Pediatric Crohn disease: A case series from a tertiary care center

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ABSTRACT

Crohn disease (CD) is an inflammatory bowel disease that causes transmural inflammation of the gastrointestinal tract. Growth failure is a major complication and can occur before gastrointestinal manifestations in children with CD. We present here four such cases where short stature and undernutrition constituted major symptomatology, along with enteric features. Median age of presentation was 13 years. Intermittent abdominal pain and growth failure were the predominant clinical manifestations. Features of imaging and colonoscopy were suggestive of CD. A poor response was noted to corticosteroids and azathioprine in three children. Clinical remission was not achieved as per abbreviated pediatric CD activity index score. One child succumbed to illness secondary to dilated cardiomyopathy. A good therapeutic response with significant weight gain was observed in two children after starting biologicals. Only one child responded to oral corticosteroids and mesalamine. Considering biologicals early in chronically active moderate to severe CD can help in altering the prognosis.

Key words: *Biologicals, Growth failure, Mesalamine, Pediatric Crohn disease activity index*

Crohn disease (CD) is an inflammatory bowel disease (IBD), wherein the involvement of gastrointestinal tract (GIT) is transmural and any part of GIT can be affected. Pediatric CD (PCD) is being reported with an increased incidence recently, even in India [1]. It is more severe in children than in adults, both in presentation and evolution, a fact that should alert the physician for an early diagnosis. Growth failure is a major complication in children. Impaired growth velocity can occur before gastrointestinal symptoms in majority of children with CD [2]. We describe here four such cases where undernutrition and short stature constituted the clinical spectrum along with enteric features. These early considerations of biologicals in the management of PCD prevent morbidity and mortality to certain extent.

CASE REPORT

Four children were diagnosed and followed up between 2015 and 2018 in a tertiary care center where pediatric surgery and gastroenterology specialty clinics are available. Informed written consent was taken from all the parents for scientific publication. Tabular representations of all the cases are given in Table 1. Diagnosis of CD was based on clinical presentation, laboratory tests, and colonoscopy with biopsy. The median age of presentation was 13 years. The average duration between onset of symptoms and diagnosis in our case series was 2 years. The presenting symptoms were intermittent abdominal pain associated with growth failure in all cases. All had body mass index of the <3rd centile as per the World Health Organization classification. The examination was marked for anemia (Mean hemoglobin – 7.9 g/dl) and clubbing. Alopecia was present in one child.

Two children were positive for anti-saccharomyces cerevisiae IgA (ASCA) antibodies. Contrast-enhanced computed tomography abdomen and colonoscopy (Fig. 1) showed classical features of CD, as mentioned in the table. Short segment involvement was noted in one child, whereas long segment thickening from jejunum to descending colon was present in the rest of the cases. Two of them had strictures in the ileum while cecal and perianal fistula were present in one child. Biopsy showed non-caseating granulomatous inflammation with cryptitis, crypt distortion, and crypt abscess in a majority of children.

As the symptomatology and clinical features were mimicking intestinal tuberculosis, a prevalent disease in our country, diagnosis of CD was delayed contributing to increased morbidity [3]. Three of our cases received antituberculosis therapy (ATT) before the diagnosis of CD. Individualized treatment was planned for each child where, mesalamine (70 mg/kg/day), a 5-aminosalicylic acid agents were the first-line drug used in all the cases. Oral prednisolone (2 mg/kg/day) was added to the regimen when the response was poor. Only one child went into remission with oral steroids. Azathioprine (2 mg/kg/day) constituted second-line management in the rest three cases. Crisis management included antibiotics such as ciprofloxacin (20 mg/kg/day) and metronidazole (30 mg/kg/day), hydration, and enteral nutrition

Table 1: Clinical profile, investigations, and outcome

Clinical details	Case 1 (Male, 13 years)	Case 2 (Female, 13 years)	Case 3 (Male, 17 years)	Case 4 (Male, 11 years)
Clinical profile				
Recurrent abdominal pain	+	+	+	+
Melena/hematochezia	-	+	-	-
Growth failure	+	+	+	+
Anemia	+	+	+	+
Clubbing	−	+	+	+
Alopecia	−	−	−	+
Oral ulcers	+	+	+	+
Hepatomegaly	+	+	+	-
Investigations				
1. Abdominal imaging findings (CECT/MRI)				
Segment thickening	Long	Long	Long	Short
Increase mesenteric vascularity	+	+	+	+
Comb sign	-	+	+	−
Mesenteric lymphadenopathy	+	+	+	+
2. Colonoscopy				
Pseudopolyps	+	+	+	+
Mucosal ulcers	+	+	+	−
Skip lesions	−	−	+	+
3. Biopsy				
Granulomas	−	+	+	−
Crypt distortion	+	+	+	−
4. ASCA	Negative	Positive	Negative	Positive
Empirical ATT	+	+	−	+
Response to oral steroids	Poor	Poor	Poor	Good
PCDAI after 2 months of treatment	15	30	15	10
Adalimumab	−	+	+	−
The course of the disease	Cardiomyopathy with EF=25%	Recurrent intussusceptions underwent right hemicolectomy	Recurrent symptoms, anemia, hypoalbuminemia	Receiving growth hormone therapy
Outcome	Died secondary to dilated cardiomyopathy	Asymptomatic with good weight gain	Asymptomatic average weight gain	Asymptomatic

