous architectures but increased intra epithelial lymphocyte (IELS) infiltrative

Marsh 2 = enlarged crypts, increased crypt cell division, increased IELS (hyperplastic)

Marsh 3A = Partial villous atrophy, shortened blunt villi, mild lymphocytic infiltration, enlarged hyperplastic crypts

Marsh 3B = Subtotal villous atrophy, enlarged crypts with increased immature epithelial cells, presence of inflammatory cells

Marsh 3C = Total villus atrophy, and loss of villi, severe crypt hyperplasia, infiltrative inflammatory lesions

Marsh 4 = Total villous atrophy, hypoplastic crypts with normal depth, normal numbers of IELS

Celiac crisis is treated using a gluten free diet, while some patients may need systemic steroids or oral budesonide. Potassium, magnesium, and phosphate all may be found low in children with celiac disease as in our patient. This observation is referred to as refeeding syndrome [8]. However, our patient had re-feeding syndrome, and we managed with intravenous electrolyte replacement and NPO for 2 days [9]. This treatment was followed by NGT feeding slowly over 2 weeks until a diagnosis was reached by adjusting all electrolyte disturbances without TP. Our patient had significant metabolic disturbances with hypoalbuminemia, hypokalemia, hyponatremia, and hypophosphatemia. This outcome might indicate that he had entered into celiac crisis, which is an indication to use steroids in addition to prescribing a gluten-free diet.

Vitamin D deficiency in a Celiac disease patient is related to malabsorption. Calcium, vitamin D, and other nutrients that are essential for bone health are not absorbed well in Celiac disease patients. The classical histopathological findings in Celiac disease are an increased number of intraepithelial lymphocytes [10], crypt hyperplasia, and villous atrophy. Celiac crisis as a complication of CD is very rare but life threatening. Clinically, it is characterized by severe diarrhea, dehydration and metabolic disturbances such as hypokalemia, hypomagnesemia, hypocalcemia and hypoalbuminemia [11]. Celiac disease is treated by a gluten-free diet [12,13]. After the introduction of a gluten-free diet, our patient showed clinical improvement, but the electrolyte disturbances and albumin did not improve; in addition, his weight remained static. After giving him steroids for five days, he started to gain weight, and the electrolyte abnormalities improved. This outcome was reported by other investigators, and they used steroids for patients with Celiac crises [8,14,15].

## Conclusion

CD is complicated to diagnose, as it is associated with misleading symptoms; many children may present at the clinic with symptoms such as vomiting, diarrhea, and abdominal distention. CD cannot be confirmed until a duodenal biopsy is taken and complete villus atrophy is revealed. Gluten free- diet can show improvement in treating CD, but when the case enters crisis, the introduction of steroids may become necessary to see improvement in the patient.

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