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CASE REPORT

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Uncovering the link between celiac disease and hypopituitarism: a case report and review of literature

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Abstract

Background Celiac disease, an autoimmune condition triggered by gluten-containing diet, is known to primarily manifest as intestinal symptoms, but can also lead to extraintestinal complications, including endocrine abnormalities and autoimmune disorders. This case report outlines a patient with celiac disease who developed hypopituitarism and explores the possible pathophysiological links between these two conditions.

Case presentation We report a case of a 19-year-old female who presented with lethargy, weakness, delayed menarche, and failure to thrive. Subsequent investigations revealed microcytic anemia with decreased serum ferritin and vitamin D levels. Following the identification of abnormal bone age on X-ray, a hormonal profile was requested which revealed panhypopituitarism. After undergoing a diagnostic workup for her gastrointestinal symptoms, she was eventually diagnosed with celiac disease, and her symptoms improved significantly following gluten restriction.

Conclusion Panhypopituitarism has a possible association with celiac disease, and this case highlights the importance of close monitoring and appropriate management to prevent long-term health consequences. Additional research is necessary to gain a comprehensive understanding of the link between celiac disease and endocrine disorders.

Keywords Celiac disease, Coeliac disease, Panhypopituitarism, Hypopituitarism, Autoimmune hypopituitarism, Hypophysitis, Endocrinopathy

Background

Celiac disease is a common autoimmune disorder that presents in genetically susceptible patients in response to food items containing gluten such as rye, barley, and wheat [1]. Although celiac disease is primarily associated with gastrointestinal symptoms, it has also been linked to a variety of extra-intestinal manifestations, including endocrine disorders [2]. The occurrence of hypopituitarism, a condition characterized by a deficiency of one or more pituitary hormones, has been documented in some patients with celiac disease, albeit with an indeterminate frequency [3]. Most patients present with the manifestations of deficient hormones, such as failure to grow, delayed puberty, and fatigue, which makes the diagnosis very challenging. Multiple studies have shown the association of celiac disease with type 1 diabetes mellitus and autoimmune thyroid disease, but it can rarely present with adrenal insufficiency, hypopituitarism, and hypoparathyroidism [4]. The management of these conditions hinges upon effective control of the primary disease, including strict adherence to a gluten-free diet as well as targeted hormone replacement therapy to address any specific deficiencies identified.

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Case presentation

A 19-year-old girl presented to us with a long history of lethargy, weakness, short stature, failure to thrive, and delayed puberty. The gradual and persistent progression of these symptoms had a deleterious impact on the patient's activities of daily living. On further inquiry, her parents reported that she was doing well till 10 years of age and had achieved normal developmental milestones; however, she has failed to achieve significant growth thereafter. Her past medical and surgical history was not significant. She had received all the childhood vaccination; furthermore, her past history of any allergies was not significant. All immediate family members had normal physical parameters, appropriate for their ages. The singular pertinent aspect of her medical history pertained to her menstrual cycle, whereby menarche was delayed until the age of 17 years and was subsequently initiated only upon consultation with a Gynecologist and with the aid of oral contraceptive pills (OCPs).

Upon conducting a general physical examination, a young female was observed lying in bed with a pale, thin, lean, and cachectic appearance; however, she was well-oriented and demonstrated intact cognitive function. Vitals record showed a blood pressure of 100/70 mmHg with a pulse of 75 beats per unit with normal oxygen saturation. Upon systemic examination, the patient's chest was found to be clear bilaterally, central nervous system findings were within normal limits, and the abdomen was soft and non-tender without any palpable organomegaly. Furthermore, the cardiovascular exam showed normal heart sounds without any additional sounds detected. Gynecological examination revealed stage 3 tanner staging. Laboratory findings are shown below (Table 1).

X-ray of left hand and wrist was done which showed a bone age of 15 years, while her actual age was 19 years. Ultrasonography of the abdomen and echocardiogram were done, which were normal. Following the identification of abnormal bone age on X-ray, a hormonal abnormality was suspected and subsequently, a hormonal profile was requested. The results are as follows (Table 2).

Following a presumptive diagnosis of pan-hypopituitarism based on the hormonal profile, our curiosity was aroused to pursue a definitive diagnosis. Thorough inquiry and examination helped to eliminate various potential etiologies, including but not limited to prior head trauma, radiation exposure, surgical intervention, post-partum necrosis, anorexia nervosa, and inflammatory or infiltrative causes of hypopituitarism. MRI brain was done to rule out local causes, which did not show any abnormality. Perimetry was also normal. She was started on hormone replacement therapy and was requested to come for a follow-up evaluation after 3 months. Subsequent to 3 months, she reported slight amelioration but manifested fresh symptoms of polydipsia and watery diarrhea, which led to her readmission for further diagnostic evaluation. We started proper intake and output records and measured serum and urine osmolarities (Table 3).

These results pointed towards diabetes insipidus, and she was started on desmopressin. Her fluid intake decreased to 4 L and output to 3 L, accompanied by normalization of both serum and urine osmolarities.

