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PECULIARITIES OF HISTOLOGICAL EXAMINATION BEFORE AND AFTER GLUTEN-FREE DIET IN CHILDREN WITH CELIAC DISEASE

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Rezumat

PARTICULARITĂŢILE EXAMENULUI HISTOLOGIC PÂNĂ ŞI DUPĂ REGIMUL FĂRĂ GLUTEN LA COPIII CU BOALĂ CELIACĂ

Cuvinte - cheie: boala celiacă, aspect histologic, dietă fără gluten.

Introducere: *Boală celiacă constituie una din poblemele majore ale gastroenterologiei moderne, datorită polimorfismului clinic şi creşterii incidenţei formelor atipice şi silenţioase. Pentru confirmarea diagnosticului de boală celiacă „standardul de aur” este examenul histologic, rolul anatomopatologului fiind esenţial, deoarece în stadiile de debut depistarea leziunilor histomorfologice specifice este dificilă, şi pot induce lacune în diagnostic.*

Material şi metode: *Studiu retro- şi prospectiv, lotul de cercetare a inclus 428 pacienţii internaţi în secţia gastroenterologie a IMSP Institutul Mamei şi Copilului în perioada 2012–2014, cu diagnosticul de malabsorbţie intestinală. În baza datelor clinice, serologice şi a examenului histologic diagnosticul de boală celiacă a fost stabilit la 29 copii. Ulterior, după respectarea dietei fără gluten, a fost efectuat examenul histologic repetat la interval de 1 an şi respectiv 2 ani.*

Rezultate: *Conform clasificării Marsh, au fost înregistrate modificări histologice Marsh tip 1 – 3 copii (10,34%), Marsh 2 – 2 copii (6,89%), Marsh 3a – 18 copii (62,06%) şi Marsh 3b – 8 copii (27,58%). Tabloul histologic după 1 an de dietă fără gluten a înregistrat o ameliorare cu scăderea numărului de limfocite intraepiteliale până la 20/100 enterocite la 23 copii (79,31%) şi până la 30/100 enterocite la 4 copii (13,79%), la 2 copii (6,89%) a persistat numărul crescut până la 40/100 enterocite. Atrofia parţială s-a menţinut la 7 copii (24,13%), după 1 an de regim fără gluten, şi la 2 copii (6,89%), respectiv la 2 ani.*

Concluzii: *Diagnosticul de boală celiacă este posibil numai în cazul în care atrofia vilozitară este asociată cu o creştere patologică a numărului de limfocite intraepiteliale în asociere cu datele clinice şi de laborator.*

Резюме

ОСОБЕННОСТИ ГИСТОЛОГИЧЕСКОГО АНАЛИЗА У ДЕТЕЙ С ГЛЮТЕНОВОЙ БОЛЕЗНЬЮ. ДО И ПОСЛЕ БЕЗГЛЮТЕНОВОЙ ДИЕТЫ

Ключевые слова: глютеновая болезнь, гистологический аспект, безглютеновая диета.

Введение: *Глютеновая болезнь является одной из главных проблем современной гастроэнтерологии, за счет наличия клинического полиморфизма и увеличения числа атипичных и скрытых форм. Для подтверждения диагноза глютеновой болезни, «золотым стандартом» является гистологический анализ, роль анатомопатолога в осуществлении этого анализа является самой важной, так как обнаружение гистоморфологических специфических поражений на ранних этапах является очень трудным и может вызвать пробелы в диагностике.*

Материалы и методы: *Исследование ретро- и проспективное проводилось на группе из 428 больных, госпитализированных в отделение гастроэнтерологии ИМСП Институт Матери и Ребёнка в период 2012-2014, с синдромом мальабсорбции. На основе клинических и серологических данных, а также гистологического обследования, диагноз глютеновой болезни был обнаружен у 29 детей. Впоследствии, после соблюдения безглютеновой диеты было осуществлено повторное гистологическое обследование в интервале в 1 год и соответственно – в 2 года.*

Результаты: *Согласно классификации Марша были зарегистрированы гистологические изменения Марша типа 1 у 3 детей (10,34%), Марша 2 у 2 детей (6,89%), и Марша 3а у 18 детей (62,06%), Марша 3б у 8 детей (27,58%). Гистологическая картина после одного года соблюдения диеты без глютена зарегистрировала снижение интраэпителиальных лимфоцитов до 20/100 энтероцитов у 23 детей (79,31%) и до 30/100 энтероцитов у 4 детей (13,79%), у 2 детей (6,79%) сохранился высокий уровень до 40/100 энтероцитов. Частичная атрофия сохранилась у 7 детей (24,13%) после одного года соблюдения безглютеновой диеты и у 2 детей (6,79%) соответственно после двух лет соблюдения безглютеновой диеты.*

