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Isolated polyarthritis revealing celiac disease: A case report

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Abstract

Nonclassical celiac disease is a diagnostic challenge for the practitioner. We report a case of a 28-year-old Moroccan woman who had been experiencing polyarthralgia and joint swelling for 8 weeks, despite treatment with nonsteroidal anti-inflammatory drugs and corticosteroids. On physical examination, there was effusion in the proximal interphalangeal joints, metacarpophalangeal joints, wrists, knees, and ankles. Laboratory tests revealed microcytic anemia, elevated levels of inflammation markers, low ferritin, and a low vitamin D level. An upper gastrointestinal endoscopy was performed to investigate the cause of anemia, revealing the loss of duodenal folds. Subsequently, a duodenal biopsy was performed, and serological testing for celiac disease was requested. Anti-transglutaminase-2 antibodies were elevated at 200 U/ml (normal < 15U/ml). The duodenal biopsy showed flattened duodenal mucosal epithelium. The patient was diagnosed with celiac disease. A gluten-free diet was started. Her joint symptoms resolved in 3 weeks. All blood tests returned to normal levels after 48 weeks. This case illustrates that celiac disease should be considered in cases of arthritis with an initial negative etiological workup.

Keywords

Case report, celiac disease, diagnosis, polyarthritis

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Introduction

Celiac disease (CeD) is an autoimmune disorder triggered by the ingestion of gluten in genetically predisposed individuals. The estimated average prevalence of CeD in the general population is approximately 1%.[1] CeD exhibits a wide range of clinical manifestations, leading to diagnostic challenges and affecting multiple organs and systems, resulting in diverse clinical presentations.[2] The classic form of CeD is characterized by typical digestive symptoms, including chronic diarrhea, loss of appetite, weight loss, and abdominal distension. Conversely, the nonclassical form presents with nonspecific intestinal symptoms such as recurrent abdominal pain and constipation, as well as extraintestinal manifestations such as anemia, chronic fatigue, alopecia, epilepsy, and other systemic symptoms.[1]

Several reports have highlighted the coexistence of CeD in patients with rheumatic disorders, prompting the suggestion of regular CeD screening in these individuals.[3–7] A study observed a frequency of serological markers of CeD in rheumatoid arthritis patients at 32.1%,[8] while another study reported a prevalence of CeD in juvenile idiopathic arthritis at 2.5%.[7] Joint involvement, considered a nonclassical manifestation of CeD, can even manifest as the initial symptom in the absence of gastrointestinal symptoms.[9] It encompasses peripheral joint involvement, leading to arthralgia and nonerosive arthritis, predominantly affecting the large joints. Additionally, axial manifestations can occur, resulting in back pain and sacroiliitis, which may be the sole manifestations of CeD.[9,10]

In this case report, we present the case of a 28-year-old woman who developed isolated acute polyarthritis, ultimately leading to the discovery of an underlying CeD diagnosis.

Case reports

A 28-year-old Moroccan woman presented at our hospital with an 8-week history of polyarthralgia and joint swelling. She had no prior medical history of autoimmune or rheumatic diseases. There was no family history of CeD or other

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autoimmune diseases. After a consultation with her primary care physician, a prescription for corticosteroids and non-steroidal anti-inflammatory drugs was issued. She had taken these for 1 month, but her symptoms never resolved. She denied experiencing any respiratory symptoms, gastrointestinal issues, fever, or constitutional symptoms. On examination, the patient appeared fit. Her temperature was 37°C, heart rate was 70/min, respiratory rate was 20/min, and blood pressure was 120/10 mmHg. Examination of joints showed bilateral warmth, swelling, pain, and restricted movement in the proximal interphalangeal joints, metacarpophalangeal joints, wrists, knees, and ankles. There were no signs of axial arthritis or enthesopathy, and no systemic abnormalities were found.

Initial laboratory investigations showed hemoglobin of 7.6 g/dl with a mean corpuscular volume of 68 and a red blood cell count and white blood cell count within the normal range. The C-reactive protein level was 126 mg/l, and the erythrocyte sedimentation rate was 100 mm/h. Serum protein electrophoresis showed a polyclonal increase in beta and gamma globulins. Her immunoglobulin (Ig) titers (Ig A, Ig G, and Ig M) were elevated. The prothrombin time and partial thromboplastin time were normal. An investigation of her anemia showed a serum ferritin level of 7 ng/ml. The vitamin D level was 10 ng/ml. Liver function tests, creatinine, electrolytes, albumin, total protein, lactate dehydrogenase, glucose, and thyroid function tests were normal. Arthrocentesis of the left knee yielded an inflammatory, sterile fluid rich in white blood cells without microcrystals. Streptolysin O antibody titers and procalcitonin levels were normal. Microbiological investigations, including cultures of blood, urine, and stool, and tests for markers of hepatitis B virus, hepatitis C virus, syphilis, and human immunodeficiency virus were all negative. Antinuclear antibodies, anti-cyclic citrullinated peptides, rheumatoid factor, and antineutrophil cytoplasmic antibodies were all negative. She was Human Leukocyte Antigen (HLA)-B27 negative. The complete laboratory values are presented in Table 1.

