News in Celiac Disease about Differential Diagnosis from Romania

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Abstract Evolution of celiac disease is continuously changing. Celiac disease has become a public health problem in some countries. Knowledge of the disease evolution is important to find current problems of disease. In this article, we wanted to discuss the recent medical and diagnostic discoveries from Romania.

Keywords: evolution, medical considerations, diagnostic approach, gluten-free diet, Romania, European context


1. Introduction

The first records of the study of celiac disease in Romania were reported in 1966 [1,2]. Different researcher assessed clinical and laboratory aspects and classification of malabsorption syndromes in the following years [3,4,5]. The collaborations with foreign researchers began in 1992. The conclusion of the study group was that CD diagnosing varied from many standard texts in Great Britain [6]. In Romania, the professor Nicolae Miu was the pioneer in the CD study at that time. The value of jejunal biopsy was emphasized on diagnosis and monitoring of the treatment [7]. The ultrastructural changes have been noticed in the jejunal mucosa by scanning electron microscopy in CD children [8]. A special case of a patient with fatal hemorrhage from small intestinal lymphoma complicating unresponsive CD treated with cyclosporine was reported in 1997 [9]. Therefore jejunal biopsy was not enough for preventing long-term complications in CD. Although the gold standard for CD diagnosis was the small bowel biopsy, in early of 2000 the first serological tests began to be used for the diagnosis of CD. IgA anti-tissue transglutaminase antibodies (tTG) were 100% positive in patients with clinical suspicion of CD, the diagnosis being confirmed by biopsy. Serum antiendomisium antibodies (EMA) levels correlated perfectly with histological alterations [10].

Recent years have brought constant changes in CD diagnosis. In 2010, the CD prevalence was 1% in Europe population. Many associations with CD were found, e.g. autoimmune type 1 diabetes mellitus (T1DM), osteoporosis or Sjogren's syndrome [11]. Four types were defined according to the Oslo definition of CD: 1). Classical CD – the patients present gastrointestinal signs and symptoms; 2). Non-classical CD – the patients do not present typical gastrointestinal manifestations; 3). Subclinical CD – the patients present autoimmune and genetic conditions or first degree relatives to patients; 4). Potential CD – the patients present positive serology, but minimally abnormal changes in intestinal biopsies [12]. Identification of large number of CD associations has led to the increasing prevalence of CD in recent years [13]. The introduction of serological tests as a screening test of CD has also contributed to increasing prevalence of CD from recent years [14]. DQ2 prevalence was 5-20% in Western Europe but DQ8 prevalence was < 5% in Eastern Europe [15]. Laboratory tests had a great explosion, e.g. tTG, EMA and antibodies against synthetic deamidated gliadin peptides (DGP). Gluten toxicity screening has been extensively studied [16]. The persistence of more than 6-12 months of symptoms of malnutrition and intestinal villous atrophy although the patient follows a strict gluten-free diet (GFD) was called refractory celiac disease (RFC). RFC has become a challenge in immunology [17].

The aim of our review was to follow the evolution of CD diagnosis in the last years from Romania in European context. We studied all articles about CD written by Romanian researchers or foreign researchers about Romania.

2. Results and Discussions

Intraepithelial lymphocytes were helpful in early recognising of CD but the finding was not specific. Therefore the histopathology exam of duodenal biopsy remained the gold standard of the diagnosis of CD in the years 2009-2010 [18,19]. Capsule endoscopy technology was proposed due to image quality provided with the intestinal villi [20]. Ciobanu et al. proposed capsule endoscopy for the diagnosis of CD in patients with Crohn's disease not responding to immunosuppressant or biological treatment [21].
2.1. Medical Considerations

The prevalence of CD in the pediatric population has been increasing in recent years: 4.09% [22], 8.7% [23] and 11.2% [24]. The prevalence of CD in adult population was found to be 2.22% [25], but this study is old and a new study unfortunately does not exist. Therefore a comparison between the CD prevalence in children and adults is not possible. However, the highest prevalence according to Marsh classification has it the form Marsh IIIe (46%) among adult patients with CD [26,27]. T1DM and the first degree relatives of CD patients have been identified as high risk groups. Association of CD with T1DM has been the subject of many studies [28]. The CD prevalence among the T1DM patients in Romania was 3.9% that is comparable with European studies in adult patient with CD [29]. The IgA anti-tTG prevalence in children with T1DM was 9.2%, and sensitivity and specificity of IgA anti-tTG were 80 and 82.6% [30]. Another association of CD is with Turner syndrome, in which besides GFD, the patient requires endocrine treatment [31]. Ioniță-Radu et al. presented a case of young women, who developed CD during the treatment for chronic hepatitis C. What could be the cause? The study authors concluded that interferon and ribavirin therapy are associated with induction or exacerbation of preexistent autoimmune disorders [32]. Samasca et al. proposed CD screening in hepatitis C, respectively determination of IgA anti-tTG before and after starting treatment with interferon [33]. Altered liver function was also found in 12 from 120 CD diagnosed patients [34].

