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ABSTRACT

Oksana Faiura
https://orcid.org/0000-0003-1122-9030
Department of Internal Medicine No. 1, Danylo Halytsky Lviv National Medical University, Lviv, Ukraine

Maryana Abrahamovych
https://orcid.org/0000-0002-2827-7170
Department of Internal Medicine No. 1, Danylo Halytsky Lviv National Medical University, Lviv, Ukraine

Liliya Tsyhanyk
https://orcid.org/0000-0001-6165-5586
Department of Internal Medicine No. 1, Danylo Halytsky Lviv National Medical University, Lviv, Ukraine

Solomiya Guta
https://orcid.org/0000-0002-7943-0139
Department of Internal Medicine No. 1, Danylo Halytsky Lviv National Medical University, Lviv, Ukraine

Nataliya Drobinska
https://orcid.org/0000-0002-4714-3688
Department of Internal Medicine No. 1, Danylo Halytsky Lviv National Medical University, Lviv, Ukraine

CELIAC DISEASE IN ADULTS: RECENT ADVANCES IN EPIDEMIOLOGY, PATHOPHYSIOLOGY, DIAGNOSIS AND MANAGEMENT – CLINICAL CASE REPORT

Introduction. Celiac disease (CD) is a global public health problem. Recent studies have revealed the global prevalence of approximately 1.4% in adults. It is known to manifest usually in childhood and have different symptoms similar to other diseases. In the presented case reports the case of CD in adult, manifested by various atypical symptoms, that became the obstacle to diagnosis the CD in time was described.

Methods. The review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. We performed a comprehensive literature search using such databases as Web of Science, Embase, PubMed. The search strategy included the following terms: "celiac disease", "gluten sensitivity", "pathophysiology", "diagnosis and treatment", "case report". Case description was described according to Case Report (CARE) guidelines.

Results. Recent advances in CD research have significantly enhanced our understanding of its epidemiology, pathophysiology, diagnosis, and management in adults. Advances in genetic and immunological research have deepened our understanding of disease mechanisms, paving the way for novel diagnostic and therapeutic approaches.

A female patient had the complaints of constant pain in the periumbilical and left hypochondriac areas, irregular defecation, diarrhea; legs swelling up to the level of knees. During the ultrasonography of the internal organs, free fluid in the abdominal cavity (approximately 2.0l) was detected. During the gastroscopy it was found pyloritis, gastroptosis, gastroduodenal reflux, CD was suspected, biopsy was taken. The results of the duodenal descending part biopsy: chronic

Ruslana Ivanochko
https://orcid.org/0000-0002-6211-6661
Department of Internal Medicine No. 1, Danylo Halytsky Lviv National Medical University, Lviv, Ukraine

Solomiya Tolopko
https://orcid.org/0000-0002-4940-3850
Department of Internal Medicine No. 1, Danylo Halytsky Lviv National Medical University, Lviv, Ukraine

Mariia Ferko
https://orcid.org/0000-0002-5932-6991
Department of Internal Medicine No. 1, Danylo Halytsky Lviv National Medical University, Lviv, Ukraine

enteritis with significant atrophic-inflammatory changes. To confirm the CD the serological testing also was conducted: IgA to deamidated gliadin > 9.0 (N-<1.0), IgG to deamidated gliadin 0.22 (N-<1.0), IgA to tissue transglutaminase 2 – 2.88 (N-<1.0), IgG to tissue transglutaminase 2 – 0.06 (N<1.0). After the mentioned examination the diagnosis of CD was set. The patient received symptomatic treatment followed by the gluten-free diet (GFD). After 10 days in the hospital the patient was discharged with improved condition and the main recommendation to maintain the GFD.

Discussion. CD is "getting older" and can be very similar to or accompanied by chronic pancreatitis, gastritis, irritable bowel syndrome etc. As could be seen from the clinical case description, the combination of the characteristic symptoms such as abdominal pain, bloating, continuous or frequently repeated diarrhea should lead to the thorough examination of a patient including endoscopy with biopsy and if any suspicion exists, subsequent serological testing. GFD remains the cornerstone of treatment, ongoing research into enzyme supplements, immunomodulators, and even genetic modification of wheat offers hope for additional management options.

Conclusions. Only the multifaceted approach, combining serological tests, instrumental examinations and qualified histopathological assessment, offers a comprehensive means of identifying CD and enabling the timely treatment.

Keywords: celiac disease, malnutrition, gluten intolerance, gluten-free diet, case report.