Ultrasound of her hands showed synovitis in the right third and fourth metacarpophalangeal joints and the left second and third proximal interphalangeal joints without erosive changes. Radiographs of the hands, knees, ankles, spine, and sacroiliac joints were normal. Magnetic resonance imaging of the sacroiliac joints was unremarkable. Echocardiography and electrocardiogram were normal, as was abdominal pelvic ultrasound. An upper gastrointestinal endoscopy was performed to investigate the cause of anemia, revealing the loss of duodenal folds. Subsequently, a duodenal biopsy was performed, and serological testing for CeD was requested. The anti-tissue transglutaminase-2 (TG2) antibodies were elevated at 200 U/ml (normal $<$ 15 U/ml). The duodenal biopsy showed flattened duodenal mucosal epithelium due to marked villous atrophy, hypertrophic crypts, and increased intraepithelial lymphocytes $\geq$30/100 epithelial cells (Figures 1 and 2), which align with the characteristics associated with stage 3b of the modified Marsh classification.[11]

Table 1. Summary of laboratory results.

Laboratory test	Result	Normal values
Hemoglobin (g/dl)	7.6	13–16
MCV	68	85–95
Leukocytes (/mm^3)	8000	4000–10,000
Platelets (/mm^3)	40,000	150,000–450,000
Prothrombin time (s)	12	10–13
Partial thromboplastin time (s)	30	25–37
CRP (mg/l)	126	0–5
ESR (mm/h)	100	0–10
Ferritin (ng/ml)	7	28–365
Vitamin D (ng/ml)	10	30–75
Albumin (g/l)	38	32–45
Total protein	71	66–87
Calcium (mg/l)	94	86–100
Phosphorus (mg/l)	32	25–45
Glucose (g/l)	0.91	0.7–1.09
Creatinine (mg/l)	6	7–12
ALT (U/l)	14	10–41
AST (U/l)	12	10–50
LDH (U/l)	116	0–250
ALP (U/l)	90	35–104
ANA	Negative	$<$1/160
TSH (mUI/l)	1.2	0.27–4.2
Anti-CCP (UI/l)	5	$<$25
RF (UI/ml)	5	$<$16
ANCA	Negative	$<$1/20
HLA B27	Negative	—
Syphilis serology	Negative	—
HIV serology	Negative	—
CMV serology	Negative	—
Hepatitis B serology	Negative	—
Hepatitis C serology	Negative	—
Streptolysin O antibody (IU/l)	27	$<$150
Procalcitonin (ng/ml)	0.01	$<$0.5
Ig A (g/l)	4.5	0.7–4
Ig G (g/l)	17	7–16
Ig M (g/l)	3	0.23–2.59

MCV: Mean corpuscular volume; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; LDH: Lactate dehydrogenase; ALP: Alkaline phosphatase; ANA: Antinuclear antibody; TSH: Thyroid stimulating hormone; Anti-CCP: Anti-cyclic citrullinated peptide antibodies; RF: Rheumatoid factor; ANCA: Antineutrophil cytoplasmic antibody; HIV: Human immunodeficiency virus; HSV: Herpes simplex virus; CMV: Cytomegalovirus; Ig: Immunoglobulin.

The diagnosis of CeD was made. A gluten-free diet was started. Her joint symptoms resolved in 3 weeks. After a span of 48 weeks, all blood tests returned to normal levels, and the anti-TG antibodies showed normal values (Figure 3). She has been reviewed 2 years after being on a gluten-free diet and has had no recurrence of her joint symptoms.

