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Minimal change disease in association with celiac disease; a case report and review of the literature

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Abstract

Celiac disease may be associated with a variety of autoimmune diseases such as type 1 diabetes, autoimmune thyroid disorders, Sjogren's syndrome and untypically with renal diseases such as nephrotic syndrome. These associations have been reported in nephrotic syndrome cases secondary to IgA nephropathy, membranoproliferative glomerulonephritis, membranous glomerulopathy and minimal change disease. Minimal change disease is a major cause of idiopathic nephrotic syndrome, characterized by intense proteinuria leading to edema and intravascular volume depletion. In adults, it is responsible for approximately one sixth of idiopathic nephrotic syndrome cases, whereas it stands for a much higher percentage at younger ages, for example it accounts for up to two thirds in children with an age less than two years old. The coexistence of celiac disease and nephrotic syndrome is extremely rare. Only a few cases have been reported in the corresponding medical literature so far, with both celiac disease and minimal change disease. Since the prevalence of celiac disease is overall 1%, the question arises whether the coexistence of celiac disease and minimal change disease is just a coincidence or not. As they both are immune mediated diseases, a link between them is reasonable. We are going to report a 46-year-old man who was admitted with both nephrotic syndrome (with proteinuria of 4.5 g/d) and probable mal-absorption syndrome, causing an iron deficiency anemia and weight loss. Clinically, he was diagnosed with celiac disease and minimal change disease, which was confirmed, by both small bowel and kidney biopsy. Renal biopsy showed minimal change disease and diffuse podocyte damage. The patient was treated with a gluten free diet and immunosuppressive therapy with corticosteroids, initially, followed by cyclosporine. Unfortunately, the treatment was not completely successful and later he developed chronic kidney injury that required hemodialysis for several years.

Keywords: Chronic kidney disease, Celiac disease, Minimal change disease, Nephrotic syndrome, Hemodialysis

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Introduction

Celiac disease may be associated with a variety of autoimmune diseases such as autoimmune thyroid diseases, type 1 diabetes, Sjogren's syndrome and untypically with kidney involvement such as nephrotic syndrome (1). These associations have been reported in nephrotic syndrome cases secondary to membranoproliferative glomerulonephritis, IgA nephropathy, membranous glomerulopathy and minimal change disease (2).

The simultaneous occurrence of celiac disease and nephrotic syndrome is extremely rare. Only a few cases have been reported in the corresponding medical literature so far, with both celiac disease and minimal change disease. Since the prevalence of celiac disease is overall 1%, the question arises whether the coexistence of celiac disease and minimal change disease is just a coincidence or not. As they both are immune mediated diseases, a link between them is reasonable, and thus, it is important to answer this probable connection, since, undiagnosed celiac disease cases may be a risk factor of long-term complications such as anemia, infertility, osteoporosis or malignant diseases such as intestinal lymphoma (3). Therefore, it is important to keep this probability in mind for general physicians, internal medicine providers, gastro-hepatologists and nephrologists while managing cases with iron deficiency anemia and renal diseases (4).

Case Presentation

We are going to report a 46-year-old man who was admitted with both nephrotic syndrome (proteinuria of 4.5 g/d), and probable mal-absorption syndrome, causing in an iron deficiency anemia and weight loss. Clinically, he was diagnosed with celiac disease and minimal change disease, which was documented by a small bowel, and renal biopsy. Renal biopsy showed a minimal change disease and diffuse podocyte damage. The patient was treated with gluten free diet and immunosuppressive therapy with corticosteroids, and also cyclosporine when needed. In this case, unfortunately, the treatment was not completely successful and later, he developed chronic kidney injury that required hemodialysis for several years. His para-clinical findings included hemoglobin 10.2 g/

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Implication for health policy/practice/research/ medical education

Celiac disease may be associated with renal disease such as nephrotic syndrome. Here we report as case of 46-year-old man who presented with both nephrotic syndrome and Celiac disease, which finally led to hemodialysis.

dL, albumin 1.9 g/L, and proteinuria of 4.6 g/d). Table 1 shows laboratory data of the patient. His proteinuria was not accompanied by any RBC casts in urine sediment. A biopsy of small bowel mucosa was taken through upper gastrointestinal tract endoscopy, for finding the cause of anemia. This biopsy showed total villous atrophy with remarkable inflammatory infiltration, as well as an increase in intraepithelial lymphocytes, that all, confirmed celiac disease, since anti-endomysial and transglutaminase antibody also were extremely high. The patient did not have used any drugs causing nephrotoxicity. The patient was ordered to take on a gluten free regimen and started a high dose of prednisolone (60 mg/d) firstly, and later on, an immunomodulatory agent (cyclosporine; 50 mg/d). However, the treatment was not completely successful and eventually, the patient developed chronic kidney disease that required hemodialysis for several years. Now, the patient is a candidate for kidney transplantation.

