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Case Report

Crohn's Disease in Children: A Case Report

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Abstract:

Background: Crohn's disease in children is a chronic inflammatory bowel disease (IBD). The incidence of this disease has tended to increase in recent decades. This case report aimed to increase clinician insight into Crohn's disease.

Case: We reported a case of Crohn's disease, one of the inflammatory bowel disease (IBD) type in a 16-year-old boy. The patient came with complaints of loose stools without mucus and blood, accompanied by heartburn, nausea, vomiting, and decreased appetite. The patient had a history of changes in defecation patterns in the last 4 months and decreased appetite and weight loss in the last 1 month. There was epigastric tenderness on physical examination. Inflammatory markers and fecal calprotectin values were increased. Gastrointestinal endoscopy results found pangastritis and pancolitis with histopathological examination showing results appropriate to IBD. The patient received corticosteroid methylprednisolone 1 mg/kg/day as induction therapy and experienced improvement in symptoms and laboratory results after 7 days of therapy.

Discussion: There are characteristic differences between Crohn's disease and ulcerative colitis. A definite diagnosis is made by endoscopy and histopathological examination. The current goal of Crohn's disease therapy is no longer limited to improving symptoms or optimizing growth and development, but also targeting the improvement of the gastrointestinal mucosa. Remission induction therapy can be carried out with exclusive enteral nutrition or corticosteroids which are gradually reduced.

Conclusion: This case report increases clinician insight into the characteristics, approaches to IBD diagnosis, and remission induction therapy in Crohn's disease in children.

Keywords: Crohn's disease, inflammatory bowel disease, pediatric

Introduction

Inflammatory bowel disease (IBD) is a chronic disease condition causing problems in children, such as growth and developmental disorders. Inflammatory bowel disease includes Crohn's disease (CD) and ulcerative colitis (UC). Crohn's disease involves the entire digestive tract from mouth to anus, while ulcerative colitis affects the colon. The incidence and prevalence of IBD are increasing, and 20-30% of cases occur before the age of 20 years.[1] Inflammatory bowel disease that occurs in children tends to be more progressive and aggressive than in adults. Crohn's disease is more common in children than ulcerative colitis with a male-to-female ratio of 1.8:1.[2] In recent decades, there has been an increase in cases of Crohn's disease in children. It is estimated that 10% of patients with Crohn's disease are diagnosed before the age of 17 years.[3] Data on IBD in children in Asian countries show variations, as in Singapore there has been a 10-fold increase from 0.23 to 2.28 per 100,000 population in the last 20 years.[4] Meanwhile in Korea, the incidence of IBD in children increased from 0.86 to 3.33 per 100,00 population, with an increase of 0.67 to 2.78 for Crohn's disease in children and 0.19 to 0.56 for ulcerative colitis in children.[5] Along with developments, the goals of therapy has changed from initially only relieving and controlling symptoms to now improving the mucosa (mucosal healing). This case report aimed to increase clinician insight into diagnosing and providing adequate management of pediatric patients with IBD, especially Crohn's disease.

Case

A 16-year-old boy, weight 65 kg and height 169 cm came to the Emergency Room with complaints of weakness, loose stools for 2 days before admission to the hospital accompanied by nausea and vomiting for more than 10 times, and abdominal pain in the pit of the stomach for 1 day before admission to the hospital. The patient has had a history of intermittent diarrhea for 4 months before admission to the hospital. When the patient had diarrhea, the frequency could be up to 10 times a day with the consistency varying from liquid to dregs. The average duration of diarrheal episodes lasted 1 week, interspersed with diarrhea-free episodes for 1 week, and then diarrhea returned. Recurrent diarrhea was experienced intermittently and accompanied by a stomach feeling twisted. There was no mucus or blood in the patient's stool. The patient also experienced anorexia and lost 5 kg of weight in the last 1 month. From the physical examination, the patient was fully conscious, vital signs were within normal limits, and abdominal tenderness was found in the epigastric region. Laboratory results showed leucocytosis (25.2 thousand/uL) with eosinophilia (58%) and increased C-reactive protein (CRP 48.45 mg/L). Blood sedimentation rate (ESR) was normal and IGRA was negative. The results of the stool analysis showed occult blood (+) and increased fecal calprotectin (137.6). No leukocytes, amoebas, or bacteria were found in the patient's feces. The stool culture was negative. The patient was admitted to the hospital with a normal soft diet, received fluid infusion, and was

treated medically with anti-emetics, proton pump inhibitors (PPI), probiotics, and broad-spectrum antibiotics.

