Lymphocytic colitis in a child with non-responsive celiac disease

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Abstract

In celiac disease, symptoms usually improve with strict adherence to diet. Some patients however do not show improvement despite of diet therapy. We here report a girl with non-responsive celiac disease whose diarrhea did not improve despite of a gluten free diet. A 12-year-old girl with recurrent diarrhea and failure to thrive was diagnosed with celiac disease. After six months of gluten-free diet her symptoms persisted. Adherence to diet was considered as correct and complete by a dietitian evaluation and by anti-endomysial antibodies that had become negative. Treatment with pancreatic enzymes, metronidazole or lactose free diet did not improve her symptoms. Colonoscopy was performed and lymphocytic colitis was diagnosed on histology from colonic biopsies. After mesalamine therapy diarrhea ceased, and weight and height z scores increased. Lymphocytic colitis, which is uncommonly seen in children compared to adults, should be considered in non-responsive celiac disease in children. (Acta gastroenterol. belg., **2008**, 71, **393-395**).

Key words : Celiac Disease, lymphocytic colitis, children.

Introduction

Celiac disease (CD) is a gluten sensitivity causing an immune-mediated enteropathy in genetically susceptible people (1). The only available treatment for CD is life-long gluten-free diet. With strict adherence to diet, symptoms improve and levels of the serological markers decrease within a year (1,2). On the other hand, some patients do not show improvement despite of diet therapy. In this case, non-adherence to the diet, secondary lactose intolerance, bacterial overgrowth, pancreatic insufficiency, inflammatory bowel disease and microscopic colitis should be excluded (3-5). We here report the case of a girl with non-responsive CD whose diarrhea did not improve despite of gluten free diet and lymphocytic colitis was defined in colonoscopic biopsies.

Case report

A 12-year-old girl presented with recurrent diarrhea and failure to thrive. She was feeling necessity to defecate after every meal. Her weight and height values were below the 5th percentile, weight for height value was 85%, weight z score was -2.87 and height z score was -2.6. Her daily energy intake was higher than her daily energy need. Investigations for malabsorption revealed normal results except a positive anti-endomysial antibody. An upper gastrointestinal endoscopy was performed and multiple biopsies were taken from edematous duodenal mucosa. Villous atrophy, crypt hyperplasia, increased intraepithelial lymphocyte number (40%) confirmed the diagnosis of CD (Fig. 1). She was started on gluten-free diet. After six months of diet therapy her symptoms persisted and there was no change in her weight and height z scores. Her diet was reconsidered. Adherence to the diet was complete and the anti-endomysial antibody had become negative at this time. Despite no laboratory clue of pancreatic insufficiency, pancreatic enzyme replacement therapy was begun. However her weight and height values were still below the fifth percentile and diarrhea did not cease. Therefore metronidazole therapy for bacterial overgrowth and lactose free diet for presence of possible secondary lactose intolerance were tried. Because she did not respond to these therapies, esophagogastroduodenoscopy was repeated, and colonoscopy was performed (Fig. 2). The endoscopic appearance and the histological structure of the duodenum were within normal limits. Because the histological examination of colon was concordant with lymphocytic colitis (LC) (Fig. 3), mesalamine therapy (50 mg/kg/day) was begun. Two weeks after she was started on mesalamine therapy diarrhea ceased. Within four months her weight and height increased 4 kg and 4 cm respectively. After six months of drug therapy colonoscopy was repeated and it was found that histological findings were still present. On the other hand, her weight for height value, weight and height z scores had increased (100%, -2.03 and -2.47 respectively). In addition, pubertal development started after mesalamine therapy, at the last visit breast development was stage II and pubic hair was stage III.

