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Cronkhite-Canada Syndrome:
An Analysis of Clinical Features and Follow-Up
Studies of 80 Cases Reported in Japan

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Abstract

Eighty cases of Cronkhite-Canada syndrome reported in Japan were reviewed comparing them with patients from other countries. The symptom occurs with a relatively acute onset and the age at onset is predominantly in the fifth decade. Although the main symptoms of this syndrome are diarrhea, weight loss and anorexia, hypogeusia and xerostomia were also important symptoms in Japanese patients with hypogeusia being the most common presenting symptom. Previously, the Cronkhite-Canada syndrome was thought to have a poor prognosis and to be fatal within a few months. However, in our 80 patients, seven survived over ten years after treatment and are in good health. The etiology of this syndrome is suspected to be inflammatory and these inflammatory polyps are reversible. The ectodermal changes such as hair loss and nail changes are reversible as are the gastrointestinal polyps. The recommended treatment is conservative with steroids, antiplasmin and supportive measures such as hyperalimentation. Surgical intervention should be performed only if the patients develop stomach or colon cancer, which occurred in 10% of our patients.

Introduction

In 1955, CRONKHITE and CANADA⁵⁾ reported two cases of diffuse gastrointestinal polyposis associated with hyperpigmentation, alopecia and onychodystrophia. Since that report, this syndrome has been called Cronkhite-Canada syndrome (C-C-S). Up to end of 1983, 120 cases have been reported in the world literature of which 80 cases were reported in Japan^{7,11,12)}. Several reviews about C-C-S have been written after CRONKHITE and CANADA's first report^{7,65,69,76)}. However, there are no definitive opinions concerning the etiology, pathogenesis, treatment or

Key words: Cronkhite-Canada syndrome, Follow-up study, Treatment.

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clinical course for this disease⁷⁾. In this report, the analysis of the clinical features and follow-up studies of 80 cases reported in Japan are presented with review of the cases from other countries.

Materials and Methods

Up to the end of 1983, 174 reports of the Cronkhite-Canada syndrome had been reported in Japanese publication^{11,12)}. After a careful survey, 80 separate patients have been collected the full name, date of birth and address of these 80 patients identified. Among the 80 patients, 28 were reported only in abstract. A request for the clinical material was sent to each of the 28 authors of these abstracts to confirm their patients as Cronkhite-Canada syndrome, the criteria including diffuse gastrointestinal polyposis of the juvenile type polyp, alopecia, nail dystrophia and skin pigmentation. The identifying materials such as x-rays, photographs, pathological materials or reports and dermatological pictures were received from all 28 authors and all 28 patients were diagnosed as Cronkhite-Canada syndrome after careful evaluation of these materials.

In our 80 Japanese patients, 19 were reported as deaths. Follow-up studies were requested for the remaining 61 patients. The outcome of all 61 patients were confirmed by the end of 1983.

The second questionnaire was sent to all authors requesting a detailed previous history, clinical features, laboratory data, pathological findings, response to treatment and the present status of their patients. Responses were received from the authors, co-workers, the patients themselves or their families in all 80 patients. It has taken about six years and 255 questionnaires to complete the study.

Clinical Features

Of the 80 patients, 52 were men and 28 women. The age at onset ranged from 31 to 85 years with a preponderance of the fifth decade. The mean age of diagnosis was 62.6 years. There were some patients in which treatment for the Cronkhite-Canada syndrome was done earlier at another hospital before consulting the reporting hospital. Therefore, the real age of onset will be earlier in some patients. Nevertheless, the onset of this syndrome is considered to be middle or older age (Fig. 1).

The duration from the onset of symptoms to the first consultation to doctors who diagnosed the C-C-S was less than three months in about half of the patients. This suggests a relatively acute onset of C-C-S. Some patients did not have the diagnosis confirmed until five years after their initial symptoms. However, the symptoms such as hair loss or skin pigmentation are difficult to distinguish from the signs of aging^{11,12)} (Fig. 2).

The most frequent initial symptom was hypogeusia followed by diarrhea and anorexia. Little attention has been paid to hypogeusia in the previous literature^{13,56)}. There were 19 Japanese patients in which hypogeusia appeared prior to any other symptoms. These patients could hardly distinguished sweet or salty taste. They consulted a neurologist or an oto-rhino-laryngologist for their loss of taste^{26,58)}. Other initial symptoms commonly included diarrhea or

Cronkhite-Canada Syndrome
80 cases reported in Japan
(1958-1983)

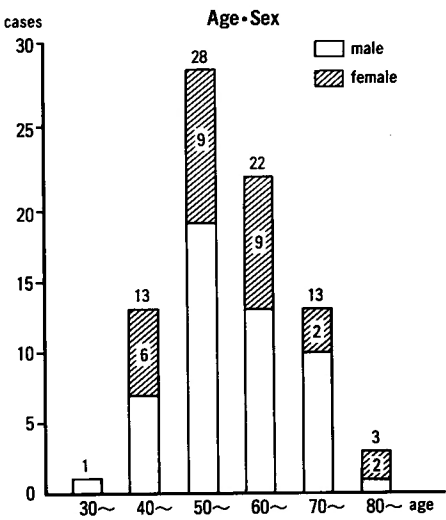


Fig. 1. Age and sex distribution

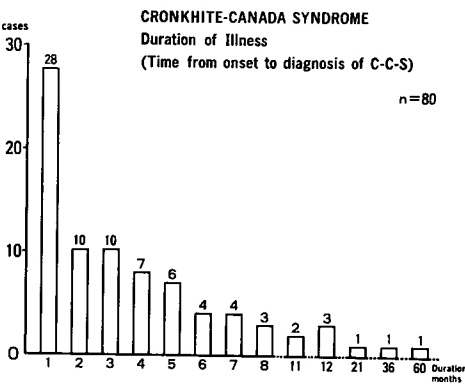


Fig. 2. Duration of illness

anorexia, followed less frequently by influenza, general fatigue, abdominal pain and others (Fig. 3).