Diagnostic endoscopy was performed on the patient. From the esophagoduodenoscopy and colonoscopy result, it can be concluded the patient had severe pangastritis and pancolitis (**Figure 1** and **Figure 2**).

Tissue biopsies were performed from the antrum, corpus, duodenum, caecum, and ascending colon to the rectum. The results of the anatomic histopathological examination of the gastric section were active chronic gastritis, non-atrophic, non-dysplastic USS grade IV, stage 0, and H.pylori was not found. Interpretation of histopathological anatomy from the duodenum to the rectum showed non-specific duodenitis, active chronic colitis, and proctitis with moderate to severe degree of activity.

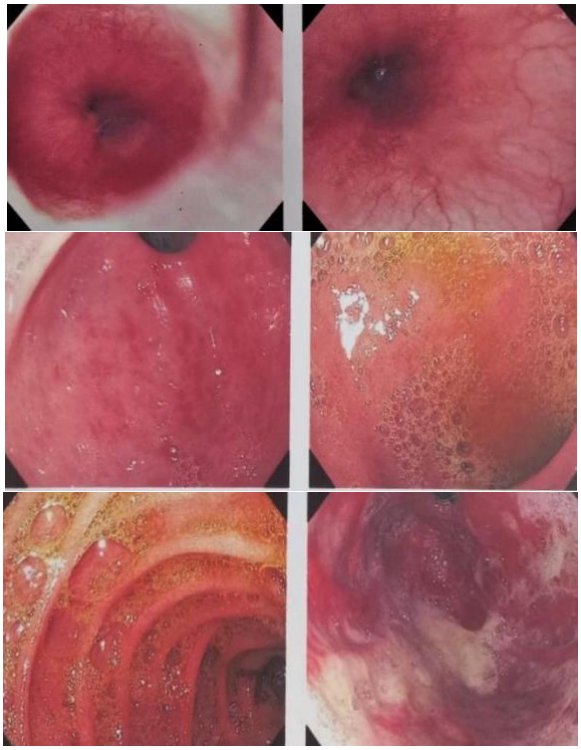

Figure 1. Esophagogastroduodenoscopy (EGD) of the patient showing diffuse hyperemic mucosa of the fundus, corpus, antrum, and pyloric with moderate edema.

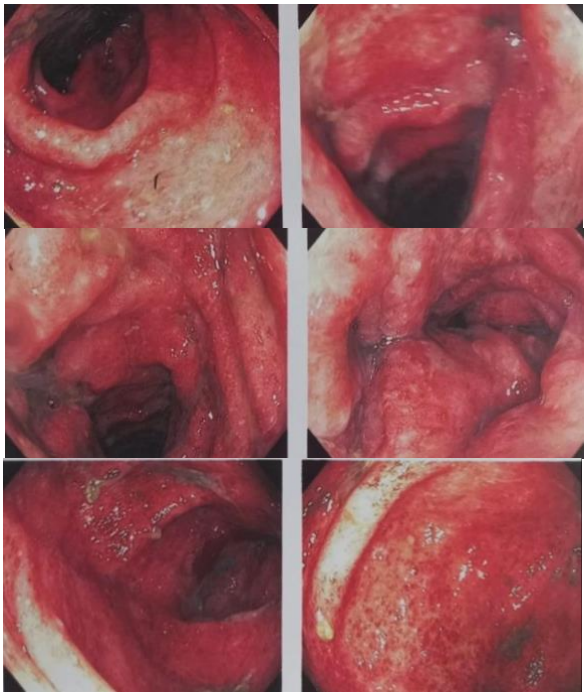

Figure 2. Colonoscopy of the patient showing diffuse erosive hyperemic mucosa of the ascending, transverse, descending colon, caecum, rectum and sigmoid.

