□ Case Report □

# Development of Crohn disease in patients with myelodysplastic syndrome : report of two children

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Crohn disease (CD) is rare, but the incidence of CD has been increasing over the past ten years. We found two cases of CD, associated with myelodysplastic syndrome (MDS), for the first time in children. In the first patient, MDS was diagnosed at three years of age and CD developed later at eight years of age. The patient presented with recurrent abdominal pain, diarrhea, bloody stools and failure to thrive. Colonoscopy revealed cobble stone like mucosa and mass like lesions with superficial ulceration and inflammatory exudates, observed from the cecum to ascending colon. Ileo-cecal biopsy samples showed ulcers with skipped areas and lymphoid infiltrations. The patient was started on treatment with mesalazine and deflazacort, and symptoms remitted. In the second patient, MDS was diagnosed at nine years of age and CD developed at 13 years of age. This patient has recurrent hematochezia, abdominal pain, vomiting and fever. Colonoscopy revealed a large, deep indurative ulceration on the cecal side of the ileo-cecal valve. Ileocecectomy was done, and histology revealed ulceration with transmural inflammation and lymphoid aggregates. Symptoms improved after ileocecectomy. **(Korean J Pediatr 2006;49:107-111)**

**Key Words :** Crohn disease, Myelodysplastic syndrome, Children

## Introduction

Crohn disease (CD) is rare. After the report of the twelve patients with CD by Seo et al.[1], the incidence of CD appears to be increasing[2, 3].

In recent years, a few adult patients with CD associated with myelodysplstic syndrome (MDS) have been reported[4-12]. These reports suggest that the association between the two disorders is not fortuitous. We report here, the first observation of two children with CD associated with MDS.

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## Case Report

### Patient 1

A 7-year-old boy was brought to our hospital for recurrent abdominal pain. During the past several years, he had bout of intensive periumbilical pain, nausea, vomiting and loose stools. Neither fever nor bloody stool was noted at the time of presentation.

He was born at 40 weeks of gestational age, and admitted because of the necrotizing enterocolitis at 22 days of life. Between the age of two and three years, he was admitted to a different hospital three times because of pneumonia, and at that time an atrial septal defect (secondum type) and pancytopenia were detected. Bone marrow aspirate revealed MDS. At four years of age, he was transferred to our hospital and has been followed up with intermittent transfusions.

The family history was noted for an elder brother who was diagnosed as MDS at four years of age and a grand-

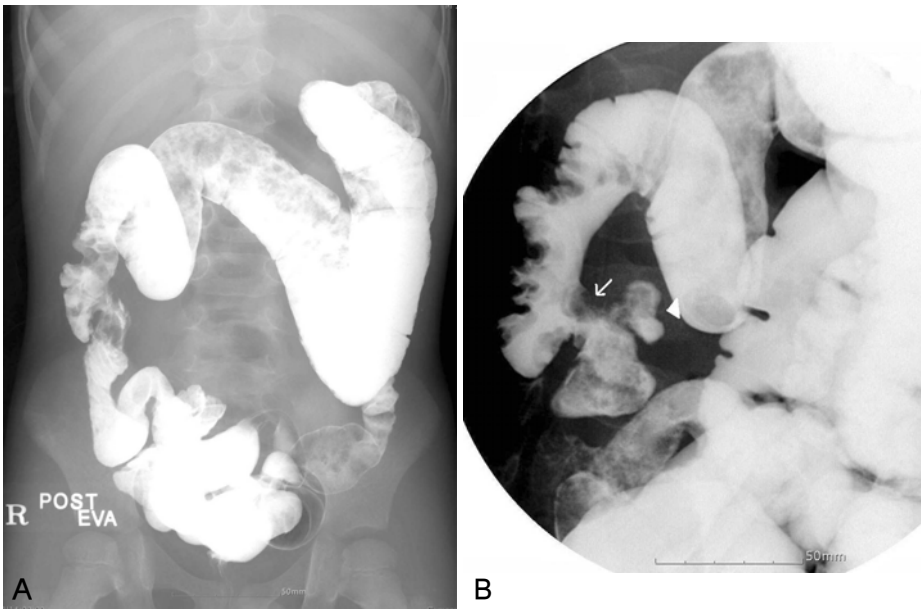


**Fig. 1.** Barium enema of the patient 1 showed shortening of the ascending colon **(A)**, and deformity and pseudosacculation (B : arrow head) of the cecum. Thickening of the ileocecal valve (B : arrow), and wall thickening and mucosal nodularity of the ascending colon, cecum and ileum were also noted.

father who died of liver disease with unknown etiology, otherwise there was no family history of malignancies, inflammatory bowel disease and so on.