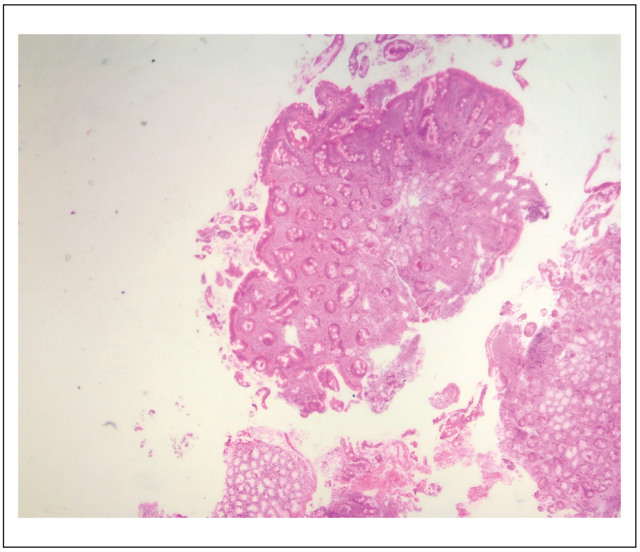

Figure 1. Biopsy image (H&E stain ×40) of the duodenum showing marked villous atrophy.

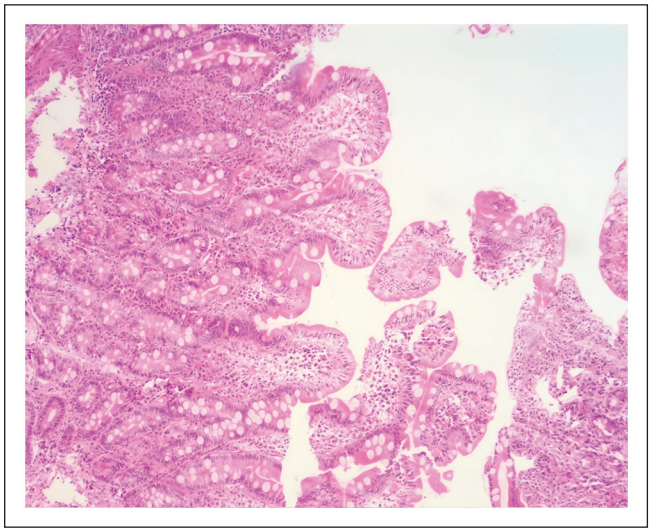

Figure 2. The biopsy image (H&E stain ×100) of the duodenum demonstrates marked villous atrophy, hypertrophic crypts, and increased intraepithelial lymphocytes, consistent with stage 3b of the modified Marsh classification.

