INFANTILE INFLAMMATORY BOWEL DISEASE

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ABSTRACT

Inflammatory bowel disease is a chronic disorder of the gastrointestinal tract that usually affects adolescents and young adults. It is rare among infants making up only less than 1% of pediatric cases. This is a case of infantile inflammatory bowel disease who presented with early onset hematochezia, with colonoscopy and histopathologic findings consistent with ulcerative colitis. He was managed with mesalazine, a 5-ASA derivative, the mainstay of treatment.

KEYWORDS: Inflammatory bowel disease, Ulcerative Colitis, Infantile Inflammatory Bowel Disease

INTRODUCTION

Inflammatory bowel disease (IBD) is a chronic, idiopathic, and destructive condition affecting the gastrointestinal tract which encompasses different disease entities namely ulcerative colitis and Crohn's disease. [1, 2] The onset of inflammatory bowel disease is most common during the period of preadolescence, adolescence, and young adulthood. Approximately 25% of IBD cases presents before the age of 20 but may also present in infants as early as first year of life. [3] Infantile and neonatal onset inflammatory bowel disease is extremely rare making up only less than 1% of pediatric cases making this a reportable case. [4]

CASE REPORT

This is a case of a two-year-old male who initially presented with hematochezia at 15 months of age. History started 10 months prior to admission where the patient was noted to have nine episodes of blood streaked yellow to greenish, loose, mucoid stools amounting to ½ cup per episode with no other accompanying symptoms. There was no fever, weight loss or decrease in appetite or activity. Patient was repeatedly managed as a case of amoebiasis and given IV hydration and antibiotics however no response was noted. He was also managed as a case of Cow's Milk Protein Allergy but still with persistence of symptoms. He was referred to a hematologist to rule out blood dyscrasia but work up showed normal results. Consult with a gastroenterologist was then advised. He was seen by a pediatric gastroenterologist and advised admission for work up.

Birth and maternal history were unremarkable. The patient was exclusively breastfed for 4 months and started on mixed feeding thereafter. Complementary feeding was started at 6 months initially with soup, infant cereal products and mashed vegetables. Table food was given starting 8 to 9 months. Currently, he eats four times a day usually consisting of 2 tablespoons of

rice with soup usually with fish, egg and vegetables and consumes 7 ounces of milk every 3 hours. For the past medical history, the patient only had mild pneumonia at 4 months of age with no other known medical illnesses and allergies. There is history of hypertension on the maternal side and no history of inflammatory bowel diseases, cancer, diabetes mellitus, asthma, allergies and blood dyscrasia. Immunization history based on the expanded program on immunization until 1 year old is complete. His development is noted to be at par with age. The personal and social history was likewise unremarkable.

On admission, the patient was seen awake, alert and not in cardiorespiratory distress. Vital signs were within normal limits. Anthropometrics is normal for age. On physical examination, the patient was sallow looking with pale palpebral conjunctivae. The rest of the physical examination including the abdominal examination was normal. The patient was initially managed as a case of Meckel's Diverticulum. Stool exam showed yellowish brown, mucoid, white blood cell count 3-6/hpf, red blood cell count 1-3/hpf with no ova or parasite. Complete blood count showed anemia with low hemoglobin at 63 g/L. WBC was elevated at 28 x 109/L with segmenter predominance at 49%. Patient was hooked to oxygen for support and was transfused with packed red blood cell. A Meckel's diverticulum scan was done but was negative. Colonoscopy showed friable, erythematous, edematous mucosa with scattered areas of whitish exudates from the rectum up to the cecum. Multiple biopsy specimens were taken from the different parts of the colon. Histopathologic findings were consistent with ulcerative colitis showing mild chronic inactive inflammation in the ileum, benign colonic type mucosa with mild chronic active inflammation in the ascending colon, benign colonic type mucosa with moderate chronic active inflammation in the transverse colon and rectum, benign colonic type mucosa with severe chronic active inflammation and reactive glandular changes in the descending colon and benign colonic type mucosa with severe chronic active inflammation and crypt abscess in the sigmoid. No atrophy, dysplasia, crypt distortion or granuloma noted. On further laboratory work up, erythrocyte sedimentation rate was 3.5 times elevated at 35 mm/hr, C-reactive protein was 2.3 times elevated at 26.9 mg/dL and fecal calprotectin showed a positive result. Due to findings consistent with ulcerative colitis and mild disease severity based on the pediatric ulcerative colitis activity index (PUCAI) score of 30, patient was started on mesalazine. On follow up consult after two weeks, patient showed response to treatment by having a decrease in frequency of hematochezia. Based on the pediatric ulcerative colitis activity index, there was a decrease in score from 30 to 20. Plan was to continue mesalazine, to monitor symptoms and to regularly follow up to monitor the patient's disease activity.

