# Extra-Digestive Manifestations of Celiac Disease: A Case Study and Review of Literature

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## Abstract

Celiac disease is a multisystem autoimmune condition characterized by an inappropriate immune response to gluten. Typical symptoms involve digestive issues, stunted growth, and malabsorption syndrome. However, extra-digestive autoimmune manifestations may precede or develop concurrently with the digestive symptoms during the disease's progression, complicating the diagnosis and prognosis.
We present a case of a 9-year-old girl initially followed for alopecia and epilepsy. The diagnosis of celiac disease was established during the assessment for nutritional rickets. The disease's progression under a gluten-free diet was marked by the onset of growth hormone deficiency (GHD), necessitating substitutive treatment. Managing multiple autoimmune conditions in this girl poses significant challenges.
**Mots-clés:** Celiac Disease, Child, Nutrition, Autoimmune Diseases.

## RÉSUMÉ

La maladie cœliaque est une condition auto-immune multi systémique caractérisée par une réaction immunitaire inappropriée au gluten. Les symptômes caractéristiques incluent des manifestations digestives, un retard de croissance et un syndrome de malabsorption. Cependant, des manifestations auto-immunes extra-digestives peuvent précéder ou apparaître simultanément avec les symptômes digestifs au cours de l'évolution de la maladie, compliquant ainsi le diagnostic et le pronostic.
Nous décrivons le cas d'une fillette de 9 ans suivie initialement pour alopécie et épilepsie. Le diagnostic de la maladie cœliaque a été établi lors de l'évaluation d'un rachitisme carentiel. L'évolution de la maladie sous régime alimentaire sans gluten a été marquée par l'apparition d'un déficit en hormone de croissance (GHD), nécessitant un traitement substitutif. La gestion de multiples atteintes auto-immunes chez cette fillette présente des défis importants.
**Key words:** Maladie Cœliaque, Enfant, Nutrition, Maladies Auto-Immunes.

## Introduction

Celiac disease (CD) is an autoimmune enteropathy characterized by an abnormal immune response to gliadin, a protein present in gluten [1]. This immune reaction results in villous atrophy and damage to the intestinal mucosa [2]. The clinical manifestations can be either absent or minimal, primarily characterized by chronic diarrhea [3]. However, there is an increasing incidence of atypical forms of the disease, which can present with diverse symptoms and may be associated with other autoimmune disorders [1,3].
Therefore, the significance of our research is to highlight the extra-digestive manifestations by investigating the association of multiple pathologies with celiac disease, as exemplified in our case study.

## Observation

We report the case of a 9-year-old girl with fourth-degree consanguinity. She had a history of epilepsy treated with Lamatrogin since the age of four years old. She presented with pallor associated with confirmed dermatological alopecia areata through biopsy (figure1).

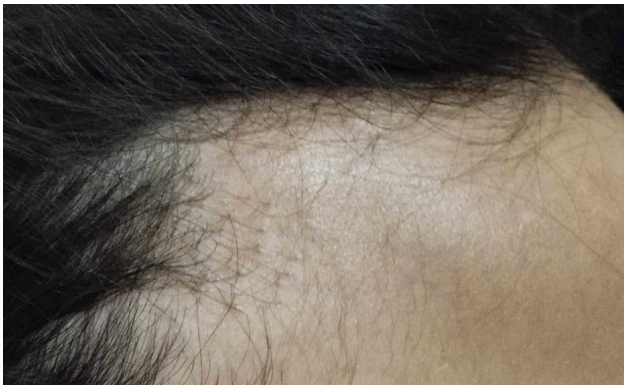

**Figure 1:** Image of the patient's alopecia areta

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Initial examination showed weight at -1Standard Deviation (SD) and height et -2 SD (figure2).
Blood tests showed a hypochromic microcytic anemia, normal liver function along with hypocalcemia and 25-OH vitamin D deficiency <8.1 ng/ml (>20 ng/ml) with a PTH level ranging from 6 to 50 pg/ml. Due to anemia, hypocalcemia, and anorexia, serology for celiac disease was requested and came positive, with anti-transglutaminase antibodies >200 mg/l (<10 mg/l). An esophagogastroduodenoscopy showed normal findings, but biopsies revealed stage 3 villous atrophy according to Marsh classification.
The evolution was marked by growth stagnation, with weight gain at 0kg per year and height 0cm per year (figure2).