Overall, it can be concluded that the picture found supports IBD with severe inflammation from the stomach to the rectum with a moderate-severe degree of activity and a chronic picture of crypt distortion in the caecum to the ascending colon. In all preparations, no dysplasia was found. Based on history, physical examination, laboratory results, and endoscopy results the patient was diagnosed with pangastritis and pancolitis e.c IBD e.c Crohn's disease. The patient tried to be given an enteral nutrition but the tolerance was not good because there was nausea and profuse vomitting. Enterall nutrition is still given in combination with total parenteral nutrition (TPN) to meet nurtitional needs. The patient received methylprednisolone 1 mg/kg/day intravenously. After 7 days of receiving steroid, the patient showed improvement in symptoms with laboratory evaluation results showing improvement in CRP to normal. The patient was allowed to discharge with oral methylprednisolone 1 mg/kg/day for 1 week which was planned to be reduced gradually according to further clinical evaluation (tapering dose).

Discussion

Inflammatory bowel disease (IBD) is an immune-mediated disease. Children with IBD show a more severe degree of disease than adults. Among pediatric IBD patients, 44% require surgery at some point, and 29% have one or more relatives with IBD.[6] A family history of IBD is often found in patients with Crohn's disease who are diagnosed before the age of 11 years.[7] The causes and pathogenesis of IBD are remain unknown. The disease is thought to involve multiple genetic components at more than 200 loci. The genes associated with IBD are broadly related to the immune response. Several genetic defects lead to impaired intestinal epithelial function or predispose to adaptive and humoral immune responses. Overall, the interaction between genetics, the immune system, and the gastrointestinal microbiota environment play an important role in the occurrence of Crohn's disease and the ongoing inflammatory process.[8] In Korean children with Crohn's disease, the IL23R gene and its variants are associated with progression to stenosis.[9] Crohn's disease in children in Asia predominantly affects the ileocolonic with the most common inflammatory phenotype.[10]

IBD in children has a variety of symptoms, both gastrointestinal and extra-intestinal symptoms. Early symptoms of patients with IBD include abdominal pain, diarrhea, and blood in the stools which are frequent manifestations[11]. In ulcerative colitis, the most common manifestations are abdominal pain and bloody diarrhea, whereas, in Crohn's disease, the manifestations are diarrhea, abdominal pain, weight loss, growth retardation, and anorexia.[1] Growth retardation has been reported in up to 20% of children with Crohn's disease and growth failure in up to 44% of children younger than the age of 6 years with IBD.[12] In our patients found abdominal pain in the pit of the stomach, symptoms of diarrhea recurrent and intermittent in which there is no visible blood, weight loss, and anorexia. The nutritional status of the patient is still good.

Some important aspects in the management of pediatric IBD in Asia are early diagnosis and referral by increasing the ability of general practitioners and public awareness, making the right diagnosis, and ruling out other diagnoses, especially infections and gastrointestinal tuberculosis (TB) where this can cause colitis and mimic Crohn's disease, and cost-effective therapy strategies. As TB is endemic in Asia, ruling out TB needs to be considered as an initial step in establishing a diagnosis.[13] In our patient, there were no leukocytes, bacteria, or amoebas in the patient's stool and the IGRA examination results were negative so the possibility of infection and intestinal TB could be ruled out.

In most children with IBD, especially Crohn's disease, inflammatory markers are increased so laboratory tests are needed including complete peripheral blood, CRP, ESR, kidney function, liver function (SGOT/SGPT, albumin), fecal calprotectin, and

stool analysis and culture. The possibility of infection must be ruled out by examination of a stool culture. The use of fecal calprotectin as an indicator of IBD is increasing. Calprotectin is significantly associated with mucosal inflammation in pediatric IBD and may be a major marker of inflammation.[14] Fecal calprotectin can also be used for disease monitoring.[15] In our patient, found leukocytosis accompanied by increased markers of inflammation (CRP 44.35 mg/L), stool analysis possitive of occult blood with increased fecal calprotectin, and negative stool culture. This supports the diagnosis of IBD.