Table 1 Basic metabolic profile

Labs	Normal range	Result
White blood cells (per mm^3)	4000–11,000	6100
Hemoglobin (g/dL)	12–16	10.1
Mean corpuscular volume (fL)	80–100	72
Platelets (per mm^3)	1,50,000–4,50,000	2,23,000
Serum sodium (mmol/L)	135–150	131
Serum potassium (mmol/L)	3.5–5	4.4
Alanine transaminase (U/L)	4–36	25
Serum bilirubin (mg/dL)	0.1–1.2	0.6
Serum creatinine (mg/dL)	0.5–1.1	0.8
Serum ferritin (ng/mL)	40–200	20
Random blood sugar (mg/dL)	70–140	101
Serum calcium (mg/dL)	8.5–10.2	8.9
Vitamin D level (ng/mL)	20–50	18

Table 2 Hormonal profile

Investigation	Normal value	Result	Interpretation
Estradiol (pg/mL)	30–400	28	↓
Testosterone (ng/dL)	15–70	14.88	↓
FSH (IU/L)	5–20	6.7	Normal
LH (IU/L)	9–76	8.25	↓
Prolactin (mIU/L)	40–530	255	Normal
Growth hormone (ng/mL)	1–14	0.88	↓
ACTH (pg/mL)	10–60	2.4	↓
TSH (mIU/L)	0.5–5	0.4	↓
Free T4 (ng/dL)	0.9–2.3	0.5	↓
Free T3 (pg/dL)	260–480	250	↓

Table 3 Workup for polydipsia

Intake in 24 h	11 L
Output in 24 h	7 L
Serum osmolarity	309 mOsm/kg
Urine osmolarity	60 mOsm/kg
Random blood sugar	104 mg/dL
HBA1c	Normal

Considering the co-occurrence of diarrhea, our index of suspicion for an underlying enteric pathology increased, and thus we initiated screening measures for celiac disease in the patient. Surprisingly, both serum anti-tissue transglutaminase (anti-TTG) IgA and anti-endomysial antibodies were positive. An esophagogastroduodenoscopy (OGD) was performed, revealing pale mucosa and early signs of celiac disease, including villous atrophy and mild inflammation. Upon obtaining these results, we arrived at a definitive diagnosis of autoimmune hypophysitis concomitant with celiac disease. She was started on a gluten-free diet along with the continuation of hormonal therapy. The patient and her parents were provided comprehensive counseling on the significance of adhering to a gluten-free diet, along with detailed elucidation of the disease prognosis. The patient attended a follow-up visit 3 months after the initial presentation and reported alleviation of her symptoms, including a resolution of the abdominal complaints of diarrhea and the urinary symptoms of polydipsia and polyuria.

Discussion

Celiac disease may manifest atypically without the classic symptoms of diarrhea and abdominal pain, thereby confounding the differential diagnosis and presenting a formidable challenge for clinicians to decipher. Since it is an autoimmune disease, it may be accompanied by many other autoimmune diseases, and sometimes patients present with the manifestations of other autoimmune diseases instead of the typical signs and symptoms of celiac disease [5]. Celiac disease has been linked with a myriad of disorders, including endocrine conditions commonly managed by endocrinologists, such as type 1 diabetes mellitus, autoimmune thyroid disease, Addison disease, osteomalacia, secondary hyperparathyroidism, vitamin D or iron deficiency, fertility issues, hypogonadism in men, and autoimmune hypopituitarism [6, 7]. In this case, the presentation of weakness, short stature, and failure to thrive in a patient with celiac disease highlights the possibility of hypopituitarism, emphasizing the challenge posed by the non-specific and elusive nature of the former condition. A study conducted in Italy was the first to report the existence of anti-pituitary antibodies (APA) in children newly diagnosed with CD, thereby establishing a foundation for the autoimmune implication of the pituitary gland [8]. Interestingly in a study on 74 treatment-naïve celiac disease patients, 8 (10.8%) patients also were found to have functional hypopituitarism and 7/54 (12.9%) having isolated hypogonadotropic hypogonadism [9]. According to the study conducted by Bozzola and colleagues, among 1066 children with short stature, three were diagnosed with celiac disease in conjunction with growth hormone deficiency [10]. Studies have reported that treating celiac disease in these patients also improves the associated endocrine diseases. The main stay of treatment in celiac disease is the gluten free diet, which helps in the overall prognosis of the disease. A comprehensive observational study revealed that individuals with subclinical autoimmune hypophysitis and celiac disease could potentially achieve remission of pituitary disease or halt its progression to a clinical stage by adhering to a gluten-free diet [11]. However, a different study put forward that autoimmune hypophysitis may ensue in children with celiac disease who do not achieve catch-up growth despite maintaining adherence to a gluten-free diet [12]. In our case, the patient showed clinical improvement in all his symptoms following gluten restriction. Further investigation is warranted to fully understand the association between celiac disease and endocrinopathies, as well as to determine the efficacy of gluten-free diet in reversing these conditions.

Conclusion

Celiac disease is an autoimmune condition which presents primarily with gastrointestinal symptoms. The possibility of concurrent autoimmune diseases in individuals with celiac disease necessitates a comprehensive evaluation. Additionally, the lack of gastrointestinal symptoms in many celiac disease cases underscores the importance of screening for the disease in young patients presenting with endocrine abnormalities especially panhypopituitarism. Such an approach not only enables early detection and appropriate management but also mitigates the risks of long-term complications associated with untreated, asymptomatic patients.

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Authors' contributions
Hameed Haidar Khan, Imran Ullah, Javeria Rufaq, Qaiser Wadood, Imad Majeed, Salman Khan, Hameed Haidar Khan, Qaiser Wadood, and Imran Ullah collected the data and prepared the manuscript. Imad Majeed, Salman Khan, and Javeria Rufaq wrote the discussion and revised the manuscript critically. All the authors approved the final manuscript.

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Declarations

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Consent for publication
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Competing interests
The authors declare that they have no competing interests.

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