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Case Report. Late-Diagnosed Celiac Disease As A Trigger Of Family History Of Gluten Related Disorders

Aissulu Kapassova[1], Gulmira Derbissalina[1]*, Dinara Zhunussova[1],
Elmira Kelimberdiyeva[1], Baurzhan Iskakov[2]

[1] General Practice Department, Astana Medical University, Nur-Sultan, Kazakhstan.
[2] Department of gastroenterology and nutrition, Kazakh Medical University of Continuous Education, Almaty, Kazakhstan.
*Corresponding author: Gulmira Derbissalina, derbissalina@gmail.com

ABSTRACT

Abstract The atypical clinical presentation of celiac disease becomes increasingly common in all specialty physician's daily practice, which requires an awareness of its many clinical faces with non-classic, silent and latent forms. Besides the common genetic background (HLA DQ2/DQ8) of the celiac disease, other non-HLA genes are now notably reported with a probable association to atypical forms [1]. Celiac disease can be difficult to diagnose because it affects to people differently. There are more than 200 known celiac disease symptoms which may occur in the digestive system or other parts of the body. Some people develop celiac disease as a child, others as an adult. And the reason of such presentation is still unknown [2]. Celiac disease is hereditary, meaning that it runs in families. People with a first-degree relative with celiac disease (parent, child, sibling) have a 1 in 10 risk of developing celiac disease [1]. Case report. We report the familial case of atypical celiac disease on an outpatient. The aim of describing this clinical case was to recall the high frequency of association of celiac disease with autoimmune and genetic diseases. Discussion. The variety of non-specific symptoms made it difficult to make a diagnosis. Perhaps the patient's father had esophageal cancer as a manifestation of a CD complication. Considering the genetic determinant of CD an examination of family members with gastrointestinal symptoms was proposed. This led to CD and a gluten hypersensitivity diagnosis at close relatives. Conclusion. It is also necessary to attract the attention of physicians of different specialties to the clinical peculiarities of celiac disease for timely detection of this disease. We suggest that even in the case of late diagnosis of CD, the patient's «family history» should be built to eliminate atypical celiac disease or gluten hypersensitivity in the patient's family. This will help identify gluten related disorders in a larger population.

Keywords: celiac disease, atypical CD, gluten related disorders, family history of CD

Correspondence:
Gulmira Derbissalina
General Practice Department, Astana Medical University, Nur-Sultan, Kazakhstan.
*Corresponding author: Gulmira Derbissalina email-address:
derbissalina@gmail.com

INTRODUCTION

Initial prevalence studies in the general population came from European countries and it was estimated to affect approximately 1% of the European population. The current worldwide prevalence of celiac disease (CD) to be 1.4% based on blood tests and 0.7% based on biopsy results [3]. Furthermore, serologic studies demonstrate that most celiac patients present with oligosymptomatic, latent, potential, and extraintestinal forms. These nonclassic clinical presentations become increasingly common and might reach about 50% of all diagnosed patients. The undiagnosed CD cases remain untreated, leaving individuals exposed to the risk of long-term complications, such as infertility, osteoporosis, or cancer [4-8].

CASE REPORT

A 43-year old female presented with epigastric pain, nausea, stomach heaviness after a meal, alternating constipation with diarrhea, foul-smelling stool, muscle hypotension, apathy, chronic fatigue, weakness, irritability, sleep disorders, depression, bone pain. These complaints have been disturbing since childhood. The deterioration was triggered after eating flour products, patient repeatedly called an ambulance due to vomiting, bloating, severe discomfort. In anamnesis the patient has been observed by various specialists for a long time. Previously, she had been followed irregularly at the outpatient unit of an *endocrinologist* due to hypogonadotropic hypogonadism, insulin resistance and autoimmune thyroiditis and was treated, also irregularly, with replaced hormones. She was seen indifferent health centers and diagnosed as having uterine myoma, iron-deficiency anemia and managed accordingly with negative response. She described regular deterioration of her symptoms further, there was associated urgency with occasional nausea, bloating and abdominal discomfort. The patient underwent an annual esophagogastroduodenoscopy (EGDS) but without histological examination. From the family medical history we found out that she has a grandfather (mother's father) died some years ago from esophageal cancer.

