

## Ulcerative colitis in infancy: Our results

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### Abstract

**Introduction:** Ulcerative colitis (UC) is a debilitating disorder of colon. The incidence of UC peaks in the age group of 15 to 25, and only 1% are infantile. Despite initial medical treatment, in refractory cases, colectomy is needed. There are few studies regarding surgical results of treatment of UC in infancy.

**Material & Methods:** In our descriptive retrospective study we reviewed medical files of infants with ulcerative colitis that consulted with us for surgery between 2009 and 2014. Age at onset, family history of inflammatory bowel disease, symptoms of onset, colonoscopic findings, duration of Medical treatment, Indication of surgery, Type of operation, surgical complications and their Management and mortality was recorded.

**Results:** We found five patients with the diagnosis of UC in their first year of life; 4 boys and 1girl. The mean age of onset of the disease was 35 days (range 3-60). The mean age of patients at the time of surgical consult was 7 months. The disease began in 3 patients with watery diarrhea. Family history was positive in only one of our cases. He had sever FTT with no response to medical treatment which was an indication for surgery and he underwent total proctocolectomy, ileoanal anastomosis and loop ileostomy which failed and 3 days after the first operation we performed an end ileostomy. Two cases had colon perforation following their colonoscopy and one of them (a 4 month girl) expired before laparotomy and the other (a 12 month boy) underwent colostomy creation while he was in septic shock. The fourth patient was a 2 day old neonate with abdominal distention and intestinal obstruction. Rectal biopsy showed agangliosis so he underwent a transanal pull through procedure with a diagnosis of hirschsprung's disease. After surgery he experienced recurrent watery diarrhea and further diagnostic investigations brought about the diagnosis of UC. Our last patient was a 3 day old neonate that underwent ileostomy in the initial surgery with suspicion of total colonic agangliosis and underwent subtotal colectomy when he was 2 months old. At 1.5 years he developed toxic mega-colon in the remnant of colon when he was old and thus was referred to us and underwent colostomy. After 3 month the final surgery was carried out.

**Conclusions:** If a child presents with recurrent bloody or watery diarrhea even in infancy, UC should be considered as a differential diagnosis. The pattern of the disease in infancy appears more rigorous. Evidence-based management of UC presenting in infancy is incomplete but early surgical attempt can reduce catastrophic results.

### Keywords

- infancy
- ulcerative colitis
- Inflammatory Bowel Disease

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### Introduction

In recent years not only the incidence of pediatric IBD has increased<sup>1, 2</sup> but also there are reports from decreased age for onset of inflammatory disorders.<sup>3</sup> UC routinely presents at the age of 15 to 25 years and 55 to 65 years<sup>4</sup>; But, symptoms in our cases begun at early infancy. Appearance of UC in this age is very rare. Perhaps this early manifestation of UC predicts its genetic talent. In the present case series we presented the data of 5 children who experienced the onset of ulcerative colitis in infancy.

### Methods

In this descriptive retrospective study we assessed medical files of infants with ulcerative colitis between 2009 and 2014. Crohn's disease was ruled out by biopsy in all cases. Stool culture was performed for them and was negative for gastro-intestinal infection. Allergic colitis was also excluded by dietary modification. Biopsy of colonic mucosa also showed absence of eosinophilic infiltration. Immunodeficiency disorders were excluded. We measured age at onset, family history of inflammatory bowel disease, symptoms of onset, colonoscopic findings, duration of medical treatment, Indication of surgery, Type of operation, surgical complications and their management and mortality rates.

### Results

From 2009 to 2014, only 5 infants (4boys, 1girl) were identified. The mean age for onset of the disease was 35 days (range 3-60). The mean age of patients at the time of surgical consult was 7 months. The disease began in 3 patients with watery diarrhea. Three of our cases expired.

#### Case 1:

Patient was a 12 month old male with sever FTT and watery diarrhea. He had watery diarrhea since he was 3 days old. He also had a family history of the disease in his sister with similar presentation who expired when she was 3 month. His parents were related (a consanguineous marriage).

