

INFLAMMATORY BOWEL DISEASE IN INFANCY

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ABSTRACT

Background

Inflammatory bowel disease (IBD) may begin as early as the first year of life. The objective of the present study was to determine the characteristics and clinical course of children with early-onset IBD.

Materials and Methods

The records of patients with IBD admitted to Children Medical Center Hospital during 2003–2006 were screened for those with disease onset before the first year of life and who had a follow-up of at least 2 years.

Results

12 patients (8 boys, 4 girls) were identified. 9 had Crohn's disease. All of the patients had colitis. One of parents had IBD in 9 patients; 2 had a positive family history for IBD. 7 patients had weaned of breast fed when the gastrointestinal symptoms started. 10 patients had a severe onset of disease requiring total parenteral nutrition, and steroid followed by azathioprine. 3 patients with Crohn's disease needed surgery; another 3 with Crohn's disease died during the study. Of those with ulcerative colitis, one is in complete remission.

Conclusions

The prevalence of inflammatory bowel disease in infancy is unknown, but appears to be increasing. The course of the disease seems more severe..

Keywords: Crohn's disease, ulcerative colitis, Infant, Early-onset inflammatory bowel diseases

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INTRODUCTION

The onset of inflammatory bowel disease (IBD) peaks within the second decade of life with approximately 10% of patients are diagnosed in the pediatric age group. (1-3)

According to recent reports, (4-7) the incidence of pediatric Crohn's disease (CD) has been increased,

although the incidence of ulcerative colitis (UC) remained stable. Not only is the number of patients increasing but there are also data indicating onset of IBD within the first of life.(8-10) The North American pediatric IBD Consortium confirmed the onset of IBD within the first 12 months of life in 1% of their patients. (9, 11), The etiology of IBD is unknown, recent research data point to an altered immune homeostasis within the intestinal mucosa in genetically predisposed individual. (9, 12, 13) This may result in an exaggerated and uncontrolled inflammatory response probably triggered by the intestinal flora and/or other environmental factors. (9, 14) In the present study we analyzed the data of 12 children with onset of IBD before the first year of life.

PATIENTS AND METHODS

From those pediatric patients who were diagnosed as IBD and who attended the Children Medical Center during 2003–2006, we identified those in whom the onset of the disease has begun within the first year of life. Twelve patients were found. All had a complete diagnostic work-up including upper gastrointestinal (GI) series with small bowel follow through, barium enema or abdominal computed tomography (CT), and upper and lower GI endoscopy.

The diagnosis of CD was made if granuloma presented in proximity to the lymphoid follicles in biopsy of the upper or lower GI tract. On endoscopy, aphthous or deep ulceration with typical skip lesions all along the GI tract with macroscopic findings of focal inflammatory changes as well as the presence of perianal lesions or transmural inflammation (fistulizing or stricturing disease) were also used for the diagnosis of CD.

UC was diagnosed if a continuous inflammatory disease confined to the colon without any evidence of small bowel involvement (other than back wash ileitis) was present. Infectious or allergic disorders (using IgE and skin prick test) as well as immunologic disorders (using lymphocyte phenotyping, immunoglobulin levels, and NBT)

were ruled out in all patients.

Stool examination for culture and direct smear for pH, white blood cell (WBC), red blood cell (RBC) and parasites were done. PPD in all patients and mycobacteria were routinely searched in patients with suspected CD. Perinuclear anti-neutrophilic cytoplasmic antibody (PANCA) or anti-saccharomyces cerevisiae IgA antibody (ASCA) was routinely tested for all patients.

Steroid was given to all patients. Prednisolone was administered orally at a dose of two mg/kg per day; in patients who could not tolerate oral medication, intravenous hydrocortisone was administered. Following corticosteroid tapering, azathioprine and 6-mercaptopurine were given.

RESULTS

Out of 316 patients reviewed between 2003 and 2006, 12 (eight boys, four girls) were found to have IBD presented in the first year of life. The final diagnosis made was CD in nine and UC in three patients. Family history for IBD was positive in two patients; in one for there was a family history of autoimmune hemolytic anemia.

The mean age of patients was 30.3 months. The mean age of onset of the disease was 5.2 (range: 3–9) months. The disease began in four patients with watery diarrhea and in eight with bloody diarrhea. Seven patients had history of using antibiotics before beginning of the disease; the antibiotics included metronidazole, cefixime, amoxicillin-clavulanic acid, and vancomycin. Eleven of 12 patients had fever at the time of admission. Significant blood loss due to bloody diarrhea requiring blood transfusion happened in seven patients. Weight and length of patients were assessed in all patients; all had growth failure. Six of 12 patients were less than fifth percentile and the remaining six were less than twenty-fifth percentile (Table 1).

Perianal lesions were seen in one patient (Fig 1). Extra-intestinal involvement was seen as oral aphthous lesions in five of 12 and arthritis in two patients. No liver involvement was seen.

Table 1. Initial clinical presentations in 12 patients with IBD.

Characteristics	Number
FTT*	12
Oral aphthous	5
Perianal lesions	5
Bloody diarrhea	9
Watery diarrhea	3
Pyoderma gangrenosum	1
Arthritis (knee involvement)	2
Family history for IBD	2
Consanguineous parents	9

*FTT: Failure to thrive

**Figure 1.** Perianal lesion in crohn's

Serological markers including ASCA and PANCA remained negative in all patients (Table 2).

The results obtained from colonoscopy and pathology are presented in (Fig 2) (Table 3). Abdominal CT was performed in only two infants to rule out abscess.