Corresponding author: *Oksana Faiura, Department of Internal Medicine No. 1, Danylo Halytsky Lviv National Medical University, Lviv, Ukraine; tel. - +380968141749, e-mail: fayurchuk@ukr.net*

РЕЗЮМЕ

Оксана Фаюра
https://orcid.org/0000-0003-1122-9030
Кафедра внутрішної медицини № 1, Львівський національний медичний університет імені Данила Галицького, Львів, Україна

Мар'яна Абрагамович
https://orcid.org/0000-0002-2827-7170
Кафедра внутрішної медицини № 1, Львівський національний медичний університет імені Данила Галицького, Львів, Україна

Лілія Циганик
https://orcid.org/0000-0001-6165-5586
Кафедра внутрішної медицини № 1, Львівський національний медичний університет імені Данила Галицького, Львів, Україна

Соломія Гута
https://orcid.org/0000-0002-7943-0139

ЦЕЛІАКІЯ ДОРОСЛИХ: ОСТАННІ ДОСЯГНЕННЯ В ЕПІДЕМІОЛОГІЇ, ПАТОФІЗІОЛОГІЇ, ДІАГНОСТИЦІ ТА ЛІКУВАННІ; ОПИС КЛІНІЧНОГО ВИПАДКУ

Вступ. Целіакія є глобальною проблемою охорони здоров'я. Нещодавні дослідження виявили, що поширеність целіакії становить приблизно 1,4% серед дорослих з деякими регіональними варіаціями. Відомо, що хвороба може проявлятися, зазвичай у дитинстві, мати різні прояви, схожі з іншими хворобами. В описі клінічного випадку описано випадок целіакії у дорослого, який проявлявся різними нетиповими симптомами, що стало перешкодою для її своєчасної діагностики.

Методи. Огляд літератури проведено згідно з рекомендаціями Preferred Reporting Items for Systematic Reviews and Meta-Analyses - PRISMA. Комплексний пошук літератури здійснено за допомогою баз даних PubMed, Embase та Web of Science. Стратегія пошуку включала такі терміни: «целіакія», «чутливість до глютену», «патофізіологія», «діагностика та лікування», «опис клінічного випадку». Опис клінічного випадку було проведено відповідно до інструкцій для опису клінічного випадку (Case report (CARE) guidelines).

Результати. Останні досягнення в дослідженні целіакії значно покращили наше розуміння її епідеміології, патофізіології, діагностики та лікування у дорослих. Досягнення в генетичних та імунологічних дослідженнях поглибили знання механізмів хвороби,

Кафедра внутрішної медицини № 1, Львівський національний медичний університет імені Данила Галицького, Львів, Україна

Наталія Дробінська
https://orcid.org/0000-0002-4714-3688
Кафедра внутрішної медицини № 1, Львівський національний медичний університет імені Данила Галицького, Львів, Україна

Руслана Іваночко
https://orcid.org/0000-0002-6211-6661
Кафедра внутрішної медицини № 1, Львівський національний медичний університет імені Данила Галицького, Львів, Україна

Соломія Толопко
https://orcid.org/0000-0002-4940-3850
Кафедра внутрішної медицини № 1, Львівський національний медичний університет імені Данила Галицького, Львів, Україна

Марія Ферко
https://orcid.org/0000-0002-5932-6991
Кафедра внутрішної медицини № 1, Львівський національний медичний університет імені Данила Галицького, Львів, Україна

проклавши шлях для нових діагностичних і терапевтичних підходів.

Пацієнтка скаржилась на постійний біль у навколопупковій та підреберній ділянках зліва, нерегулярну дефекацію, рідкий кал; набряки ніг до рівня колін. При ультразвуковому обстежені внутрішніх органів в черевній порожнині виявлено вільну рідину (близько 2,0 л). Під час гастроскопії виявлено пілорит, гастроптоз, гастродуоденальний рефлюкс, запідозрено целіакію, тому забрано біоптати для гістологічного дослідження. У біоптаті низхідного відділу дванадцятипалої кишки виявлено хронічний ентерит зі значними атрофічно-запальними змінами. Для підтвердження ЦК також проведено серологічне дослідження: IgA до дезамідованого гліадину > 9,0 (N-<1,0), IgG до дезамідованого гліадину 0,22 (N-<1,0), IgA до тканинної трансглутамінази 2 – 2,88 (N-<1,0), IgG до тканинної трансглутамінази 2 – 0,06 (N<1,0). Після зазначеного обстеження встановлено діагноз целіакії дорослих. Хвора отримувала симптоматичне лікування з дотриманням безглютенової дієти. Після 10 днів перебування в стаціонарі пацієнтка виписана із покращенням стану та рекомендаціями щодо дотримання безглютенової дієти.

Дискусія. Целіакія «старіє» і може бути дуже схожою за симптомами або і супроводжуватися хронічним панкреатитом, гастритом, синдромом подразненої кишки тощо. Відповідно до інформації, поданої в описі клінічного випадку, поєднання характерних симптомів, таких як біль у животі, метеоризм, безперервна або часто повторювана діарея, має стати передумовою для всебічного обстеження хворого, включаючи фіброскопію/колоноскопію з біопсією, а за наявності будь-яких підозр – наступне серологічне дослідження з визначенням маркерів целіакії. Безглютенова дієта залишається наріжним каменем лікування целіакії, тривають дослідження ферментних добавок, імуномодуляторів і навіть генетичної модифікації пшениці, даючи надію на впровадження альтернативних методів лікування.

