The Korean Journal of Internal Medicine
Vol. 3, No. 2, July 1988

A case with Some Components of Cronkhite-Canada Syndrome in a Family with Peutz-Jeghers Syndrome

Young Woo Kang, M.D. and Soong Kook Park, M.D.

Department of Internal Medicine, College of Medicine, Keimyung University, Taegu, Korea

Hong Kim, M.D.

Department of Diagnostic Radiology

Ok Suk Bae, M.D.

Department of General Surgery

Eun Sook Chang, M.D.

Department of Pathology

A case with some components of Cronkhite-Canada syndrome such as onycholdystrophy, a large amount of diarrhea, hypoproteinemia and hypoalbuminemia in a 16 year-old man with Peutz-Jeghers syndrome was studied.His family members were conirmed to have Peutz-Jeghers syndrome by biopsy of polyps in the rectum and duodenum. This is the first case report of Peutz-Jeghers syndrome associated with some components of Cronkhite-Canada syndrome.

Key Words: *Peutz-Jeghers syndrome, Cronkhite-Canada syndrome*

INTRODUCTION

Peutz-Jehgers syndrome, a familial disease which appears to be inherited in an autosomal dominant pattern, is characterized by mucocutaneous pigmentation and gastrointestinal polyposis and was nominated by Bruwer et al in 1954.[1] In Korean literature about 16 cases have been reported, almost all of which describe its complications and malignant changes.[2]

Generalized gastrointestinal polyposis associated with hyperpigmentation, hair loss and nail atrophy was first described by Cronkhite and Canada in 1955 and is generally recognized as the Cronkhite-Canada syndrome.[3] Approximately 55 cases have been described in world literature,[4] but no cases have been reported in Korea.

A rare case of Peutz-Jeghers syndrome associated with some components of Cronkhite-Canada syndrome is reported with special reference to its correlation between the histologic finding of polyps and clinical manifestations.

CASE REPORT

A 16-year old man was admitted to the Department of Internal Medicine of Dongsan Medical Center with the chief complaint of hematochezia. He had suffered on 4-5 occassions from hematochezia and dizziness for 5 months. About 1 month prior to admission, he complained of a large amount of diarrhea (3-4 times a day)and swelling of the face and lower extremities. Eight years previously he underwent an operation for intestinal intussusception.Family history revealed that his father and younger sister also had pigmentation of the lips and oral mucosa, palms, and soles at birth (Fig.1).

Adress reprint requests: Young Woo Kang, M.D., Department of Internal Medicine, Dongsan Medical Center, Keimyung University #194, Dongsan-Dong, Chung-gu, Taegu, 700-310 Korea

A summary of this article was presented at the 24th congress of the Korean Society of Gastrointestinal Endoscopy, 1988.

On physical examination, the patient appeared to be chronically ill.His blood pressure was 100/60mmHg, pulse rate 76/minute, respiration rate 20/minute, and temperature 36.9°C. The face was puffy and the conjunctiva was pale. There were multiple, dark blue colored pigmentations of the lips, buccal mucosa, palms, and soles (Fig.2) and especially onychodystrophy such as a longituidinally ridged, spoon-like deformity and distortion in all fingernails (Fig.3), and pitting edema of the lower extremities. The other parts were normal.

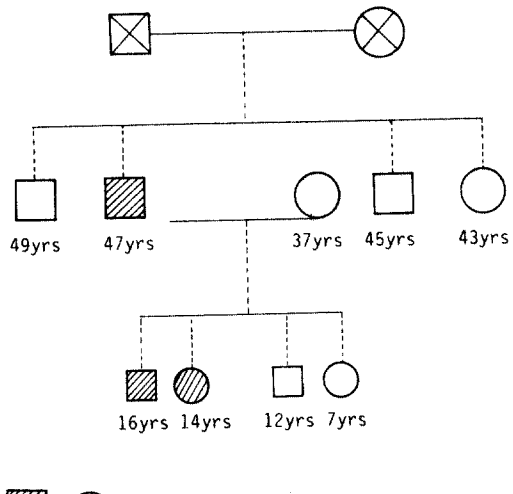

Fig 1. *Pedigree of case.*

The laboratory findings on admission were as follows: hemoglobin 5.9g%, hematocrit 19.0%, WBC count 9100/mm^3 with 60% neutrophils, serum iron 6ug/dl, TIBC 174 ug/dl, ferritin Ong/ml, total protein 3.2g%, albumin 1.2g%, calcium 6.4mg%, inorganic phosphorus 5.0g%, sodium 142 m Eq/L, and potassium 3.3m Eq/L. Fecal occult blood test was positive.

