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Presenting features and disease course of pediatric ulcerative colitis

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Abstract

Clinical variables and disease course of pediatric ulcerative colitis (UC) have been poorly reported. The aim of this study was to retrospectively describe the phenotype and disease course of pediatric onset UC diagnosed at a tertiary referral Center for Pediatric Gastroenterology.

Patients and methods: 110 patients with a diagnosis of UC were identified at our Department database. Records were reviewed for disease location and behavior at the diagnosis, family history for inflammatory bowel disease, pattern changes at the follow-up, need of surgery and cumulative risk for colectomy.

Results: Thirty-five % of patients had an early-onset disease (0–7 years). At the diagnosis, 29% had proctitis, 22% left-sided colitis, 15% extensive colitis and 34% pancolitis. Fifteen % presented with a rectal sparing, while a patchy colonic inflammation was reported in 18%. Rectal sparing was significantly related to the younger age (p: <0.05). Disease extension at the follow up was reported in 29% of pts. No clinical variables at the diagnosis were related to the subsequent extension of the disease. The cumulative rates of colectomy were 9% at 2 year and 14% at 5 years. An extensive disease as well as acute severe colitis and corticosteroid therapy at the diagnosis were significantly associated with an increased risk of colectomy.

Conclusions: Pediatric UC is extensive and severe at the diagnosis, with an overall high rate of disease extension at the follow-up. Endoscopic atypical features are common in young children. The colectomy rate is related to the location and severity of the disease at the diagnosis.

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1. Introduction

Ulcerative colitis (UC) and Crohn's disease (CD) are chronic, unremitting, immune-mediated disorders, known as inflammatory bowel diseases (IBD). Up to 25% of IBD first develop in childhood and adolescence, with recent studies suggesting an increasing incidence of pediatric CD in the last 20–30 years, whereas the incidence of UC seems to be remained stable or slightly decreased.[1–5]

UC is classically defined as a chronic inflammation characterized by a continuous involvement of the colonic mucosa in the absence of histological granulomas, affecting the rectum and a variable extent of the colon in continuity, with a course that is characteristically relapsing and remitting.[6] However, it is widely known that pediatric UC may present with atypical phenotypes, thus the above mentioned definition is not always applicable to the pediatric-onset disease.[7]

The clinical features at the diagnosis and the natural history of pediatric UC are poorly described, and only few population-based studies are available, most of them having been carried out before the era of immunomodulators and biological agents. Some data do suggest that most of children with UC present with moderate/severely active disease already at the diagnosis and 25–30% will become corticosteroid-dependent by 1 year.[8–10] The aggressive nature of the pediatric disease is marked by a relatively high rate of early colectomy: studies in 1990 showed a rate of colectomy around 25%[11] and, despite medical progresses, recent data have shown similar colectomy rates,[12] thus, raising the question as to whether the conventional therapeutic strategy in pediatric UC should be revised.

In the context of pediatric disease, early-onset (EO) UC is the most poorly described because this age group represents a small subgroup of IBD patients. However, few data suggest that it is more severe than the late-onset disease both in terms of phenotype and course.[13,14]

Given the high risk of a disabling course of disease and risk for surgery, children with UC have much to gain from therapeutic strategies altering the predicted course of the disease.[15] To date, there are no data on the history of pediatric UC following the wide use in clinical practice of immunomodulators and biologics in early phases of the disease. It is thus warranted in this population to identify predictive factors of severe disease course in order to optimize the therapeutic armamentarium.

The aims of this study, performed in a cohort of UC children followed at a single tertiary referral center for Pediatric Gastroenterology, were to describe clinical features of early- and late-onset pediatric UC, to evaluate the use of current therapy, including infliximab, and responses to treatment, and to identify factors that may predict extension of the disease and need of surgery.

2. Patients and methods

This is a retrospective longitudinal study conducted at a tertiary referral Center for Pediatric Gastroenterology and Hepatology. The department database was screened for all children diagnosed with UC by 2006 to 2011. Diagnosis of UC was made using widely agreed clinical, endoscopic and histological criteria.[16] All patients had a full colonoscopy with retrograde ileocolonoscopy. Until 2007, upper gastrointestinal endoscopy was mainly performed in patients who had not a definite diagnosis of UC based on colonoscopy. Since 2008, according to Porto criteria,[16] all patients at the diagnosis had both lower and upper gastrointestinal endoscopy. After the diagnosis, all patients were followed according to a standardized protocol including an annual ileocolonoscopy.

Case records were reviewed for clinical variables at the diagnosis and during follow-up. EO-UC was defined as a diagnosis of UC made in children aged between 0 and 7 years. Disease location at diagnosis and at follow-up was defined according to the Paris classification.[17] Ulcerative proctitis (E1) was defined as an involvement limited to the rectum (i.e., proximal extent of inflammation distal to the rectosigmoid junction). Left-sided UC (E2) as an involvement limited to the portion of the colorectum distal to the splenic flexure. Extensive UC (E3) as a disease extending proximally to the splenic flexure but distally to the hepatic flexure, while pancolitis (E4) included a colitis extended proximally to the hepatic flexure. Rectal sparing was defined as a normal rectum (endoscopically and/or histologically) when definite proximal disease was present. Patchy colonic inflammation was defined as areas of normal mucosa (endoscopically and/or histologically) amid areas of apparent inflammation. Disease extension was defined as the involvement, during follow-up, of at least one additional colonic segment. Disease activity was scored by the Pediatric UC Activity Index (PUCAI)[18]; an episode of severe colitis was defined as a PUCAI score >65.[19] Extra-intestinal manifestations (EIMs) included skin, joint and ocular manifestations, and primary sclerosing cholangitis. A family history for IBD was defined by the presence of CD or UC in first-degree relatives only. Laboratory tests included full blood count, C-Reactive Protein (CRP), Erythrocyte Sedimentation Rate (ESR), perinuclear Anti-Neutrophil Cytoplasmic Antibodies (p-ANCA), nutritional, renal and liver function parameters. Medical (i.e. mesalamine, corticosteroids, immunomodulators, infliximab) and surgical treatment received were also evaluated as well as intolerance or failure to therapy. One year after induction of the first course of corticosteroids (CS) treatment, CS-dependency and resistance were reported. The former was defined as a relapse of the disease within 30 days of cessation of treatment or relapse when dose reduction was attempted; the latter as a persistent active disease under CS therapy.[15] The study protocol has been approved by the ethical committee of the hospital.

2.1. Statistical analysis

All data were summarized and displayed as the mean ± SD for the continuous variables. Categorical data were expressed as frequencies and percentages. Comparison of groups was performed using Student's *t* test for unpaired data in two group comparison and one way analysis of variance (ANOVA) with Bonferroni's test for multiple group comparison. Chi square test with Fisher's correction was used to evaluate the differences for categorical variables wherever needed. A p value of 0.05 or less was considered significant. The Kaplan–Meier survival method was used to estimate the interval free from colectomy and from disease extension during follow-up. Differences between curves were tested using the Log-Rank test. Factors associated with disease extension were analyzed