Allergic proctocolitis (AP) can be hard to differentiate and diagnose in neonates who manifested watery diarrhea and failure to thrive. The initial symptoms are not specific and colonoscopic findings share similar ulcerated and erythematous lesions as in ulcerative colitis of infancy and infectious colitis. A 3-day-old infant was admitted to the hospital due to loose, blood-tinged stools. An initial workup, including abdominal ultrasound and hepatobiliary scan, was performed, and all results were negative. The patient subsequently required readmission due to pervasive watery diarrhea, severe weight loss, and lethargy. After further investigation, he was eventually diagnosed of allergic proctocolitis by rectosigmoidoscopy and biopsy. Treatment was started with a corticosteroid (prednisone 2 mg/kg/day) due to severe symptoms. After 7 days of steroid therapy, the stools slowly normalized, and the patient started to gain weight. He was discharged home and followed regularly at the outpatient clinic.

Key Words: Failure to thrive, Diarrhea, Infant, Steroids

INTRODUCTION

Allergic proctocolitis (AP) can be hard to differentiate and diagnose in neonates who manifested watery diarrhea and failure to thrive. The initial clinical features and laboratory findings are not specific and colonoscopic findings share similar ulcerated and erythematous lesions as in ulcerative colitis in infancy and infectious colitis. Because a number of severe and potentially treatable diseases may mimic allergic proctocolitis, a comprehensive evaluation is very important. Early diagnosis is possible and treatment can be instituted earlier for a better outcome when colonoscopy is performed. The most highly associated findings in colonoscopy in allergic proctocolitis is large numbers of eosinophils in colonic mucosal biopsy specimen, therefore, even in neonates with severe GI symptoms, colonoscopy should be done to confirm the diagnosis. Allergic proctocolitis is usually associated with mild and transient clinical
manifestations with good prognosis. The symptoms are mostly occurring in healthy looking infants with appropriate growth rate for their age. We report a 3-day old neonate who manifested chronic diarrhea and failure to gain weight and eventually diagnosed with allergic proctocolitis.

**CASE REPORT**

A 3-day-old, 2.7 kg (50-75 percentiles), male infant born at 36 weeks gestation by cesarean section was transferred to our neonatal intensive care unit (NICU) due to loose, blood-tinged, and grey-colored stools. His mother had been diagnosed with ulcerative colitis 8 years prior to this pregnancy and was on mesalamine treatment. His older brother was diagnosed with congenital hepatic fibrosis and choledochal obstruction at 8 months of age and was being regularly assessed at another tertiary center. The patient was admitted to our NICU on his 3rd day, and an initial workup, including abdominal ultrasound and hepatobiliary scan was performed. All results, including initial laboratory findings, were negative. At the 7 days after admission, no more blood tinged stool was found and discharge was planned. However, because the patient’s follow up lab showed an increased C-reactive protein level, he was started on antibiotics and observed for any probable signs of infection. Meanwhile, he was fed with formula milk, because his mother was on mesalamine and refused to breast feed her baby. At 1 week after discharge, the patient’s vital signs were unstable with hypotension and intermittent hypoxemia, consistent with shock. He was admitted to pediatric intensive care unit and treated for dehydration and septic shock, and was found to be positive for rotavirus. After a complete resolution of symptom, the patient was diagnosed with rotaviral enteritis and discharged home. His formula milk was changed to hypoallergenic formula milk due to continuous loose and mucoid stools. However, 1 week later at an outpatient clinic visit, when he is 50 days old, he still manifested a failure to gain weight and continued to have frequent watery and mucoid stools. Therefore, he was admitted for further investigation.