The patient had a body weight of 15 kg (below 3 percentile), height 109 cm (below 3 percentile) and head circumference 47.3 cm (below 3 percentile). His face looked like an inverted triangle, and the cutaneous vessels were prominent. Periumbilical tenderness was noted. His oral cavity and perianal area were clear and lymph nodes were not enlarged.

Laboratory examinations showed pancytopenia and macrocytic anemia (white blood cell 2,860/$\mu$L, hemoglobin 8.2 g/dL, hematocrit 28.0%, mean corpuscular volume 63.6 fL and platelet $147\times10^3/\mu$L). Erythrocyte sedimentation rate was 70 mm/hr, and C reactive protein was 2.95 mg/dL. Anti-ds DNA was 5.3 IU/mL, C3 191 mg/dL and C4 19 mg/dL. Anti-neutrophil cytoplasmic antibody was negative, immunoglobulin G, A and M were 2,559 mg/dL, 151 mg/dL and 110 mg/dL repectively. HBs Ag, anti-HBs, anti-HCV, anti-HIV, Ebstein-Barr virus and parvovirus B19 were all negative. The bone marrow exam done 6 months ago revealed myelodysplastic syndrome/myeoproliferative syndrome, and the karyotype was normal.

Stool cultures were negative. An abdominal sonography revealed wall thickening of the cecum and terminal ileum and multiple mesenteric lymph node enlargement. Barium enema showed shortening of the ascending colon, and deformity and pseudosacculation of the cecum. Thickening of the ileocecal valve, and wall thickening and mucosal nodularity of the ascending colon, cecum and ileum were also noted (Fig. 1).

Mesalazine (200 mg/dose, twice per day) was started 1 month later because of the aggravated abdominal pain.

One year later, the patient had a recurrence of lower abdominal pain, loose stools and vomiting. Colonoscopy revealed cobble stone like mucosa and mass like lesions from the cecum to the proximal portion of the ascending colon. Superficial ulceration and inflammatory exudates were noted in the mucosa (Fig. 2). Colonoscopy biopsy of non-ulcerated areas situated near the ulcers showed a relatively normal looking appearance but plasma cells and lymphocytic infiltrations of the lamina propria, and those findings were competent with Crohn disease (Fig. 3). The patient was treated with mesalazine (750 mg/day) and deflazacort (18 mg/day). He responded well to the treatment, and deflazacort was discontinued. He is now in remission.

### Patient 2

A 13-year-old boy presented to our hospital with complaints of hematochezia and vomiting. Three weeks prior to the visit, left lower abdominal pain and hematochezia developed. He was not febrile.

The past medical history revealed that at the age of two years pancytopenia was first detected when he was evaluated for pneumonia. At the age of nine years, a bone marrow aspirate showed findings consistent with MDS. He was treated with alfacalcidol and deflazacort, and has waited for stem cell transplantation. Neutropenic fevers were problems for this patient several times. Four months prior to the visit, multiple hepatic adenomas were found due to right upper abdominal and epigastric pain. He denied smoking and a family history that might relate to these problems.

His body weight was 47.6 kg (between 50 and 75 percentile) and height 155.7 cm (between 50 and 75 percentile). His bowel sounds were increased and his abdomen was mildly tender. His oral cavity and perianal area were clear. Lymph nodes were not enlarged.

Laboratory tests showed pancytopenia and macrocytic anemia (white blood cell 1,090/$\mu$L, hemoglobin 4.2 g/dL, hematocrit 11.9%, mean corpuscular volume 85.6 fL and platelet $65\times10^3/\mu$L). Erythrocyte sedimentation rate was 48 mm/hr, and C reactive protein was 1.76 mg/dL. A bone marrow aspirate done four months ago revealed hypoplastic MDS. The karyotype revealed trisomy 8 (46XY, inv(9)(p11q13)[8]/47XY, idem, +8[10]). Stool cultures were negative. He was treated conservatively and symptoms were relieved.