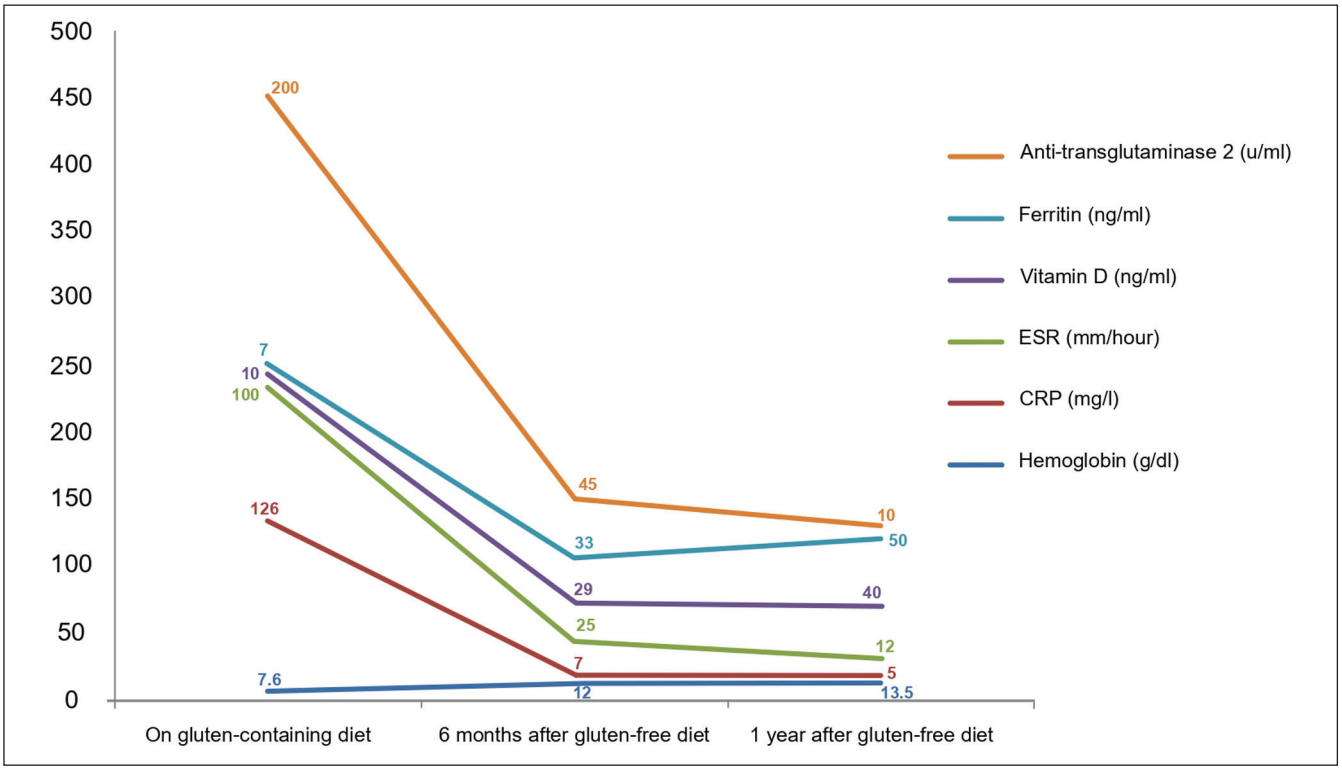

Figure 3. Longitudinal course of main laboratory parameters over time.

Discussion

This clinical case represents an unusual presentation of CeD, specifically isolated polyarthritis. It highlights the diagnostic challenge encountered in such a situation. Indeed, evaluating and diagnosing polyarthritis is challenging as several conditions must be considered, including rheumatoid arthritis, spondyloarthritis, gout, pseudogout, infectious arthritis, connective tissue disorders, polymyalgia rheumatica, sarcoidosis, and rheumatic fever.[12] CeD can coincidentally be associated with various conditions, emphasizing the need for a rigorous diagnostic approach to establish the

Table 2. Summary of cases with non-chronic arthritis revealing CeD reported in literature.

First author, Ref. Year	Age (years)	Sex	Clinical presentation	Localization	Arthritis duration	Associated symptoms	Evolution of arthritis after gluten-free diet
Chakravarty, (17) 1992	24	Male	Oligoarthritis	Both knees	2 months	Weight loss	Resolved in 6 months
Borg, (20) 1994	42	Male	Monoarthritis	Talonavicular joint	3 weeks	—	Persisted for 12 months
Bagnato, (13) 2000	37	Female	Polyarthritis	PIP DIP Both knees	2 months	- Myalgia - Fever - Anxiety	Signicant clinical improvement after 2 months
Slot, (10) 2000	50	Male	Monoarthritis	Knee	—	- Uncharacterized dermatitis - Weight loss	Gradually subsided in the following couple of months
Efe, (18) 2010	34	Female	Polyarthritis	Knees Wrists PIP MCP	2 months	—	Resolved in a 4 weeks

CeD: Celiac disease; Ref.: References; PIP: Proximal interphalangeal; DIP: Distal interphalangeal; MCP: Metacarpophalangeal.

underlying cause of polyarthritis.[13,14] A meta-analysis has demonstrated a cumulative incidence of arthritis in CeD of 22.1%, suggesting that CeD should be considered in cases of arthritis with an initial negative etiological workup.[15]

The pathophysiology of arthritis in CeD remains unclear. However, available evidence suggests that there is an immunologically mediated injury occurring in individuals with a genetic susceptibility (HLA-B8 DR3). This susceptibility enhances the interaction between tissue transglutaminase present in the synovial membrane and undigested gliadin, leading to a cellular or humoral immune reaction within the joint. Consequently, this immune response ultimately results in the development of arthritis.[10,16–18]

Arthritis may present as the initial symptom of CeD, even in the absence of any gastrointestinal symptoms.[9] A study utilizing ultrasound has revealed the existence of subclinical synovitis in patients diagnosed with CeD. Interestingly, this study found that the occurrence of synovitis was more prevalent among individuals adhering to a gluten-containing diet.[19] A few cases have been previously reported where acute arthritis revealed silent CeD (Table 2).[10,13,17,18,20]

The gluten-free diet is the gold standard of treatment for CeD. It leads to a variable improvement in arthritis symptoms, as indicated by various studies.[9] In the study conducted by Iqbal et al.,[3] improvement was observed in 30% of the participants. Other studies have demonstrated that arthritis tends to be more prevalent in untreated patients with CeD compared to those following a gluten-free diet.[19] Improvement of joint manifestations under a gluten-free regime reinforces the hypothesis of the pro-inflammatory and pro-oxidative effects of gluten, as well as its capacity to suppress regulatory T-cell activity[21,22]

Conclusion

This case underscores the importance of considering CeD in the differential diagnosis of patients with isolated joint involvement, to avoid misdiagnosis and the subsequent delay in initiating a treatment regimen. A gluten-free diet is the mainstay of treatment and can effectively reduce joint symptoms.

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Author contributions

A.M. followed the patient closely, collected and analyzed the data, and took the lead in writing and structuring the article. I.E. conducted a comprehensive review of the article, provided critical feedback, and contributed significantly to the overall improvement of the article.

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