The x-ray film of the upper GI tract, small intestine series and barium enema revealed variable sized, scattered, grouped, multiple polyps in the C loop of the duodenum, proximal jejunum, and from the rectum to the ascending colon (Fig. 4). Endoscopy of the upper GI tract and rectosigmoid showed red colored, variable sized, grouped, multiple polyps in the first portion of the duodenum to the distal (Fig. 5), and in the rectum at 12cm, 15cm, and 18cm from the anal verge.

The culture and semar of nail scrapings were

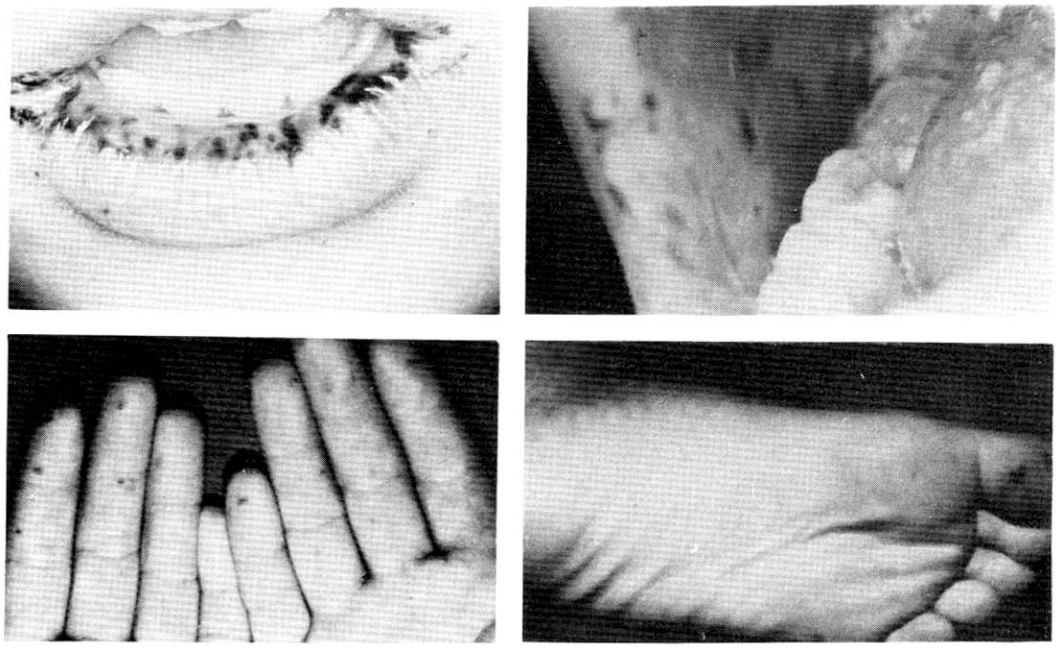

Fig 2. *Dark blue colored pigmentation in the lips, buccal mucosa, palms, and soles.*