Physical examination at admission showed a good general condition, body temperature 36.4° C, weight 77 kg, height 160 cm, body mass index 30.1kg/m^2, pale skin with areas of hyperpigmentation on the face. Respiratory rate 18/min, heart rate 90/min, normal lungs and heart sound, the abdomen is swollen and painful on palpation in the epigastric region and right hypochondrium. Normal neurologic exam.

Preliminary investigations showed a normal full blood count. Biochemical blood tests were all normal, except for low folate levels - 1.80 ng/ml (norma 3-17,0 ng/ml). Blood test for hormones: thyroid-stimulating hormone - 3.00 mU/L (norma 0.4 and 4.0 mU/L), antibodies to microsomal thyroperoxidase (Anti-MTP) - 635 ml/IU (norma 0-34).

Findings on electrocardiogram, chest radiograph, ultrasound examination of abdomen and fibrocolonoscopy were all normal.

Specific markers of CD have been significantly changed: Antibodies to endomysium, IgA-titer 1:20 (increased). Antibodies to endomysium, IgG titer 1:20 (increased). Antibodies to transglutaminase (tTG) IgA- 65.9U/ml (increased). Antibodies to transglutaminase (tTG) IgG - 4,3U/ml (increased). Antibodies to deaminated gliadin (DeaGlia), IgA 44.1U / ml (increased). Antibodies to

deaminated gliadin (DeaGlia), IgG-78.5U / ml (increased). Total IgA was normal.

Real-time PCR analysis revealed the DQ2.5 mutation of the class II HLA gene.

EGDS: esophageal lumen is normal. The mucous esophagus is pink with a smooth surface. The walls of the esophagus are elastic. The Z-line is located at a distance of 40.0 cm from the picks, at the proximal edge of the gastric folds. There's a light, foamy secret with a small amount of bile in the opening of the stomach. Stomach folds are wavy, normal sizes. The walls of the stomach are elastic. The mucous membrane of the proximal sections is pink with moderate hyperemia. The antral mucosa is pink with focal hyperemia. The surface of the mucosa is smooth. Peristalsis can be traced along all the walls to the gatekeeper. The lumen of the bulb of the duodenum and post bulbar department is normal. The mucous membrane of the bulb and post bulbar pink, dull with a villous surface. Folds are a little smoothed. There is a light secret in the lumen of the duodenum.

Histology of duodenal biopsies confirmed the diagnosis: the duodenal mucosa had a partial atrophy with desquamation and intraepithelial lymphocytes with an admixture of neutrophilic leukocytes, and inflammatory infiltration, consisting of lymphocytes, plasma cells, eosinophils, focal sclerosis in the bulb (Fig. 1) and subtotal lint atrophy with loss of brush border in the superficial epithelium and inflammatory infiltration consisting of lymphocytes, plasma cells, eosinophils were found in the second part of the duodenum (Fig. 2)

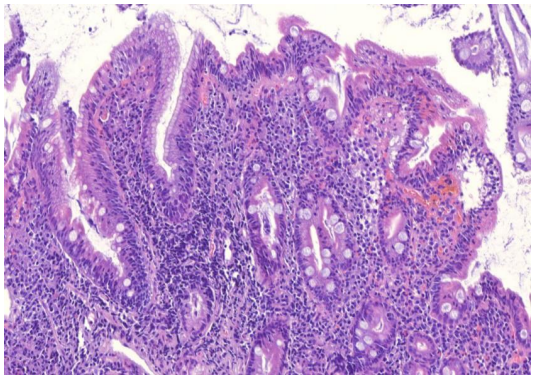

Fig. 1. Histopathology: partial atrophy with desquamation and intraepithelial lymphocytes with an admixture of neutrophilic leukocytes, and inflammatory infiltration, consisting of lymphocytes, plasma cells, eosinophils, focal sclerosis in the bulb.