Discussion

Non-responsive CD is defined as lack of initial response or recurrence of symptoms despite gluten-free diet (6). After starting gluten free diet, clinical improvement occurs within the first few weeks of therapy, which is followed by histological improvement (6). Clinical

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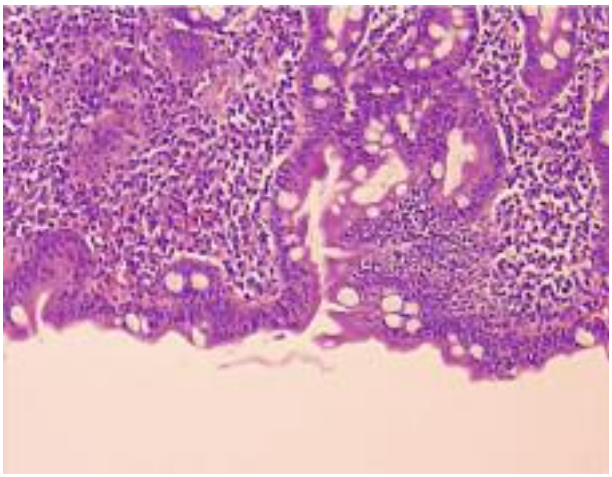

Fig. 1. — Duodenal biopsy. Histologic examination revealed total villous atrophy, cryptitis and crypt hyperplasia suggestive of Celiac disease (×10, H&E).

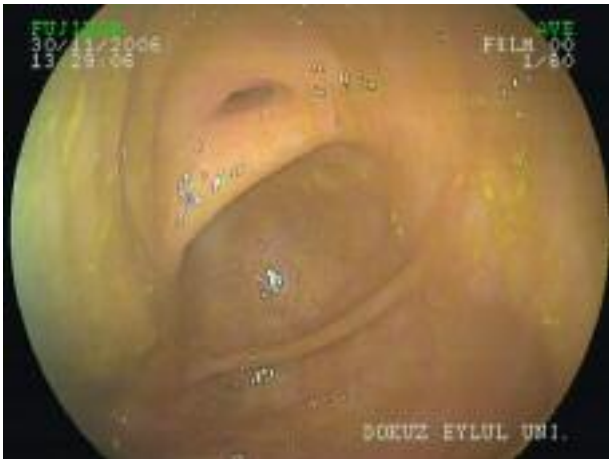

Fig. 2. — Macroscopically normal appearance of colon

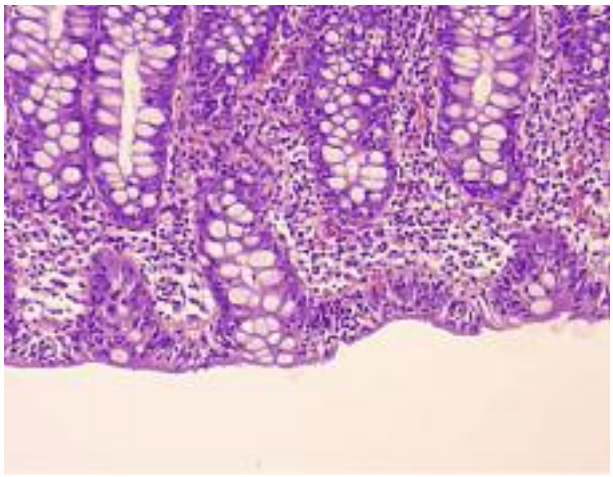

Fig. 3. — Lymphocytic colitis. Dense lymphocytic infiltrate in the epithelium associated with many lymphoid follicles (×10, H&E).

improvement may take as long as two years until histological improvement is complete. Rarely, clinical symptoms persist in spite of histological improvement like it was in our patient (6). After 18 months of gluten free diet, her symptoms persisted while the histological evaluation of duodenum was normal.

In cases with non-responsive CD, other reasons should be sought. Gluten contamination, bacterial overgrowth, pancreatic insufficiency, LC, collagenous colitis, secondary lactase deficiency, coexisting inflammatory bowel disease, irritable bowel syndrome, ulcerative jejunitis, autoimmune enteropathy and other food intolerances are the disorders that should be taken into consideration (4-6). Diet of our case was re-evaluated by the dietician and serum anti-endomysial antibodies revealed normal results. These findings supported the adherence to the gluten free diet. Metronidazole, pancreatic enzyme replacement therapy and lactose free diet did not produce improvement. Colonoscopy revealed normal macroscopic findings, but histological evaluation was in concordant with LC. Therefore we accepted LC as the diagnosis and started mesalamine therapy.

Lymphocytic colitis, which consists of expansion of lamina propria with chronic inflammatory cells and elevated number of intraepithelial lymphocytes (7), is found in 6-10% of adult non-responsive CD (6,8). Even though LC is a disorder of the elderly, it might be seen in children also, only less commonly (9,10).