DISCUSSION

Inflammatory bowel disease is a complex, multifactorial and lifelong disease which may present in any age group. It is most common among those aged 15 to 29 years old with 25% of cases seen during

childhood and adolescence, and male predominance at all age groups [4,5].

Early onset inflammatory bowel disease (<6 years) constitutes 4 to 10% of pediatric IBD cases while neonatal (< 28 days) or infantile onset (< 2 years) IBD is extremely rare and develops in less than 1% of pediatric patients. [4, 6]. In the Philippines, there are only 30 out of 4,599,665 cases among aged 1-4 years old diagnosed with ulcerative colitis and 8 out 4,601,720 cases among aged 1-4 years old diagnosed with Crohn disease based on data gathered from the Philippine Pediatric Society, Inc. In Philippine Children's Medical Center, there are only 12 reported cases of inflammatory bowel disease, three of which were ulcerative colitis. Of the 12 cases, three were very early onset inflammatory bowel disease and two were infantile onset inflammatory bowel disease. There is no case of neonatal onset inflammatory bowel disease in our institution.

The pathophysiology of inflammatory bowel disease is not clearly understood. It is believed that the development of inflammatory bowel is largely influenced by the interplay between genetics, immune system, microbiome and environment. [3, 5] Children with very early onset inflammatory bowel disease are at higher risk of having a monogenic cause. With over 200 genes associated with inflammatory bowel disease, 52 of these are linked with monogenic diseases often presenting in infancy or those younger than 6 years. The functions of these genes are linked to immune regulation. Presence of genetic mutations result in immune dysregulation leading to disruption of epithelial barrier function, mucosal invasion of bacteria, abnormal immune receptors, increased inflammatory response, disrupted downstream immune signaling and abnormal handling of bacteria resulting in primary immunodeficiency which eventually leads to inflammatory bowel disease. Thus, in patients who present with early onset IBD, further investigation for rare monogenic disorders should be considered especially among those with atypical presentation such as skin problems, frequent infections or dysmorphism. [3, 5] A strong family history is also a risk factor in the development of early onset inflammatory bowel disease. Approximately 44% of children diagnosed with ulcerative colitis under the age of 2 years have a first degree relative with IBD. [3, 5] Aside from genetic causes, environmental factors play a significant role in the disease process. Inflammatory bowel disease may be attributed to improved sanitation and hygiene together with decreased exposure to enteric organisms during early childhood, which is associated to a greater susceptibility to develop an inappropriate immunologic response exposure to new antigens. Moreover, diet and nutrition specifically those rich in processed food, sugar, sweeteners, fats and oil may alter the composition of the normal flora in the intestinal tract or disrupt the intestinal barrier contributing to the disease process. [5,9] Early exposure to antibiotics may interfere in the normal process of developing tolerance to enteric bacteria which may result to inflammatory bowel disease. Vaccination specifically live attenuated

measles vaccine has been linked as a risk factor for development of inflammatory bowel disease. However, evidence is still lacking to confirm this association [3,9] In our patient's case, there was no history of inflammatory bowel disease in the family. Moreover, he did not have any atypical presentation and had no history of recurrent infections making monogenic cause less likely thus not warranting immunology work up. In terms of environmental factors, patient had multiple and early exposure to antibiotic use which may have contributed to the development of his inflammatory bowel disease.

