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CASE REPORTS

REFRACTORY ULCERATIVE COLITIS IN A TODDLER AND RESPONSE TO INFLIXIMAB - A CASE REPORT AND REVIEW OF LITERATURE

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ABSTRACT

Ulcerative Colitis (UC) in younger age group has poor response to medical line of management and surgical treatment is more successful. Here we present a 2-year-old boy who had recurrent diarrhea with failure to thrive from first week of life. He was detected to have UC on colonic biopsy and histopathology with a high stool calprotectin (425.9 ug/g). He was started on oral prednisolone and sulfasalazine but due to poor response, was subsequently treated with infliximab and azathioprine to which he responded with a fall in stool calprotectin (28 ug/g) and weight gain of 2.9 kg in 4 months.

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Introduction

Inflammatory bowel disease (IBD) is a chronic condition of the gastrointestinal tract, comprising mainly Crohn's disease (CD) and ulcerative colitis (UC). CD presents a diagnostic annual rate in children between 0.2 and 8.5 per 100,000 individuals, while UC is encountered at a rate between 0.5 and 4.3 per 100,000. In developing countries, IBD in adolescents and children accounts for approximately 30% of total IBD.[1] IBD can occur at any age. According to the age at onset, IBD can be classified into pediatric onset (<17 years), early onset (<10 years), very early onset (<6 years).[2] Generally, UC is found to be more common than CD in the preschool age group, whilst CD is three times more frequent than UC in older children.[3] Aloi et al studied features and disease course of pediatric ulcerative colitis in 110 patients of which 35% of patients had an early-onset disease (0–7 years).[4] Regular treatment of IBD includes glucocorticoids, 5-ASA preparations, immunomodulators, antibiotics, and surgical treatment. It has been found that UC under 1 year of age has poor response to medical line of management and surgical treatment is more successful than medical therapy in this age group.[5] We present a 2-year-old boy who had recurrent diarrhea with failure to thrive from first week of life. He was detected to have UC on colonic biopsy and histopathology with a high stool calprotectin (425.9 ug/g). He was started on oral prednisolone and sulfasalazine but had no response and was subsequently treated with infliximab and azathioprine to which he responded.

Case Report

A 2 years-old male presented with recurrent watery diarrhea since one week of life along with failure to thrive. There was no blood in stools or vomiting. He had received multiple antibiotics (cefixime, amikacin, cefotaxime) for the same but had no response. On examination, he was malnourished with height 66 cm (<3rd percentile) and weight 4.8 kg (<3rd percentile). He had pedal edema, pallor and diffuse abdominal pain. Bowel sounds were present on auscultation and other systems were normal. Investigations showed anemia with hemoglobin of 8.4 gm/dl, white blood count of 22900 cells/cu mm (polymorphs 73%, lymphocytes 27%), erythrocyte sedimentation rate (ESR) was 80 mm at end of 1 hour, C-reactive protein of 41 mg/dl. Liver transaminases, urea, creatinine, stool culture, and stool examination for ova and parasites were normal. There was no cryptosporidium seen in the stool. HIV, Hepatitis C Elisa and HBsAg were negative. Blood culture did not grow any organism. Tissue transglutaminase IgA and IgG were negative. Serum immunoglobulins showed raised IgE antibody (1659 ku/l; normal: 0-114) with normal IgG 1260 mg/dl (Normal = 700-1600), IgA 355 mg/dl (Normal = 70-400) and IgM levels 213 mg/dl (Normal = 40-230). Colonoscopy up to terminal ileum showed multiple deep ulcerations in rectosigmoid region suggestive of IBD (Figure 1). Histopathology showed flattening of mucosal surface epithelium, focal ulceration, crypt abscess, cryptitis, mixed inflammatory infiltrate of lymphocytes, plasma cells, eosinophils and neutrophils suggestive of UC (Figure 2). Stool calprotectin levels were 425.9 ug/g (Normal <50). p-ANCA and anti-saccharomyces antibody (ASCA) were not done due to non-affordability. Pediatric ulcerative colitis activity index (PUCAI) (6) was 40 indicating moderate disease activity. He was started on IV methyl prednisolone (2 mg/kg/day) for 3 days followed by oral prednisolone at 2 mg/kg/day along with oral sulfasalazine at 30 mg/kg/day and probiotic lactobacillus acidophilus in. Child initially showed good clinical response with decrease in frequency of stools and improved stool consistency. However, one week later he again developed watery stools along with perianal abscesses. Steroids were tapered and stopped in one month, the pus was drained. Pus culture grew Escherichia coli, and he was treated with cefuroxime for

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Figure 1. Colonoscopy up to terminal ileum showed multiple deep ulcerations in rectosigmoid region.

