

Case Report

An Eleven Months Old Infant with Very Early Onset Inflammatory Bowel Diseases (IBD): A Rare Case Report

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Abstract

Inflammatory bowel disease (IBD) in pediatric cases has been seen rapidly increasing in number over the last decade. Now a days four types of pediatric IBD has been identified: less than ten years of age - early onset IBD, less than six years of age - very early onset IBD, less than two years of age- infantile IBD and less than twenty eight days of age - neonatal onset IBD. Young children presented with more aggressive clinical features and severity is more than the older children and adults. Early onset disease presenting in children may have a monogenic basis. Infantile IBD or neonatal IBD having the high rates to affect the first-degree relatives and there is very high chance to develop resistance against immunosuppressive treatment. Very early onset IBD (VEO-IBD) most commonly presenting per rectal bleeding with or without mucous stools, isolated colonic disease, perianal involvement, skin lesions, whereas early onset IBD (EO-IBD) commonly presented with abdominal pain and weight loss. A thorough history, physical examination, biochemical markers, endoscopic evaluation with macroscopic and microscopic findings are the only way to reach the diagnosis. The treatment of VEO-IBD is the same as that given to the adolescents and adults with IBD (eg, anti-inflammatory agents, immunomodulators, biologics, antibiotics, and surgical approaches). Here, we report a rare case of very early onset IBD of a 11 months old male infant, who presented with the complaints of blood and mucus mixed loose watery stool for

10 days, having similar episodes for last five months. He was mildly pale, and had thrombocytosis with raised C reactive protein (CRP), features of colitis in stool routine microscopic test. The diagnosis was confirmed by colonoscopy and histopathology study, which showed features of Crohn's colitis. He was treated by anti-inflammatory drugs (steroid and mesalazine) with a significant improvement in a short time.

Keywords: Pediatric inflammatory bowel disease, monogenic VEO-IBD, very early onset IBD

INTRODUCTION

Inflammatory bowel disease (IBD) in children constitutes about 25% of all patients of IBD.¹ "very early-onset IBD" (VEO-IBD) means key symptoms of IBD or is diagnosed before six years of age. Compared with children whose IBD develops later in life, those with VEO IBD and particularly those with infantile IBD are more likely to have single gene defects that alter immunity or epithelial barrier function may disturb, and often have a more severe disease course^{2,3}. The common disorders are interleukin-10 (IL-10) signaling defects, atypical severe combined immunodeficiency (SCID), common variable immunodeficiency, chronic granulomatous disease and other neutrophil defects, hyperimmunoglobulin M syndrome, Wiskott-Aldrich syndrome, agammaglobulinemia, familial hemophagocytic lymphohistiocytosis, and IPEX (immune dysregulation, polyendocrinopathy, enteropathy, X-linked) or other autoimmune related enteropathy.⁴

Near about, 50 genetic variants have been associated with IBD and these disorders are collectively called as monogenic IBDs.⁵

Clinical features that give suspicion for monogenic IBD include:⁶

- Early age of onset (eg, younger than six years, particularly younger than two years of age)
- Family history of IBD and/or immunodeficiency in multiple family members, usually with male predominance, or consanguinity

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- Frequent attack of infections or unexplained fever
- Associated features suggestive for autoimmunity (eg, primary sclerosing cholangitis, arthritis, anemia, or endocrine dysfunction)
- Very severe IBD and/or resistance to conventional therapies for IBD
- Symptoms and/or signs suggestive of hemophagocytic lymphohistiocytosis (fever, hepatomegaly, cytopenias, high ferritin)
- Lesions of the skin, hair, or nails
- Current or previous history of cancer in the patient

Laboratory investigations include complete blood count with ESR, intestinal inflammatory markers, stool RME and C/S. For immunodeficiency, identification of immunological panel is important. For diagnosis of VEO-IBD, endoscopy of lower and upper GIT now remain the gold standard. Colonoscopy may show ulcer, pseudopolyps and histopathology confirms the diagnosis by showing features of chron's colitis or ulcerative colitis.⁷ We hereby report a case of an 11 months old male infant who presented with blood and mucus mixed loose watery stool for 10 days and was diagnosed as very early onset IBD on the basis of laboratory, colonoscopy and histopathology findings.