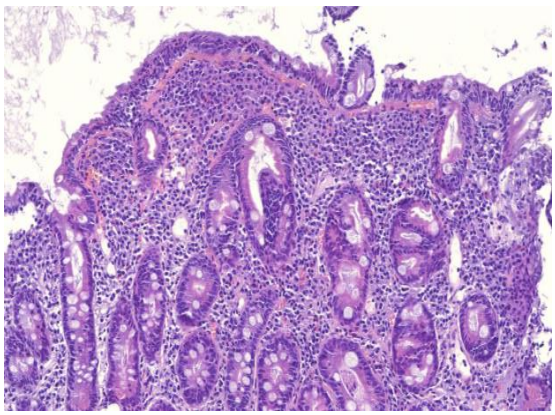

Fig. 2. Histopathology: subtotal lint atrophy with loss of brush border in the superficial epithelium and inflammatory infiltration consisting of lymphocytes, plasma cells, eosinophils were found in the second part of the duodenum.

Conclusion: Picture of superficial gastroduodenitis. Histological conclusion: moderate changes in morphological criteria of Marsh III B.

After 2 months of GFD, with significant improvement of gastrointestinal symptoms, thyroid function and even blanching hyperpigmentation on the face, all laboratory parameters had normalised, and now the patient managed only with the strictest GFD.

Further supportive evidence occurred when her 13-year youngest daughter presented with gastrointestinal symptoms and was tested and found to have a strongly positive EMA and TTG positive CD. The patient's 8- year nephew (her brother's son) with complaints of abdominal pain, flatulence, constipation for up to 5 days, loose stools, lack of appetite, poor weight gain, fatigue, tearfulness and weakness was also examined. His specific markers of CD were normal, except for an increase of DeaGlia to IgG - 17.9 U/ml. Intestinal irrigoscopy showed dolichosigma, dolicholon. We treated him with a diagnosis of gluten hypersensitivity with positive response.

DISCUSSION

Our case report demonstrates the difficulty of making a diagnosis of CD once again, especially by primary care physicians. CD affects around 1% of the general population, but most cases are unrecognised, and diagnosis is often delayed considerably [9 -12]. Screening programs are not conducted in Kazakhstan to detect all forms of gluten enteropathy at an early stage, so a typical form of CD is more frequently diagnosed. Effective detection of people suffering from CD is possible only if both clinicians of various specialties and endoscopists are highly alert to the possible presence of this disease. Our patient has a long history of the disease since childhood and a late diagnosis. CD easily was misdiagnosed as endocrinological disease (hypogonadotropic hypogonadism, autoimmune thyroiditis) and chronic anemia.

The variety of non-specific symptoms such as muscle hypotension, apathy, chronic fatigue, weakness, irritability, sleep disorders, depression, bone pain made it difficult to make a diagnosis. The clinical symptoms of our patient are so diverse that it was rather difficult to diagnose the disease and start treatment on the basis of complete and lifelong exclusion of gluten from the diet. The main role in the occurrence of celiac disease belongs to hereditary factors. In the pedigrees of those suffering from this disease, relatives had several pathologies, including diseases, which are based on a violation of the body's immune system. For example, oncological diseases, among which about one third were tumors and diseases of the gastrointestinal tract, diabetes. Perhaps the patient's father had esophageal cancer as a manifestation of a CD complication. Considering the genetic determinant of CD an examination of family members with gastrointestinal symptoms was proposed. This led to CD and a gluten hypersensitivity diagnosis at close relatives.

CONCLUSION

The presence of many non-specific, diverse symptoms or multiple autoimmune diagnoses should alert physicians to the CD diagnosis. We recommend not stopping at a single patient's CD diagnosis. Building a family history with a detailed specification of classic and nonclassic symptoms helps to clarify atypical, latent, hidden forms of CD or gluten hypersensitivity at an earlier stage and expose a family case

of CD. This will help identify gluten related disorders in a larger population.

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