In Fig. 4, the most frequently mentioned symptom was diarrhea which was seen in 65 patients. The second most common was hypogeusia, detected in 43 patients after careful studies on each patient. Anorexia, xerostomia, abdominal pain, weight loss and general fatigue were common symptoms. Xerostomia or thirst was detected in 27 patients. This symptom has been considered due to the intestinal polyps and diarrhea by previous papers⁶⁵⁾. However, the dry sensation in the oral cavity or thirst was present in some of our patients before their

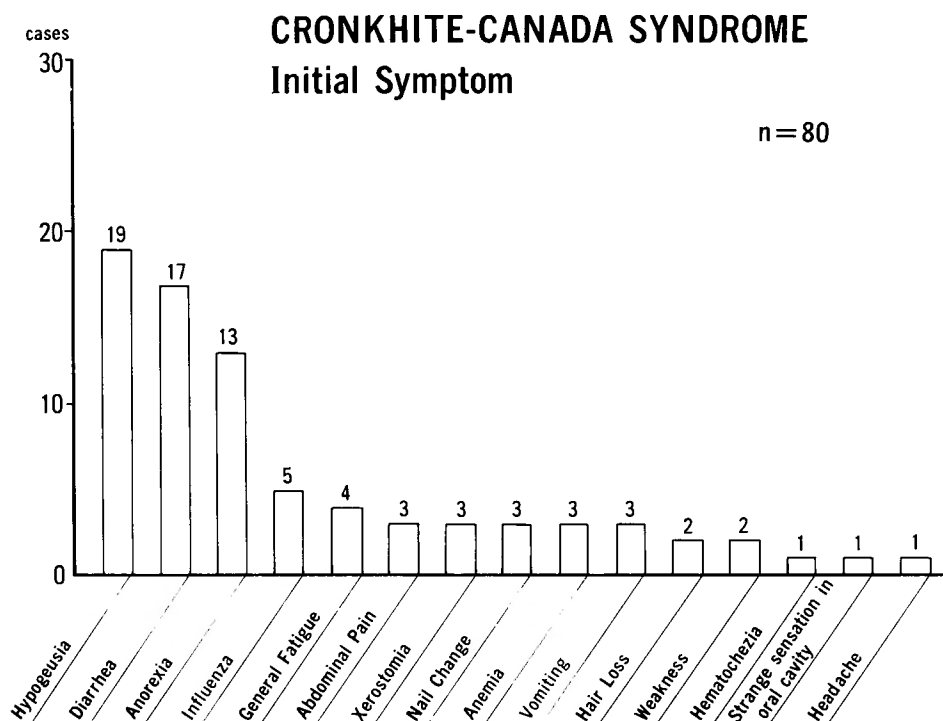


Fig. 3. Initial symptoms

diarrhea^{55,57,72}). Although their mouth was dry, they didn't want water at that time. The swallowing disturbance was found in some patients in which a decreased salivary function was suspected^{44,53,64}

By physical examination, the ectodermal changes such as hair loss and hyperpigmentation of skin (Fig. 5) and nail change or onychodystrophy (Fig. 6) were observed in most patients. However, in some patients, hyperpigmentation was not detected throughout their clinical course^{21,68}. Anemia, edema and glossitis were also detected in many patients (Fig. 4).

Diffuse polyposis was found throughout the entire digestive tract in most patients (Table 1, Fig. 7-A, B). One patient has been reported with polyposis of the esophagus thus including the entire digestive tract¹⁸). Four patients showed only gastric polyposis^{22,49,52,77}) and one patient had only colonic polyposis⁴). However, in this last patient, an erosive gastritis was detected after a thorough search of the stomach by x-ray and gastroscope.

Histologically, the polyps in the gastrointestinal tract resembled juvenile polyps (Table 2). They showed cystic dilatation of the glands with prominent inflammation (Fig. 8). Cancer was associated with polyposis in 10 patients. There were 4 gastric^{30,49,61,77}) and 6 colo-rectal cancers noted^{10,27,43,47,54,63}. In 9 patients, the juvenile type polyps and adenomatous polyps were mingled within the same patients^{10,17,27,35,54,61,68,77}). The juvenile type polyps decreased in size and number after treatment in 31 patients^{21,28,42,43,45,50,57,67,70}

Figure 9 shows that the total serum proteins were low in 49 of 55 patients with values