Radiological imaging in pediatric IBD includes ultrasonography (USG), computed tomography (CT-scan), and magnetic resonance enterography (MRE). Ultrasonography can be used to visualize characteristics of Crohn's disease such as bowel thickening, dilatation, strictures, presence or absence of abscesses, fistulas, or inflammation of the mesentery. CT scan and MRI can be used to find out other abnormalities that may accompany or cause symptoms similar to IBD. The American College of Radiology (ACR) mentions that for pediatric patients with suspected Crohn's disease, CT-enterography and MRE examinations are equally good. Nevertheless, a definite diagnosis of IBD must be established by endoscopic examination of the gastrointestinal tract accompanied by histopathological examination.

Gastrointestinal endoscopy should be performed in all cases with suspected IBD and multiple histological biopsies taken from all parts of the gastrointestinal tract to differentiate Crohn's disease from ulcerative colitis.16 Total colonoscopy with ileum intubation, upper gastrointestinal endoscopy, multiple biopsies and exploration of the bowel are recommended as diagnostic procedures.17 The difference between Crohn's disease and ulcerative colitis is sometimes not clearly defined. Involvement of almost the entire digestive tract with a wide distribution of inflammation and the presence of granulomas makes the diagnosis more suggestive of Crohn's disease than ulcerative colitis. In our patient, endoscopic results found pangastritis and pancolitis which indicated involvement of almost the entire digestive tract accompanied by a wide distribution of inflammation.

Complete comparison of Crohn's disease and ulcerative colitis is presented in **Table 1**.

Table 1. Comparison of the characteristics of Crohn's disease and ulcerative colitis[1]

Characteristics	Crohn's disease	Ulcerative Colitis
Gender	boy > girl	boy = girl
Symptoms and signs	Abdominal pain, diarrhea, anorexia, weight loss, growth failure	Massive bloody diarrhea, abdominal pain
Location	Mouth to anus, involving all layers of the mucosa - serosa	Colon, involving only the mucosa
Endoscopic findings	Segmental distribution, aphthous ulcers, deep ulcers, cobble stones, strictures, fistulas	Diffuse and continuous erythema
Histological Findings	Pathognomonic non-caseating granuloma, ileitis	Cryptitis, crypt abscess, distal Paneth cell metaplasia
Radiological findings	Skip area, rigid stenotic segment	Colonic dilatation in toxic megacolon

Based on the history, symptom characteristics, laboratory results, endoscopy results, and histopathological examination results, the diagnosis of Crohn's disease was made in our patient.

Initially, the goals of IBD therapy in children were to relieve symptoms, optimize growth, and improve the patient's quality of life. To achieve these, tight control of inflammation is essential. However, the new paradigm of the current goal of IBD therapy in children is to achieve mucosal healing.[18] (**Figure 3** and **Table 2**). Achievement of mucosal healing is associated with better long-term outcomes.[19] Normal histological features are the main focus of current therapy. In Asia, the goals of Crohn's disease therapy in children include normal growth, absence of disability, and improvement of quality of life, as well as mucosal healing as a long-term goal of therapy.[20] However, in some parts of Asia Pacific with limited resources, it may not be possible to achieve the goal of endoscopic mucosal healing.