It was demonstrated in previous studies that CD is associated with diffuse epithelial T-cell infiltration at all levels of gastrointestinal tract (7,11). Only the frequency of monoclonal T cell receptor γ gene rearrangements was discriminating CD patients on gluten free diet and active CD patients from refractory CD (11). Depending on this data it may be proposed that lymphocytic colitis may not be a different entity from CD. On the other hand, it was stated that CD patients with microscopic colitis generally did not respond to gluten free diet (9). However, why one group with microscopic colitis and CD respond to gluten free diet while another group does not is controversial (9). An explanation for this was that, patients might be reacting to minute amounts of gluten or another luminal antigen other than gluten (9). Diagnostic importance of LC on the response to gluten free diet and its relation with CD might be a topic for further research. After mesalamine therapy, our patient's symptoms improved and the weight for height, weight and height z scores increased. On the other hand, no improvement was present histologically. This may be due to taking the control biopsies too early.

In conclusion, lymphocytic colitis, which is seen uncommonly compared to adults, should be considered in non-responsive CD of children. Even though this may be accepted as a part of CD, with an appropriate therapy patients may display improvement.

References

1. LEFFLER DA., DENNIS M., HYETT B., KELLY E., SCHUPPAN D., KELLY C.P. Etiologies and predictors of diagnosis in nonresponsive celiac disease. *Clin. Gastroenterol. Hepatol.*, 2007, **5** : 445-450.
2. HILL I.D., DIRKS M.H., LIPTAK G.S., COLLETTI R.B., FASANO A., GUANDALINI S., HOFFENBERG E.J., HORVATH K., MURRAY J.A., PIVOR M., SEIDMAN E.G., NORTH AMERICAN SOCIETY FOR PEDIATRIC GASTROENTEROLOGY, HEPATOLOGY AND NUTRITION. Guideline for the diagnosis and treatment of Celiac disease in children : recommendations of North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. *J. Pediatr. Gastroenterol. Nutr.*, 2005, **40** : 1-19.
3. ABDULKARIM A.S., BURGART L.J., SEE J., MURRAY J.A. Etiology of nonresponsive celiac disease : results of a systematic approach. *Am. J. Gastroenterol.*, 2002, **97** : 2016-2021.
4. DAUM S., CELLIER C., MULDER C.J. Refractory coeliac disease. *Best Pract. Res. Clin. Gastroenterol.*, 2005, **19** : 413-424.
5. GREEN P.H.R., JABRI B. Coeliac disease. *Lancet*, 2003, **362** : 383-391.
6. MASHAKO M.N., SONSINO E., NAVARRO J., MOUGENOT J.F., GARGOURI A., BOIGE N., CEZARD J.P. Microscopic colitis : a new cause of chronic diarrhea in children ? *J. Pediatr. Gastroenterol. Nutr.*, 1990, **10** : 21-26.
7. BIAGI F., CORAZZA G.R. Defining gluten refractory enteropathy. *Eur. J. Gastroenterol. Hepatol.*, 2001, **13** : 561-565.
8. TAGKALIDIS P., BHATHAL P., GIBSON P. Microscopic colitis. *J. Gastroenterol. Hepatol.*, 2002, **17** : 236-248.
9. MAKI M, LOHI O. Celiac disease. *In* : WALKER W.A., GOULET O., KLEINMAN R.E., SHERMAN P.M., SHNEIDER B.L., SANDERSON I.R. (eds). Pediatric Gastrointestinal Disease Pathophysiology, Diagnosis, Management Volume 1. 4th ed. BC Decker Inc., Ontario, 2004 : 932-943.
10. MATTEONI C.A., GOLDBLUM J.R., WANG N., BRZEZINSKI A., ACHKAR E., SOFFER E.E. Celiac disease is highly prevalent in lymphocytic colitis. *J. Clin. Gastroenterol.*, 2001, **32** : 225-227.
11. VERKARRE V., ASNAFI V., LECOMTE T., PATEY MARIAUD-DE SERRE N., LEBORGNE M., GROSDIDIER E., LE BIHAN C., MACINTYRE E., CELLIER C., CERF-BENSUSSAN N., BROUSSE N. Refractory coeliac sprue is a diffuse gastrointestinal disease. *Gut*, 2003, **52** : 205-211.