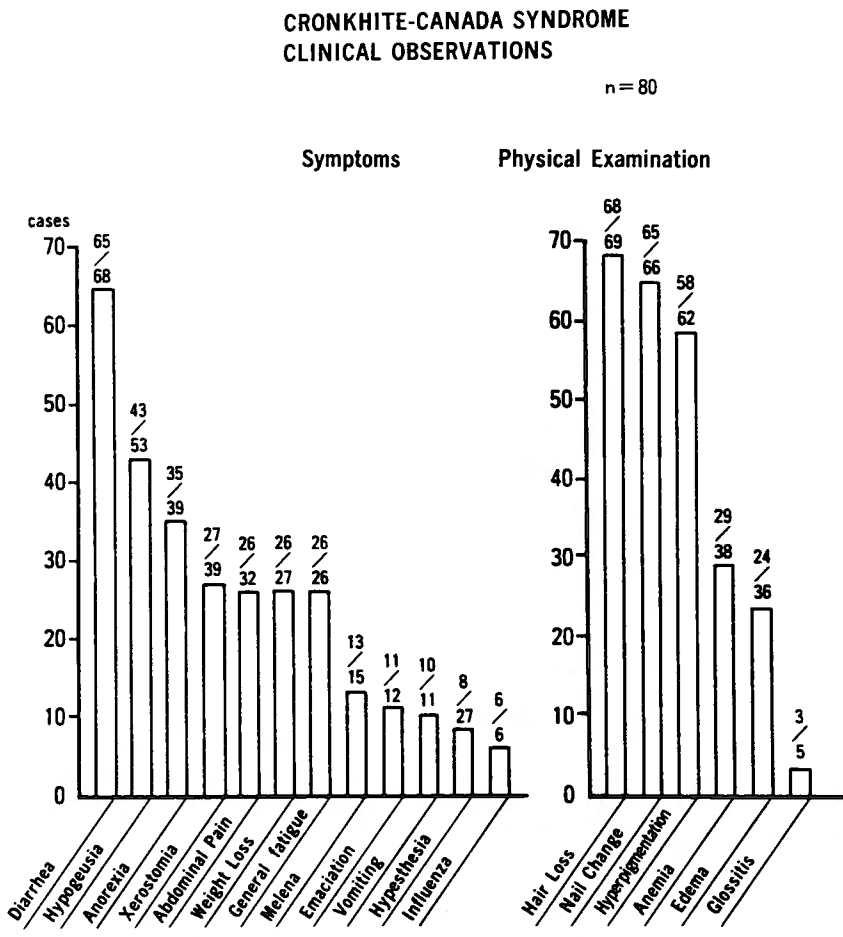


Fig. 4. Symptoms and physical examinations

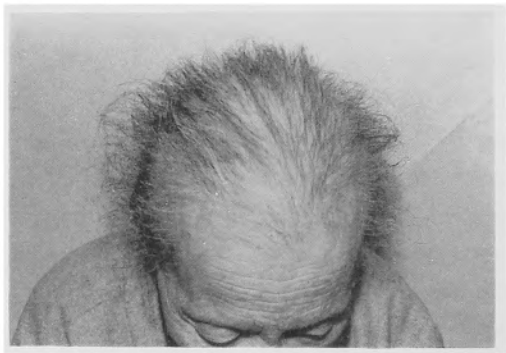


Fig. 5. Hair loss in a 55 yr. woman



Fig. 6. Nail changes in a 43 yr. man

Table 1. Distribution of polyps

Location	Cases	%
Esophagus, Stomach, Large bowel	1	1.3
Stomach, Small intestine, Large bowel	45	56.2
Stomach, Large bowel	29	36.2
Stomach	4	5.0
Large Bowel	1	1.3
	80	100.0

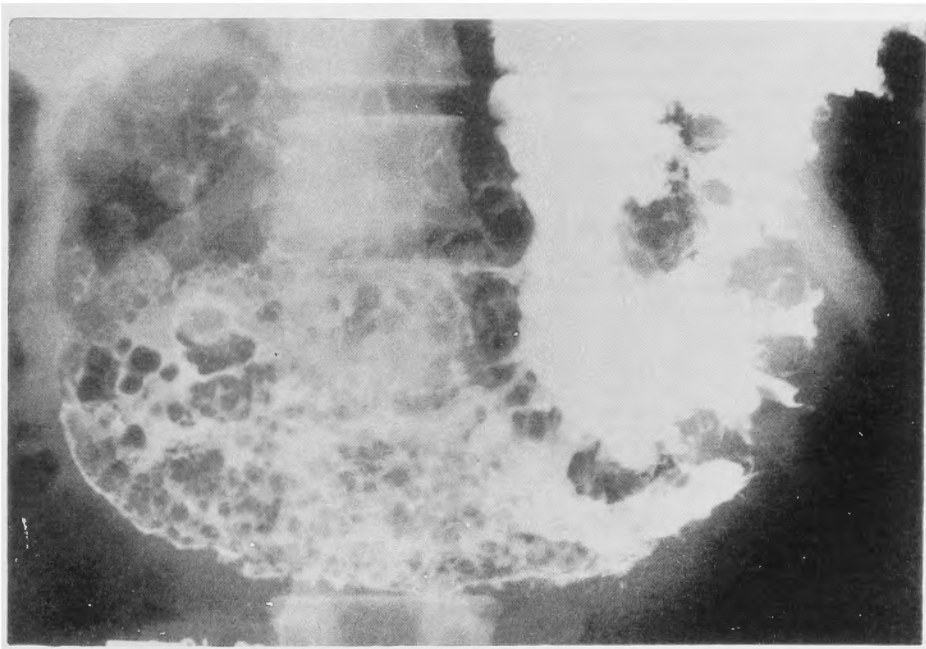


Fig. 7-A. Diffuse polyposis involving the stomach in a 43 yr. male.

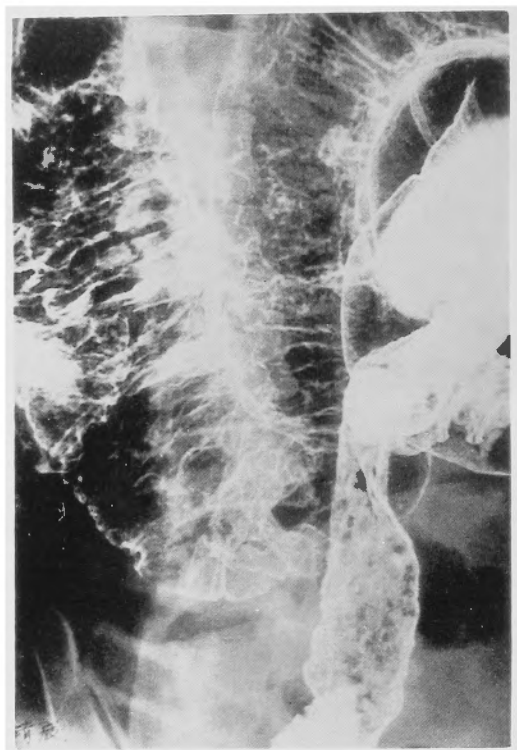


Fig. 7-B. Diffuse polyposis involving the colon in a 43 yr. male.

