Tokai J Exp Clin Med., Vol. 6, No. 4, pp. 393–402, 1981

Clinical Investigations in Patients with Juvenile Gastric Atrophy Compared with Senile Gastric Atrophy

Shigeru HARASAWA, Tetsu NOMIYAMA, Norio TANI, Sohtaro SUZUKI, Masahiko MIWA, Hiroyuki WATANABE, Issei SENOUE, Kazuhiro KIKUCHI and Takeshi MIWA

Department of Internal Medicine, School of Medicine, Tokai University

(Received April 28, 1981)

Juvenile atrophy (JA; under 30 years of age with a MAO value below 6.0 mEq/h) was studied clinically in comparison senile atrophy (SA; over 60 years of age with a MAO value below 6.0 mEq/h).

Items examined were as follows: 1. subjective gastrointestinal symptoms, 2. gastric endoscopic findings, 3. peripheral blood lymphocyte counts, 4. PPD and DNCB skin tests, 5. HLA phenotype, 6. serum complements, 7. parietal cell antibody (PCA), 8. endoscopic congo-red pattern, 9. gastric emptying, and 10. endoscopic methylene blue method.

The folloowing results were obtained:

1. GI symptoms were found more frequently in JA than in SA. The endoscopic findings of JA were a hyperplastic change of the gastric mucosa while those of SA were uneven color and transparent vessels.

2. Peripheral lymphocyte counts were lower in JA than in SA, in spite of the age difference of 40 years. In the skin tests (PPD and DNCB), JA was positive more frequently than SA. JA showed lower C3 values for serum complements.

3. In the study of HLA antigen, JA without intestinal metaplasia had low frequencies of A9 and B15 and high frequencies of BW52 and BW54. Three out of 27 cases of JA were positive for parietal cell antibodies.

4. Endoscopic congo-red patterns were mainly of the C2-C3 type in JA but of the O2 type in SA. Also by the endoscopic methylene blue method, intestinal metaplasia was not found in 11 cases with JA, but in only two cases with SA.

(Key Words: Juvenile Gastric Atrophy, Chronic Gastric Atrophy, Endoscopic Congo-red Method, Intestinal Metaplasia)

INTRODUCTION

It is common and natural for the gastric mucosa to become gradually atrophied with advancing age. This atrophic change of the gastric mucosa is considered as antralization (type B atrophic gastritis) (21) accompanying various types of gastritis and gastric disease.

Gastric atrophy is also an underlying cause in the pathogenesis of pernicious anemia in which autoantibodies in the stomach react with parietal cells and intrinsic factors. Their incidence is particularly high and gastric atrophy is marked in the gastric corpus with no antral damage (9) (10) (21).

The pathogenic features of chronic atrophic gastritis were first defined by Faber and Bloch (1900), and gastric atrophy was first recognized his-

Shigeru HARASAWA, Department of Internal Medicine, School of Medicine, Tokai University, Bohseidai, Isehara, Kanagawa 259–11, Japan

tologically by Fenwick (1870) in a postmortem study of a case of pernicious anemia. Schindler (1947) recognized gastritis by the flexible gastrofiberscope which made possible the observation of the gastric mucosa *in vivo* (1).

Recently, we have recognized atrophic change of the gastric mucosa in juvenile patients with abdominal complaints from endoscopical findings and gastric acid secretion. Therefore, we studied clinically juvenile gastric atrophy in comparison with senile atrophic gastritis.

MATERIALS

Juvenile gastric atrophy (JA) was defined by the endoscopic presence of atrophic gastitis in patients under 30 years of age with a MAO value below 6.0 mEq/h stimulated by 4r/kg of tetragastrin intramuclarly.

In comparison, senile gastric atrophy (SA) as control group was considered to be gastric atrophy endoscopically with gastric hypoacidity (MAO value below 6.0 mEq/h) in patients over 60 years of age.

Forty four patients were studied including 27 cases with JA and 17 cases with SA, with no evidence of other gastrointestinal disease.

JA patients consisted of 13 males and 14 females, 18—29 years of age (mean: 25 years); SA patients consisted of five males and 12 females, 60—75 years of age (mean: 65.8 years).

