


CASE REPORT

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Renal amyloidosis: a hidden complication of celiac disease (a case report)

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Abstract

We report a case of a 36-year-old female with untreated celiac disease, exhibiting both digestive discomfort and extra-digestive symptoms, including anemia. She subsequently developed a nephrotic syndrome. Biopsy of the accessory salivary gland confirmed amyloid deposits, as indicated by positive Congo red staining. Esophago-gastroduodenal fibroscopy revealed characteristic signs of celiac disease and ruled out lymphoma. Further etiological screening identified celiac disease as the only possible cause of the amyloidosis. Complete remission was achieved after 3 months on a gluten-free diet, with later laboratory assessments indicating the absence of nephrotic syndrome and hematological abnormalities.

Keywords Celiac disease, Nephrotic syndrome, Amyloidosis

Background

Celiac disease (CD) is a chronic inflammatory autoimmune disease of the intestine, due to the ingestion of gluten in genetically predisposed subjects [1].

The gliadin found in gluten has a toxic effect acting directly on the intestinal epithelium causing recruitment of intraepithelial lymphocytes and an immunogenic effect on the T lymphocytes of the lamina propria.

These two effects are intertwined and induce an inflammatory reaction and tissue damage in the intestine.

Celiac disease generally takes the form of a malabsorption syndrome, which can manifest itself in different ways. The clinical presentation is frequently digestive (discomfort, diarrhea, bloating) but can also be extra-digestive: anemia symptoms, renal manifestations, osteopenia, and depression.

The gold standard for diagnosis involves serological tests and histological examination of duodenal biopsies.

Treatment is a total gluten avoidance. It results in the symptoms disappearance.

Case report

We report the case of a 36-year-old North African woman, suffering from celiac disease since the age of 10-year-old (diagnosis confirmed initially on an esophago-gastroduodenoscopy and serological findings including positive IgA tissue transglutaminase and IgA anti-endomysial antibodies (Table 1). She is not adhering to a gluten-free diet, because of noncompliance, and experiences digestive discomfort, bloating, and diarrhea, and also extra-digestive signs, as microcytic and hypochromic anemia. She was admitted with pure nephrotic syndrome.

On clinical examination, the patient was conscious, in good general condition, afebrile, heart rate 81 bpm, blood pressure 100/60 mmHg, respiratory rate 19 cpm, and arterial oxygen saturation 99% on room air. Abdominal examination revealed moderate ascites, and the rest of the examination was normal.

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Table 1 Laboratory results (immunological tests) on admission

	Admission
IgA dosage (g/L) [0.7–4]	2.5
C3 (g/L) [0.83–1.93]	1.41
C4 (g/L) [0.15–0.57]	0.24
ANA	Negative
Anti-dsDNA antibodies	Negative
ANCA	Negative
APL antibodies	Negative
AntiSM antibodies	Negative
AntiSSA antibodies	Negative
AntiSSB antibodies	Negative
Antiribosome antibodies	Negative
IgA tissue transglutaminase	Positive
IgA anti-endomysial antibodies	Positive

Table 2 Laboratory results (complete blood count) on admission, at 3 months, and after 1-year follow-up

	Admission	3 months	1 year
White blood cell (/ μ L) [4000–10,000]	5200	4800	
Neutrophil (%)	61	64.4	
Lymphocyte (%)	28.7	24.3	
Eosinophil (%)	1.7	2	
Basophil (%)	1.1	1	
Monocyte (%)	7.5	8	
Hemoglobin (g/dL) [11.5–15.5]	6.8	10	11.9
Platelet (/ μ L) [0, 0–400]	194,000	188,000	

Table 3 Laboratory results (urinalysis) on admission, at 3 months, and after 1-year follow-up

	Admission	3 months	1 year
Urine red blood cell (/mm ³) [<15]	3	4	
Urine white cells (/mm ³) [<10]	2	0	
Proteinuria (g/day) [<0.3]	17	1.8	0.9

Urine dipstick showed three-cross proteinuria, negative hematuria, and leukocyturia. Laboratory findings showed microcytic hypochromic anemia (hemoglobin: 6.8 g/dL) low ferritin, normal thyroid markers, normal renal function, hypoproteinemia at 45 g/L, and hypoalbuminemia at 16 g/L, with nephrotic-range proteinuria at 17 g/24 h (Tables 2, 3 and 4).