On admission, he only weighted 2.9 kg on his 50th day after birth. A complete blood count showed a hemoglobin level of 10.9 g/dL, white blood cell count of $8,570 \times 10^9$/L (neutrophils 40.6%, lymphocytes 36.3%), and platelet count of 261,000/mm$^3$. Liver function and renal function tests were normal. Gastrointestinal infections were ruled out by culture and sensitivity testing. A Clostridium difficile test was also negative. Erythrocyte sedimentation rate (ESR) and C-reactive protein were increased to 78 mm and 9.84 mg/dL, respectively. The autoimmune study was proceeded. Anti-nuclear antibody (ANA) was positive at 1:800 with both nucleolar and cytoplasmic patterns. Specific systemic lupus erythematosus (SLE) profile antibodies were all negative. Anti-neutrophil cytoplasmic antibodies (ANCA) were also negative. The immunologic studies included as following; Lymphocyte subsets were all within normal range (CD3: 77.9%, CD4: 56%, CD8: 20.7%, CD19: 13.9%). The allergic study indicated a slightly elevated immunoglobulin (Ig) E-Fe level of 2.21 IU/mL (normal <0.35) to milk. The IgG level was 1420 mg/dL, IgA was 158 mg/dL, and IgM was 51 mg/dL, which were all within the normal range. However, the IgE level was elevated at 459 IU/mL (normal range 0-230 IU/mL). C3 and C4 levels were decreased at 40 mg/dL (normal 76-139 mg/dL) and 1.4 mg/dL (normal 12-37 mg/dL), respectively. Blood lactate was elevated to 35.3 mg/dL (normal <20 mg/dL). Thyroid function tests, TORCH (toxoplasma, rubella, cytomegalovirus, and herpes) and HIV (human immunodeficiency virus) antibodies were all negative.

![Figure 1. Rectosigmoidoscopy showing multiple areas of ulcerated, erythematous and inflammatory intestinal mucosa.](image-url)
Rectosigmoidoscopy revealed multiple ulcerated, erythematous and inflammatory areas of intestinal mucosa starting at 60 cm above the anorectal valve. At the region around the rectum, multiple areas of patchy erythemas and ulcerations were observed (Figure 1). The oral cavity was intact. Biopsies from the stomach, duodenum, and colon indicated moderate chronic colitis with prominent eosinophil infiltration (125/10 high power field) which is a typical feature of allergic proctocolitis (Figure 2).

The child couldn’t be breast fed due to her mother’s medication. Our patient was continuously given hypoallergic formula milk. Unlike mild symptoms of allergic proctocolitis, severe watery and mucoid stools and failure to gain led to the initiation of corticosteroid treatment (prednisone 2 mg/kg/day). After 7 days of steroid therapy, the loose stool slowly normalized, and the patient started to gain weight. He was discharged home and followed at the outpatient clinic. At 3 months of age, with tapered steroid treatment (0.3 mg/kg/day), he remained symptom-free with an appropriate weight gain of 6.7 kg (10-25 percentile). At a recent follow-up visit at 15 months of age, he had no recurrence of symptoms without steroid. His weight was 9.1 kg (5-10 percentile), and height was 75.2 cm (5-10 percentile).

DISCUSSION

Allergic proctocolitis is a clinical manifestation of food allergy during the first months of life. It is the most common cause of rectal bleeding in infancy. Bloody stools occur irregularly for only a few days during the following months. Allergic proctocolitis is non-IgE mediated disease and classified as type IV hypersensitivity which is cell-mediated and delayed response. In addition to dietary antigens, intraluminal microbial agents challenge the gut mucosa. Although controlled in the mature gut, these infectious antigens may induce inflammation in the developing gastrointestinal tract like our case when he was infected with rotaviral enteritis. In biopsy, allergic proctocolitis can be diagnosed when eosinophil infiltrations are greater than 60/10 high power field (HPF). Our biopsy revealed 125/10 HPF eosinophil infiltrations which led us to diagnose allergic proctocolitis. After one year of age, all infants eventually show food tolerance and become tolerate cow’s milk without any difficulties. As a result, allergic proctocolitis is a benign and self-limiting disorder.

Unlike most allergic proctocolitis cases, our 3-day-old patient did not reveal mild symptoms like bloody stool in healthy looking appearance. Rather, he was looking very ill with pervasive diarrhea and failure to thrive which was more likely suited to ulcerative colitis of infancy. In a study by Cannioto et al, 6 out of 12 cases eventually diagnosed as very early onset inflammatory bowel disease (IBD) when allergic colitis was initially considered since the stool analyses revealed the presence of eosinophils. Furthermore, both studies by Cannioto et al. and Marx et al. mentioned improper diagnosis of allergic colitis caused a diagnostic delay of at least 6 months in very early onset of IBD patients. Therefore, empiric dietary approach (elimination diet) should be approached and when lack of clinical improvement persists in a few days of elimination diet, then, ulcerative colitis of infancy should be considered.