2.2. Diagnosis Approach

A combination of most specificity and sensitivity IgA anti-EMA and IgA anti-tTG was used as screening tests for risk populations such as T1DM, Turner syndrome, William’s syndrome, immunoglobulin A deficiency and first degree relatives of CD patients [35]. Samasca et al. proposed IgA anti-tTG as a screening methods [36], as did their predecessors [37]. Possible association between asymptomatic CD and dermatitis herpetiformis was revealed [38]. New tests (IgG-F-actin antibodies) have been evaluated in CD and dermatitis herpetiformis but the results were not relevant [39]. IgA+IgG DGP were evaluated as a new serological test. Conclusion was that IgA+IgG DGP is a useful test as serological marker for the CD screening and at the same time in the immunoglobulin A deficit for the 0-3 years age group. IgA+IgG DGP was also a test of high precision diagnostic value in all child age groups [40]. Recently, Belei and Marginiane have proposed a new test, a combination of DGP and tTG, namely IgA/IgG DGP/tTG screen assay for CD detection among symptomatic and at risk young children [41]. Genetic tests have been introduced to the diagnosis and prognosis of CD. The study authors have emphasized the genetic testing importance in relatives of patients with CD, where serological tests were negative but genetic tests were positive [42,43].

A question was whether serological tests can replace duodenal biopsy? Duodenal biopsy during the routine gastrointestinal endoscopy has recommended being included in clinical practice as a diagnostic method of CD in high risk symptomatic patients and those with anemia and / or chronic diarrhea [44]. Samasca et al. presented a case report that brings a question about a rapid and certain diagnosis in CD with secondary lactose intolerance, given by serological tests compare with duodenal biopsy, a more invasive, children unpleasant [45]. The same opinion is shared by Nur Arslan, related to the performance of IgA/IgG DGP/tTG in young children compared with duodenal biopsy [46]. Popp et al. concluded that high IgA anti-tTG titres do not require endoscopy with duodenal biopsies for CD diagnosis in children with T1DM. But the patients with lower IgA anti-tTG positive antibodies need duodenal biopsy [47]. These conclusions are in line with the recommendations of the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) [48]. A rare manifestation of CD was described, namely: the cavitating mesenteric lymph node syndrome with an estimated mortality rate of 50% [49]. Mosteanu et al. proposed spiral enteroscopy for patients who are developing complications during CD follow-up [50].

2.3. Gluten-free Diet

GFD is difficult to follow. Improving quality of life (QOL) of patients with CD that follows a GFD has been an important concern in Europe [51]. Anca et al. established that supported groups, better prices and food labeling would improve the QOL of CD patients [52]. But Samasca et al. concluded that GFD should be understood first by the families of children with CD [53]. Unfortunately, we have same circumstances among Romanian immigrants in northern Italy. The twin nostalgia of immigrant children for foods and tastes from the native country represents a problem that will be difficult to resolve [54]. A balanced caloric GFD, fat and protein to make sure an ideal nutritional status and prevent long-term complications is also necessary [55]. The genetic variability of wheat [56], the use of microbial biotechnology [57], bake-off technology [58] can also provide solutions to gluten-free products of CD patients. The immunochromatographic assay was an efficient rapid tool for gluten toxicity screenings, as an alternative to the enzyme-linked immunosorbent assay (ELISA) techniques [59]. This is an important issue for detection of gluten in dietary products that is highly important to the safety of products consumed by CD and gluten-sensitive patients [60]. Therefore, a special attention should be given to gluten screening toxicity.

3. Conclusions

Following the diagnosis of CD in the last years, we established the following: 1). New diagnostic methods (serological tests, capsule endoscopy technology) but with persistent of duodenal biopsy as gold standard have characterised the years 2008-2010; 2). Studies were focused on the CD association from 2010. Serologic tests have identified CD as being associated with many other autoimmune diseases, like T1DM, osteoporosis, Sjogren’s syndrome, Turner syndrome, William’s syndrome, immunoglobulin A deficiency. The serological importance increased compared with duodenal biopsy in the last years. Genetic testing is also important to relatives of CD patients as a risk factor.