Висновки. З метою своєчасного діагностування та лікування целіакії у дорослих потрібен багатогранний підхід, який поєднує серологічні тести, інструментальні обстеження та кваліфіковану гістопатологічну оцінку.

Ключові слова: целіакія, мальнутриція, непереносимість глютену, безглютенова дієта, опис клінічного випадку.

***Автор, відповідальний за листування**: Оксана Фаюра, кафедра внутрішної медицини № 1, Львівський національний медичний університет імені Данила Галицького, Львів, Україна; tel. - +380968141749, e-mail: fayurchuk@ukr.net*

INTRODUCTION

The celiac disease (CD) is an enteropathy, mediated by the immune system and triggered by ingestion of gluten-containing grains (wheat, barley, rye etc.) in genetically susceptible individuals [1]. CD manifests as a chronic enteropathy with potential far-reaching consequences beyond the gastrointestinal tract. Once considered rare, CD is now recognized as a global health issue affecting approximately 0.5% to 1.0% of the population worldwide. The prevalence and diagnosis of the disease have increased over the last two decades. CD is more common among people with autoimmune diseases, especially type 1 diabetes mellitus (DM). The risk of CD in the first-degree relatives of people with CD is about 1 in 10. In the past decade the significant advancements in our understanding of CD, particularly in adults, have developed [2, 3]. Recent years have seen paradigm shifts in our understanding of disease prevalence, genetic and environmental risk factors, and potential therapeutic approaches beyond the gluten-free

diet (GFD). It is crucial for clinicians and researchers to stay abreast of these developments to provide the optimal care for adult patients with CD and to guide the future research.

MATERIALS AND METHODS

The literature review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. We performed a comprehensive literature search using such databases as Web of Science, Embase, and PubMed. The literature review was made using the terms: "celiac disease", "gluten sensitivity", "epidemiology", "pathophysiology", "diagnosis and treatment". Inclusion criteria were: original research articles, systematic reviews, and meta-analyses, articles addressing epidemiology, pathophysiology, diagnosis, or management of CD. Exclusion criteria were case reports and small case series ($n < 10$), articles not peer-reviewed or published in predatory journals. The quality of included studies was assessed using Newcastle-Ottawa Scale for the observational studies and Cochrane risk of bias tool with grading the evidence level using the guidelines of the Oxford Centre for Evidence-Based Medicine. The clinical case was described according to Case reports (CARE) guidelines after the receiving the informed concent from the patient in compliance with the principles of the Declaration of Helsinki on Human Rights, the Council of Europe Convention on Human Rights and Biomedicine, and the relevant laws of Ukraine.

RESULTS

Literature review. Recent epidemiological studies have provided new insights into the prevalence and distribution of CD among the adults worldwide. A comprehensive analysis by Gatti et al. (2024) found that the global prevalence of CD in adults ranges between 0.7% and 2.9% in general population, with higher frequency in females and well-defined at-risk groups, such as relatives of CD patients and patients with autoimmune diseases [4].

Key findings from our recent epidemiological research:

1. Increasing prevalence. Rubio-Tapia et al. (2023) reported a steady CD prevalence increase in the adult population during the past decades, with rates approximately doubling in North America and Europe over the past 25 years [5].

2. Regional variations. Abadie et al. (2024) conducted a global survey highlighting the significant differences in CD prevalence across the regions. Western countries showed the prevalence rates of 1.0–2.0%, while some Middle Eastern countries reported the rates exceeding 1.5%. East Asia, traditionally considered a low-prevalence area, showed increasing rates, although still generally below 0.5%. India showed variable rates, with some regions reporting prevalence as high as 1.0%, while others had much lower rates. Data from Africa remains limited, but the available studies suggested the prevalence rates below 0.5% in most regions, with some exceptions in North Africa. Prevalence rates varied widely, from less than 0.5% in some countries to over 1.0% in others, particularly in areas with significant European ancestry [6].

3. Demographic patterns. Catassi et al. (2022) confirmed the previous studies that CD is more common in women than men, with a female-to-male ratio of approximately 2:1 [7]. The reasons for this gender disparity are not fully understood but may involve hormonal factors and differences in healthcare-seeking behavior. Gutowski et al. (2020) identified two peak periods of CD diagnosis in adulthood: in the third to fourth decades and again in the sixth to seventh decades of life [8]. These epidemiological findings underscore the importance of increased awareness and screening for CD in adult populations, particularly in high-risk groups and regions with growing prevalence.

Interestingly, some studies have suggested a correlation between the higher socioeconomic status and increased prevalence of CD. Zingone et al. (2024) in their analysis, proposed that this association might be due to differences in dietary habits, healthcare access, or environmental exposures [9].

The recent advances in understanding the pathophysiology and genetics of CD have provided new insights into disease mechanisms and potential therapeutic targets.