The child was investigated and worked up for chronic diarrhea with blood in stool. Gastrointestinal infections were ruled out by

culture. Liver function tests and renal function tests were normal. Serum immunoglobulin level was normal. At the age of 7 months, the patient underwent colonoscopy and biopsy. In colonoscopy pseudopolyps formation in colon and diffuse ulcers were seen and biopsy showed diffuse inflammation in mucosa and submucosa along with crypt abscess and depletion of goblet cells. After diagnosis of UC when he was 7 months old, the child was managed with dietary modification along with various antibiotics and immunosuppressive therapy; But the patient did not improve with this treatment and at 12 month age the surgical service was consulted while he was in a very bad condition with sever FTT. He underwent total proctocolectomy, ileoanal anastomosis and loop ileostomy but it failed and 3 days after the first operation we performed end ileostomy while he was in septic shock. One month after surgery he was discharged with acceptable conditions and gradually grew. But 6 month after remission he was admitted to the hospital with severe abdominal distention and septic shock and expired 2 hours after admission.

#### Case 2:

Patient was a 4 month old girl with bloody diarrhea, growth failure, and moderate pallor since she was one month old. She underwent many investigations and other conditions such as infectious colitis and allergic colitis were ruled out. With IBD in mind she underwent colonoscopy and biopsy and UC was revealed. At 4 month age we were consulted for emergency surgery since perforation of colon had occurred following phosphate enema, but she was in septic shock and died with sepsis before surgical intervention could be carried out.

#### Case 3:

Patient was a 12 month old boy with bloody watery diarrhea; which had started since he was 40 days old. He had colon perforation following colonoscopy and biopsy, and underwent urgent colostomy creation. Pathology reported severe chronic crypt destructive inflammation with moderate to severe activity and ulceration. All of the colorectal tube was involved but the small intestine was intact. He had perianal abscess too. After beginning of medical treatment for UC, colostomy was closed when he was 14 month old but 3 month later he was referred to us in a very



bad general condition and ultimately expired while in septic shock.

#### Case 4:

Patient was a 2 day old neonate with abdominal distention and intestinal obstruction that rectal biopsy showed agangliosis thus transanal pulthrough was carried out on him but after surgery he had recurrent watery diarrhea and further investigation showed UC. He is currently under medical treatment.

#### Case 5:

The last case was a 3 day old neonate that underwent ileostomy, in initial surgery with suspicion of total colonic agangliosis and then underwent subtotal colectomy when he was 2 month old. When he was 18 month old he was referred to us with toxic megacolon in the remnant of his colon and underwent colostomy. Pathology reported ulcerative colitis with presence of ganglion cells in the colon. Three months later he underwent his final surgery. Now he is under corticosteroid therapy and has an acceptable condition.

### Discussion

In recent reports IBD has been rising in children. The occurrence of inflammatory bowel disease in infancy is unknown, but seems to be rising. The pathway of the disease appears more rigorous.<sup>19</sup> Ulcerative colitis (UC) is a chronic, idiopathic, mortal disease of colon with extra colonic disorders in 60% of children. UC is more prevalent in the male population.<sup>5</sup> twenty percent of patients with UC, present before 20 years of age and approximately 1% of them include infants.<sup>6</sup> Other pediatric centers reported about 1%–2% of children with UC with the disease beginning within the first two years of life.<sup>24-26</sup>

The Asia-Pacific area has been reported as a region with a low incidence of IBD, however there has always been the question that is this low rate due to a diagnostic error or is it an accurate low rate.<sup>7</sup>

Failure to thrive is usually the primary beginning symptom in children with early-onset IBD and leads to continuous illness in childhood, sometime it is accompanied by catastrophic problems especially in those with refractory disorders. Six to 10% of children experience severe growth retardation. All

5 cases in this study had growth retardation.<sup>4</sup> Many disorders with diarrhea present similar to UC such as Crohn's disease, infective colitis, allergic colitis, Meckel's diverticulum, intussusceptions, and immunodeficiency.<sup>1</sup> Unfortunately presence of similar symptoms leads to delay in diagnosis thus the majority of these patients die without a correct diagnosis and appropriate treatment.

Evidence-based treatment for UC demonstrated in infancy is very limited thus these patients need more attention. Perhaps early initiation of medical therapy in UC in infants can lead to early remission for them and prevent relapse and catastrophic complications.<sup>9</sup> unfortunately many of infants presented here suffered irrecoverable morbidities or even mortality during diagnostic investigations.