Table 1. Laboratory data of the patient

Test	Result	Unit	Reference value
Urea	55	mg/dL	M: 19-44; F: 15-40
Creatinine	1.36	mg/dL	0.7-1.4
Na	140	mEq/L	136-145
K	4.1	mEq/L	3.6-5
Ca	7.7	mEq/L	8.5-10.5
Phosphorus	4.2	mEq/L	3.5-5.2
WBC	6100	×1000/mm³	4.0 - 11
Hb	7.2	g/dL	M:14 -18 ; F:12-16
Alb	2.3	g/dL	3.5-5.2
CPK	110	IU/L	21 to 215 IU/L
CK-MB	16	IU/L	5 to 25 IU/L
Troponin	0.2	ng/mL	0 and 0.4 ng/mL
Ferritin	127	ng/mL	20 to 250 ng/mL
Iron	41	mcg/dL	60 to 170 µg/dL
TIBC	240	mcg/dL	240 to 450 µg/dL
HBsAg	Negative	IU/L	Negative
MCV	68	fL.	80–100 fL.
Platelets	336	PLT per microliter of blood	150000 to 450000 platelets per microliter of blood.
UA USG	1020	1.005 to 1.030	1.005 to 1.030
FBS	76	mg/dL	70-110
Cholesterol	158	mg/dL	120-200
Triglyceride	70	mg/dL	150-200
SGOT	27	IU/L	M: 0-31 - F: 0-37
SGPT	14	IU/L	M: 0-41 - F: 0-31
ALP	148	IU/L	Adult: 64-306
LDH	347		
25(OH)D	19.20		
TSH	9.43		
Free T4	0.99		
RBC	4.91	×10^6/mm³	M:4.5-5.8 F:4-5.2

CPK, creatine phosphokinase; CKMB, creatine kinase myocardial band; TIBC, total iron binding capacity; HBsAg, hepatitis B surface antigen; MCV, mean corpuscular volume; UA USG, urine analysis specific gravity; FBS, fasting blood sugar; SGOT, serum glutamic-oxaloacetic transaminase; SGPT, serum glutamic-pyruvic transaminase; TSH, thyroid stimulating hormone; RBC, Red blood cell; Free thyroxine, free T4; 25 hydroxy vitamin D, 25(OH) D; PLT, platelet.

Discussion

Celiac disease is a systemic disease, rather than a disease, which limited to the digestive system. This disease is frequently associated by a variety of extra-gastrointestinal symptoms, making it a true mystery. This is primarily explained by the fact that celiac disease is one of the autoimmune types. Its etiology is linked to a permanent intolerance to gluten containing foods. Notably, celiac disease may accompany extra-intestinal symptoms, which may appear either at the time of diagnosis or at later stages. Minimal change disease is one of the causes of nephrotic syndrome, marked by massive proteinuria alongside with edema. In adults, it is responsible for almost one sixth of patients with idiopathic nephrotic syndrome. In children, it reaches 2/3 of cases (5). Examination by light microscopy reveals no visible alterations; however, electron microscopic study shows foot process effacement. Immunologic disturbance and malfunction of the podocyte results in altered integrity of the glomerular basement membrane, and therefore, cause proteinuria. The goal of the treatment is the inhibition of immunologic disturbance with corticosteroids, like prednisolone, but occasionally, relapses occur in steroid-sensitive forms of the disease, since some patients need second-line therapy that includes immune-suppressive drugs for steroid-sparing (6).

Ultrasonography reports of the kidneys shows, right kidney size of 105 mm, left kidney size of 110 mm with normal parenchymal echogenicity. Other components of urinary tract including renal pelvis, ureter, and urinary bladder, were normal. Peripheral blood smear disclosed anisocytosis 2+, hypochromia 2+ and poikilocytosis 2+. The 24-hour collection of urine showed proteinuria of 4600 mg/d. Additionally, urine sediment was negative for RBC or WBC.

Conclusion

It is possible that, cases with complete response to steroid therapy, rarely lead to renal failure, but others with incomplete response or no response to steroids, may finally lead to chronic renal failure. Our case report is an example of unresponsiveness of nephrotic syndrome to current treatments and led to chronic kidney disease due to coexistence of celiac disease and nephrotic syndrome, since further attention to this possibility coexistence of celiac disease with nephrotic syndrome is necessary.

Authors' contribution

AG and AHG both involved in the patient management; manuscript write up and literature review. All authors read and signed the final paper.

Conflicts of interest

We hereby declare that all authors meet the criteria for authorship and do not have any financial or non-financial conflicts of interest. We also declare that we do not have any funding from or shares in organizations that stand to gain or lose from the publication of this case, holding patents related to the case, or any other competing interests that may cause embarrassment were they to become public after the publication of the case.

Ethical issues

Ethical issues including plagiarism, double publication, and redundancy have been completely observed by the author. The patients gave his consent to publish as a case report.

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