METHODS

Items examined were as follows; 1) subjective gastrointestinal symptoms, 2) endoscopical findings of the stomach, 3) peripheral blood lymphocyte counts, 4) skin test for delayed hypersensitivity: PPD and/or DNCB (2, 4-dinitro-1-chlorobenzene), 5) HLA antigen frequency (26), 6) serum complements (13), 7) parietal cell antibody (PCA) (8), 8) endoscopic congo-red pattern (11), 9) gastric emptying (6), and 10) intestinal metaplasia by the endoscopic methylene blue method (17).

These studies were performed during hospitalization.

RESULTS

1. Subjective gastrointestinal symptoms

Twenty six out of 27 JA patients had some positive symptoms with a high frequency (Table 1), especially abdominal pain and/or gastric fullness followed by anorexia. SA patients had almost no GI symptoms. There was tendency to want more sweet foods and pungent foods in JA patients than in SA patients. In their familial history, there was nothing associated with cancer, especially GI tract cancer, in both JA and SA patients.

2. Endoscopical findings of the stomach

Fig. 1 shows the representative endoscopic findings of the JA stomach. Diffuse-fine-irregular mucosal surface, i.e. hyperplastic change of the mucosa, was the predominant finding. Table 2 shows a summary of the endoscopic findings of the body and the antrum of the stomach. Hyperplastic changes of the mucosa were found in JA patients with uneven color and transparent vessels which suggested atrophic and inflammatory changes of the mucosa.

Table 1 Subjective symptoms in patients with juvenile atrophy and senile atrophy

	Juvenile atrophy	senile atrophy
Gastrointestinal symptom (+)	26/27	7/17
Epigastralgia	14	2
Heavy sensation	10	1
Anorexia	2	4
Nausea, Vomiting	2	0
Hematemesis	1	0
Gastrointestinal symptom (−)	1	10

positive/total

Table 2 Endoscopic findings of gastric mucosa in patients with juvenile atrophy and senile atrophy

	Juvenile atrophy	Senile atrophy
ANTRUM		
Hyperplastic change	4	1
Uneven color	11	16
BODY		
Hyperplastic change	2	0
Uneven color	11	17
Transparent vessels	0	10

3. Lymphocyte counts in peripheral blood

The counts were $1,969 \pm 497/mm^3$ (M ± SD) in JA patients and $2,117 \pm 539/mm^3$ in SA patients. In spite of the age difference of 40 years in the mean age, the lymphocyte counts in JA patients were lower than those in SA patients. In juvenile controls with normal gastric acid secretion, the value was $2,127 \pm 855/mm^3$.

4. Delayed hypersensitivity skin test (PPD and DNCB)

PPD and DNCB skin tests are considered to reflect cellular immunity. The positive rate of PPD was 79% in JA patients and 44% in SA patients. The positive rate of DNCB was 80% in JA patients and 87% in SA patients.

5. HLA phenotype frequency

HLA-A and B loci were studied in the Department of Transplantation and Immunology of Tokai University (16) (26). There was no significant difference in the phenotype frequency between JA and SA patients. With difference in the phenotype frequency between JA and SA patients. Table 3 shows the HLA-antigen phenotype frequency with respect to intestinal metaplasia in JA and SA patients. The frequencies of A9 (AW 24) and B15 were significantly lower in JA patients without intestinal metaplasia than in SA patients with intestinal metaplasia ($X^2 = 3.93, 2.18$). The frequencies of A-Blank and BW52 were significantly higher ($X^2 = 2.5, 6.3$).

6. Serum complements

Three serum complements (C3, C4 and CH50) were studied (Table 4). The man ± SD values at the C3 level were 69.2 + 15.5 mg/dl in JA patients and 81.3 ± 14.9 mg/dl in SA patients. At the C4 level, the values were

31.5 ± 7.9 mg/dl in JA patients and 41.0 ± 13.5 mg/dl in SA patients. At the CH50 level, the values were 30.1 ± 6.1 CH50U in JA patients and 32.2 ± 4.5 CH50U in SA patients. The value of the C3 level was relatively but not significantly lower in JA patients than in SA patients.