Table 2. Histology of polyps. This table was based on the original description of authors, respectively.

Histology	Cases (Cancer)	%
Juvenile type polyp	62(5)	77.5
Adenomatous polyp	3	3.7
Mixed type of juv. polyp & adenom	9(4)	11.3
Hyperplasia	5(1)	6.2
Benign adenoma	1	1.3
	80(10)	100.0

ranging from 3.1 to 5.9 g/dl. Protein loss into the gastrointestinal tract was detected in 26 of 31 patients by protein excretion tests using ^{131}I -PVP or ^{131}I -RISA.

The electrolyte disturbances seen in these patients are shown in Fig. 10. Hypocalcemia under 9.4 mg/dl was found in 49 of 51 patients with only three of these patients showing muscle weakness^{14,62,70)} Hypokalemia was found in 25 of 64 patients and hypophosphotemia in 12 of 28 patients. These electrolyte disturbances may be due to the abnormal loss and malabsorption of electrolytes from the gastrointestinal tract and these abnormalities were correlated with

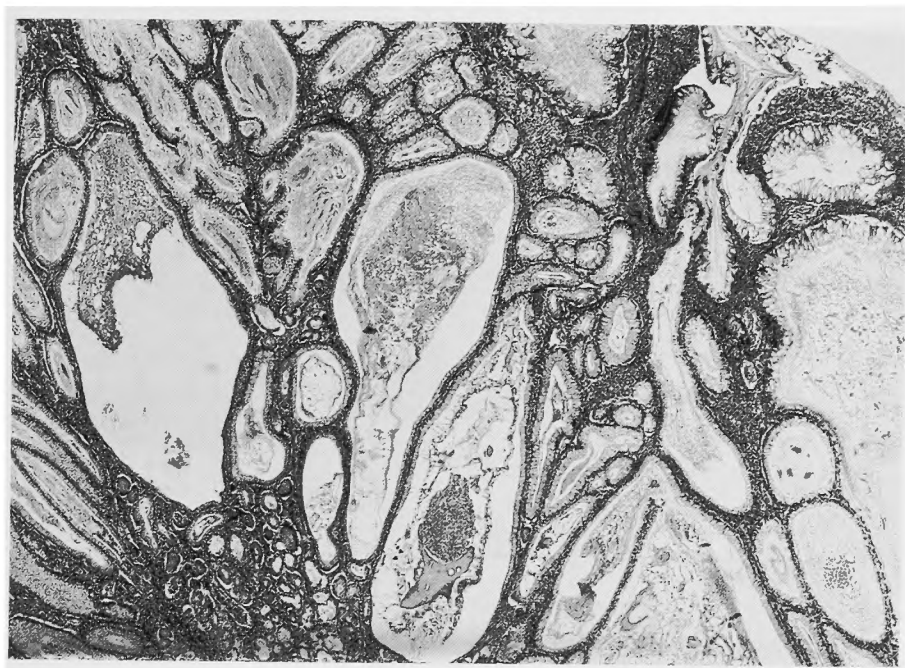


Fig. 8. Stomach polyp in a 43 yr. male. H. & E. $\times 100$.

CRONKHITE-CANADA SYNDROME SERUM PROTEIN and PROTEIN EXCRETION TEST

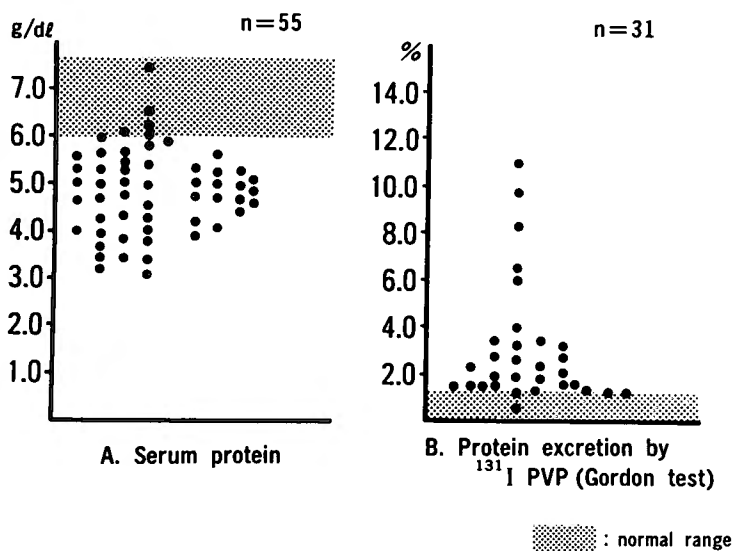


Fig. 9. Serum protein levels and protein excretion studies

CRONKHITE-CANADA SYNDROME
SERUM ELECTROLYTE

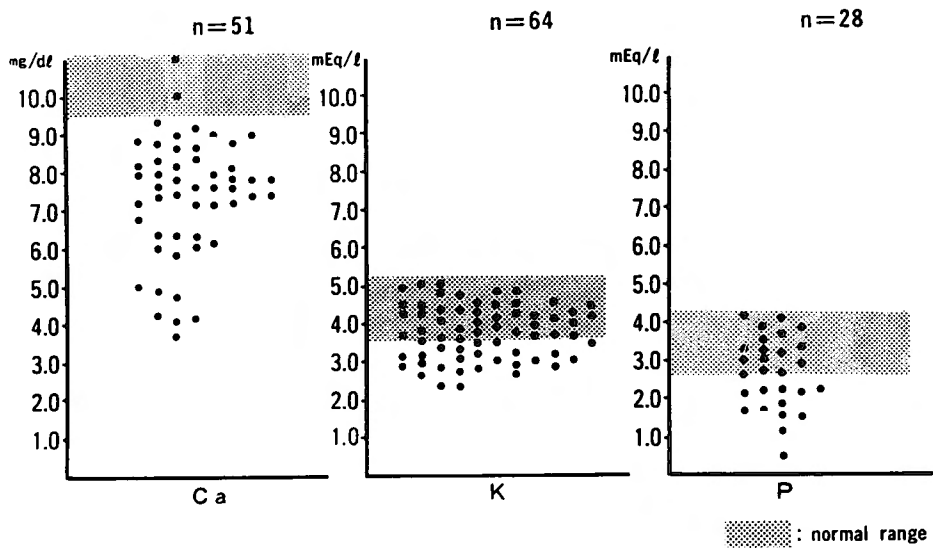


Fig. 10. Electrolyte determinations

diarrhea in the clinical course of many patients.