Patients were followed for at least 1.5 years. All of the patients were treated with long steroid therapy and azathioprine. Three patients with CD died in the first month of treatment because of severe failure to thrive and sepsis; two of them underwent

surgery because of perianal abscess and bowel stenosis. Two patients with UC and six with CD are currently in partial remission and need repeated parenteral nutrition. One patient with UC is currently in complete remission.

DISCUSSION

The incidence and prevalence of IBD, mainly CD, have markedly rose during the last several decades. It is well established that both CD and UC occur in children younger than 10 years.(1-3,10,15)

There are only few reports that analyzing the onset and outcome of IBD in different pediatric age groups, with three series dealing specifically with children younger than five years of age.(8, 10, 15) To the best of our knowledge, this is the first report of IBD in Iranian infants. The ratio of infantile IBD to total IBD patients in our study was 3.8% which was 1%–2% in Rumele, et al, syudy. (8), Diagnosis of IBD in this age group is particularly difficult. Reports of other pediatric centers indicated that about 1%–2% of children have the disease onset within the first two years of life. (2, 8, 10, 11), The differential diagnoses of IBD in this age group are infectious and allergic colitis, that are the major causes of infantile colitis. Rare conditions such as immune defects (e.g., septic granulomatosis) or GSD type 1b can mimic IBD. (16), All of these were ruled out in our patients. All of the 12 patients had colitis; most of them had isolated colonic disease. This was the same as report of Heyman, et al,(11) and Mamula, et al. (15), This finding, however is in contrasts with observations in older children and adults with CD who have mostly predominant small bowel or ileocecal disease. (6-8), Only four patients with CD had ileal involvement (stenosis, thickening of intestinal wall with rigid loop; two had colic fistula). Since small bowel fallow through and abdominal CT are stressful, cause high exposure to radiation and are not sensitive, especially in infants, the pediatric gastroenterologists face a diagnostic dilemma. (16)

Table 2. Lab findings in 12 patients with IBD
No. of patients

Lab test	Number
Hb<10 g/dl (mean= 8.2)	10
ESR (18–85) (mean=45)	7
CRP (+ to 4+)	7
WBC in stool	12
ASCA/PANCA*	0
Immunological studies	normal

*ASCA (Anti-saccharomyces cerevisiae antibody); PANCA (Perinuclear antineutrophilic cytoplasmic antibody)

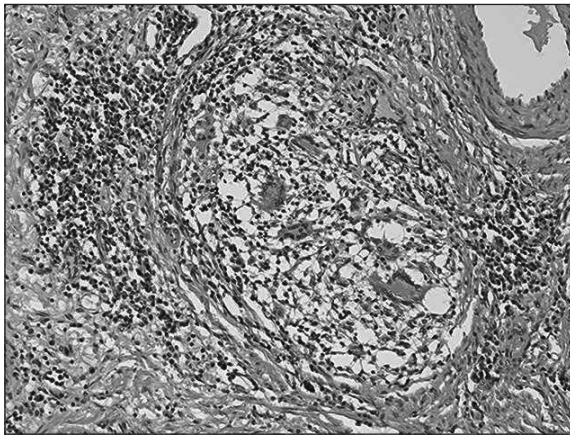


Figure 2. Granuloma in crohn's disease

Furthermore, PANCA and ASCA tests were not helpful for the diagnosis of IBD. (6-7-15) Recent reports indicated that a positive ASCA reflects small bowel or ileocolic CD, whereas patients with colonic CD are often negative for or have only low titers of ASCA.(8, 17, 18) PANCA is detectable in 15% of patients with CD. (7), However, serological markers were negative in all of our patients.

Two of 12 patients had a positive family history of IBD; one had a family history of hemolytic anemia. The reported rate was 29% in Heyman, et al, (11) and four of 10 in Ruemal, et al, studies.(8), Nine of 12 patients had consanguineous parents. This has not been reported in earlier studies. The epidemiologic data supported a positive family history of IBD as the strongest risk factor for the Steroid was given to all patients. (11, 19, 20) Seven patients had the history of using antibiotics. Altered interaction between the normal gut flora and the intestinal mucosa is a major triggering factor for IBD (2, 9, 21) and some studies indicated a link between the antibiotic use and the development of IBD(22, 23). Eleven of 12 patients requiring total parenteral nutrition and the use of immuno-suppressants such as azathioprine and 6-

Table 3. Colonoscopy, pathology and SBFT* in 12 patients

Colonoscopy	Pancolitis (3 with UC and 7 of 9 with CD) Left-sided colitis in 2 of 9 with CD Aphthous ulcers, deep ulcer, pseudopolyp, skip lesions in 9 of 9 patients with CD Erythema, edema, fragility, ulceration in 3 of 3 with UC
Granuloma	2 of 10 with CD
Cryptabscess	3 of 3 with UC
Eosinophils (in biopsy)	Rare
Small bowel fallow through	4 of 9 with CD had ileal involvement (stenosis, thickening of intestinal wall with rigid loop) 2 of 9 with CD had ileocolic fistula

* SBFT: Small bowel fallow through

mercaptopurine. Three of our patients needed surgery. The need for surgery was markedly higher and earlier in this age group.(24) Recent reports have special attention to prebiotics and probiotics,(24, 25) although we did not use it in our patients. Compared with older IBD patients, these patients required 1) more aggressive therapeutic efforts to achieve remission, 2) parenteral nutrition, 3) administration of steroids and immunosuppressants, 4) more surgical interventions, and 5) have more relapses. (3,8,16,24), development of IBD.(11, 19, 20), Seven patients had the history of using antibiotics. Altered in-

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CONCLUSION

Not only the number of pediatric IBD patients is steadily increasing, but also the affected children are increasingly younger. The major factor is probably a genetic predisposition for development of IBD. Several arguments indicate that a change of the intestinal flora make individuals prone to IBD.

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