ANA, anti dsDNA, ANCA, APL, antiSM, antiSSA, antiSSB, and antiribosome antibodies were negative. Serum complement fractions C3 and C4 are normal

Table 4 Laboratory results (chemistry) on admission, at 3 months, and after 1-year follow-up

	Admission	3 months	1 year
AST (U/L) [5–34]	24	27	
ALT (U/L) [0–55]	18	30	
Total protein (g/L) [64–83]	45	66	
Serum albumin (g/L) [35–52]	16	32	
Blood urea [0.15–0.55]	0.51	0.3	
Creatinine [5.7–12.5]	8.2	7.5	
eGFR (mL/min/1.73 m ²)	78	87	
Na (mEq/L) [136–145]	132	136	136
K (mEq/L) [3.5–5.1]	4	4.8	5
Cl (mEq/L) [98–107]	102	105	104
Calcium (mg/L) [84–102]	89	90	
Phosphate (mg/L) [23–47]	37	37	
Uric acid (mg/L) [26–60]	39	35	
Plasma glucose (g/L) [0.7–1.1]	0.9	1.01	0.9
TSH us (μ UI/mL) [0.35–4.94]	1.96		
FT3 (pg/mL) [1.71–3.71]	1.71		
FT4_6 (ng/dL) [0.7–1.48]	0.73		
Ferritin (ng/mL) [4–204]	10	87	

AST aspartate transaminase, ALT alanine transaminase, eGFR estimated glomerular filtration rate, IgG immunoglobulin G, IgA immunoglobulin A, IgM immunoglobulin M, TSH thyroid-stimulating hormone, CMV Cytomegalovirus, EBC Epstein-Barr virus

Table 5 Laboratory results (virology) on admission

	Admission
CMV antibody IgM (S/CO)	0.1
CMV antibody IgG (UA/mL)	85.6
EBV antibody IgM VCA (S/CO)	0.06
EBV antibody IgG EBNA (S/CO)	9.04
EBV antibody IgG VCA (S/CO)	39.77

(Table 1). Autoimmune disorders were then ruled out. Hepatitis B and C and HIV viral serology were negative (Table 5).

The patient underwent CT chest and abdomen imaging to search for infectious or malignant processes. Biopsies of the accessory salivary glands were performed and have shown amyloid deposits, Congo red-positive, and apple green birefringence under polarized light (Figs. 1, 2 and 3).

An esophagogastroduodenoscopy showed a reduction in the density of duodenal folds. Biopsies performed during it revealed total villous atrophy, with intraepithelial lymphocytes equaling 50%, and no evidence of lymphoma (Fig. 4).

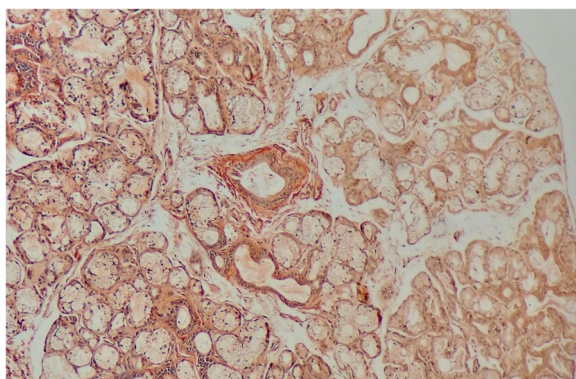


Fig. 1 Salivary parenchyma showing eosinophilic deposits in interstitial and pericanal areas with Congo red staining showing red amyloid deposits in the pericanal area

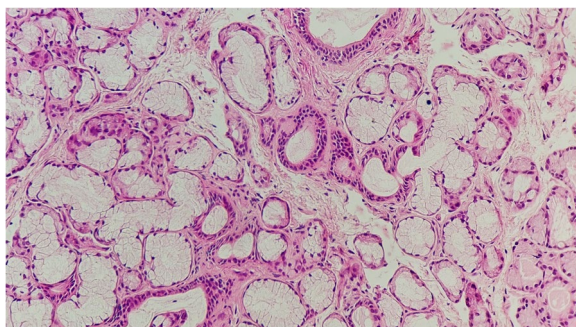


Fig. 2 Salivary parenchyma showing eosinophilic deposits in the interstitial and pericanal areas (x 10) H&E stain

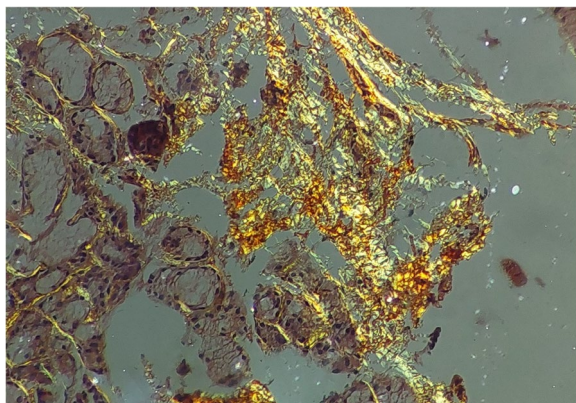


Fig. 3 Congo red staining showing birefringent amyloid deposits in polarized light with apple green color (x 10)

The myelogram, bone marrow biopsy, electrophoresis, and serum protein immunofixation are not in favor of a lymphoma that could complicate celiac disease.