Genetic factors. Trynka et al. (2011) identified 42 non-HLA loci that contribute to CD risk, highlighting the polygenic nature of disease susceptibility [10]. Cukrowska et al. (2023) discussed that DNA methylation patterns and histone modifications can influence gene expression relevant to CD [11]. A landmark study by Andrén Aronsson et al. (2022) explored how genetic risk interacts with early-life gluten exposure to influence the CD development. They found that high-risk genotypes combined with higher gluten intake in infancy significantly increased the risk of developing CD [12].

Immunological mechanisms. Iversen and Sollid (2023) demonstrated that innate immune responses play a crucial role in the early stages of CD pathogenesis, identifying the specific innate lymphoid cells activated upon gluten exposure in celiac patients [13]. Lee et al. (2024) characterized the T-cell receptor repertoire in CD, providing insights into the specificity of the immune response to gluten peptides [14]. Beyond the well-known tissue transglutaminase (TG) antibodies, new research by Yu et al. (2018) described the new

autoantibodies targeting TG type 3, which may explain some of the extraintestinal manifestations of CD [15].

Intestinal barrier function. Cardoso-Silva et al. (2019) demonstrated that gliadin peptides directly affect tight junction proteins, leading to increased intestinal permeability. In turn, the alterations in the gut microbiome can influence the intestinal barrier function and modulate the immune response to gluten [16].

Environmental triggers. Beyond gluten, other environmental factors have been implicated in CD development. Bouziat et al. (2017) provided evidence that certain viral infections, particularly reovirus, can trigger CD in genetically susceptible individuals by altering the immune response to dietary antigens [17]. Beyond gluten, other dietary components have been implicated. Additionally, Mazzola et al. (2024), in "Nutrients", discussed how the modern wheat varieties with higher gluten content and food additives might contribute to increased CD prevalence [18]. Lebwohl et al. (2014) found an association between the proton pump inhibitor use and increased risk of CD diagnosis, potentially due to alterations in protein digestion and intestinal pH [19].

These advances in understanding the pathophysiology and genetics of CD have important implications for the diagnosis, treatment, and potential prevention strategies.

The clinical presentation of CD in adults has proven to be more diverse than previously recognized, and diagnostic approaches have evolved to meet this challenge. Caio et al. (2019) described the shift in understanding from a primarily gastrointestinal disease to a systemic disorder, noting that non-classical presentations, including neurological, dermatological, and hematological manifestations, are increasingly recognized [20]. Gala et al. (2022) provided an in-depth analysis of neurological manifestations of CD, including ataxia and peripheral neuropathy [21]. Raiteri et al. (2022) explored the prevalence and significance of silent CD, where patients have positive serology and villous atrophy but minimal or no symptoms [22]. They found that these patients still benefit from GFD, highlighting the importance of CD detection.

As CD symptoms may occur at any age, it is worth highlighting that serology is the first step in the diagnostic process. The American Gastroenterological Association recommends to begin the diagnostic process with the detection of TG type 2 (TG2) IgA and total Ig A (tIgA). IgA deficiency in adults also requires the detection of TG2 IgG or deamidated gliadin peptide (DGP) IgG or endomysial antibodies (EMA) IgG. In symptomatic adult patients with high (>10 times more than upper limit of norm (ULN)) TG2 IgA titers and positive EMA in a second blood sample, esophagogastroduodenoscopy and intestinal biopsy cannot be omitted [23]. However, a discussion has already begun regarding the possibility of omitting the biopsy when high TG2 IgA concentrations are present in the serum of adult patients [24]. Aboulaghras et al. (2023) discussed how genetic testing can be used to rule out or confirm the CD in high-risk individuals or in cases where diagnosis is unclear. Human leukocyte antigens (HLA)-DQ2 allele due to its high frequency in the population is related to CD. Homozygous and heterozygous DQ2 status frequency is increased in most adults with CD. The connections between DQ2/DQ8 and CD were confirmed in meta-analysis, and fewer CD cases were developed in case of predisposing HLA haplotypes absence. The analysis of major histocompatibilty complex (MHC) in the CD patients with DQ2-negative profile should lead to improved knowledge of CD susceptibility genes. Recent studies of the microbiome in patients with CD [25] concluded the importance of thorough HLA screening, because it was found that some bacteria were associated with CD when the classical HLA risk alleles were absent. However the real role of non-HLA genes is unknown [26]. Advancements in the endoscopic techniques have improved the detection of subtle mucosal changes. Taavela et al. (2021) proposed a quantitative method for assessing the villous height: crypt depth ratio, potentially improving the accuracy of histological diagnosis [27]. Emerging technologies are making the CD testing more accessible.

CD can be differentiated with the conditions characterized by the intraepithelial lymphocytosis without villous atrophy, in particular, the effects of medicatons, *Helicobacter pylori* (HP) gastritis, duodenal parasitic infestations, Whipple disease, autoimmune diseases, tropical sprue, etc. [28, 29]. Prolonged use of nonsteroidal anti-inflammatory drugs (NSAID), antineoplastic medications, immunomodulatory substances may result into the condition that can mimic CD histologically, but real villous atrophy can be rarely described. Additionally, the NSAID use can usually cause the mucosal erosions or ulcerations with the presence of inflammatory infiltrate containing neutrophils and plasma cells [30]. In contrast, disorders of the crypt architecture, infiltration with neutrophils, ischemia, villous blunting, apoptosis of the epithelial cells in crypts and neutrophilic cryptitis were rarely seen in patients that were treated by the kinase inhibitors [31, 32]. Olmesartan was also found to cause the villous atrophy, thus mimicking CD histologically [33].