Table 3 HLA phenotype in patients with juvenile atrophy and senile atrophy associated with intestinal metaplasia

Antigen group	Juvenile atrophy (JA) Intestinal metaplasia					Senile atrophy (SA)				Normal control Japanese	
	Int. met. −			Int. met. +		Int. met. −		Int. met. +			
	n	PF%	x^2	n	PF%	n	PF%	n	PF%	n	PF%
A-Locus											
A9(AW24)	7/12	58	3.9↓	5/8	63	1/2	50	10/12	83	213/355	60.6
A26	0/12	0	(3.8↓)	1/8	13	2/2	100	1/12	10	85/355	24.8
A-Blank	7/12	58	2.5↑	1/8	13	1/2	50	2/12	17	138/355	39.2
B-Locus											
B15	0/12	0	2.2↓	2/8	25	0/2	0	2/12	17	18/355	5.1
BW52	5/12	42	6.3↑	2/8	25	0/2	0	0/12	0	48/355	13.8
BW54	4/12	33	(4.9↑)	1/8	13	0/2	0	2/12	17	42/355	12.2

X^2: $p < 0.05$ JA int. met. − vs SA int. met. + (vs Normal control)

Table 4 Serum complements (C_3, C_4, CH_{50}) in patients with juvenile atrophy and senile atrophy

	C_3	C_4	CH_{50}
Juvenile atrophy (JA) n = 27	69.2 ± 15.5	31.5 ± 7.9	30.1 ± 6.1
Senile atrophy (SA) n = 17	81.3 ± 14.9	41.0 ± 13.5	32.3 ± 4.5

$C_3 = \beta_1C/\beta_1A$ 80 − 140 mg/dl
$C_4 = \beta_1E$ 20 − 40 mg/dl
$CH_{50} = 30 - 40$ CH_{50} u

7. Autoimmune antibodies

Serum autoimmune antibodies such as parietal cell antibody (PCA), antinuclear antibody factor and the thyroid test were studied. Three JA patients and one SA patient were positive for PCA. No other antibodies were detected in this study.

8. Endoscopic congo-red patterns

Endoscopic congo-red patterns were classified by Kimura's classification (11). Fig. 2 shows endoscopic congo-red findings in JA patients. The atrophic border was of the closed type (C2-C3) in spite of gastric hypoacidity, and the unchanged color area was found to be spotty or islet-like within the changed color area. Table 5 shows endoscopic congo-red patterns in JA and SA patients. The patterns in JA patients were of the closed-type, mainly the C2-C3 type, but in SA patients, they were of the open-type (O2 type).

Table 5 Endoscopic congo-red pattern in patients with juvenile atrophy and senile atrophy

	Congo-red pattern					
	C-1	C-2	C-3	O-1	O-2	O-3
Juvenile atrophy (JA)	0	4	16	3	3	1
Senile atrophy (SA)	0	1	2	3	8	3

Kimura's Classification

9. Gastric emptying

Gastric emptying was measured using the acetaminophen method to ingest test meal (6). The values of gastric emptying were $10.1 \pm 4.1 \mu g/ml$ in JA patients and $12.9 \pm 4.0 \mu g/ml$ in SA patients. Gastric emptying in JA patients was delayed when compared with SA patients.

10. Serum gastrin concentration

The fasting serum gastrin level (FGL) was 71.2 ± 47.7 pg/ml in JA patients and 51.8 ± 39.1 pg/ml in SA patients with no significant difference. The integrated gastrin response (IGR) to the test meal was 3.4 ± 2.6 ng·min/ml in JA patients and 2.4 ± 2.0 ng·min/ml in SA patients. Both FGL and IGR were relatively higher in JA patients than in SA patients, but there was no significant difference.

11. Intestinal metaplasia

Intestinal metaplasia was studied by the endoscopic methylene blue method and was classified by a modification of Sano's classification (17). Twelve out of 27 JA patients were non metaplastic. Fifteen JA patients were positive cases, consisting of eight of the antral type, and seven of the diffuse type.