We performed an etiological screening of this amyloidosis, and no other cause was found. The nephrotic

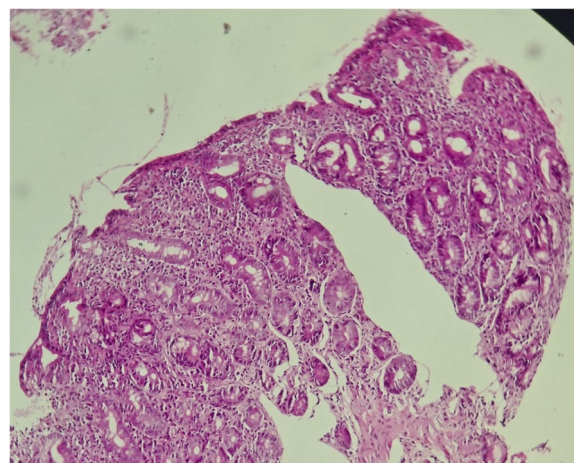


Fig. 4 Duodenal biopsy showing total villous atrophy, with intraepithelial lymphocytes = 50% (x 10) H&E stain

syndrome was finally attributed to renal amyloidosis due to her celiac disease. A gluten-free diet for celiac disease is started associated with renin-angiotensin-aldosterone system inhibitors. Total remission is achieved after 3-month diet. Laboratory findings show no nephrotic syndrome signs and no hematological disorders.

Discussion

Celiac disease (CD) is an autoimmune disease whose antigen is gluten. The frequency of CD in North Africa is close to that in Europe [2]. Its prevalence in the general population is about 0.5 to 1% [3]. Its prevalence remains underestimated, due to its generally silent nature and atypical expression [4]. Currently, the female-to-male ratio stands at 1.5:1 [5].

It can be associated with other autoimmune conditions, such as type 1 diabetes, autoimmune thyroiditis, autoimmune hepatitis, Sjögren's syndrome, and IgA nephropathy [2].

CD is diagnosed clinically, serologically, and histologically and is confirmed by a favorable response to a gluten-free diet.

Extra-digestive manifestations of CD may be secondary to the resulting malabsorption syndrome or to autoimmune phenomena that have yet to be fully elucidated [6].

These include hematological, osteoarticular, neurological, cardiovascular, endocrine, immuno-allergic, and renal manifestations [7].

Renal involvement in CD is uncommon; the occurrence of celiac disease is elevated in individuals with chronic kidney diseases. While there is some debate surrounding this, there have been documented instances of an elevated risk of progressing to end-stage renal disease

in individuals with celiac disease [7]. The most robust links are observed with IgA nephropathy [8] and diabetic nephropathy.

On the other hand, only a few sporadic cases of renal amyloidosis due to CD have been reported [1, 9]. Gluten gliadin penetrates the lamina propria massively. It triggers an inflammatory and immune response, which results in a release of inflammatory cytokines [10].

The latter are responsible of an increase in SAA protein levels, a major factor in amyloid deposits. Gluten-free diet is crucial in CD management; it can not only resolve symptoms but also prevent long-term complications (small intestinal adenocarcinoma, intestinal lymphoma) [11].

As for our patient, we obtained a full recovery (renal and extra-renal) after a 3-month well-respected gluten-free diet.

Conclusion

Celiac disease is essentially known for its digestive manifestations but can also cause extra-digestive signs, as renal ones. Hence, it is crucial to recognize the potential renal involvement in celiac disease.

Abbreviations

CD	Celiac disease
HIV	Human immunodeficiency virus
ANA	Antinuclear antibodies
Anti dsDNA	Anti-double-stranded DNA antibody
ANCA	Antineutrophil cytoplasmic antibodies
APL	Antiphospholipid
AntiSM	Anti-Smith antibody
CT	Computed tomography
SAA	Serum amyloid A
AST	Aspartate transaminase
ALT	Alanine transaminase
eGFR	Estimated glomerular filtration rate
IgG	Immunoglobulin G
IgA	Immunoglobulin A
IgM	Immunoglobulin M
TSH	Thyroid-stimulating hormone
CMV	<i>Cytomegalovirus</i>
EBV	Epstein-Barr virus

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None.

Authors' contributions

ZK is involved in the clinical care of the patient, the drafting of the text, sourcing, editing of clinical images, writing the review, and editing. TB has revised the work. All authors read and approved the final version of the manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

A consent was obtained from the patient for an anonymous publication.

Competing interests

The authors declare that they have no competing interests.

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