HP, intestinal parasitic organisms such as *Giardia lamblia*, sometimes can cause villous atrophy. Enteropathies, especially food protein-sensitive, can cause CD-like histologic changes, but usually they are

transient or respond to the dietary allergen withdrawal. In the patients with pernicious anemia the partial villous blunting, chronic inflammatory infiltration of the mucous membrane along with the epithelial megaloblastic changes in the duodenal biopsies may be found [34]. Collagenous sprue may be often misdiagnosed as CD. But nowadays the thick subepithelial collagen type I band with inflammatory cells and capillaries entrapped identification will help to set the appropriate diagnosis [35].

Common variable immunodeficiency enteropathy may have the similar to CD symptoms. But the depletion of plasma and follicular lymphoid hyperplasia in the duodenal samples of such patients can be found. The pathologists should always check a patient for the presence of *Giardia lamblia* infection (reported in 23.0 % of patients) [34].

Autoimmune enteropathy may have the symptoms of active enteritis, characterized by the CD-like histoloical patterns, but may show areas of apoptotic epithelial cells, goblet and Paneth cells number decrease can occasionally be observed. The biopsies from other gastrointestinal parts usually show the histologic disorders helping to set the diagnosis [36]. The different forms of idiopathic villous atrophy may also cause the diagnostic challenges. Some of the patients may have spontaneous recovery, whereas others show the persistent villous atrophy, with or without associated lymphoproliferative diseases [37].

Recent research has influenced the screening recommendations for CD, especially in first-degree relatives of celiac patients and individuals with associated type 1 DM or autoimmune thyroiditis [38]. The management of CD in adults significantly developed in the recent years, with a focus on improving the adherence to the GFD and exploring the new therapeutic options. Patients with CD must adhere to a lifelong GFD as it is currently the best-known treatment. Treatment of such patients should be done at an early age, as younger individuals tend to show more significant reversal of gastrointestinal symptoms and healing from the damage to the gut mucosa [39].

Besides the diet, the treatment of CD complications plays an important role too. Reduced bone mineral density (BMD) and higher risk of fractures are the confirmed complications of untreated CD [40]. According to the recent data, osteoporosis can be seen in 4.0%–20.0% of males and premenopausal females with CD, osteopenia – in 10.0%–50.0% [41]. BMD measurement could be made in patients with prolonged disease duration or its severe course. Vitamin D, calcium and use of specific medications follow the general guidelines. Bisphosphonates may be used in newly diagnosed CD patients with documented osteoporosis [42]. Untreated CD may cause the hormonal imbalance in childhood [43]. The females have the increased risk for pregnancy complications, infertility, miscarriages and menopause [43, 44]. The few studies have reported fertility issues in CD males comparable to the controls [45, 46].

The principles of atherosclerosis, coronary heart disease prevention and treatment in CD patients follow the general recommendations [47]. It was found that CD is associated with the certain neurological disorders, varying from the transient symptoms (headache, ‘brain fog’) to permanent conditions such as cognitive impairment, epilepsy with cerebral calcifications, ataxia etc. [48–51]. Further studies are needed to confirm the effect of GFD on cognitive dysfunction [52]. Many psychiatric illnesses like depression, anxiety, eating disorders, are also overrepresented, at least in patients with untreated CD. Recent research has highlighted the importance of addressing the psychosocial aspects of CD: life quality, mental health, diet support programs offer new hope for improving outcomes in adult celiac patients, while also highlighting the need for a comprehensive, multidisciplinary approach to care [53, 54]. The enteropathy-associated T-cell lymphoma or intestinal adenocarcinoma are the rare complications of refractory CD affecting 0.1%–3.2% of all CD patients [55]. The cancer risk increases in CD patients with such comorbities as obesity, autoimmune diseases, in smokers, alcohol abusers etc.[56, 57].

The CD research is rapidly evolving, with several exciting areas of investigation that promise to shape future approaches to prevention, diagnosis, and treatment. Recent research has focused on the potential strategies to prevent CD development through the early-life interventions, microbiome modulation, environmental factor mitigation etc. Developing of the emerging diagnostic approaches has aim to improve the accuracy and ease of CD detection. Artificial intelligence for detecting and classifying the duodenal lesions in CD during endoscopy shows the positive prospects in improving the accuracy and consistency of endoscopic diagnosis [58]. Fernández-Bañares et al. (2022) described a new approach – the measurement of the activated gut-homing $CD8^+$ T cell, as a highly accurate blood test for the CD diagnosis in patients using GFD. Further studies are needed to confirm the diagnostic accuracy, especially in non-HLA-DQ2/5 patients. [59]. Rostami-Nejad et al. (2024) explored the use of metabolomic and lipidomic profiling to find the non-invasive diagnostic tool for CD, as gluten cause the intestinal microbiota damage resulting into dysbiosis, metabolomic and lipidomic states changes [60]. The research on new treatment using CD-gene therapy is at the preclinical study stages [61, 62].