CASE REPORT

A 11 months old male infant got admitted in the Department of Pediatric Gastroenterology and Nutrition, BSMMU with the complains of blood and mucus mixed loose watery stool for 10 days for 10-12 episodes per day. Occasionally he also complains mucoid stool without blood several episodes with moderate in amount. He had history similar type of illness for previous five months but not regularly. Duration of each attack persist for two weeks and managed with few antibiotics that results decrease the frequency of purging but not complete recovery. So that he visited several registered physician and condition not so improved. He had history of exclusive breast feeding (EBF) for first six months, then complementary feeding was started with formula milk for 1 month. But after starting complementary feeding, he developed watery diarrhea. Then after recovery only breast milk was continued with rice suji and occasionally chicken based diet was given. He had no history of cow's milk ingestion

or related foods. On examination, baby was fretful, mildly pale and anicteric, all vitals were within normal limit, no signs of dehydration and bilateral pedal oedema absent, skin survey revealed normal findings, severe wasting was present (weight- 6.6 kg, length: 69 cm WLZ score -3.6), abdomen examination revealed no organomegaly and ascites was absent. Laboratory investigation showed haemoglobin (Hb)- 9.1 g/dl, WBC count- 16500/cmm, platelet count 8,50,000/cmm, ESR 90 mm in 1st hour, liver function test and fasting blood sugar were normal. Stool RME showed Mucus and RBC ++, pus cell plenty, stool C/S was normal, S. albumin was 27 gm/l, C-reactive protein 21 gm/l, fecal calprotectin was 850 µg/gm, S. tTG IgA was negative, stool for Clostridium difficile toxin negative, USG of whole abdomen showed loaded bowel loops having peristalsis. Primary immunodeficiency panel was normal and HIV testing was negative. Initially we managed this patient by giving lactose free diet with management of severe acute malnutrition due to its secondary cause and some antibiotics. But patient's condition did not improve rather there was persistent passage of mucoid stool, so we planned to do endoscopy of lower GIT. Upto transverse colon was seen through colonoscopy due to friable gut wall and there might be chance of bleeding. Macroscopically colonoscopy (Fig.1) showed erythematous mucosa, friable with shallow ulcer and few pseudopolyps in descending colon but there was no rectal involvement. For biopsy, tissue took from descending colon and sent for histopathologic examination. Histopathology report (Fig.2) showed infiltration of chronic inflammatory cell that suggestive of colitis with absence of crypt abscess, cryptitis, goblet cell depletion and absence of any granuloma. Usually for chron's disease getting definitive submucosal tissue by biopsy not always possible, so granuloma may be absent now a days. Then we treated the patient with oral prednisolone 1mg/kg/day and oral mesalazine 40mg/kg/day. Gradually, the frequency and amount of mucoid stool was reduced significantly, baby was gaining weight and he became playful. After 1 week CRP, was reduced to 18 mg/l, Hb 9.9 gm/dl, ESR 55 mm in 1st hour and platelet count 7,50,000/cmm. Our final diagnosis was very early onset IBD (Chron's disease) and we discharged the patient with advice for periodic follow up.

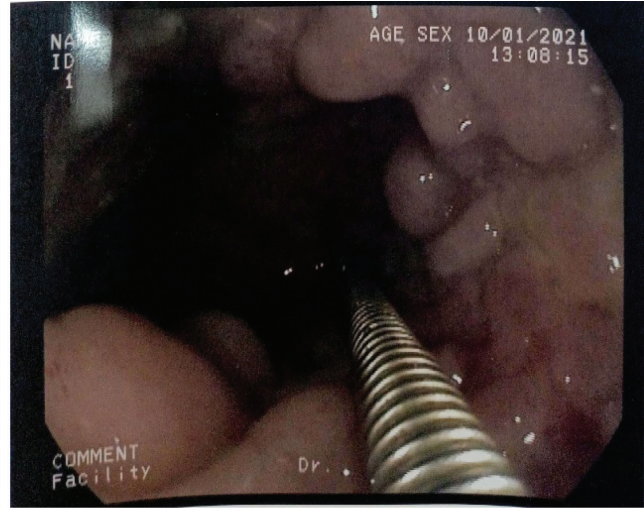


Fig.1 Colonoscopy showing erythematous mucosa, friable with shallow ulcer and few pseudopolyps in descending colon.