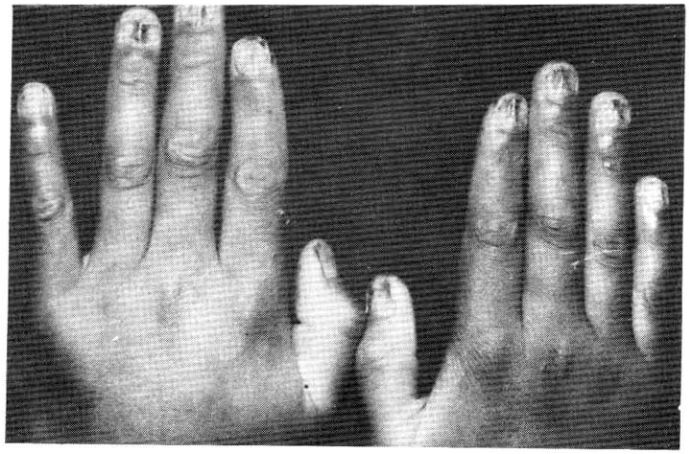

Fig 3. *Onychodystrophy in all fingernails.*

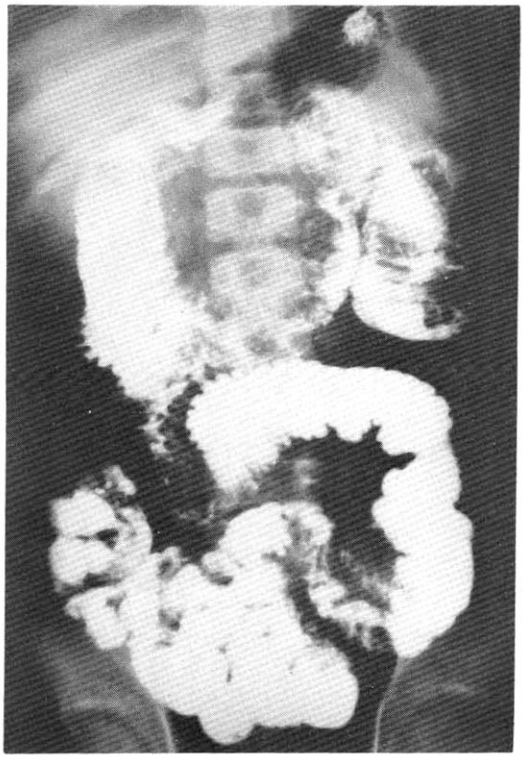

Fig 4. *Small intestine series showing multiple polyps in the C loop of the duodenum and proximal jejunum.*

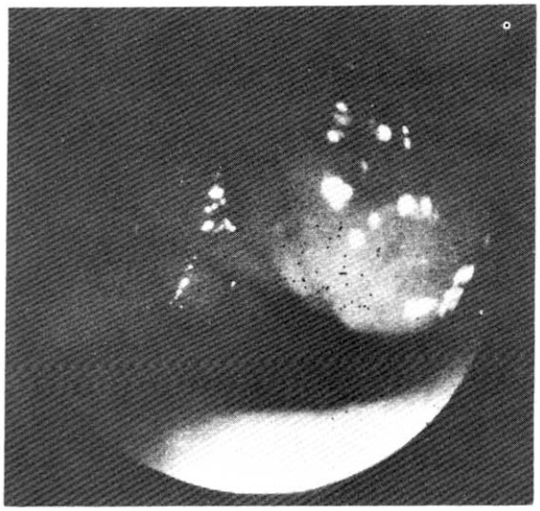

Fig 5. *UGI endoscopy showing variable sized, multiple polyps in the first portion of the duodenum.*

negative for fungi.

The microscopic finding of specimens taken from rectal polyps showed hamartomatous polyps with cystic dilatation of glands and containing smooth muscle bundle supports, epithelial proliferation and infiltration of plasma cells, lymphocytes, and neutrophils (Fig. 6). The microscopic finding of specimens taken from duodenal polyps also showed Peutz-Jehgers polyps with columnar and goblet cells in the superficial portion and some inflammatory cell infiltration.

During admission, the patient was treated with blood transfusion, albumin infusion, and iron tablet medication, thereafter he was discharged with improvement. At present he is in good general condition with disappearance of the onychodystrophy,

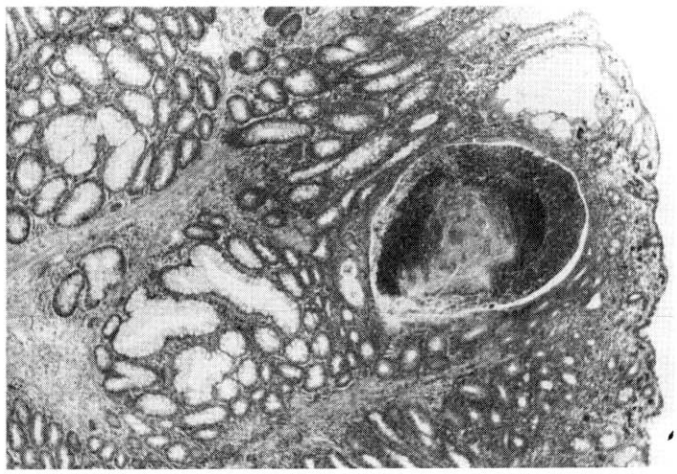

Fig 6. *Hamartomatous polyp showing ramifying central stalk containing muscle bundle supports and epithelial proliferation with many cystic dilated glands, the largest one in mid-left field is filled with neutrophils. (H&E X40)*