Some therapeutic strategies for UC in infancy were presented as case reports or case series that included beginning with elemental diet. If response to nutritional therapy fails; steroids will be administered. For refractory cases to elemental diet, prednisolone and mesalamine; other drugs such as 6-mercaptopurine, tacrolimus, azathioprine, and infliximab will use. In unresponsive cases to medical therapy, colectomy is indicated.<sup>10</sup>

Rukunuzzaman<sup>8</sup> reported an eight-month-old girl with UC in whom the diagnosis was established by colonoscopy and biopsy. After initial induction therapy with parenteral steroid and infliximab, the patient is now on remission with azathioprine and mesalamine. Recurrent bloody diarrhea in infancy has many differential diagnoses one of which is ulcerative colitis. Thus when coming across bloody diarrhea, UC should be in mind. All our patients also presented with refractory diarrhea and growth failure.

Although a few infants with IBD have been reported, but cases of neonatal disease are rare. Allergic colitis is the first differential diagnosis for non-infectious colitis in neonate<sup>11&12</sup>; but all 5 patients did not response to elemental formula, and pathologist reported no histological evidences for allergy. There are recommendations for evaluation of immunodeficiency in infants with suspicion of IBD<sup>13&14</sup>; thus all of our cases were investigated for Immunologic abnormalities. In all cases immunoglobulin, serum complement, total lymphocytes and lymphocyte subsets were normal.



Nitroblue tetrazolium test was done in one case and excluded the possibility of chronic granulomatous disease.

Ayodele\_Ojuawo<sup>15</sup> et al investigated on non-infective colitis in infancy. Food allergy is a main reason of non-infective colitis in the first two years of life. On the other hand ulcerative colitis and Crohn's disease are unusual in infancy period. They mentioned that minor immunodeficiency is popular in infants with non-infective colitis.

The fundamental reasons of IBD are unknown, but recent investigations confirm the basic role for immunodeficiency in the expansion of ulcerative colitis and Crohn's lesions. Some forms of inborn immunodeficiencies affect the cellular innate immune system and lead to noninfectious, inflammatory bowel disease. So in all cases of IBD in infancy, these potential associations must be considered.<sup>16</sup>

Indications for surgical intervention in children with IBD are similar to adult patients. Elective resection is considered when medical therapy fails in improvement of symptoms; there is delay in normal growth and an intolerable quality of life. Special attention to normal growth is the chief concern in children in comparison to adults; so, decision for colectomy should be taken as the epiphyses are still open in order to achieve the most favorable growth.

Medical therapy is the first line for treatment of UC and it usually results in different durations of remission, but UC can be cured by resection of the involved colon and rectum most of the times. Irrational delay of surgical intervention leads to catastrophic morbidities. Up to 40% of patients with UC will need surgical intervention, since

operative resection has supplied supreme long-standing consequences.

Unfortunately there is no specified practical guide line for childhood IBD; which is due to the delay in identifying the disease, low number of cases, and innovation of novel cure modalities and absence of randomized controlled trials concerning kids. On the other hand, the need to take full advantage of growth potentials may convince pediatricians to consider surgery earlier.<sup>17, 18</sup>

Pediatric ulcerative colitis is distinguished by widespread intestinal involvement, speedy development and a higher need for colectomy for disease control as compared to adults.<sup>21,22</sup>

Mehri Najafi et al<sup>23</sup> recorded patients with IBD onset before the first year of life during 2003–2006. They had a follow-up of at least 2 years. Twelve patients (8 boys, 4 girls) were recognized. Nine had Crohn's disease and 3 had UC. Family history for IBD was positive in two patients. The mean age of patients was 30.3 months. The mean age of beginning of the disease was 5.2 (range: 3–9) months. They reported that sever onset of illness necessitated total parenteral nutrition in 10 patients and they prescribed steroid followed by azathioprine. Three cases of Crohn's disease needed surgery; another 3 with Crohn's disease died through this study. One patient with ulcerative colitis went in to complete remission and the two other patients were in partial remission and needed repeated parenteral nutrition.

For children with UC, colectomy should be advised before severe disability occurs. However, in order to maximize growth potential and facilitate puberty pediatrician should consider surgery earlier in the course of treatment.

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