Two months later, hematochezia and abdominal pain recurred. Severe anemia and thrombocytopenia (hemoglobin 3.9 g/dL, hematocrit 10% and platelet $10\times10^3/\mu$L) were noted. Red blood cell and platelet transfusions were started. A bleeding scan was done, and there was suspected bleedings in the transverse colon. At CT colonography, a 3.5×2 cm sized large ulcer was detected in the cecum near ileocecal valve. The patient was treated with mesalazine (2,250 mg/day), prednisolone (45 mg/day) and ciprofloxacin (1,000 mg/day for 2 weeks). Abdominal pain and bloody diarrhea improved, and after a month of treatment follow-up CT colonography revealed improvement of the cecal ulcer.

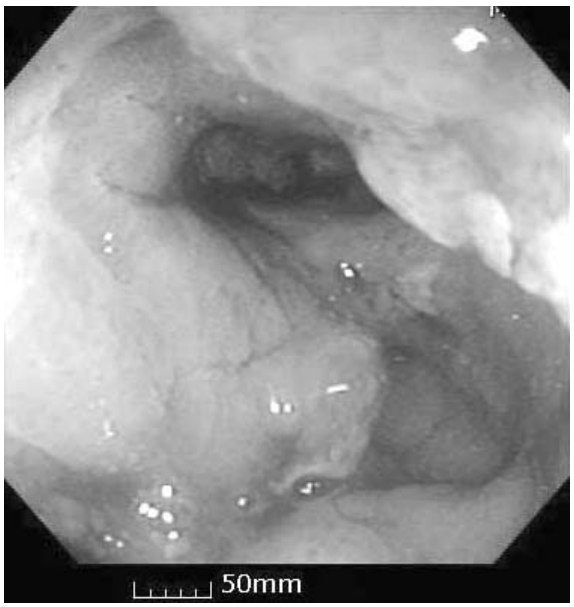


**Fig. 2.** Colonoscopic finding of patient 1 revealed cobble stone like mucosae with superficial ulcerations and inflammatory exudates.

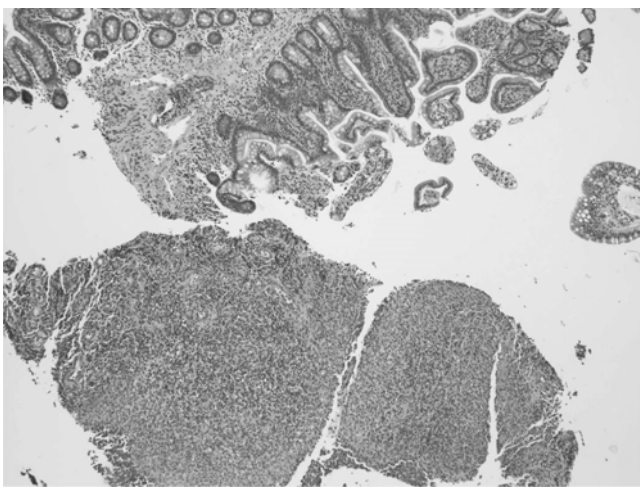

**Fig. 3.** Photomicrograph of ileocecal biopsy samples showed ulcerated areas (lower half of the figure) and non-ulcerated areas. Non-ulcerated areas demonstrated some alteration of villous configuration and increased lympho-plasma cell infiltration into lamina propria (H&E stain, ×100).

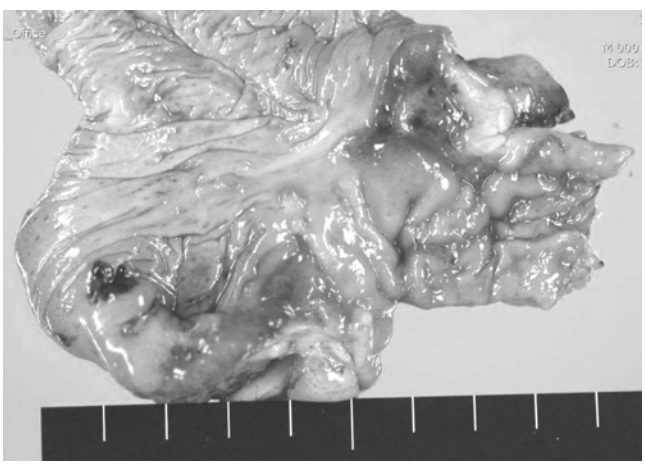

**Fig. 4.** Ileocecectomy specimen of the patient 2 showed a 2.5 ×2×0.6 cm sized large deep ulcer at cecum (medial aspect of ileocecal valve).