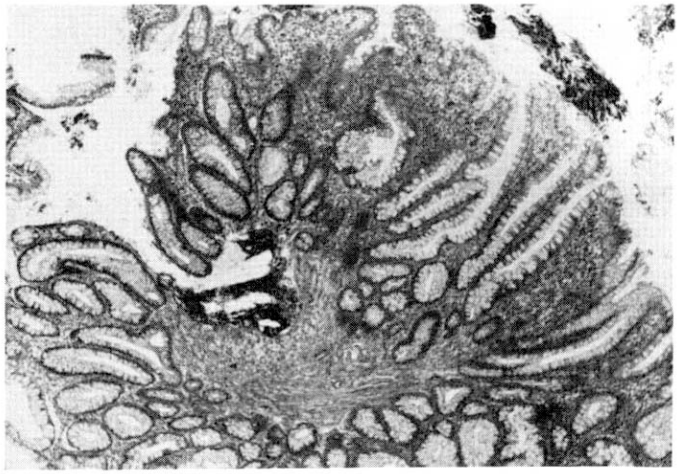

Fig 7. *Microscopic finding showing hamartomatous polyps. (H&E X40)*

edema of face and lower extremities, and he showed improvement in laboratory tests during the OPD follow up check.His father and sister also revealed similiar findings of the upper GI tract, small intestine series, barium enema, and endoscopy without hypoproteinemia, hypokalemia, and onychodystrophy. The microscopic findings of rectal polyps showed hamartomatous polyps having smooth muscle fibers from muscularis mucosa and chronic inflammatory cell infiltration without cystic dilated glands (Fig. 7). The younger sister developed two segmental intestinal intussusceptions in the proximal and distal jejunum, one at a time, and underwent an operation recently.

DISCUSSION

The Peutz-Jeghers syndrome is defined as mucocutaneous pigmenation, gastrointestinal polyposis, and transmission of an autosomal dominant trait.[1] On the other hand, the Cronkhite-Canada syndrome is characterized by the following cardinal

features: 1. gastronitestinal harmartomatous polyps of the juvenile (retention) type, 2. ectodermal changes consisting of alopecia, onychodystrophy, and hyperpigmentation, 3. the absense of a family history of polyposis, and 4. adult onset.[3]

In this case, the findings of mucocutaneous pigmentation in the lips, buccal mucosa, palms and soles, intestinal polyposis, and the proved family history are consistent with Peutz-Jeghers syndrome. Besides these, some clinical components of Cronkhite-Canada syndrome are associated as follows: onychodystrophy in all fingernails, edema of face and lower extremities, large amounts of diarrhea, hypoproteinemia, hypoalbuminemia, and hypokalemia. In patients with Cronkhite-Canada syndrome, hypokalemia below 3.5mEq/L was reported in 48.6%, hypocalcemia in 92.6% and in 51.9% when corrected for coexisting hypolalbuminemia, hypoproteinemia in 93.8% and hypoalbuminemia in 86.8%. Serum protein electrophoresis revealed a decrease in the albumin fraction in 50% of patients and elevation of α_1 globulin in 59.1%. Excessive enteric protein loss was documented in 88.9% by one or more of the following means: 51 Cr labeled albumin, 131 I PVP, and 131 I albumin.[4] These studies indicated that hypoproteinemia in these patients is due, at least in part, to a protein losing enteropathy. Although a study of protein losing enteropathy was not conducted in this case, the microscopic findings of inflammatory change and cystic dilated glands with mucin pool formation and infiltration of neutrophils were highly suggestive of a protein losing enteropathy. There was no cause of protein loss other than a clinical gastrointestinal tract problem.