Выводы: *Диагноз глютеновой болезни возможен только в случае, когда ворсинчатая атрофия сочетается с патологическим увеличением числа интраэпителиальных лимфоцитов, в сочетании с клиническими и лабораторными данными.*

Introduction. Celiac disease or gluten intolerance is an autoimmune disease triggered by the ingestion of gluten in genetically susceptible individuals. Currently celiac disease remains one of the major problems of modern gastroenterology, due to clinical polymorphism and increased incidence of atypical and silent types. Histological examination is the „gold standard" to confirm the diagnosis of celiac disease, the anatomopathologist`s role being essential, because it is difficult to detect specific histomorphological lesions at early stages, inducing some gaps in diagnosis. Normal intestinal mucosa presents a digitiform appearance, the ratio of villi and crypts is always in favor of villi (3:1 or more) [1]. According to individual variability, the number of intraepithelial lymphocytes ranges between 25 and 29 per 100 epithelial cells [1, 2, 3, 4].

In patients with celiac disease the increase of the number of intraepithelial lymphocytes has a fundamental importance, among less specific lesions being: enterocyte height decrease, enterocytes flattening, crypt hyperplasia, villous atrophy with villi height decrease, modification of the normal ratio of crypt/villi (3:1) until the complete disappearance of villi [5, 6]. The issues that raise doubts and require anatomopathologist`s caution in the diagnosis of celiac disease concern initial lesions (Marsh 1-2/Grade A).

The diagnosis of celiac disease is based on histological identification correlated with clinical and serological lesions. To simplify and standardize the activity of this condition, Marsh classification was proposed, modified recently by Corazza and Villanacci [7, 8].

Subsequently children followed the gluten-free diet for a two-year period, the histological evaluation being repeated after 1 year and 2 years, respectively.

Purpose of study: To assess the histological peculiarities in patients with celiac disease and to estimate the histological response to gluten-free diet.

Materials and methods: The research was based on a retro- and prospective study that included 428 patients hospitalized in gastroenterology department of PMSI Institute of Mother and Child within 2012 - 2014 diagnosed with intestinal malabsorption. The study group comprised children aged between 2 and 17 years. Based on clinical and serological data as well as histological examination, the diagnosis of celiac disease was made in 29 children. The histological lesions were evaluated according to Modified Marsh Classification (Oberhuber), Corazza - Villanacci. All the patients included in the study complied with the gluten-free diet, being subjected to clinical, serological and histological assessment after 1 year and 2 years, respectively.

Results: The distribution of children by sex showed the prevalence of female patients - 19 girls (65,51%), mean age 6.4 years. The histological examination of patients with celiac disease in the study group showed an increase in intraepithelial lymphocytes over 35 per 100 enterocytes in 13 children (44,82%), over 45/100 enterocytes in 9 children (31,03%), and over 60/100 enterocytes in 7 patients (24,13%). Crypt hyperplasia