ASCA: Anti-saccharomyces cerevisiae IgA, ATT: Antituberculosis therapy, PCDAI: Pediatric Crohn's disease activity index, MRI: Magnetic resonance imaging, CECT: Contrast-enhanced computed tomography

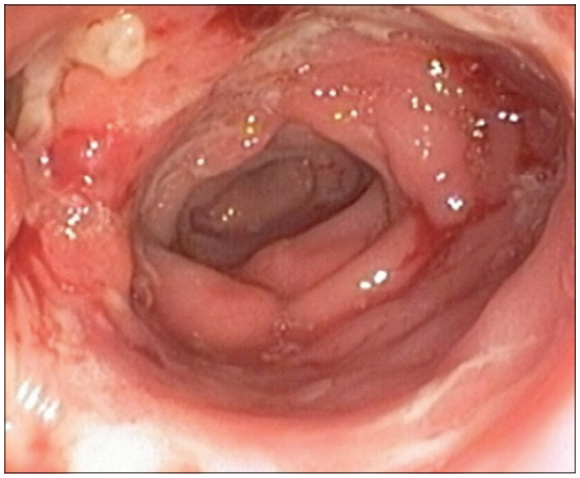

Figure 1: Multiple ulcerations and pseudopolyps noted in ascending colon associated with thickened ileocaecal valve

which included high-protein diet formula (100 k.cal/kg/day) and probiotics.

Disease activity as per abbreviated PCD activity index (abbreviated PCDAI) after 2 months of therapy was ranging between 10 and 30 with a mean score of 17 (abbreviated pediatric Crohn's disease activity index [PCDAI] <10 indicates remission), signifying the need for biological [4]. Due to financial constraints and irregular follow-up, biologicals were not started initially in three of the cases; whereas, one child succumbed to illness due to dilated cardiomyopathy. Recurrent intussusceptions and need for multiple packed RBC transfusions due to microbleeds in the large intestine, one girl needed surgical intervention. Two children received adalimumab (loading dose of 80 mg; subsequent doses at 40 mg given subcutaneously once in 15 days) and are on regular follow-up.

DISCUSSION

Incidence of PCD has been rising in both developed and developing countries [5,6]. Of all cases of CD, 15–25% occurs in pediatric population [6]. Commonage of onset is during preadolescence and young adulthood. PCD can involve any part of GIT, most commonly terminal ileum and right colon. The common clinical features include constellation of abdominal pain, diarrhea, growth failure, weight loss, poor appetite, and unexplained fever. However, most characteristic symptoms include insidious onset of abdominal pain and weight loss. Growth failure can be an important initial clue in suspecting PCD since approximately half of the children have a delay in height velocity, before obvious intestinal manifestation, as seen in our case series [7]. Findings on physical examination such as pallor and abdominal tenderness are not specific; however, abdominal mass, aphthous ulcers, erythema nodosum, digital clubbing, arthritis, or perianal tags are highly suggestive of CD.

A positive ASCA test in children with IBD is suggestive of CD (sensitivity 49% and specificity 97%) [8]. Radiographic features include narrowing of the lumen of the small intestine or colon with ulceration, string sign, fistulae, and abscess formation which were present in all of our cases. Colonoscopic features range from subtle focal aphthoid ulcers to diffuse areas of edema and ulceration that creates a polypoid mucosa (Fig. 1) and give a cobblestone appearance. Skip lesions, pseudopolyps with traversing mucosal ulcers are key features of CD [9]. Intestinal complications contribute to significant morbidity in PCD. They include fistulae between different segments of bowel or from bowel to adjacent organs, abdominal abscess, intussusceptions, small bowel obstruction, and localized peritonitis. One child had recurrent intussusceptions requiring surgery in our case series. Most common extraintestinal complications in PCD include arthritis, aphthous stomatitis, and osteopenia [10]. Alopecia was present in one child which is a less frequent manifestation associated with CD [11]. One child succumbed to illness secondary to dilated cardiomyopathy, a rare complication noted in PCD [12].

Antitumor necrosis factor agents are used in children with steroid-refractory IBD or in combination with immunomodulators, as dual therapy, are more effective than single agent alone. These agents are considered superior to immunomodulators and induce complete mucosal healing of intestine. In children with severe mucosal ulcerations, perianal fistulas, and/or significant growth failure, these are considered as the first-line agents [13]. Remission in PCD on biological therapy is reported as 50% by the end of the 1st year with reasonable safety profile [14]. Two children were started on adalimumab therapy. Good therapeutic response was noted, wherein abdominal pain, decreased need for blood transfusions, and weight gain were documented.

A decline in the growth chart percentiles for weight and height with respect to the age and gender should arouse suspicion of an underlying systemic disease. Growth failure can precede gastrointestinal symptoms in CD, needing thorough evaluation. An early diagnosis is of prime importance in managing these children, thereby preventing morbidity associated with the disease.

CONCLUSIONS

Diagnosis of CD needs to be considered in children where initial diagnosis of intestinal tuberculosis was made and had poor response to ATT. Considering biologicals early in CD can help in altering the prognosis of CD.

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