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The value of focally enhanced gastritis in the diagnosis of pediatric inflammatory bowel diseases

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Abstract

Background and aims: Focally enhanced gastritis (FEG) has been suggested as a diagnostic marker for patients with Crohn's disease. In this study we evaluated the prevalence of FEG in children with inflammatory bowel diseases (IBD) and assessed the ability of FEG to distinguish IBD from non-IBD patients.
Methods: A retrospective study of the children who underwent esophagogastroduodenal endoscopy (EGD) during 2004–2011 was performed, after excluding individuals with H. pylori infection and celiac disease. Two groups were studied: patients with IBD (IBD group, n=185) and non-IBD patients who underwent endoscopy of the upper gastrointestinal tract for various abdominal complaints (non-IBD group, n=684). Relation of FEG to age and gender was also assessed.
Results: FEG was found significantly more frequently among children with IBD (35.7% vs 3.4%, respectively, $p<0.001$). Children with FEG were 15.4 times more likely to have IBD than to belong in the non-IBD group. All types of IBD had significantly higher frequencies of FEG compared to non-IBD individuals (Crohn's disease: 54.1%, ulcerative colitis: 21.6%, IBD unclassified: 18.4%, all three comparisons with the non-IBD group: p-values<0.001). FEG positivity was more common in females compared to males with Crohn's disease and ulcerative colitis and in children younger than 2 years in the IBD-unspecified group. FEG achieved a sensitivity of 35.7% and specificity of 96.6% in distinguishing between IBD from non-IBD patients.

Abbreviations: FEG, Focally enhanced gastritis; IBD, Inflammatory bowel disease; CD, Crohn's disease; UC, Ulcerative colitis; PPV, positive predictive value; NPV, negative predictive value.

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Conclusions: FEG has significantly higher prevalence in children with IBD, particularly Crohn's disease and can be a valuable supporting finding in cases of indefinite diagnosis.

1. Introduction

The diagnosis and classification of pediatric inflammatory bowel disease (IBD) are a complex task incorporating clinical, endoscopic, radiologic and histologic information.[1] In children, a macroscopically normal gastroscopy and ileocolonoscopy do not preclude the diagnosis of IBD. In this context the pathologist's report becomes even more crucial in the diagnostic process. The histopathological features of Crohn's disease (CD) and ulcerative colitis (UC) are well described; however, distinguishing between these two entities in clinical practice can be, occasionally, difficult.[1] Especially in children, problems with definitive diagnostic classification are more common considering that 4–30% of pediatric IBD patients are classified as having inflammatory bowel disease unclassified (IBDU).[1,2] Today, early and accurate distinction between CD, UC and IBDU is becoming increasingly important, as refinements in treatment are being identified.

Involvement of the upper gastrointestinal tract was traditionally considered to be a characteristic of Crohn's disease. In nowadays, it is well recognized that UC and IBDU may also affect the upper gastrointestinal tract.[3] Several studies in adults have shown that focally enhanced gastritis (FEG) is being recognized with increasing frequency in IBD.[3] The term "focally enhanced gastritis" was first introduced by Oberhüber in 1997.[4] It is used in order to describe perifoveolar or periglandular mononuclear or neutrophilic infiltrates around gastric crypts.[5] The lymphocytes are typically CD3 positive and the histiocytes are CD68R positive. The prevalence of FEG seems to differ among IBD patients, being more commonly identified in CD patients (up to 76%)[6] compared to UC (approximately 20%)[7] and in younger patients compared to older.[3,8] Data in pediatric IBD populations are scarce and the few published reports indicate that FEG could be a useful marker in diagnosing IBD, as well as discriminating between CD, UC and IBDU. The assessment of the diagnostic value of focal gastritis requires knowledge of the likelihood of FEG in non-IBD patients. Pediatric data in this field are even more limited and based on small samples. The prevalence of FEG in the general adult population is approximately 3%, once H. pylori gastritis and reactive gastropathy have been excluded.[3]

In this study we aimed at estimating the prevalence of FEG in a large number of newly diagnosed, treatment-naive children with IBD and in non-celiac, non-H. pylori children undergoing upper gastrointestinal endoscopy. We also assessed gender and age variations of FEG in both IBD and non-IBD individuals. Finally we evaluated the performance of FEG as a criterion in the distinction of IBD from non-IBD children, as well as between CD, UC and IBDU.

2. Methods

This retrospective study was conducted at the Gastroenterology Unit of the 1st Department of Paediatrics in the University of Athens, in "Aghia Sophia" Children's Hospital. The Ethics Committee of the hospital approved permission for medical review, waiver of informed consent and anonymous publication of data according to the Declaration of Helsinki.

Initially, all endoscopic and pathology reports during an 8-year period (2004–2011) were retrieved. We constrained the retrospective collection of data in that period in order to ensure that all procedures, including endoscopies, biopsies and microscopic analyses, would be complete and comparable for all individuals without any missing data. Subsequently, only children undergoing their first upper gastrointestinal endoscopy were included. Children who were later diagnosed with celiac disease or H. pylori infection, as well as children who had received, prior to the endoscopy, steroids, proton pump inhibitors or H_2 antagonists were excluded. Finally two groups were formed: children with a diagnosis of IBD and the control group which consisted of non-celiac, non-H. pylori children undergoing a first upper gastrointestinal endoscopy for investigation of abdominal complaints. Diagnosis of IBD was based on the Porto criteria[9] and further classified into three subgroups: CD, UC and IBDU.

The endoscopies were performed by trained pediatric gastroenterologists and the following biopsies were taken in all cases: second part of duodenum (2–4 biopsies), duodenal bulb (1 biopsy), antrum (1 biopsy), body (1 biopsy) and esophagus (3–6 biopsies). Specimens, were fixed in 10% formalin, and embedded in paraffin, and sections were stained with hematoxylin–eosin and modified Giemsa or Masson trichrome and assessed under light microscopy. All histological analyses were performed by a single, highly experienced histopathologist. Classification of gastritis was according to that of the updated Sydney system.[10] Focal enhanced gastritis was defined as presence in biopsy material of focal inflammatory lesions composed mainly of lymphocytes and histiocytes, and occasionally neutrophils involving at least one or a few adjacent foveolae/glands.[1,5] The definition of FEG was uniform across the study groups and patients with Crohn's disease and gastric involvement were not characterized as FEG-positive unless they fulfilled the described criteria.

In the IBD group, patients with Crohn's disease were classified as proposed by the Paris classification[11]: L1: distal 1/3 ileum ± limited cecal disease, L2: colonic disease, L3: ileocolonic disease and with regard to the involvement of the upper gastrointestinal tract (L4a+: involvement of the upper gastrointestinal tract, proximal to the ligament of Treitz, L4a−: no involvement). As different imaging modalities were used for detection of small bowel disease, the L4b classification was not applied.

Categorical variables are presented as absolute (n) and relative frequencies (%) and compared by Fisher's exact test. Quantification of the effect of categorical variables on the probability of IBD diagnosis and type of IBD diagnosis was done by logistic regression analysis and exact logistic regression analysis. Results are reported as odds ratios (OR) with 95%