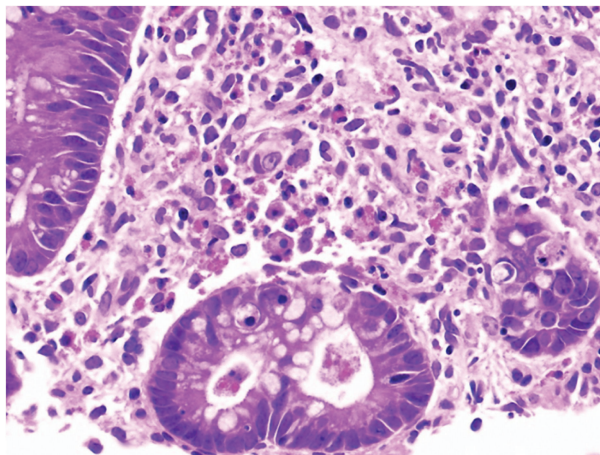


Fig.-2: Histopathology with features of Chron's colitis

DISCUSSION

Inflammatory bowel disease (IBD) in children below 6 years of age defined as very early-onset IBD (VEO-IBD). Infantile onset IBD also presents before 2 years of age and neonatal onset IBD present before <28 days of age. In pediatric IBD, around 6 to 15% of population presents at below 6 years of age.⁴ The phenotype of VEO-IBD is considered to be heterogeneous and while some children have mild disease, others can present with aggressive and severe disease rather than adult IBD.⁹⁻¹² Due to more aggressive phenotype, strong family history and involving primary immunodeficiency gene, VEO-IBD is now considered to be a monogenic disease.¹³⁻¹⁵ Our patient presented in his infancy period and we consider he had

monogenic form, though he had no family history and his genetic study was not done due to financial constraints.

Variable presentation may show in pediatric IBD. Usually the onset is insidious, blood and mucus stained small volume loose watery stool may be present. Children with immune dysregulation polyendocrinopathy enteropathy X linked (IPEX) syndrome may presented with severe extensive volume of diarrhoea.¹⁶ In children with IL-10 signalling defect, chronic granulomatous disease (CGD), and X-linked inhibitor of apoptosis protein (XIAP) may presented with intestinal fistula.¹⁷ Children also may presented with repeated infections with lesions of the skin, nails, or hair.⁶ On physical examination, pallor and tender abdomen may be present. Children must be evaluated for Perianal disease, folliculitis, arthritis, and gout. Some monogenic variants of VEO-IBD can present with palpable spleen or lymphnode.^{18,19} Our patient presented with blood and mucus mixed loose watery stool and he was mildly pale, severely wasted.

The routine laboratory investigations for VEO-IBD include complete blood count (CBC) with ESR, important inflammatory markers. CBC picture may show low hemoglobin, high platelet count. Neutrophils defects can be associated with VEO-IBD, and low neutrophil as well as leukocytosis (seen in leukocyte adhesion deficiency) can be seen in some cases. There can be raised C-reactive protein. Looking for immunological panel is important for immunodeficiency disorders. Colonoscopy may show friable ulcer, pseudopolyps and histopathology confirms the diagnosis with features of chronic inflammation in

bowel wall and changes associated with IBD. Besides, monogenic form of VEO-IBD may show features of eosinophilic infiltrates, atrophied vilous, apoptosis, and increased intraepithelial lymphocytes.⁷ Our patient had typical lab features of IBD (pallor, thrombocytosis and raised CRP). Other differentials- like allergic colitis, celiac disease, primary immunodeficiency disorder were excluded in this case. Colonoscopy showed ulcer and pseudopolyps in descending colon with no rectal involvement. Histopathology report showed features of Crohn's colitis.

Like other IBD, the treatment options for VEO-IBD include both medical (anti-inflammatory agents, immunomodulators, biologics, antibiotics) and surgical management (colectomy or ileal diversion). Hematopoietic stem cell transplantation (HSCT) is beneficial for specific genetic defect.⁷ Our patient showed dramatic response both clinically and biochemically after treatment with steroid and mesalazine. So, now immunomodulatory therapy or biological agents were not required in our patient.

He was discharged with advice for periodic follow up.

CONCLUSIONS

Monogenic VEO-IBD has high rates of morbidity and mortality, and it might require different treatment strategies. So, starting the early pharmacologic treatment can be effective step. Early initiation vaccination therapy for children with VEO-IBD is necessary, due to the age of onset of disease. It is recommended to avoid immune suppressive drugs for at least 1 month for corticosteroid administration and 3 months for azathioprine/6-MP and biological medication.^{20, 21}

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