Pediatric epidemiological data from the European countries and the United States show a relatively constant incidence of pediatric ulcerative colitis, in contrast to an increased incidence of pediatric Crohn’s disease. Although rare, inflammatory bowel disease (IBD) may have a very early onset in childhood, before the age of 2 years. Recently published data showed the onset of IBD within the first year of life in 1% of patients. As regard to IBS symptoms, almost all present with chronic diarrhea followed by failure to grow. Growth failure in ulcerative colitis is multifactorial, caused by chronic diarrhea, decreased oral intake, increased catabolism, and production of certain growth inhibitory cytokines. Diagnosis of IBD in infancy is very difficult because its presentation is often atypical, and neonatal IBD has seldom been described. In addition, several conditions may appear similar to ulcerative colitis. The major conditions to exclude are allergic colitis, infectious colitis and Crohn’s colitis.
Serological markers of IBD like pANCA (peripheral antineutrophil cytoplasmic antibodies) or ASCA (anti-saccharomyces cerevisiae antibody) are not useful in the diagnosis of IBD in an infancy group compared to that for older children with IBD. The diagnosis of ulcerative colitis must be confirmed by endoscopic and histologic examination of the colon. Typical histologic findings are cryptitis, crypt abscesses, separation of crypts by inflammatory cells, focal of acute inflammatory cells, edema, mucus depletion, and branching of crypts in adults. In some ulcerative colitis patients, eosinophilic infiltration may precede like our case. Early onset of ulcerative colitis indicates its genetic predisposition, and several genetic risk factors have been identified. NOD2 (nucleotide-binding oligomerization domain containing 2)/CARD15 (caspase activation recruitment domain 15) mutations are highly correlated with ulcerative colitis.

Unlike allergic proctocolitis, early inflammatory bowel disease (IBD) is characterized by unpredictable and severe prognosis which often needs an aggressive therapeutic approach. Controlling disease symptoms and progression is hard to curb and the long-term prognosis is very bad in ulcerative colitis of infancy. Ulcerative colitis also reveals large bowel with acute and chronic inflammation, ulceration, cryptitis and crypt abscess formation in colonoscopic findings. Therefore, because both allergic proctocolitis and ulcerative colitis share consistent active inflammation features, differential diagnosis is necessary to improve outcomes. If an elemental diet does not relieve symptoms, corticosteroids (Prednisone 1 to 1.5 mg/kg per day, to a maximum of 40 to 60 mg/day), and mesalamine are commonly prescribed. Surgical treatment is reserved for fulminant and destructive colitis. As a treatment modality, our patient was given hypoallergic formula milk on his second hospitalized day because he could not be breastfed due to his mother’s medication. His dietary option was limited and he consistently failed to gain weight and had severe intestinal symptoms which led us to initiate oral steroid which was very effective in this case. In some cases, corticosteroids and novel steroid-sparing agents may be required in patients with refractory or relapsing eosinophilic gastrointestinal disorders.

In conclusion, allergic proctocolitis can also be manifested with severe initial symptoms with failure to growth. Therefore, neonates with chronic diarrhea and bloody, mucoid stools should be evaluated for both allergic proctocolitis and ulcerative colitis of infancy at the same time even though it is rare in a neonatal period. Early diagnosis with colonoscopy and biopsy is important to prevent any additional adverse impact upon growth, nutrition, and treatment modality. Corticosteroid treatment was effective for a neonate with severe symptoms of allergic proctocolitis followed by failure to grow who can’t be breast fed or have different dietary approach.

REFERENCES

알레르기성 직결장염은 증상이 비특이적이고 직결장 내시경술에서 관찰되는 궤양과 발적이 영아 궤양성 대장염 및 감염성 대장염과 유사하다. 그래서 설사와 성장장애가 있는 신생아에서 알레르기성 직결장염을 감별 진단하는 것은 어렵다. 생후 3일 된 환아가 묽은 혈변을 주소로 내원하여 입원치료 후 퇴원하였다. 이후에도 지속적인 혈변과 성장장애가 있어 재입원하여 직결장 내시경술로 알레르기성 직결장염을 확진하였다. 환아는 혈변과 성장장애와 같은 심한 증상이 지속되어 스테로이드 치료를 하였으며 호전 후 외래에서 추적 관찰 중이다. 저자들은 직결장 내시경 검사와 조직검사로 확진된 영아 궤양성 대장염과 유사한 알레르기성 직결장염 1례를 보고하는 바이다.