On the other hand, only two patients with SA were of the non-metaplastic type. From the standpoint of intestinal metaplasia, comparisons with FGL, IGR and intestinal metaplasia are shown in Table 6. IGR was significantly higher in JA patients of the non-metaplastic type than in SA

Table 6 Serum gastrin and gastric emptying in patients with juvenile atrophy and senile atrophy associated with intestinal metaplasia

	Methylene-blue method	FGL	IGR	GE
Juvenile atrophy n = 27	negative (12)	79.2 ± 56.6	4.5 ± 2.6*	9.8 ± 3.9*
	positive (15)	63.8 ± 36.2	2.8 ± 2.5	10.8 ± 4.2
	antral type (8)	51.4 ± 27.1	1.5 ± 0.9*	8.5 ± 3.2
	diffuse type (7)	80.3 ± 40.0	4.6 ± 2.8	13.3 ± 4.1
Senile atrophy n = 19	negative (2)	/	/	/
	positive (17)	51.8 ± 39.1	2.4 ± 2.0*	12.9 ± 4.0*
	antral type (7)	58.1 ± 32.0	1.6 ± 1.1	14.1 ± 2.9*
	diffuse type (10)	63.3 ± 64.3	4.3 ± 3.9	11.4 ± 4.2

FGL: fasting gastrin level, IGR: integrated gastrin response, GE: gastric emptying
*$p < 0.025$

patients with intestinal metaplasia and JA patients with the antral type of intestinal metaplasia (4.5 ± 2.6 ng·min/ml versus 2.4 ± 2.0 ng·min/ml and 2.8 ± 2.5 ng·min/ml respectively, $p < 0.05$).

DISCUSSION

According to Shindler, the first mention of gastritis in the medical literature should be credited to G.E. Stahl (1728). A discription of "gastritis" is to be found in the second volume of "Histoire des Phlégmasies ou Inflammations Chroniques", which first appeared in 1808 (Broussais). Several years later Handfield Jones (1855) described the occurrence of "atrophy of the gastric tubuli with fibrinoid replacement" in several autopsy cases. Austin Flint (1860) linked gastric atrophy to pernicious anemia, while Samuel Fenwick published his paper on gastric atrophy in 1870.

Another important step in the knowledge of gastritis was the design by Shindler of the flexible gastroscope which made possible the observation *in vivo* of the gastric mucosa.

It is thought that chronic atrophic gastritis in aged persons is due to antralization associated with erosive gastritis and/or zonal gastritis of gastric ulcers. Actually, atrophic gastritis has been defined by endoscopic findings and histological findings of the gastric mucosa, and is also related to hypoacidity of gastric secretion. Strickland *et al.* (21) proposed the separation of chronic atrophic gastritis into two distinct types, "Type A and Type B", on the bases of gastric morphology and function, and pathogenesis. Type A atrophic gastritis shows sparing of the antral mucosa, a positive PCA reaction, changes in the corpus of diffuse character and severe impairment of gastric secretion. Type B atrophic gastritis shows antral involvement, a negative PCA reaction, changes in the corpus of focal character and moderate impairment of gastric secretion. Atrophic gastritis may accompany intestinal metaplasia (20), gastric ulcers, and gastric cancer (19).

Recently we have experienced juvenile patients with atrophic gastritis which was considered to have a low incidence in young people. Clinical symptoms and pathophysiology of juvenile atrophy are discussed in this paper in comparison with patients with senile atrophy which is considered to be type B atrophic gastritis.

Criteria of JA were as follows: 1) juvenile patients under 30 years of age, 2) observation of endoscopic mucosal atrophy, and 3) gastric acid secretion with a MAO value below 6.0 mEq/h (4 r/kg tetragastrin stimulated). Therefore, there are many clinically undefined points concerning criteria of JA. As a control group, atrophic gastritis in the aged (over 60 years of age) with MAO values below 6.0 mEq/h was studied.

The grade of subjective GI symptoms was more severe in JA patients than in SA patients and a high frequency of GI symptoms was found in JA patients. Inveterate or frequent GI symptoms are considered to be the key point in the material selection. Epigastralgia and epigastric distress in JA patients are difficult to treat.