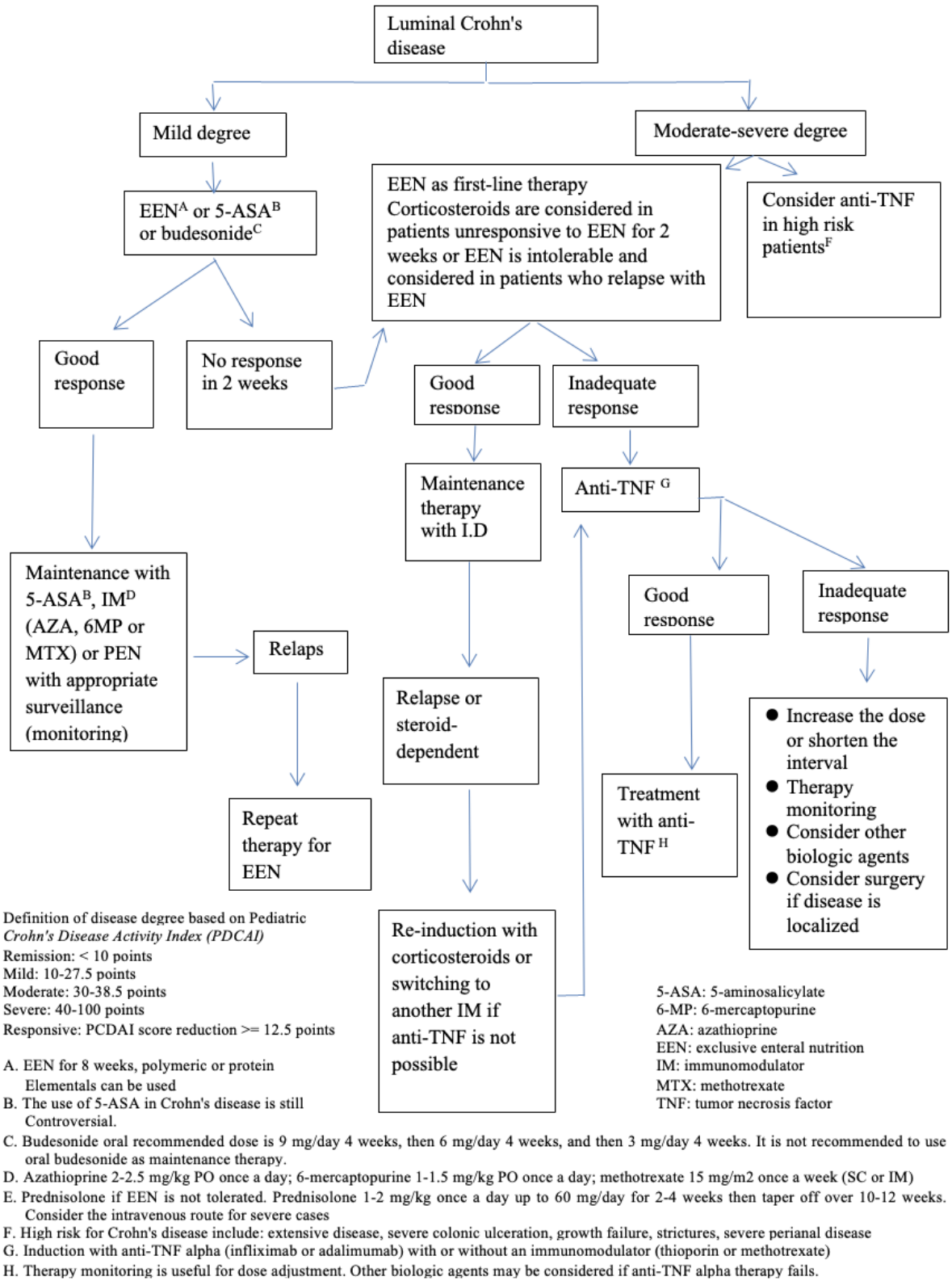

Figure 3. Management of pediatric Crohn's disease in Asia.[21]

Table 2. Treatment recommendations for pediatric inflammatory bowel disease (PIBD) in Asia.[21]

1. Induction Therapy

1.1 Gastrointestinal infections and other causes of diarrhea, especially gastrointestinal TB, need to be ruled out before diagnosing IBD in Asian children.

1.2 EEN is recommended in the induction and re-induction phases as the therapy of choice in Asian children who have just been diagnosed with Crohn's disease or relapse cases who are not high-risk factors.

1.3 EEN is not recommended for induction therapy in complicated Crohn's disease, including strictures, intestinal penetration, and perianal disease.

1.4 In children with Crohn's disease who do not tolerate or respond to EEN after 2-4 weeks, oral corticosteroids should be considered.

1.5 In areas where resources are limited and where EEN is not available, 5-ASA may be considered as induction therapy in mild Crohn's disease.

1.6 EEN is not recommended as induction therapy in Ulcerative Colitis.

1.7 Oral 5-ASA preparations are recommended as first-line therapy for mild to moderate ulcerative colitis.

1.8 Corticosteroids are recommended as the treatment of choice in moderate to severe ulcerative colitis

1.9 Biologic agents may be considered as first-line therapy in high-risk pediatric Crohn's disease and second-line therapy for steroid-refractory ulcerative colitis or patients with ASC.