Treatment

The various treatments and responses for the 80 patients with Cronkhite-Canada syndrome are given in Table 3. In the early case reports, the patients received symptomatic treatment including anabolic steroids, amino acids, albumin, plasminase with fluids and crystalloids. Corticosteroid became frequently used after the report of Takahata in 1972⁶⁷⁾. The steroids were

Table 3. Medical treatment. Parenthesis means the cases with other combined treatments.

	Effective	Temporally effective	None	Total
Symptomatic Tx	8	1	4	13 (3)
Anabolic steroid	5	1		6 (2)
Amino acid	3	1	3	7 (2)
Plasmanate	9	4	6	19 (7)
MCT	3	2		5 (1)
Antibiotics	2	1		3
Corticosteroid	15	5	2	22 (6)
Antiplasmin	7	1	2	10 (2)
Hyperalimentation	5	1		6
Total	57	17	17	91(23)

Table 4-A. Surgical treatment.

No,	Author Ref	Year	Age	Sex	Operative indication	Operative method	Response to op	Postop Follow-up	Status at Follow-up (Cause of death)	Addendum
1	Sasagawa ⁶³⁾	1971	59	M	Rect ca	Pancolectomy	Death	2w	(Ileus)	
2	Takahata ⁶⁷⁾	1972	31	M	Ileus	R-hemicolectomy	Remission	45m	(G.I. bleed)	
			35		Perf D.U.	Gastrojejunostomy	Death	2m		
3	Goto ¹⁰⁾	1973	58	F	Rect ca	Rectal resection	Death	6d	(Cardiac arrest)	
4	Imai ¹⁹⁾	1973	57	F	Diagnosis	Jejunal resection	Remission	158m	Alive	
5	Kazumi ³¹⁾	1973	62	M	Ileus	Removal of adhesion	Death	2m	(Intestinal bleed)	
6	Tsurumi ⁷⁰⁾	1974	50	F	Poor response medical treatment	Colon resection	Remission	40m	(Cachexia)	
7	Fujita ⁹⁾	1976	44	F	Diagnosis	Endoscopic polypectomy	Remission	106m	Alive	Polyp disappear
8	Murayama ⁴⁷⁾	1976	60	F	Colon ca	Endoscopic polypectomy	Remission	8m		
					Recurr colon ca	Sigmoidectomy	Death	11m	(Liver metastasis)	
9	Mito ⁴³⁾	1977	55	M	Rect ca	Colo-Rect resection	Remission	99m	Alive	Polyp disappear
10	Kishimoto ³⁵⁾	1979	62	F	Gast Polyposis	Gastrectomy resection	Remission	98m	Alive	Polyp disappear
11	Nakamura ⁴⁹⁾	1979	46	F	Gast ca	Gastrectomy	Remission	75m	Alive	Polyp disappear

Two cases of endoscopic polypectomy were included in this table.

Table 4-B.

No.	Author Ref	Year	Age	Sex	Operative indication	Operative method	Response to op	Postop Follow-up	Status at Follow-up (Cause of death)	Addendum
12	Harada ¹³⁾	1980	57	M	Gast polyposis	Gastrectomy	Remission	86m	Alive	
13	Uchida ⁷¹⁾	1980	61	M	Gast dolyposis	Gastrectomy	Remission	127m	Alive	Polyp disappear
14	Kitagaki ³⁶⁾	1980	72	M	Susp Gast ca	Gastrectomy	Death	21m	(Pneumonia)	
15	Uchida ⁷²⁾	1980	52	F	Poor response med treat	Gastrectomy & R-hemicolectomy	Remission	56m	Alive	Polyp disappear
16	Nagashima ⁴⁸⁾	1981	50	F	Ménétrir disease	Gastrectomy	Remission	39m	Alive	Polyp disappear
17	Kamagami ²⁵⁾	1982	67	F	Gast polyposis	Gastrectomy	Remission	94m	Alive	
18	Muratani ⁴⁶⁾	1982	49	F	Ileus Poor response med treat	R-hemicolectomy Gastrectomy	Remission Remission	51m 9m	Alive	
19	Matsunami ⁴²⁾	1983	43	M	Diagnosis	Surgical polypectomy	Remission	110m	Alive	Polyp disappear
20	Yokoyama ⁷⁷⁾	1983	70	M	Gast ca	Gastrectomy	Death	5m	(Liver metastasis)	
21	Sagara ⁶¹⁾	1983	71	M	Gast ca	Gastrectomy	Remission	47m	Alive	Polyp disappear
22	Katyama ²⁷⁾	1983	52	M	Rect ca	Pancolectomy	Remission	17m	Alive	

effective in 20 of the 22 patients where it was used. Recently, antiplasmin drugs have been given with good results in 7 of 10 patients^{17,21,28,38,45,61,65}. Hyperalimentation or elemental diet was used in several patients in combination with corticosteroid and gave good results in five patients^{18,20,51,61,66} (Table 3).