Endoscopic findings such as uneven color and transparent vessels which are commonly found in SA patients are rare in JA patients. A fine irregular

mucosal surface, i.e. hyperplastic change of the mucosa, was found chiefly in JA patients. These findings indicate the absence of inflammation and presence of hyperplastic change of the mucosa.

Peripheral blood lymphocyte counts (15) which are considered to indicate the immunity of an individual clinically were lower in JA patients than in SA patients in spite of age difference of about 40 years. Decrease of blood lymphocytes may mean a low immune response, but because subpopulations of lymphocytes were not evaluated in this study, this point is not clear.

In addition, serum immunoglobulins (IgG, IgA and IgM) showed no significant differences between JA and SA, as in the previous reports. PPD and DNCB as indicators of cellular immunity were unexpectedly more positive in JA patients than in SA patients.

It has been thought that HLA-antigen or the site of immune response genes may be on the VI chromosome (26). The results of our study of reactivity of a variety of anti HLA antisera on lymphocytes from patients with JA showed no significant difference from SA patients. Therefore, because intestinal metaplasia may accompany gastric cancer, HLA antigens were studied again in addition to the factors of intestinal metaplasia. There were significant differences between JA patients and SA patients; the frequencies of A9 and B15 were significantly lower in JA without intestinal metaplasia than in SA with intestinal metaplasia, and the frequencies of A-Blank and BW52 were significantly higher in JA without than in SA with intestinal metaplasia. Tuji *et al.* (26) have reported that HLA-A2, A9, A10, A11 and B15 phenotype frequencies were significantly higher in Japanese patients with gastric cancer than in normal controls. It may be possible that A9 and B15 phenotypes are sensitive antigens for intestinal metaplasia, while A-Blank and/or BW52 phenotypes are resistant antigens for intestinal metaplasia and gastric cancer.

There have been many reports on gastritis and HLA antigens including those on chronic atrophic gastritis by Fung *et al.* (2), pernicious anemia by Mawhinney *et al.* (14), thyroid gastric autoimmune disease by Whittingham *et al.* (27) and pernicious anemia by Dausset *et al.* They said that the frequencies of A3 and A7 are significantly higher in autoimmune gastritis. Their results deny that JA is a hereditary disease due to an immunological disorder.

The results of our study on serum complements disclosed low values of C3 in JA patients, as in other reports (13) concerning gastritis and gastric ulcers, but it is uncertain what the low value of C3 means in JA patients. PCA is found in about 90% of pernicious anemia patients and also in some of their relatives. They are present in variable percentages in the sera of patients with chronic atrophic gastritis, and there is some indication that they might be more common among relatives of these patients than among the general population. In a large group of donors used as controls, the incidence of PCA was 5%. PCA tends to be absent in people under 30 years of age and to appear over 60 years of age in agreement with the age prevalence of chronic gastritis (8).

The results of our study on PCA in which there out of 27 JA patients

were positive for PCA suggested that positive of PCA is not always specific to pernicious anemia. Katayama *et al.* (10) have reported that patients with active chronic gastritis with recurrences or exacerbation are positive for PCA. Therefore it may be possible that the progress of gastritis is correlated with some antigen-antibody reaction.

Generally, the gastric atrophic border is demonstrated by the endoscopic congo-red method and is considered to be related to gastric acid secretion. A significant percentage of cases diagnosed as "atrophic gastritis" by gastroscopy have, on biopsy, proved to have histological atrophic change of the mucosa (3). Recent evidence has vindicated the diagnostic significance of gastric hypoacidity or anacidity for the recognition of gastric atrophy (3). It is of interest that the endoscopic congo-red pattern in JA patients was the closed type in spite of hypoacidity with a MAO value below 6.0mEq/h. Especially in the area of the congo-red color, there were macular, islet-like areas of no change or imperfect change in the color.

