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Celiac Disease Revealed by Prolonged Unexplained Fever: A Diagnostic Challenge

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Abstract **Case Report**

Celiac disease (CD) is a chronic immune-mediated disorder triggered by gluten ingestion in genetically predisposed individuals, increasingly recognized for its diverse extra-intestinal manifestations. We report a rare case of a 32-year-old woman presenting with prolonged fever of unknown origin as the sole manifestation of CD. The patient experienced recurrent high-grade fevers associated with fatigue over several months, without gastrointestinal symptoms. Initial investigations revealed iron-deficiency anemia and elevated inflammatory markers, while infectious, neoplastic, and autoimmune workups were unremarkable. Further evaluation demonstrated markedly elevated tissue transglutaminase IgA levels. Upper gastrointestinal endoscopy showed characteristic duodenal mucosal changes, and histopathology confirmed villous atrophy with intraepithelial lymphocytosis (Marsh 3a), establishing the diagnosis of CD. Initiation of a strict gluten-free diet resulted in rapid resolution of symptoms and normalization of serological markers within six months. This case highlights CD as a potential and rare cause of fever of unknown origin, emphasizing its status as a clinical chameleon with atypical presentations. Incorporating CD screening into the diagnostic approach for unexplained fever may facilitate early diagnosis and prevent long-term complications.

Keywords: Celiac disease, Fever of unknown origin, Extra-intestinal manifestations, Tissue transglutaminase, Iron-deficiency anemia, Gluten-free diet.

INTRODUCTION

Celiac disease (CD) is a chronic immune-mediated enteropathy triggered by gluten ingestion in genetically predisposed individuals. It is increasingly recognized as a multisystem autoimmune disorder that can present with a broad spectrum of clinical manifestations, often diverging markedly from the classic malabsorption syndrome and creating substantial diagnostic challenges [1]. Although historically linked to overt gastrointestinal symptoms, contemporary evidence shows that non-classical phenotypes now predominate, rendering CD a "clinical chameleon" with diverse extra-intestinal features that frequently mislead clinicians. Among these atypical presentations, fever of unknown origin (FUO) emerges as a noteworthy, albeit uncommon, manifestation of CD [2].

Here, we present a rare case of a young female patient who presented a prolonged isolated fever that revealed a celiac disease.

CASE PRESENTATION

A 32-year-old woman with no prior medical history presented to our hospital for a prolonged fever that has been evolving over several months. Fevers ranged from 38,5 to 39,5 degrees Celsius with marked fatigue, occurring monthly with each episode lasting 5 days per episode, without having any gastrointestinal symptoms or extra-intestinal manifestations. The physical examination was normal. Laboratory tests revealed an iron deficiency anemia (11 g/dL), C reactive protein concentration (CRP) was 56 mg/l, with normal liver and kidney function. Procalcitonin and tumor markers were negative.

Laboratory findings are summarized in Table 1.

Table 1: Initial laboratory findings on presentation

Test	Patient's value	Reference range
Haemoglobin (Hb)	13	12−16 g/dL
Platelets (PLT)	230	150–400G PLT/µL
WBC	7590	4,500 – 11,000 cells/µL
CRP	18	<10 mg/L
ALT	22	7 to 56 U/L
AST	17	8 to 48 U/L
Creatinine	0,8	0.6-1.3 mg/dL
Tumor markers	Normal	-

WBC, white blood cell; CRP, C-Reactive Protein; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

All viral serologies (Epstein–Barr virus, cytomegalovirus, parvovirus B19, HIV, hepatitis B and C) as well as Wright and Felix serologies were negative. Both chest X-ray and abdominal ultrasound were without anomalies, as well as thoracic echocardiography.

Her work up continued with further evaluation for autoimmune diseases and she was found to have a positive tissue transglutaminase IgA over 150 UI. She underwent upper gastro intestinal endoscopy that showed a mosaic pattern of the duodenal mucosa with reduced duodenal folds (Figure1).

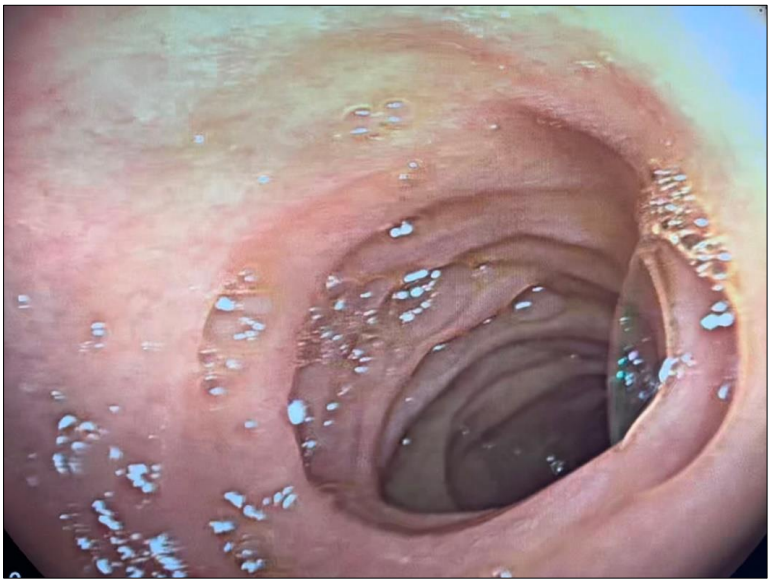

Figure 1: Endoscopic image showing reduced duodenal folds

The histopathology report revealed mild villous atrophy with crypt hyperplasia and increased intraepithelial lymphocytosis (>30/100 enterocytes), corresponding to Marsh 3a classification. The diagnosis of a celiac disease was established. The patient was then started on a strict gluten free diet (GFD), which led to a rapid resolution of her fevers and fatigue with the normalization of her serologies after six months.