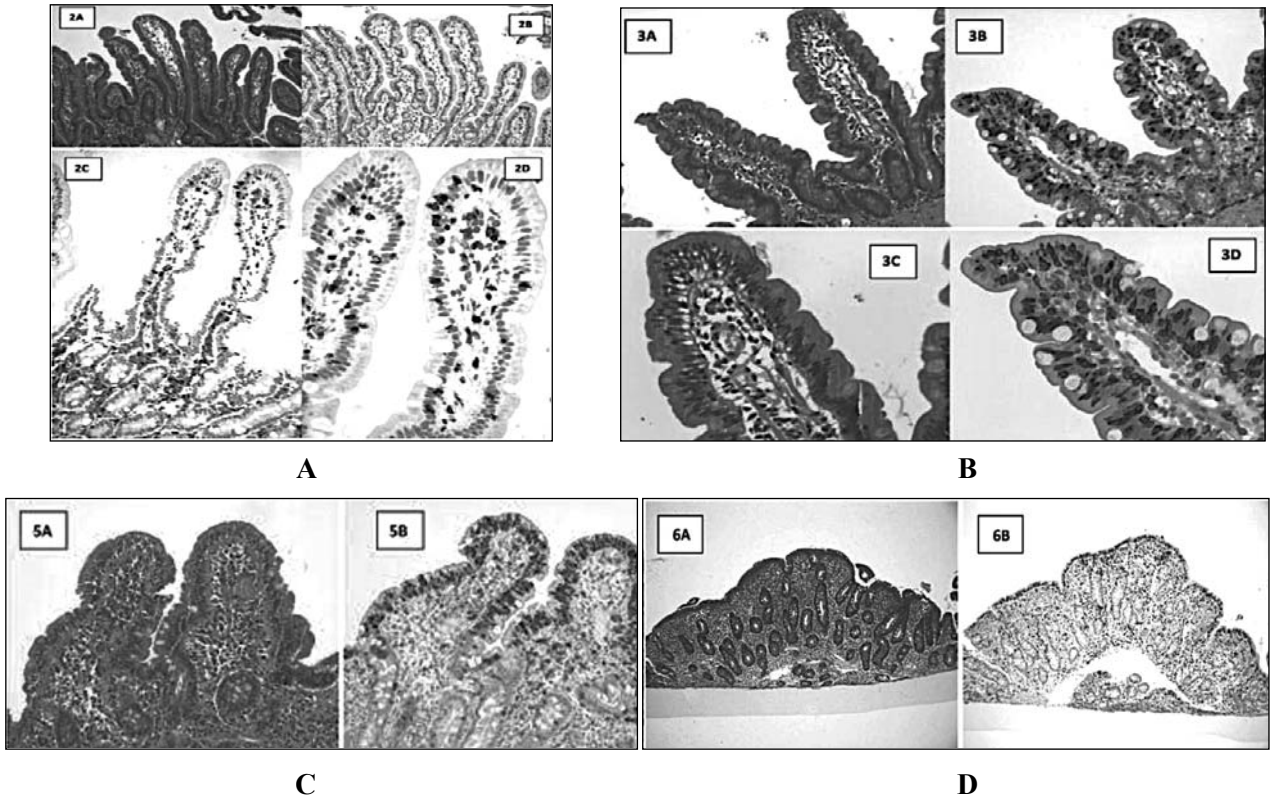

Figure 1. Normal duodenal mucosa, A, Marsh 1 - 2, B, Marsh 3a - 3b, C, Marsh 3c, D.

Table 1.

Histological classification by Modified Marsh Classification (Oberhuber) Corazza - Villanacci [6, 7]

Histological criteria				Corazza - Villanacci
modified Marsh (Oberhuber)	**Increased intraepithelial lymphocytes ***	**Crypt hyperplasia**	**Villous atrophy**	
Type 0	absent	absent	absent	
Type 1	present	absent	absent	Grade A
Type 2	present	present	absent	
Type 3a	present	present	present (partial)	Grade B1
Type 3b	present	present	present (subtotal)	
Type 3c	present	present	present (total)	Grade B2
Note:	* > 40 intraepithelial lymphocytes per 100 enterocytes for modified Marsh (Oberhuber) > 25 intraepithelial lymphocytes per 100 enterocytes for Corazza			

was revealed in 27 children (93,10%), its absence being recorded in 3 children (10,34%). Partial villous atrophy with villi height decrease was estimated in 19 children (65,51%), 4 children (13,7%) had subtotal villous atrophy, while 1 child (3,44%) had total atrophy. Based on Marh classification, there were recorded histological changes of Marsh type 1, only the increase of intraepithelial lymphocytes in 3 children (10,34%), Marsh 2 - crypt hyperplasia in 2 children (6,89%) and Marsh 3a - partial villous atrophy being determined in 18 children (62,06%), and subtotal villous atrophy Marsh 3b in 8 children (27,58%). Later, after following the gluten-free diet, the histological examination was repeated after 1 year and 2 years, respectively. The clinical response to gluten-free diet was fast within some days or weeks. However, it was observed that histological recovery may take several months and is not complete. The improvement of histological picture was recorded after 1 year of gluten-free diet, with a decreased number of intraepithelial lymphocytes up to 20/100 enterocytes in 23 children (79,31%) and up to 30/100 enterocytes in 4 children (13,79%). The increased number up to 40/100 enterocytes persisted in 2 children (6,89%). Despite strict adherence to gluten free diet, partial atrophy remained in 7 children (24,13%) after 1 year, and persisted in 2 children (6,79%) after 2 years of diet.

Conclusions:

1. To establish the diagnosis of celiac disease, it is necessary to have a multidisciplinary collaboration and an adequate number of qualitative biopsies.

2. The diagnosis of celiac disease is only possible if villous atrophy is associated with a pathological increase in the number of intraepithelial lymphocytes in combination with clinical and laboratory data.

3. Histological recovery may take several months and is not complete, despite strict diet followed by each patient.

4. Both early diagnosis and initiation of gluten-free diet are necessary to improve the quality of life of these children and to avoid complications, which are sometimes irreversible, having a reserved prognosis.

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