There are many diseases that may mimic the presentation of inflammatory bowel disease. Given the rarity of infantile inflammatory bowel disease, other more common conditions such as allergic and infectious colitis, which were initially considered in our patient, should be part of our differential diagnosis. Primary immunodeficiency states should also be considered especially in patients with early onset inflammatory bowel disease with atypical presentation, recurrent infections and skin or hair manifestations. [3]

Diagnosis of inflammatory bowel disease is based on clinical presentation and is confirmed by endoscopy and histological findings. [5] Expected findings on endoscopy include erythema, edema, loss of vascular pattern, granularity, and friability. [3, 5] An isolated colonic involvement, as seen in our patient, is characteristic of patients with very early onset IBD. [3] On biopsy, chronicity and inflammation that is usually limited to the mucosa is expected. Other histological findings include cryptitis, crypt abscesses, separation of crypts by inflammatory cells, acute inflammatory cells, edema, mucus depletion and branching of crypts. [3] On laboratory studies, they are expected to have anemia, elevated ESR and CRP, elevated WBC count in severe colitis and elevated fecal calprotectin which are all consistent with our patient's laboratory work up. [9]

The goal of treatment in inflammatory bowel disease is to obtain and maintain remission, achieve mucosal healing, and prevention of surgical intervention and development of cancer. [7] Treatment is given to control symptoms and to reduce the risk of recurrence. [3] The recommended first line induction and maintenance therapy for mild to moderate ulcerative colitis is oral 5 – aminosalicyclic acid (5-ASA). [8] It is effective in cases of active ulcerative colitis and in preventing recurrence. [3] Since our patient was considered to have a mild disease activity based on his PUCAI score on admission, he was started on mesalazine, a 5-ASA derivative, which is an anti-inflammatory that works locally on the colonic mucosa and reduces inflammation through a variety of anti-inflammatory processes. It is usually given at 60 to 80 mg/kg/day with a maximum dose of 4.8 grams daily. [8] In patients with moderate to severe disease activity unresponsive to aminosalicylate treatment, corticosteroids are usually given. In severe cases unresponsive to both aminosalicylate and steroids, immunomodulators may be started. Patients with uncontrolled severe disease activity despite 3 to 5 days of intravenous treatment may already require surgical

intervention. The optimal approach is to do total colectomy with endorectal pull-through to maintain continence. Besides medical and surgical management, psychosocial support and counseling especially on diet and lifestyle is important. Processed food and those rich in sugar, sweeteners, fats and oil must be avoided while high intake of dietary fiber is recommended. Close monitoring is recommended especially in early onset inflammatory bowel disease since the risk of developing malignancy begins to increase after 8 to 10 years of disease for about 0.5 – 1% per year. Thus, monitoring every 1-2 years with endoscopy and biopsy is recommended. In cases where significant dysplasia will be detected on biopsy, colectomy may be warranted. [8]

Inflammatory bowel disease is a lifelong condition. It is marked by remissions and exacerbations. [3,5] Early onset IBD has a more severe disease course compared to late onset inflammatory bowel disease as it impacts growth, psychological wellbeing, nutrition, and schooling. [5] Moreover, patients with early onset inflammatory bowel disease are associated with a more aggressive disease course usually refractory to conventional therapies thus requiring greater immunosuppression or in some cases even surgery. [5] In children with ulcerative colitis, most will usually respond to medical management. However, there is a risk of developing colon malignancy secondary to chronic inflammation if not controlled. [8]

In summary, we present a two-year-old male with a 10 month history of lower gastrointestinal bleeding associated with loose mucoid stools, colonoscopy findings of friable, erythematous, edematous, with scattered areas of whitish exudates and histopathologic findings of mild to severe acute to chronic inflammation of the mucosa of the entire colon with crypt abscess in the sigmoid which are all consistent with ulcerative colitis. Having been categorized with mild ulcerative colitis based on the score of 20 to 30 on pediatric ulcerative colitis activity index, he is being managed and maintained on mesalazine, a 5-ASA derivative, which is the first line of treatment for mild to moderate ulcerative colitis. Management does not only warrant medical or surgical interventions. Psychosocial support is also important to promote a good quality of life among these patients.

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