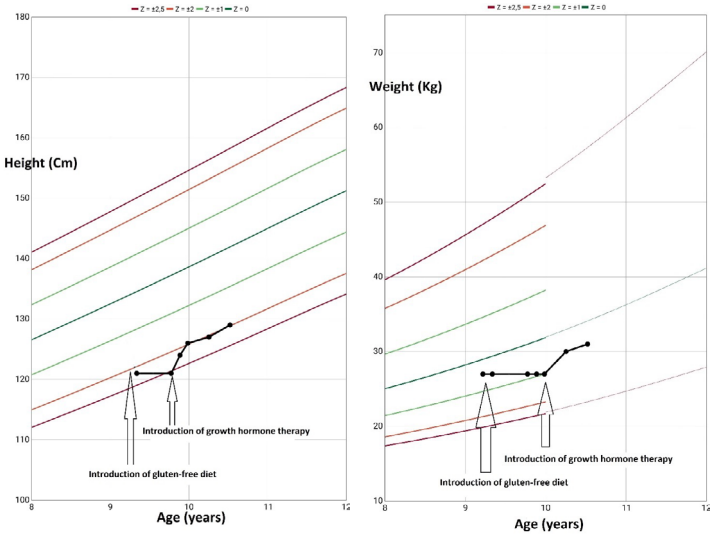


**Figure 2:** Weight (Kg) and Height (Cm) versus age (Year) curvue.

Bone age showed a 5-year delay compared to chronological age. A karyotype was performed, resulting in 46, XX . Endocrines causes have been suspected and a thyroid panel came within the normal range, with TSH at 4.6 UI/ml (<4 UI/ml). IGF1 levels were decreased compaired to liver function at 132.31 ng/ml (>247 ng/ml and <396 ng/ml). In view of these results, insuline stimulation test was made and confirmed a complete deficiency in growth hormone response at 7.1mUI/L (< 10 mIU/L (3.3 µg/L)).
Furthermore, she didn't exhibit any corticotrope deficiency. Despite the presence of epilepsy and growth hormone deficiency, the suspicion of lymphocytic hypophysitis was discarded due to the absence of anti-NMDA receptor antibodies and normal findings on the cerebral MRI.
The diagnosis of celiac disease associated with growth hormone deficiency was established, and she was placed on a gluten-free diet and hormone growth therapy. The evolution was marked by improvement in stunted growth, with height at -2 SD (figure2) and improvement in rickets with correction of vitamin D deficiency and serum calcium levels.

## Discussion

A 9-year-old girl, with fourth-degree consanguinity and epilepsy, showed pallor and confirmed alopecia areata. Initial examination revealed underweight and stunted growth. Blood tests indicated anemia, hypocalcemia, and vitamin D deficiency. Positive serology for celiac disease, along with growth hormone deficiency, led to gluten-free diet and hormone therapy. Treatment led to improved growth and corrected deficiencies.
Celiac disease has traditionally been defined in children as a chronic enteropathy with villous atrophy resulting from an inappropriate immune response of the intestinal mucosa to gluten found in wheat, barley, and rye [3] . The prevalence in Tunisia is estimated to be from 1/157 to 1/175 [4].
ypically, in its classical form, celiac disease manifests in infants older than 6 months, shortly after the introduction of gluten into their diet [3]. It is characterized by chronic diarrhea with bulky, malodorous stools, along with symptoms such as loss of appetite and lethargy [1,2]. Clinical examination reveals abdominal bloating and signs of malnutrition, including muscle and adipose tissue wasting [3,4]. The nutritional impact is confirmed by a deviation from the weight growth curve, sometimes accompanied by a secondary slowdown in stature growth rate [2,4].
Over the past few decades, the incidence of atypical forms of celiac disease has been steadily increasing, leading to delayed diagnosis and treatment [5]. Indeed, celiac disease is now recognized as a multi-system autoimmune disorder that affects various organs, with a significant impact on the skin, resulting in dermatological manifestations [3]. The most common manifestation is dermatitis herpetiformis (DH), also known as Duhring's disease, with a prevalence ratio of 1:8 between DH and CD in Finland and the United Kingdom [6]. Urticaria and atopic dermatitis are also commun with CD [3,6]. Alopecia areata has been associated with celiac disease and has been described in the literature [7], as seen in our case where the initial presentation was pallor associated with confirmed histological alopecia. The prevalence of gliadin antibody in patients with alopecia areata is estimated to be about 1 in 116 [3,7]. Another study estimated the prevalence of anti-gliadin antibodies in patients with alopecia areata to be about 18 in 100 [6]. These results raise the question of whether screening for celiac disease should be considered in all individuals presenting with alopecia areata.
Neurological manifestations have also been described, such as epilepsy in our patient who has been on anti-epileptic medication for the past 4 years. Epilepsy is one of the most common neurological disorders, affecting approximately 50 million individuals worldwide, mainly in developing countries [8]. In pediatric patients with epilepsy of unknown cause, the prevalence of celiac disease was found to be 1.83% [6,8]. Neurological complications are estimated to occur in 6%-10% of patients with celiac disease [3,8] such as peripheral neuropathy and cerebellar ataxia, also known as gluten ataxia, which is one of the most common neurological symptoms in patients with celiac disease, with a prevalence of 0.6% [8].

In our described case, the patient also presented with stunted growth that was not improved by a gluten-free diet. Associations with endocrine disorders have been described, including an association between celiac disease and growth hormone deficiency (GHD). The clinical similarities between GHD and celiac disease can pose diagnostic challenges [9], as both conditions can present with stunted growth and symptoms of malabsorption [3,9]. This can lead to misdiagnosis or delayed diagnosis.
It is important for clinicians to maintain a high level of suspicion and consider alternative diagnoses when treatment responses are unsatisfactory [9]. The association between GHD and celiac disease in children is rare [10], as highlighted by a review of the literature. The limited number of reported cases may be due to the rarity of this association and difficulties in recognition. Only 0.23% of children with celiac disease are at risk of having growth hormone deficiency [10]. The mechanism of impaired hypothalamic control of growth hormone secretion in the context of celiac disease is not well understood [6,10]

## Conclusion

In conclusion, celiac disease is a chronic enteropathy characterized by an inappropriate immune response to gluten, primarily affecting the intestinal mucosa. While it traditionally presents with gastrointestinal symptoms in infants, atypical forms of the disease have become more prevalent, leading to delayed diagnosis and treatment. Clinicians should be aware of the various associated conditions and consider them in the diagnostic process to ensure timely intervention and appropriate management.

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