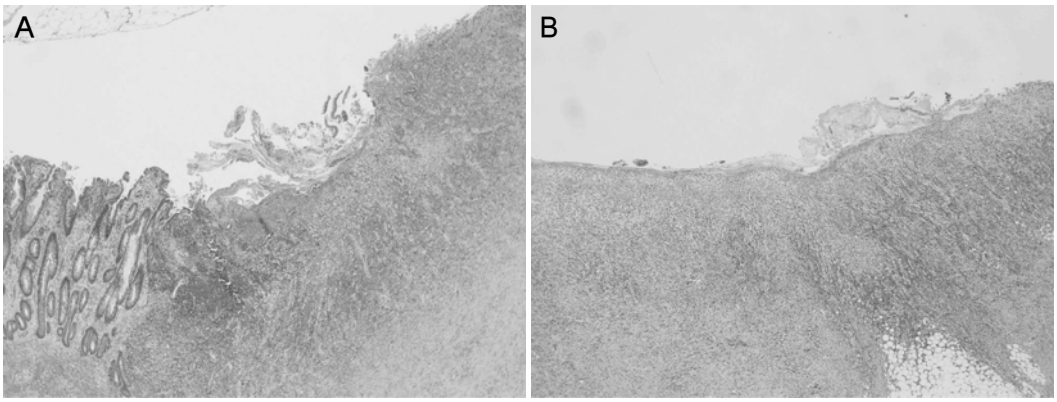


**Fig. 5.** Photomicrograph of the resected specimen of the patient 2 displayed a wide area of ulceration with increased transmural lympho-plasmocytic infiltration and a non-ulcerated portion with architectural distortion of crypts (H&E stain, ×40).

After two months of treatment with mesalazine, the patient developed massive hematochezia with hypotension. Admission to the intensive care unit, and conservative managements with transfusion and somatostatin infusion followed. Colonoscopy showed a large deep indurative ulceration that was detected in the previous CT colonography. There was no ulceration or inflammation in terminal ileum or other area of the colon. Capsule endoscopy was performed to examine the small bowel, and there were no abnormalities.

Ileocecectomy was performed because there was no lesion except in the cecal side of ileocecal valve. The resected specimen showed a 2.5×2×0.6 cm sized ulceration in the cecal side of ileocecal valve (Fig. 4). Histology revealed ulceration with transmural inflammation and lymphoid aggregates and adjacent mucosa with mild cryptitis and crypt architecture distortion (Fig. 5). These findings were competent with Crohn disease. Symptoms disappeared after surgical resection.

## Discussion

The association between CD and MDS has previously been reported in adults[4-12]. In most of the reported cases, CD was diagnosed first or CD and MDS were coexistent. In just one case of an 87-year-old woman, MDS was diagnosed first four years prior to CD[9]. To the best of our knowledge, our patients represent the first report of CD with MDS in children.

The etiology of CD is unclear. It is hypothesized that chronic immune-mediated intestinal injury results from complex interactions between predisposing genetic factors and exogenous or endogenous triggers[13, 14]. There are also hypotheses presented to explain a possible link between MDS and immunological disorders[15]. Though the association between CD and MDS still remains unknown, this report could give some clues for elucidating the pathophysiology of these rare diseases.

## 한 글 요 약

### 골수이형성 증후군으로 진단받은 소아에서 발생한 크론병

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크론병은 매우 드문 질환이나 지난 10년간 발생률이 꾸준히 증가하고 있다. 저자들은 골수 이형성 증후군을 가진 환아에서 크론병이 발병한 2례를 소아에서는 최초로 보고하는 바이다. 첫 번째 환아는 3세에 골수 이형성 증후군으로 진단받았고, 수 년간 지속된 반복적인 복통 및 설사, 혈변, 성장 부전이 있어 8세에 크론병으로 진단받았다. 대장 내시경 검사에서는 맹장에서 오름 결장에 걸쳐 조약돌상 점막과 표재성 궤양 및 염증성 삼출이 있었으며, 조직 소견은 궤양 사이에 정상 점막을 포함하고 있으면서 림프구 침윤을 보였다. Mesalazine과 deflazacort로 치료 후 증상은 호전을 보였다. 두 번째 환아는 9세에 골수 이형성 증후군으로 진단받았으며, 13세에 반복되는 혈변과 복통, 구토, 발열로 크론병으로 진단받았다. 대장 내시경 검사에서 크고 깊은 경화성 궤양이 회맹판에서 맹장 쪽 주위에서 발견되었다. 이 외의 부위에는 병변이 없어 병변을 절제하였고, 조직은 경벽 염증과 림프구 집합을 동반한 궤양 소견을 보였다. 절제술 후 증상은 호전을 보였다.

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