The microscopic finding of Cronkhite-Canada syndrome is characterized by proliferated tortuous glands cystically dilated and filled with proteinaceous fluid or inspissated mucus, abundant stroma with edematous chronically inflamed lamina propria, and intact surface epithelium.[4] The microscopic findings in this case also showed many cystic dilatations of the glands; the largest one was filled with neutrophils and there was infiltration of plasma cells, lymphocytes, and neutrophils in the lamina propria. The above finding is analogous to that of Cronkhite-Canada syndrome with the exception of branching smooth muscle bands. Microscopically, the polyps in Peutz-Jeghers syndrome are clearly distinguishable from those in Cronkhite-Canada syndrome by the presence of characteristic branching core muscular tissue.[5,6]

The gastric mucosa of Cronkhite-Canada syndrome is microscopically similiar to that of Menetrier's disease,[7] which is confined to the stomach and not usually associated with ectodermal changes. Both are associated with protein losing enteropathy and symptomatic remission.

Similiar histopathologic findings were reported by Kyriakos et al[8] in 1978, the first case of enteritis cystica profunda to occur in association with Peutz-Jeghers syndrome. It is characterized microscopically by mucosal glands and mucinous cysts within the bowel wall including penetration through the serosa, and is occasionally misdiagnosed as mucinous adenocarcinoma. The differentiation of this lesion from adenocarcinoma is of major improtance. Enteritis cystica profunda does not exhibit atypical or malignant cytologic features at all and the cells have the appearance of normal mucosal cells. Follow up studies have verified the benign nature of this disease. After reviewing the published articles of carcinoma arising in Peutz-Jeghers syndrome, Reid[9] and Kyriakos et al[8] considered that such misplaced glands are comparable to those in enteritis cystica profunda.

Ectodermal changes in Cronkhite-Canada syndrome have also been seen in cases associated with hypoparathyroidism, kwashiorkor, and administration of 5-fluorouracil, which may be responsible for the observed ectodermal changes.[4] However, neither symptoms nor signs in this case indicated malnutrition and hypoparathyroidism. The culture and smear of nail scrapings were also negative for fungi. Onychodystrophy and other symptoms disapperared after blood transfusion, albumin infusion, and iron tablet medication.

Therefore we considered that some components of Cronkhite-Canada syndrome could be seen in a patient with Peutz-Jeghers syndrome who showed such histopathologic findings as cystic dilated glands and chronically inflammed lamina propria.

REFERENCES

1. Bruwer A, Bargen JA, Kierland RR: *Surface pigmentation and generalized intestinal polyposis (Peutz-Jeghers syndrome). Mayo Clin. Proc 29:168, 1954.*
2. Lee JS, Hwang SH, Lee JS, Kang JS: *A case of Peutz-Jeghers syndrome accompanied with intussusception. The Korean J of Gastroenterology 7:47, 1987*
3. Cronkhite LW Jr, Canada WJ: *Generalized gastrointestinal polyposis: an unusual syndrome of polyposis, pigmentation, alopecia and onychotrophia. N E J M 252:1011, 1955*
4. Daniel ES, Ludwig SL, Lewin KJ, Ruprecht RM, Rajacich GM, Schwabe AD: *The Cronkhite-Canada syn-*

drome: an analysis of clinical and pathologic features and therapy in 55 patients. Medicine 61:293, 1982.

5. Bartholomew LG, Dahlin DC, Waugh JM: *Intestinal polyposis associated with mucocutaneous melanin pigmentation (Peutz-Jeghers syndrome). Gastroenterology 32:434, 1957*
6. Morson BC, Dawson IM: *Gastrointestinal pathology, p74, 175, 224, 590, London, Blackwell Scientific Publ , 1792*
7. Gill W, Wiken BJ: *Diffuse gastrointestinal polyposis associated with hypoproteinemia. J Roy Coll. Surg Edinb , 12:149, 1967*
8. Kyriakos M, Condon SC: *Enteritis cystica profunda. A J C P. 69:77, 1978*
9. Reid JD: *Intestinal carcinoma in the Peutz-Jeghers syndrome. JAMA 229:833, 1974*