Surgical intervention was performed in 22 patients of whom 25 operative procedures were undertaken. A diagnostic exploratory laparotomy was performed in two patients^{19,42}. Three other patients were underwent surgery for complications such as perforation of a duodenal ulcer⁶⁷ or ileus^{31,46}. Gastrectomy only was performed in 9 patients, 3 of whom had cancer^{49,61,77} and 6 of whom had gastric polyposis^{13,25,35,36,48,71}. Colon resection alone was performed in 3, one of whom had cancer⁴⁷, the others ileus⁶⁷ and polyposis⁷⁰, rectal resection was done in 2, both for cancer^{10,27}. Gastrectomy and colectomy was done in 2 patients for polyposis^{46,72} and pan-colectomy in 2 for polyposis with cancer^{27,63}. Endoscopic polypectomy was performed in 2 patients^{9,47} (Table 4-A, B).

Follow-up Study

Of the 80 patients of this survey, 41 are alive and 39 dead. Of these 39 patients, 23 died of complication of C-C-S and 16 of non-related disease after a complete remission of their symptoms. Eighteen patients died after transient remission of their symptoms. The cause of death were cachexia, ileus, heart failure, coronary infarct, pneumoia and others. Most of the deaths occurred less than two years after the diagnosis of C-C-S was established. Three patients died from recurrence of gastric^{30,77} and colon cancer⁴⁷ (Table 5).

The longest surviving patient died 213 months after the onset of his disease⁵⁸. Complete remission had occurred after conservative treatment for two years. However, 13 years later, the disease recurred with symptoms of hypogeusia, xerostomia, hair loss and nail changes. After three months of conservative treatment, this patient again recovered completely and engaged in

Table 5 Cause of death before 1975 and after 1976.

Disease	1955-1975	1976-1983	total
Cachexia	6	7	13
Ileus	4	2	6
Heart failure	2	2	4
Coronary infarct	1	2	3
Pneumonia	1	2	3
Cancer		3	3
Cerebral bleeding	1	2	3
Decrepitude	1		1
Digestive bleeding	1		1
Intoxication	1		1
Accident	1		1
Death number/Tot. no.	19/24	20/56	39/80

Table 6. Follow-up study.

Duration from onset to death (months)	Death attributable to C.C.S.	Death not attributable to C.C.S.	Alive at 1983
less than 24	23(34)	7(34)	4(34)
25 to 60		4(18)	14(18)
61 to 120		2(21)	19(21)
121 to 213		3 (7)	4 (7)
Total	23(34)	16(80)	41(80)

C.C.S.: Cronkhite-Canada syndrome
Parenthesis means the total cases of Cronkhite-Canada syndrome

his daily work for 10 years, then, suddenly died of heart failure after a brain stroke. There were 7 patients alive more than 10 years after their treatment of C-C-S^{4,19,29,40,55,58,71)} and three of them died of heart failure⁵⁸⁾, decrepitude²⁹⁾ and pulmonary failure after pneumonia⁵⁵⁾. Twenty one patients were alive more than 5 years after the diagnosis and treatment of their disease^{11,12)}. Two of these 21 died of cerebral bleeding¹⁶⁾ and pneumonia⁷¹⁾ (Table 6).

In many of the long term survivors, the gastrointestinal symptoms such as diarrhea or abdominal pain improved along with an increase in body weight. The ectodermal change such as hair loss and nail atrophy also improved^{28,42,43,45,50,67)}. As these signs and symptoms improved, there was a coincidental normalization of the serum proteins and electrolytes. The hypogeusia

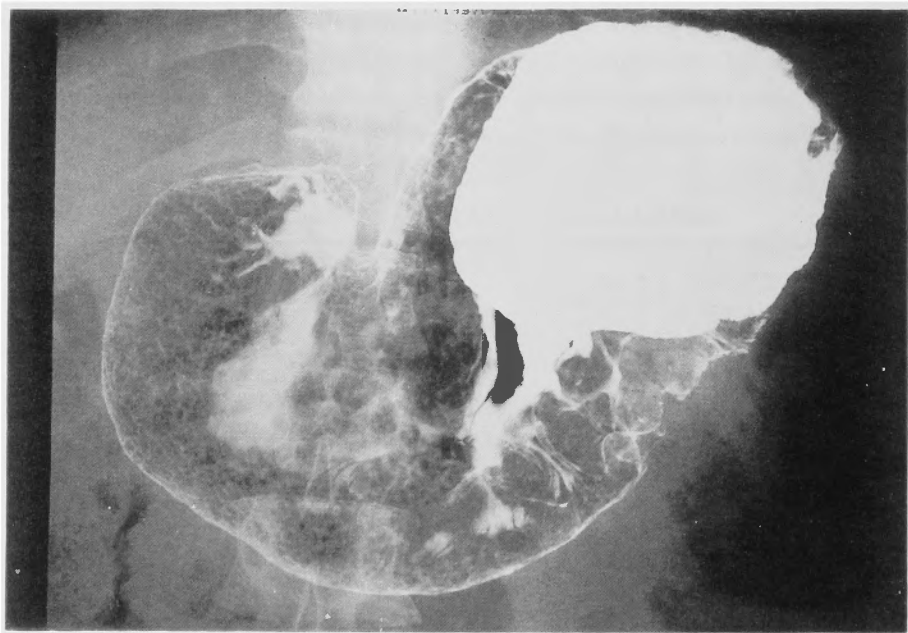


Fig. 11. Marked reduction in gastric polyps after 8 years of medical treatments in a 43 yr. male (refer Fig. 7-A).