It is thought that there is a partial absence or decrease of parietal cells in the fundic gland area, exclusive of the atrophic border. There also may be a problem because the sensitivity of the parietal cell receptors is dissimilar in character. In a few patients with JA, or gastric acid analysis stimulated by tetragastrin, histamine or insulin was performed, but all of them showed the same gastric acid secretion as in the case of tetragastrin stimulation. Therefore, in spite of the closed-type of endoscopic congo-red pattern, gastric hypoacidity may be related to a decrease in the parietal cell distribution rather than the sensitivity of the parietal cell receptors.

Gastric emptying studies related to the pathophysiology of peptic ulcers have been reported by various investigators and the authors (7). Any type of gastric abnormality associated with longstadnding stasis of gastric contents within the stomach lumen may produce chronic gastritis, usually accompanied by erosions. Delayed gastric emptying in JA patients when compared with SA patients is thought to be related to subjective symptoms such as epigastric distress, and nausea or vomiting.

Takeuchi *et al.* (24) reported that the early stage of intestinal metaplasia was found in juvenile-aged subjects. Intestinal metaplasia is one of the most remarkable features of chronic gastritis. It is particularly prominent in gastric atrophy where it may replace practically the entire gastric mucosa. Gastroscopic biopsy has shown that it is very common around the lesser curvature of the stomach and rather infrequent near the greater curvature (23). More than half of the patients with JA have intestinal metaplasia and some of them may be in the early stage of intestinal metaplasia reported by Takeuchi.

Previous studies have indicated that the serum gastrin response to a standard protein meal provides an indirect measurement of the mass of functioning gastrin-secreting ("G") cells (4) (5). The relationship between intestinal metaplasia and serum gastrin level has been reported by several investigators (12) (22). Many reports disclosed that relation between the grade of intestinal metaplasia on the antral mucosa and the antral G cell mass was inversely proportional. Although the test meal used in our study may not be a satisfactory stimulus of antral G cells (25), integrated gastrin

response to this test meal was higher in JA patients without intestinal metaplasia than in those with intestinal metaplasia or in SA patients. However, this relation between intestinal metaplasia and the antral G cell mass may have no connection with the pathophysiology of JA.

Various degrees of gastritis have been found in practically almost all patients over 60 years of age. Chronic gastritis may be rare in young patients with abdominal complaints (18). These discrepancies may be due entirely to different criteria for selection and histologic analysis. The natural history of chronic gastritis is yet to be determined. Further studies are required to define the pathogenesis of the chronic gastritis involved.

CONCLUSION

Juvenile atrophy was studied with respect to various clinical points in comparison with atrophic gastritis in the aged.

The following results were obtained: 1) Pathophysiology of atrophic gastritis was different from ordinary antralization of the fundic gland, and partial atrophic areas existed in the fundic gland area. 2) Gastritis in JA was different from atrophy associated with immunological disease. 3) The HLA antigen study showed no relation between JA and gastric cancer.

ACKNOWLEDGEMENTS

We are grateful to Dr. K. Tsuji and a his co-workers for their helpful suggestions and discussions on the HLA antigen study.

We wish to thank Miss A. Takizawa and K. Yamazaki for their technical assistance. We also want to thank Miss T. Maeda for her skillful secretarial assistance in preparing the manuscript.

