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Does Inflammatory Bowel Disease Develop in Infants?

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Crohn disease (CD) and ulcerative colitis (UC), collectively known as inflammatory bowel disease (IBD), are chronic, idiopathic, destructive disorders of the gastrointestinal tract. IBD manifests during childhood or adolescence in up to 25% of patients, and the incidence has been increasing over the last two decades. Although a small percentage of children may present with IBD in infancy, a thorough evaluation is necessary in this age group as a number of conditions may mimic inflammatory bowel disease. This chapter reviews the epidemiology, differential diagnosis, and natural history of infantile IBD; we do not address acute infectious ileo-colitis.

The development of IBD in infancy is extremely rare. Published data from epidemiological studies and IBD registries in North America and Europe suggest that less than 1% of children with IBD present during the first twelve months of life. (Table1).[1-5] Although the numbers are small, CD seems to be more prevalent than UC in these and other studies. Additionally, it is not uncommon for infants initially diagnosed with UC or indeterminate colitis to have their diagnosis changed to CD during subsequent follow-up. Therefore, the distinction between CD from UC in infants is complicated, and many clinicians prefer an initial diagnosis of indeterminate colitis.

Because IBD is extremely rare in infants, thoughtful consideration of conditions that mimic IBD in this age group is warranted (Table 2). Allergic colitis is the most common etiology of non-infective colitis in infancy, comprising 62% of cases in a report of 42 infants with histologically proved non-infective colitis.[6] A well-known complication of Hirschsprung's disease, ileocolitis, may also resemble IBD. Autoimmune enteropathy may present in this age group, classically with intractable diarrhea and failure to thrive. Infants with congenital immune deficiencies can develop an IBD-like illness, and present with failure to thrive and colitis. Examples include HIV, chronic granulomatous disease, glycogen storage disease Ib, Hermansky-Pudlak syndrome, Wiskott Aldrich syndrome, NEMO (NF- κ B essential modifier) deficiency, leukocyte adhesion deficiency, and severe combined immunodeficiency. [7] Additionally, minor deficiency of mucosa-associated immune globulins such as IgA, IgG2, and IgG4 can occur in over 50% of infants with non-infective colitis, and may play a role in the pathogenesis of this disorder. [6] Infants with Behcet's syndrome may present with predominantly gastrointestinal involvement, and those with inherited malignancies such as hemophagocytic lymphohistiocytosis (HLH) may have inflammatory colitis. Finally, typhlitis (inflammatory ileo-cecitis) may occur in infants with neutropenia of any etiology. Since many of these conditions are life threatening and potentially treatable, detailed investigation and multi-specialty consultation may be extremely important (Table 3).

The clinical presentation of IBD in infants is heterogeneous; however, nearly all will have symptoms of chronic diarrhea. Other symptoms commonly reported in infantile IBD include failure to thrive, hematochezia, perianal disease, oral ulcerations, and small bowel obstruction. [8]

In contrast to older children and adults, almost all infants with IBD have disease involving the colon. [8] [9] Additionally, there may be a higher prevalence of perianal involvement in this age group. [10]

The natural history of IBD presenting in infancy is poorly defined. Although many reports describe a high morbidity (need for surgery, parenteral nutrition, etc), others do not indicate that very early age at presentation implies a poor prognosis.[9]

Evidence-based treatment of IBD presenting in infancy is limited. Therapeutic strategies have evolved from anecdotal experience and published series and case reports. For infants with significant colitis or ileocolitis, a small number will respond to an elemental diet. Those unresponsive to nutritional therapy are customarily treated with steroids; many will experience initial improvement. Very little has been written about the use of 5-aminosalicylates in the treatment of IBD in infancy, aside from its value as a maintenance agent in a few published cases. Despite initial responses to elemental nutrition or steroids, many patients eventually require 6-mercaptopurine/azathioprine, or, ultimately, colectomy. [9] In addition, tacrolimus and cyclosporine have also been used in infants with refractory disease, particularly when surgical resection was to be delayed or avoided. For infants with more limited perianal involvement, management with perianal hygiene and metronidazole may be appropriate.[10]

In conclusion, IBD will rarely develop in infancy. Very early presentation occurs in less than 1% of cases of pediatric IBD. IBD with onset in this age group is likely a heterogeneous group of disorders, and as such, there is variability in the clinical presentation and prognosis. It appears that, when compared to older children and adults, infants are more likely to demonstrate colonic involvement and may have a higher incidence of perianal disease. Though onset in infancy is more frequently associated with a CD-type illness, distinguishing between CD and UC is often complicated. Because a number of severe and potentially treatable illnesses may mimic inflammatory bowel disease in infants, a comprehensive, multidisciplinary evaluation is of paramount importance.

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Table 1

IBD Registries and Epidemiological Studies involving Infants

Study Group/Location Location	Number of children less than 1 year of age at presentation	Total number of children with IBD in Study	% of children with IBD who presented as infant	Predominant Diagnosis in Infancy
Wisconsin	0	199	0	N/A
Stockholm	1	152	0.6	IC
Netherlands	2	546	0.3	Not reported
Pediatric IBD consortium	13	1370	1	CD
Pediatric IBD Collaborative Group Registry	1	571	0.2	UC

Table 2

Conditions associated with IBD-like Illness in Infancy

Allergic colitis
Hirschprung's disease
Autoimmune enteropathy
HIV
Chronic granulomatous disease
Glycogen storage disease Ib
Hermansky-Pudlak syndrome
Wiskott Aldrich syndrome
NEMO (NF- κ B essential modifier) deficiency
Leukocyte adhesion deficiency
Severe combined immunodeficiency
Other immune deficiencies
Behcet's syndrome
Hemophagocytic lymphohistiocytosis
Typhlitis

Table 3

Evaluation of the infant with suspected IBD

Careful history to identify infectious exposures or possible immune deficiency (eg, late loss of umbilical cord, recurrent infections)
Family history of chronic infections, immunodeficiency, and autoimmune disorders
Physical examination to identify failure to thrive, oral ulcers, otitis, skin rash, abdominal distention, hepatosplenomegaly, lymphadenopathy, perianal disease, genital ulcers, and tight rectal sphincter
Laboratory evaluation to include complete blood count, platelet count, and examination of blood smear, immunoglobulin determination, nitroblue tetrazolium test, HIV antibody, anti-enterocyte antibodies, and fasting glucose
Specific tests to exclude other entities described in Table 2
Infection must also be excluded with appropriate cultures and serological markers
Specialized procedures including computerized tomography, upper gastrointestinal endoscopy with biopsies and ileo-colonoscopy with biopsies, liver biopsy as indicated