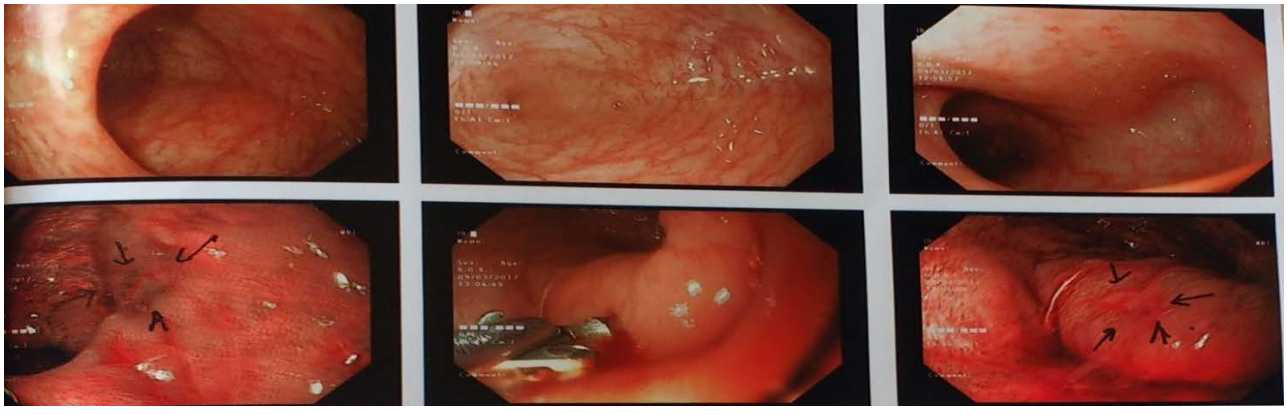
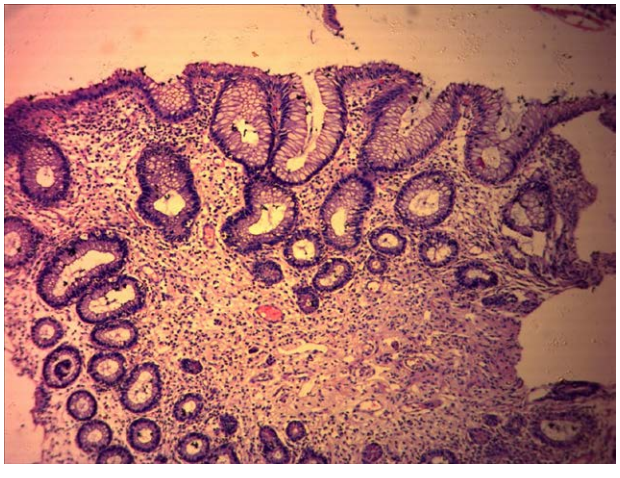


Figure 2. Histopathology of the sigmoid colon showed flattening of mucosal surface epithelium, focal ulceration, crypt abscess, cryptitis, mixed inflammatory infiltrate of lymphocytes, plasma cells, eosinophils and neutrophils.



7 days. Steroids were restarted at 1 mg/kg/day upon recovery. Mesalamine suppository was also added at 20 mg/kg/day, but he continued to have diarrhea. He was subsequently given infliximab (5 mg/kg/day) after 2 months of presentation to us. Steroids and sulfasalazine were continued. However, there was no improvement with a PUCAI of 20 and thus azathioprine (1 mg/kg/day) was also added. Second dose of Infliximab was given 3 weeks after the first dose to which he responded. He was subsequently discharged from the hospital on oral steroids, sulfasalazine and azathioprine. Steroids were gradually tapered and omitted within 4 months of treatment. On his follow up at 4 months of treatment, his weight has increased to 7.7 kg, his stools were now well-formed and were only 3-4 times a day. Stool calprotectin had dropped to 28 ug/g.

Discussion

The etiology of IBD is not fully understood, being a multifactorial disease. The pathological mechanism of IBD consists in a dysregulation of the immune interaction concerning the relationship between enteric antigens and the enteral mucosa leading to a chronic, immune-mediated inflammation.[2] Rectal bleeding, bloody diarrhea, abdominal pain and weight loss dominate the clinical picture of this disease. The patients with IBD can present different gastrointestinal symptoms at presentation with a variable severity, including abdominal pain, diarrhea, gastrointestinal bleeding, intestinal fistula, intra-abdominal abscess, perianal disease, or failure to thrive.[2] Though our patient did not have bloody diarrhea, he had recurrent watery diarrhea with high fecal calprotectin and colonoscopy and histopathology suggestive of UC along with hypoalbuminemia and high ESR. He also developed perianal abscesses which is known to occur with IBD. Histologic features in UC include crypt architectural distortion, cryptitis, and crypt abscesses.[7] Microscopic diagnosis of UC is based on crypt architectural distortion, a diffuse transmucosal inflammatory infiltrate with basal plasmacytosis, cryptitis and crypt abscesses.[8] Histopathology examination in our child showed flattening of mucosal surface epithelium, focal ulceration, crypt abscess, cryptitis, mixed inflammatory infiltrate of lymphocytes, plasma cells, eosinophils and neutrophils suggestive of UC.