2. Maintenance Therapy

2.1 Corticosteroids are not recommended as maintenance therapy in pediatric IBD.

2.2 Partial enteral nutrition may be considered as adjunctive therapy to immunomodulators to prolong remission in pediatric Crohn's disease patients with luminal disease without fistulas or strictures.

2.3 In ulcerative colitis, 5-ASA monotherapy is recommended in maintaining remission in children with mild disease. In children with frequent relapses on 5-ASA or corticosteroid-dependent maintenance therapy, AZA is recommended as maintenance therapy.

3. Immunomodulator

3.1 AZA is recommended as first-line maintenance therapy for Crohn's disease and ulcerative colitis

3.2 Where NUDT15 genotyping and TPMT enzyme assay are not available, it is recommended that complete peripheral blood count and liver enzymes should be monitored weekly. After the AZA dose is fixed, monitoring can be paused for up to three months. Complete peripheral blood count and liver enzymes are still required although NUDT15 genotyping and TPMT enzyme assay are available.

3.3 Routine screening for EBV prior to starting thiopurine therapy is not recommended

3.4 MTX may be considered in Crohn's disease both as main maintenance therapy and as replacement therapy in cases of intolerance and non-response to thiopurines.

3.5 TAC may be considered as a short-term agent in cases of steroid-refractory ulcerative colitis as well as replacement therapy in ASC.

4. Biologic

4.1 The use of biologic agents, IFX and ADA is recommended in inducing and maintaining remission in chronic luminal Crohn's disease despite adequate immunosuppressant therapy or steroid refractoriness. In addition, biologic agents should be used as primary induction and maintenance therapy in severe luminal disease and active perianal disease.

4.2 In ulcerative colitis, both IFX and ADA are indicated in steroid-dependent and refractory cases, as well as for active or recurrent disease despite adequate 5-ASA and thiopurine therapy.

4.3 The main considerations for using biologic agents in the Asia Pacific region are the very expensive price, limited materials, and the potential risk of infection, especially TB.

5-ASA: 5-aminosalicylic acid; ADA: adalimumab; ACS: acute severe colitis; AZA: azathioprine; EBV: Epstein Barr Virus; IBD: inflammatory bowel disease; IFX: infliximab; MTX: methotrexate; EEN: exclusive enteral nutrition NUDT-15: nudix hydrolase 15; TAC: tacrolimus; TB: tuberculosis.

The use of antibiotics needs to be considered in patients with Crohn's disease because of the possibility of bacterial overgrowth or to prevent infections that can worsen.[18] In a randomized control trial (RCT) of pediatric patients, it was stated that giving the combination of antibiotics azithromycin and metronidazole during the induction period was more effective in improving symptoms than the metronidazole group alone.[22] The fecal calprotectin values decreased significantly in the group that received the combination antibiotic. Our patient has been administered with broad-spectrum combination antibiotics.

The specific management of Crohn's disease in children is to start giving nutrition and steroids as the initiation of therapy. Exclusive enteral nutrition (EEN) is recommended using a complete liquid formula as a food source for the initial 6-8 weeks.[18] The selection of polymeric formula nutrition can be considered the first choice. In a study by Kadim M et al.,[23] it is stated that giving EEN is as effective as corticosteroids for inducing Crohn's disease remission in children, but giving EEN is more recommended because of its better mucosal healing effect and there are no long-term side effects on growth. A study in Southeast Asia shows that after using EEN for 8 weeks, 91% of children with Crohn's disease achieved remission with significant weight gain and improvement of inflammatory markers and PCDAI scores.[24] A study by Chan et al.,[25] in Malaysia, also shows that EEN is as effective as primary induction therapy in new cases and re-induction in relapsed cases of Crohn's disease in children.