DISCUSSION

Celiac disease is now recognized as a multisystem autoimmune disorder that can present as fever of unknown origin. This atypical presentation is rooted in the gluten-driven activation of lamina-propria CD4 T cells, which release pro-inflammatory cytokines such as interleukin-1(IL-1), (IL-6), tumor necrosis factor-alpha (TNF-α), and interferon-gamma (IFN-γ). These cytokines act as endogenous pyrogens on the hypothalamus to raise the temperature set-point [3].

The clinical profile of CD has shifted significantly over the past decades, with non-classical phenotypes now prevailing over the classical malabsorption syndrome. As a true clinical chameleon, CD manifests through a diverse array of extra-intestinal symptoms that frequently mislead the diagnosis [4]. Beyond fever, common atypical presentations include musculoskeletal disorders such as osteopenia or osteoporosis, which may affect up to 52% of patients, and hematologic abnormalities like iron-deficiency anemia (34%) or hyposplenism [5]. Neurological manifestations, including gluten ataxia, peripheral neuropathy, and migraines, are increasingly reported, alongside reproductive complications such as infertility and recurrent miscarriages. Furthermore,

mucocutaneous signs like dermatitis herpetiformis and recurrent oral aphthous ulcers often serve as the sole indicators of underlying enteropathy [6, 7].

In this case, the patient's markedly elevated tissue transglutaminase IgA (>150 UI) exceeded the 10× upper-limit threshold that recent guidelines of the ACG and European Society for the study of coeliac disease endorse as sufficient for a non-biopsy approach [8, 9]. However, diagnosis was supported by the endoscopic "mosaic pattern" and Marsh 3a histology. Prompt initiation of a strict gluten-free diet led to rapid symptom resolution, which is vital as delayed diagnosis has been linked to chronic endothelial activation, accelerated atherosclerosis, and increased risk of CD-related malignancies such as small-bowel adenocarcinoma or lymphoma [10].

While the GFD remains the cornerstone of therapy, adherence challenges affect up to 70 % of adults, prompting investigation of adjunctive agents. Emerging non-dietary options like zonulin antagonism (larazotide acetate) and gluten-degrading enzymes (e.g., IMGX-003) have shown promise in phase II/III trials, aiming to restore barrier integrity and reduce gluten-induced immune activation, and may eventually complement the GFD for patients with refractory symptoms [11-13].

Conclusion

This case underscores the importance of incorporating CD serology into the diagnostic algorithm for FUO and unexplained systemic inflammation, even when classic gastrointestinal symptoms are absent. Prompt recognition and GFD initiation can prevent prolonged inflammation and its downstream complications.

References

1. Daley SF, Haseeb M. Celiac Disease. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025
2. Cooney MJ, El-Matary W. Celiac disease presenting as fever of unknown origin. Case Rep Gastrointest Med. 2013;2013:676327. 10.1155/2013/676327.
3. Cioni G. Celiac disease presenting as fever of unknown origin in the adult: the role of undiagnosed celiac disease in systemic atherosclerosis. Pol Ann Med. 2018;47:1-4.
4. Blom JJ, Gidrewicz D, Turner J, et al. Diagnosis and management of celiac disease. CMAJ. 2025;197:E1258-E1265. 10.1503/cmaj.230091.
5. Volta U, Caio G, Stanghellini V, et al. The changing clinical profile of celiac disease: a 15-year experience (1998-2012) in an Italian referral center. BMC Gastroenterol. 2014;14:194. 10.1186/1471-230X-14-194.
6. Caio G, Volta U, Ursini F, et al. Celiac disease: a comprehensive current review. BMC Med. 2019;17:142. 10.1186/s12916-019-1380-z.
7. Valitutti F, Fasano A. Breaking down barriers: how understanding celiac disease pathogenesis informed the development of novel treatments. Dig Dis Sci. 2019;64:1748-1758. 10.1007/s10620-019-05646-y.
8. Rubio-Tapia A, Hill ID, Kelly CP, et al. American College of Gastroenterology guidelines update: diagnosis and management of celiac disease. Am J Gastroenterol. 2023;118:59-76. 10.14309/ajg.0000000000002075.
9. Al-Toma A, Zingone F, Branchi F, et al. European Society for the Study of Coeliac Disease 2025 updated guidelines on the diagnosis and management of coeliac disease in adults. Part 1: diagnostic approach. United European Gastroenterol J. 2025;13:1855-1886. 10.1002/ueg2.70119.
10. Caio G, Volta U, Ursini F, et al. Small bowel adenocarcinoma as a complication of celiac disease: clinical and diagnostic features. BMC Gastroenterol. 2019;19:45. 10.1186/s12876-019-0964-6.
11. Segura V, Ruiz-Carnicer A, Sousa C, et al. New insights into non-dietary treatment in celiac disease: emerging therapeutic options. Nutrients. 2021;13:2146. 10.3390/nu13062146.
12. Slifer ZM, Krishnan BR, Madan J, et al. Larazotide acetate: a pharmacological peptide approach to tight junction regulation. Am J Physiol Gastrointest Liver Physiol. 2021;320(6):G983-G989. 10.1152/ajpgi.00386.2020
13. Mazzola AM, Zammarchi I, Valerii MC, et al. Gluten-free diet and other celiac disease therapies: current understanding and emerging strategies. Nutrients. 2024;16:1006. 10.3390/nu16071006.