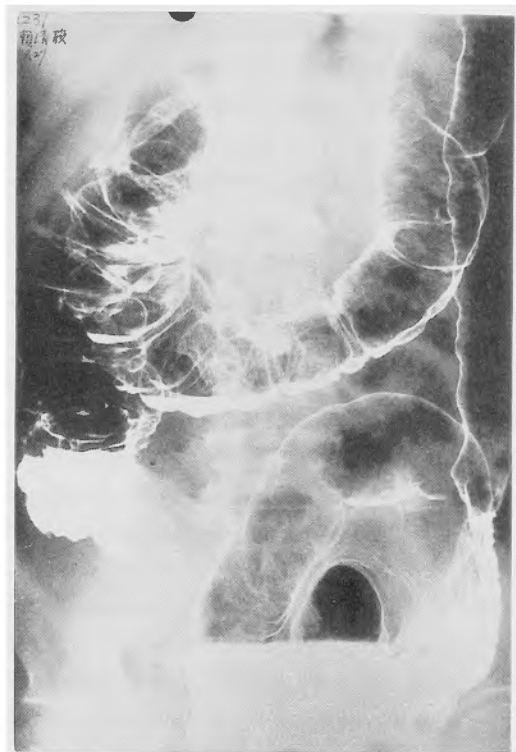


Fig. 12. Complete remission of colon polyp after 8 years of medical treatment in a 43 yr. male (refer Fig. 7-B).

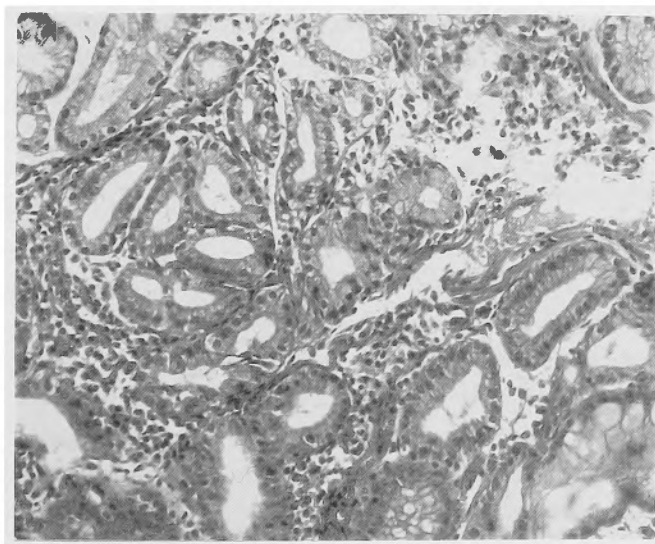


Fig. 13. Biopsy of gastric polyp in a 43 yr. male after 8 years of medical treatment.

and xerostomia also improved in most patients. The polyps in the stomach and colon completely disappeared in 2 patients^{44,78)} and diminished in size and number in 29 patients after their medical treatment^{11,12)}. The histological examination of those polyps showed a decreased dilatation of the gland elements and a decreased edema of the stroma (Fig. 11, 12, 13).

Discussion

Cronkhite-Canada syndrome is a well recognized relatively rare disease in which generalized gastrointestinal polyposis, hyperpigmentation, alopecia and onychodystrophia are the main features. This syndrome has a world wide distribution. However, two-third of the 120 reported cases in the world were reported from Japan. The reason for this is unknown. It may be that the cases were discovered because of the mass surveys of the gastrointestinal tract done in Japan, or due to some unknown predisposition for this syndrome in the Japanese people.

This disorder develops during middle or older age, a mean age of 62 in Japan with the same tendency in other countries. There is no familiar occurrence in the 120 patients reported in the world. The sex incidence shows a marked male predominance in Japan (male 52 and female 28). However, there is no sex difference in the other countries (male 21 and female 19).

The duration from onset of symptoms to the first consultation with a physician is from three months to one year. In other countries, 27 out of 40 patients consulted a physician within one year from their onset of symptoms.

Diarrhea, weight loss, abdominal discomfort and anorexia are frequently written as the characteristic symptoms of C-C-S. However, hypogeusia is the most common symptom in this study. This hypogeusia was the presenting symptom in 19 patients and occurred in 43 out of 53 patients during their illness. In the other countries, only 5 cases with hypogeusia were reported^{2,23,32,34)}. It has been postulated that the hypogeusia was secondary to the diarrhea and abdominal discomfort. However, there were many patients who complained of hypogeusia prior to any other symptom such as diarrhea or anorexia. However, there is no definite explanation for the hypogeusia in this syndrome. A change of taste may result from a disturbance of zinc absorption¹⁵⁾, possibly secondary to the diarrhea or a mucosal change in gastrointestinal tract due to unknown cause. However, there were very few patients in whom the level of serum zinc was examined^{13,57)}.

Diarrhea is the most frequent symptom of C-C-S reported in many cases. But there are a few patients in whom no diarrhea was observed throughout their clinical course^{43,52,72,76)}. Xerostomia is another frequent symptom in this syndrome. This symptom may result from the diarrhea or abdominal disturbance. However, there were 13 patients who complained of this symptom first, prior to any other symptom^{10,55,57,62,72)}. It is postulated that the xerostomia is a secondary symptom resulting from the dysfunction of the salivary glands. One patient was suspected of having Sjögren syndrome because of the xerostomia⁵¹⁾. However, only one case with xerostomia was reported in the other countries²³⁾. The ectodermal changes such as nail atrophy, hair loss and skin pigmentation are present in most patients in Japan as well as other countries. These clinical features were noted before or after diarrhea or other abdominal sym-

ptoms. And there are two patients in whom systemic dermatological disease such as scleroderma¹³ and lupus erythematosus²⁶⁾ were associated. However, no relevance between these dermatological disease and C-C-S was reported.

Gastrointestinal polyposis is a dominant feature in C-C-S and these polyposis are observed in the stomach, small intestine and large bowel in 75 patients in Japan. In one patient, an esophageal polyp was confirmed by x-ray and endoscopic examination¹⁸⁾. A C-C-S patient with an esophageal polyp was reported from England³²⁾. Four cases have been reported from Japan with only gastric polyps^{22,49,52,77)}, and one from West Germany³⁹⁾. No gastric polyps were seen in one patient with erosive gastritis⁴⁾.