The course of the disease is chronic, with periods of exacerbations and remissions. UC treatment depends on the disease activity and the endoscopic assessment of the extent of inflammatory lesions. UC of mild-to-moderate severity should initially be treated with oral sulfasalazine (40 to 70 mg/kg/day) or a combination of oral and topical mesalamine. Levine et al found good results by adding mesalamine enemas to oral mesalamine for induction of remission in 38 children with UC in age group 4-18 years.[9] Our patient was treated with similar therapy but did not respond. Patients who do not respond to this treatment within 10-14 days or who are already taking appropriate maintenance therapy should be treated additionally with a course of oral steroids. In the case of steroid-dependency or steroid refractory course, azathioprine (2.5 mg/kg per day) or 6-mercaptopurine (1.5 mg/kg per day) should be introduced for induction of remission and remission maintenance.[10] Ivanczack et al studied infliximab for induction and maintenance in 42 children aged 4-18 years with moderate to severe ulcerative colitis and concluded that infliximab therapy induces remission and proves to be effective in preventing early colectomy.[11] Our patient also did not respond to

addition of azathioprine and went into remission only after 2nd dose of infliximab. Infliximab is a chimeric anti-TNF-α mouse monoclonal antibody.[12] Its Fab fragment consists of the mouse variable TNF binding region (25% of the protein) and a human Fc fragment (75% of the protein). The antibody binds both the soluble and transmembrane forms of TNF-α with high affinity and blocks their action (association constant 1010/M), with a serum half-life of 10 days.[13]

There is evidence for the probiotic Escherichia coli Nissle 1917 for patients with mild UC who are intolerant to 5-ASA or as adjuvant therapy. In pouchitis, a combination probiotic is useful in reducing the risk of further episodes of pouchitis[6] Lactobacillus GG was shown to be more effective then mesalamine in prolonging relapse free time in UC[14]. Though our patient was on lactobacillus acidophilus right from beginning, the response was only achieved with infliximab. Whether the probiotic will maintain a remission for a longer time will be determined on the follow-up.

Conclusion

Inflammatory bowel disease in infants and young children is difficult to treat with poor response to immunomodulators and steroids. Infliximab may be useful to induce remission in these patients to prevent early surgery.

Compliance with Ethical Standards

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Conflict of Interest: None

References:

1. Ye Y, Pang Z, Chen W, Ju S, Zhou C. The epidemiology and risk factors of inflammatory bowel disease. Int J Clin Exp Med. 2015;8:22529-42.
2. Mărginean CO, Meliţ LE, Mocanu S, Mărginean MO. Inflammatory bowel diseases: a burden in pediatrics: Case series and a review of the literature. Medicine (Baltimore). 2017;96:e6329.
3. Day AS, Ledder O, Leach ST, Lemberg DA. Crohn's and colitis in children and adolescents. World J Gastroenterol. 2012;18:5862-5869.
4. Aloi M, D'Arcangelo G, Pofi F, Vassallo F, Rizzo V, Nuti F, et al. Presenting features and disease course of pediatric ulcerative colitis. J Crohns Colitis. 2013;7:e509-e515.
5. Ein SH, Lynch MJ, Stephens CA. Ulcerative colitis in children under one year: a twenty-year review. J Pediatr Surg. 1971;6:264-271.
6. Fell JM, Muhammed R, Spray C, Crook K, Russell RK, BSPGHAN IBD working group. Management of ulcerative colitis. Arch Dis Child. 2016;101:469-474.
7. Romano C, Syed S, Valenti S, Kugathasan S. Management of Acute Severe Colitis in Children with Ulcerative Colitis in the Biologics Era. Pediatrics. 2016;137:e20151184.
8. Dhakhwa R, Shrestha HG, Acharya IL. Histopathological evaluation of ulcerative colitis in colonoscopic biopsies. J Pathol Nepal. 2016;6:932-936.
9. Levine A, Yerushalmi B, Kori M, Broide E, Glassberg YM, Shaoul R, et al. Mesalamine Enemas for Induction of Remission in Oral Mesalamine-refractory Pediatric Ulcerative Colitis: A Prospective Cohort Study. J Crohns Colitis. 2017;11:970-974.
10. Meier J, Sturm A. Current treatment of ulcerative colitis. World J Gastroenterol. 2011;17(27):3204-12
11. Iwańczak BM, Kierkuś J, Ryżko J, Szczepanik M, Więcek S, Czaja-Bulsa G, et al. Induction and maintenance infliximab therapy in children with moderate to severe ulcerative colitis: Retrospective, multicenter study. Adv Clin Exp Med. 2017;26:57-61.
12. Baugh JA, Bucala R. Mechanisms for modulating TNF alpha in immune and inflammatory disease. Curr Opin Drug Discov Devel. 2001;4:635-650.
13. Levin A, Shibolet O. Infliximab in ulcerative colitis. Biologics. 2008;2:379-388.
14. Garud S, Peppercorn MA. Ulcerative colitis: current treatment strategies and prospects. Therap Adv Gastroenterol. 2009;2:99-108.