Celiac Disease Case Report. While the CD is traditionally considered a pediatric condition, recent years have witnessed a growing recognition of it in adults. The symptoms of CD can vary widely – abdominal pain of different localization, infectious-like diarrhea, general or localized edema, etc., making diagnosis more elusive. Such symptoms are usually treated as the signs of pancreatitis, chronic enteritis or irritable bowel syndrome without any specific serological screening or the specific biopsy done.

Woman, 31 years old, biologist, had the complaints of constant pain in the abdomen (umbilical and left subcostal areas), abdomen enlargement, legs edema, nausea, periodic diarrhea, bloating, fatigue, dry skin, dizziness. Medical history: the patient denied the presence of venereal diseases, viral hepatitis, malaria, DM, rheumatic diseases, surgeries in the past, allergies. Family, and psycho-social history, heredity – not burdened. Patient denied professional harmfulness, smoking, alcohol intake.

The significant physical examination findings: the general condition severity is moderate, skin is pale, dry, elastic; on the face – erythematous rash, which does not rise above the skin; mucous membranes – pale, moist. Respiratory rate – 20/min, heart rate – 90 bpm, blood pressure – 100/60 mm Hg. Tongue is moist, with white coating; abdomen is enlarged; percussion sound – dull; during palpation soft, painful in the periumbilical and left hypocostal areas; defecation is not regular, stool is brown, irregular, liquid. There was edema of legs till the level of knee joints.

For the first time the patient felt ill 2 years ago, when began to notice the periodic abdominal pain, bloating. After acute respiratory infection, she noticed the onset of diarrhea and significant body weight loss in 1 month (from 65.0 to 45.0 kg). She has been taking the multienzymes (pancreatin 25,000 IU + amylase 22,500 IU + protease 1250 IU) daily for a week to treat the possible pancreatitis, after which her condition slightly improved. In 3 months the patient was admitted to the hospital with the diagnosis: “Gastropathy. Chronic enterocolitis. Iron deficiency anemia”. After the treatment (albumin, mesalazine, ademetionine, iron supplements, multienzymes), she felt better. But soon after the discharge the patient noticed the above mentioned symptoms due to which she was admitted to the gastroenterological department of Lviv Regional Clinical Hospital.

In the complete blood count: white blood cells – $4.5x10^9$/l; red blood cells – $4.77x10^{12}$/l; hemoglobin – 102.0 g/l; hematocrit – 0.338; platelets – $354.0x10^9$/l; color index – 0.64; bands – 0; segments – 60; lymphocytes – 28; eosinophils – 6; monocytes – 6; hypochromia, estimated sedimentation rate – 8 mm/h. In urinalysis, no changes were found. In biochemistry, the levels of total bilirubin, glucose, creatinine, blood urea nitrogen, cholesterol, β-lipoproteins, triglycerides, high density lipoproteins, low density lipoproteins, atherogenic index, uric acid, K^+, Na^+, calcium, Cl^-, amylase, aspartate aminotransferase, alanine aminotransferase; alkaline phosphatase, γ-glutamiltransferase, C-reactive protein, coagulogram parameters were within the normal limits. The level of Fe^{2+} was 5.1 (N-10.7-21.5 mmol/l), antistreptolysine "O" – 500.0 U (N-<250.0 U); rheumatoid factor – 13.07 (N – negative). In the proteinogram, the level of total protein was 68.3 g/l (N-65.0–85.0 g/l), albumins – 49.0 % (52.0–65.0%), α_1-globulins – 5.2 % (2.5–5.0%), α_2-globulins – 10.8 % (7.0–13.0%), β-globulins – 14.2 % (8.0–14.0%), γ-globulins – 20.8 % (N – 12.0–22.0%). Also the patient was negative for hepatitis B, C viruses, HP.

In the stool, excess of fatty acids was present, helminths: absent. Bacteriological examination: E. coli – 114.0 million/g (N–150.0–600.0 million/g), hemolyzing *E. coli* – $17.0x10^6$ (N – absent), *E. cloacae* – 10^4 (N<10^4), *Enterococcus* – 10^7 (N-10^5–10^6), *Candida albicans* – $2.0x10^4$ (N<10^3).

Electrocardiography: sinus bradycardia, heart rate – 51 bpm. Echocardiography: no changes, ultrasonography of the abdomen: free fluid in the abdominal cavity (approximately 2.0l) was detected.