Histologically, most of the polyps were reported to be juvenile type polyps with cystic dilatation of the glands and round cell infiltration of the stroma. CRONKHITE and CANADA gave the description of adenomatous polyps in their initial paper in 1955⁵⁾. DINER (CANADA) revised her pathological report of two patients calling the polyps "inflammatory pseudopolyps" in 1972⁸⁾. However, there have been patients reported in which juvenile type polyps and adenomas are mixed in the same patient^{9,10,54,61)}. Cancer of the stomach was found in 4 patients^{30,49,61,77)} and colo-rectal cancer in 6 patients from Japan^{10,27,43,47,54,63)}. The complication of cancer in 3 reports from the other countries are the stomach in one case⁷⁴⁾ and colorectum in 2 cases^{3,6)}. The malignant potential of those polyps is still under consideration. There are a few reports in which the juvenile polyps has very low malignant potential^{60,73)}. In this study, there are three patients in which malignant degeneration of a stomach polyp was demonstrated during their illness^{49,61,77)}. More patients must be studied to answer this problem.

Cronkhite-Canada syndrome is considered to be a relentless disease, progressive and usually fatal within a few months^{7,33)}. In this study, there were 28 patients who succumbed within two years in spite of early treatment^{11,12)}. In those patients, few ones had only temporary remission in their course^{19,66)}. However, several papers report the recovery from this disease after conservative treatment for several months in the other countries^{7,59,75,79)}. About one-half of the 80 Japanese patients were alive at the end of 1983^{11,12)}. When the patients recovered, the polyps disappeared or diminished in size or number. This observation was confirmed by x-ray or fiberoptic examination^{14,42,44,59,75)}. And ectodermal change and abdominal symptoms also decreased or disappeared in 20 cases^{11,12)}.

The etiology of this disease is still unknown. There is no report documenting a hereditary or familial incidence as seen in Familial Polyposis and Peutz-Jeghers syndrome. Several articles implicated nutritional deficiency^{5,55,59)} metabolic imbalance²⁴⁾, hormonal disturbance^{6,41,70)} and congenital abnormality²³⁾ as etiologic factors. Recent reports, including our own, have presented patients with complete recovery from this disease^{7,37,41,42,44,59)}. As the patients recover, their hair and nails again regrow and the gastrointestinal polyps diminish or disappear along with a subsidence of the abdominal symptoms^{11,12)}. The histology of these polyps are inflammatory in nature and are reversible. These phenomenon show that this disease may be caused by an inflammatory change in the gastrointestinal mucosa. This inflammatory change theory is supported by the fact that steroids or antiplasmin are effective in treating these lesions.

Conclusion

Eighty cases of Cronkhite-Canada syndrome reported in Japan were reviewed comparing them with patients from other countries. Although the main symptoms of this syndrome are diarrhea, weight loss and anorexia, hypogeusia and xerostomia are also important symptoms in our Japanese patients with hypogeusia being the most common presenting symptom. Previously, the Cronkhite-Canada syndrome was thought to have a poor prognosis and to be fatal within a few months. However, in our 80 patients, many survived over ten years after treatment and are in good health. The etiology of this syndrome is suspected to be inflammatory and these inflammatory polyps are reversible. The treatment is conservative with steroids, antiparasitic and supportive measures such as hyperalimentation. Surgical intervention should be performed only if the patients develop stomach or colon cancer.

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和文抄録

Cronkhite-Canada 症候群： 本邦報告80例の臨床的特徴と予後について

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Cronkhite-Canada 症候群は下痢を主症状とし、全消化管ポリポージス、皮膚色素沈着、脱毛、甲爪脱落を伴う稀な症候群であるが、Cronkhite と Canada (1955年) による2症例の報告以来1983年末までに、世界で120例の報告がある。そのうち、本邦よりの報告は80例で、その2/3を占めている。本症候群については、すでに内外に若干の集計ならびに総説が書かれているが、その病因、病態、治療法、予後については、いまだ、一定の見解がない。そこで、自験例2例を含めた1983年末までの本邦報告80例の臨床的特徴および予後調査を中心に検討した。

本症候群の好発年齢は50代、60代で、平均年齢は62才である。臨床症状は下痢、食欲低下、味覚異常、爪の変化、脱毛、腰痛、体重減少などである。下痢は90%にみられ、消化管ポリープからの蛋白漏出に基くものとされている。消化管ポリープでは胃、十二指腸、小腸、大腸に発生しているが、食道の発生は少ない。ポリープは嚢胞状拡張、間質の浮腫および炎症性細胞浸潤を主とした若年性ポリープに類似したポリープが多いが、腺腫の合併例もある。低蛋白血症は89%にみられ、蛋白漏出試験では83%に異常がみられている。電解質異常ではカルシウム、カリウムの低下例が多い。治療はこれまで保存的治療が行なわれ、蛋白同化ホル

モン、アミノ酸製剤、プラズマネートなどが使用されていたが、近年、ステロイドホルモン、抗プラスミン剤が有効とする報告が多くなり、完全静脈栄養、ED食などの栄養管理が重要とされている。外科的治療はこれまで、保存的治療の無効例に実施されていたが、近年、癌合併やまたは合併症のため手術を必要とする以外は適応はないとされている。

本症候群の予後はこれまで不良とされ、たとえ、一時的に軽快することがあっても、発症後、数年以内に死亡するとされていたが、今回の調査により80例の中、本症候群による直接の死亡は23例、本症候群の軽快後、脳出血、心疾患など関連のない疾患による死亡は16例であり、現在、41例(50%)が健在である。この中、5年以上生存は21例であり、10年以上生存は7例である。大部分の症例は消化管症状が改善し、毛髪、爪も再生し、ポリープの消失した症例も多い。これまで、消化器癌の合併が少ないのが、本症候群の特徴とされていたが、胃癌4例、結腸、直腸癌6例を認めている。

本症候群の成因は不明であるが、ステロイドホルモン、抗プラスミン剤などの著効例のみられることや消化管ポリープの可逆性のことより炎症性因子が推定される。