The use of EEN as an induction therapy for Crohn's disease in children is especially relevant in Asia where the incidence of infectious diarrhea is high and there is concern over the use of biologic agents in TB endemic areas.[26] In cases where the diagnosis of Crohn's disease is uncertain, EEN is an appropriate choice to avoid the side effects of immunosuppressants and is also an effective therapy in the Asian child population.[27] The use of nasogastric tube is worth considering so that EEN can be given adequately and avoid rejection. The side effects of EEN administration are diarrhea and vomiting. Crohn's Disease exclusion diet (CDED), a diet rich in complex carbohydrates and low in animal fat with a moderate amount of fiber has been shown to be effective in inducing remission in children with Crohn's disease. When compared to EEN alone, CDED added with partial EEN therapy provides better tolerance and patient acceptance, and induces more remissions in children with mild-moderate Crohn's disease.[28]

In pediatric Crohn's disease patients, oral corticosteroids are effective at inducing remission.[29] If EEN is not effective after 2-4 weeks of administration or is not well tolerated, then systemic corticosteroids should be given. The initial dose of prednisolone follows the patient's weight (weight-dependent) and should be tapered immediately when clinical improvement is achieved, a maximum of 4 weeks after

initiation of therapy. In general, oral prednisolone or prednisone may be given once a day at a dose of 1 mg/kg/day (maximum 40 mg per day) and may be increased to 1.5 mg/kg/day (maximum 60 mg per day) if the response to therapy with an initial dose of 1 mg/kg/day is not satisfactory.[18] For children weighing more than 40 kg, an initial dose of budesonide can be given 9-12 mg once a day for 6 weeks. A dose of up to 12 mg may be given during the first 4 weeks.[30] Then it is gradually lowered as follows: 6 mg once a day for 2 weeks and 3 mg once a day for 2 weeks. The total duration of budesonide administration from initiation to tapering down is 10-12 weeks. If oral administration is not well tolerated, intravenous steroid administration is an option. Ideally, EEN should be given, but in our patient the tolerance was not good because there was severe vomitting. Because enteral nutrition could not be fulfilled properly, steroid was given. For induction therapy, the patient was given methylprednisolone 1 mg/kg/day. An intravenous route is an option because the patient had symptoms of nausea and vomiting. The patient felt improvement in clinical symptoms and CRP significantly after 7 days of receiving corticosteroids, then he was allowed to discharge with oral methylprednisolone 1 mg/kg/day for 1 week which was planned to be tappering down gradually according to further clinical evaluation during outpatient check-up. (**Table 3**)

Table 3. Laboratory work up result.

Laboratory Workup	Result		Unit
	Before steroid treatment	After steroid treatment	
Hemoglobin	17.3	15.3	g/dL
Hematocrit	53	46	%
Erythrocytes	6.4	5.6	Million/uL
Leucocytes	25.2	12.8	Thousand/uL
Thrombocytes	280	421	Thousand/uL
Basophil	1	0	%
Eosinophil	58	3	%
Neutrophil	28	87	%
Lymphocytes	8	5	%
Monocytes	7	5	%
CRP	48.45	0.67	mg/dL
Procalcitonin	N/A	< 0.05	ng/mL
IGRA-TB	Negative	N/A	N/A
Fecal calprotectin	137.6	N/A	N/A
Fecal analysis	Occult blood (+)	N/A	N/A
Fecal culture	Negative	N/A	N/A

N/A: not available

Stenosis as a complication of Crohn's disease is frequently found in Asian children[31]. Therapy using Biologic agents is recommended as initial therapy in children with stenosis without prestenotic dilatation. However, in resource-limited settings where biologic agents are not readily available, endoscopic or surgical dilation should be considered.[32] Indications for surgery in pediatric Crohn's disease include strictures, stenosis, obstructive symptoms, and perianal fistula.[33] Surgery also needs to be considered in children who are entering puberty where the growth of bone age decreases in the range of 6-12 months despite optimal medical and nutritional therapy. There were no signs of obstruction or complications in our patient, so no operative management was required.

Conclusion

Crohn's disease belongs to the category of IBD involving the entire upper and lower digestive tract. This disease can cause complications such as growth and development disorders in children. Crohn's disease can be differentiated from ulcerative colitis by several characteristics. Calprotectin fecal examination, gastrointestinal endoscopy, and histopathological examination results are necessary in all cases of suspected IBD. The current goals of Crohn's disease therapy are to achieve optimal growth, eliminate or reduce symptoms, and achieve the mucosal repair. Exclusive enteral nutrition or corticosteroids is the main pillar in the management of Crohn's disease in the induction phase.

Conflict of Interest

None declared

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