Fibrogastroscopy: gastroptosis, hiatal hernia, the cloudy mucus in stomach, hyperemic mucous membrane, swollen pylorus. A biopsy was taken from the few areas of the bulb and retrobulbar zone (about 20.0 cm behind the bulb) (CD is suspected). Conclusion: pyloritis, gastroptosis, gastroduodenal reflux. Fibrocolonoscopy: mucous membrane of the intestine was hyperemic, colon – contact bleeding on the folds, dolichocolon. Biopsy was taken. Conclusion: dolichocolon, enteritis.

In the biopsy of the descending part of the duodenum the surface epithelium was prismatic, had multiple areas of sclerosis, and contained significant number of intraepithelial leukocytes. Villi were atrophied, single, follicle-like accumulations of lymphocytes were found only in bioptate N 4. The number of crypts was unevenly reduced, the cellular composition was uniform. The lamina propria contained a significant and diffuse mixed cellular infiltrate, foci of sclerosis. Conclusion: chronic enteritis with significant atrophic-inflammatory changes. In the biopsy of the intestines taken during colonoscopy, chronic enteritis with significant atrophic-inflammatory changes was found.

The serological testing was also conducted: DGP IgA > 9.0 (N-<1.0), DGP IgG – 0.22 (N-<1.0), TG2 IgA – 2.88 (N-<1.0), TG2 IgG – 0.06 (N<1.0).

The patient was consulted by hematologist – iron deficiency anemia.

No diagnostic challenges except the well-timed diagnosis were present.

Diagnosis: "CD: typical form, with malabsorption syndrome (II severity degree with a predominant disorder of protein metabolism); decompensation phase; chronic gastritis: with localization in the pyloric part of the stomach, exacerbation phase; duodeno-gastral reflux; chronic pancreatitis: of alimentary etiology, with the exocrine dysfunction by hyposecretory type; dolichocolon; gastroptosis, hiatal hernia; digestive failure of the 3rd degree. Anemia: iron-deficient, hypochromic, microcytic, moderate severity".

The prognosis for celiac disease is generally good if the condition is properly managed. Since celiac disease is a lifelong autoimmune disorder, there is no cure, but a strict gluten-free diet can help manage symptoms and prevent complications.

The patient received the preventive and pharmacologic treatment: GFD, Pantoprazole 0.04 g (+ sol. NaCl 0.9% 100.0 ml) – IV once daily, multienzymes (pancreatin 25,000 IU + amylase 22,500 IU + protease 1250 IU) – 1 capsule 3 times daily during meals, iron+folic acid supplements (iron (0.08 g), folic acid (0.00035 g)) – 1 tab. twice a day, sol. Glucose 5.0% 200.0 ml – IV once daily.

After 10 days in a hospital the patient was discharged with improved condition, by the clinician's and patient's assessments, and recommendations to maintain the GFD, continue the treatment under the supervision of a gastroenterologist: multienzymes (pancreatin 25,000 IU + amylase 22,500 IU + protease 1250 IU) – 1 capsule 3 times daily during meals, iron+folic acid supplements (iron (0.08 g), folic acid (0.00035 g)) – 1 tab. twice a day for 2 weeks.

After the 2-week ambulatory treatment at the follow-up visit the serum Fe^{2+} increased: 10.3 mmol/l (N – 10.7–21.5 mmol/l). At 6-month follow up visit the immunological analysis was done: DGP IgA – 0.37 U/ml (N-<1.0), DGP IgG – 26.07 U/ml (N-<1.0).

The intervention adherence and tolerability to treatment were well-assessed by the patient.

No adverse or unanticipated events happened during the period of observation.

In the period before the last hospitalization the biopsy of the intestine was not provided for the patient, and all the visualized changes were treated as the signs of usual chronic enteritis. During the last hospitalization the endoscopy with multiple biopsies (6 samples) were taken from different areas of the duodenum, including the bulb and distal duodenum, to increase diagnostic accuracy. Endoscopy results assumed and biopsy of the small intestine mucous membrane confirmed the presence of characteristic histological changes, such as villous atrophy and intraepithelial lymphocytosis which are important not only for the diagnosis but also for differential diagnosis [27–29]. The important component of the CD diagnosis was serological testing, namely antibodies to TG2 and DGP determination in dynamics [15, 23]. Balancing of the serological tests with intestinal biopsies remains a crucial aspect of CD diagnosis in adults [5, 23]. This dual approach helped to achieve the more accurate diagnosis and ensured that the patient with CD was not overlooked due to potential false negatives from serological tests alone [24].

GFD, being the simple key-method of treatment, helped to minimize the symptoms in the patient and made her be able to continue rehabilitation and treatment on an ambulatory basis. Iron and folic acid supplements helped to fill the gap resulted from malnutrition and pancreatic enzymes corrected the reactive changes in the pancreas.

The combination of the characteristic symptoms such as abdominal pain, bloating, continuous or frequently repeated diarrhea should lead to the throughout examination of a patient including fibroscopy with biopsy and if any suspicion exists, next determining of IgA and IgG to TG2, DGP.

The multifaceted approach, combining serological tests and histopathological assessment, offers a comprehensive means of identification the CD in adults and timely treatment.

The patient shared her thoughts regarding the perspectives on the treatment provided: "After the treatment in the Lviv Regional Clinical Hospital I started feeling better, as the doctor provided clear guidance on following a strict gluten-free diet, which has significantly improved my symptoms. I appreciate the thorough care and regular follow-ups that ensure my nutritional needs are met and my health remains stable without a tone of tablets."

CONCLUSIONS

CD is "getting older" and can be very similar to or accompanied by chronic pancreatitis, gastritis, irritable bowel syndrome, etc. Such overlap of symptoms with complicates the diagnosis. Recent advances in CD research have significantly enhanced our understanding of its epidemiology, pathophysiology, diagnosis, and management in adults. Advances in genetic and immunological research have deepened our understanding of disease mechanisms, paving the way for the new diagnostic and therapeutic approaches. GFD remains the cornerstone of treatment, ongoing research into enzyme supplements, immunomodulators, and even genetic modification of wheat offers hope for additional management options.

Future research should focus on refining the prevention strategies, developing more accurate and accessible diagnostic methods, and advancing novel therapies to improve the life quality of CD patients. As our understanding of this complex disorder continues to evolve, a multidisciplinary approach to the research and patient care will be crucial in addressing the challenges posed by CD in the adult population.

AUTHOR CONTRIBUTIONS

Oksana Faiura – substantial contributions to the conception and design of the work; analysis and interpretation of data for the work.

Maryana Abrahamovych – final approval of the version to be published.

Liliya Tsyhanyk – analysis and interpretation of data for the work.

Solomiya Guta – substantial contributions to the conception of the work; analysis and interpretation of data for the work.

Nataliya Drobinska – interpretation of data for the work, ensuring that questions related to the accuracy and integrity of all the parts of the work are appropriately investigated and resolved.

Ruslana Ivanochko – substantial contributions to the conception and design of the work.

Solomiya Tolopko – drafting the work or revising it critically for important intellectual content.

Mariia Ferko – drafting the work or revising it critically for important intellectual content.

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The authors declare no conflict of interest.

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The authors confirm that no artificial intelligence (AI) technologies were used during manuscript writing or editing.

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INFORMATION ABOUT THE AUTHORS

Oksana Faiura, PhD, Associate Professor, https://orcid.org/0000-0003-1122-9030; Danylo Halytsky Lviv National Medical University, Department of Internal Medicine N 1 (69, Pekarska Str., Lviv, 79010; +380(32) 236 84 19); 7, Poludneva Str., Lviv; +380(96) 814 17 49; fayurchuk@ukr.net

Maryana Abrahamovych, DSci, Professor, https://orcid.org/0000-0002-2827-7170; Danylo Halytsky Lviv National Medical University, Department of Internal Medicine N 1 (69, Pekarska Str., Lviv, 79010; +380(32) 236 84 19); 8, Lytovska Str., Lviv; +380(50) 500 74 77; marjana2003@ukr.net

Liliya Tsyhanyk, PhD, Associate Professor, https://orcid.org/0000-0001-6165-5586; Danylo Halytsky Lviv National Medical University, Department of Internal Medicine N 1 (69, Pekarska Str., Lviv, 79010; +380(32) 236 84 19); 41, Naukova Str., Lviv; +380(67) 957 71 25; ltsyhanyk@gmail.com

Solomiya Guta, PhD, Associate Professor, https://orcid.org/0000-0002-7943-0139; Danylo Halytsky Lviv National Medical University, Department of Internal Medicine N 1 (69, Pekarska Str., Lviv, 79010; +380(32) 236 84 19); 5, Ozhynova Str., Lviv, +380(97) 852 22 00; solomia.guta@gmail.com

Nataliya Drobinska, PhD, Assistant Professor, https://orcid.org/0000-0002-4714-3688; Danylo Halytsky Lviv National Medical University, Department of Internal Medicine N 1 (69, Pekarska Str., Lviv, 79010; +380(32) 236 84 19); +380(93) 112 59 91; likarkanata@gmail.com

Ruslana Ivanochko, PhD, Assistant Professor, https://orcid.org/0000-0002-6211-6661; Danylo Halytsky Lviv National Medical University, Department of Internal Medicine N 1 (69, Pekarska Str., Lviv, 79010; +380(32) 236 84 19); 67, Krychevsky Str., Lviv,+380(96) 226 00 64; ruslana.ivanochko07@gmail.com

Solomiya Tolopko, PhD, Associate Professor, https://orcid.org/0000-0002-4940-3850; Danylo Halytsky Lviv National Medical University, Department of Internal Medicine N 1 (69, Pekarska Str., Lviv, 79010; +380(32) 236 84 19); 16, Masaryk Str., Lviv; +380(96) 753 10 34; solomia_tol@ukr.net

Mariia Ferko, PhD, Associate Professor, https://orcid.org/0000-0002-5932-6991; Danylo Halytsky Lviv National Medical University, Department of Internal Medicine N 1 (69, Pekarska Str., Lviv, 79010; +380(32) 236 84 19); +380(67) 285 90 21; marija353@email.ua