REFERENCES

1) Bockus HL: Chronic gastric disease and suction biopsy; Part I chronic gastritis. Gastroenterology. Vol. 1 Saunders, Philadelphia, 1974, p 527—567.
2) Fung WP, Rigby RJ, Trencher P, Matz LR: Immunological studies in chronic atrophic (superficial) gastritis. Am J Gastroenterol 69: 51—56, 1978.
3) Glass GBJ, Speer FD, Nieburgs HE, Ishimori A, Jones EL, Barker H, Schwarlz S, Smith R: Gastric atrophy, atrophic gastritis and gastric secretory failure. Gastroenterol 39: 429—453, 1960.
4) Hansky J, Korman MG, Soveny C, St John DJB: Radioimmunoassay of gastrin: Studies in pernicious anemia. Gut 12:97—101, 1971.
5) Hansky J, Soveny C, Korman MG: Effect of secretion on serum gastrin as measured by immunoassay. Gastroenterol 61: 62—68, 1971.
6) Harasawa S, Tani N, Suzuki S, Miwa M, Sakita R, Nomiyama T, Miwa T: Gastric emptying in normal subjects and patients with peptic ulcer.—A study using the acetaminophen method. Gastroenterologia Japonica 14: 1—10, 1979.
7) Harasawa S, Tani N, Nomiyama T, Sakita R, Miwa M, Suzuki S, Miwa T: Gastric emptying in patients with gastroduodenal disease. The first report: peptic ulcer and its recurrence. Journal of Japanese Society of Internal Medicine (in Japanese) 68: 733—741, 1979.
8) Hooper B, Whittingham S, Mathews JD, Mackay IR, Curnow DH: Autoimmunity in a rural community. Clin Exp Immunol 12: 79—87, 1972.
9) Inada M, Kameyama M: Immunological aspects in chronic gastritis with special refernce to antigastric antibodies. Saishin-Igaku (in Japanese) 31: 1925—1934, 1976.
10) Katayama K, Abe T: Immunological aspects in chronic gastritis. Clinical Immunology (in Japanese) 6: 29—35, 1974.

11) Kimura K, Takemoto T: Biopsy of chronic gastritis. Stomach and Intestine (in Japanese) 5: 843—851, 1970.
12) Korman MG, Strickland RG, Hansky J: The functional G cell mass in atrophic gastritis. Gut 13: 349—351, 1972.
13) Masuda N: Complements in patients with gastric disease Allergy 14: 637, 1965.
14) Mawhinney H, Lawton JWM, White AG, Irvine WJ: HLA-A3 and HLA-A7 in pernicious anemia and autoimmune atrophic gastritis. Clin Exp Immunol 22: 47—53, 1975.
15) Nomiyama T, Harasawa S, Sakita R, Suzuki S, Miwa M, Tani N, Miwa T, Tuji K: Immune response in patients with gastric cancer. Digestive Organ and Immunology (in Japanese) No. 2, Ishiyaku Publishers, Inc. 1979. P 95—101.
16) Sakita R, Harasawa S, Senoue I, Watanabe H, Nomiyama T, Miwa M, Suzuki S, Tani N, Miwa T, Tuji K: Juvenile atrophy and HLA antigen. Digestive Organ and Immunology (in Japanese) No. 4, Ishiyaku Publishers, Inc. 1980. p 23—26.
17) Sano R: Chronic gastritis in Japanese patients with various gastric diseases on surgical materials. Japanese Journal of Gastroenterology (in Japanese) 72: 1231—1239, 1975.
18) Sedlackova M, Bendnar B: Chronic gastritis in childhood. Gastroenterologia (Basel) 107: 251, 1967.
19) Segal HL, Samloff M: Gastric cancer: Increased frequency in patients with achlorhydria. Am J Dig Dis 18: 295—299, 1973.
20) Siurala M, Varkis K, Wiljasalo M: Studies of patients with atrophic gastritis; A 10-15 year follow-up. Scand. J Gastroenterol. 1: 40—48, 1966.
21) Strickland RG, Mackay IR: A reappraisal of the nature and significance of chronic atrophic gastritis. Digestive Disease 18: 426—440, 1973.
22) Strickland RG, Bhathal PS, Korman MG, Hansky J: Serum gastrin and the antral mucosa in atrophic gastritis. Brit Med J 4: 451—453, 1971.
23) Takahashi T: Gastrin cell (G cell) population of the gastroduodenal mucosa in patients with gastric ulcer and duodenal ulcer. Japanese Journal of Gastroenterology (in Japanese) 75: 1312—1321, 1978.
24) Takeuchi I , Mai M, Konishi F: Early stage of intestinal metaplasia of the gastric mucosa. Gastroenterological Endoscopy (in Japanese) 21: 1425—1433, 1980.
25) Tani N: Plasma gastrin response to test meal and gastric acid secretion, gastric emptying: [1] Basal study. Japanese Journal of Gastroenterology (in Japanese) 75: 1534—1544, 1978.
26) Tsuji K, Inoue H: Human major histocompatibility complex and malignancey. Saishin-Igaku (in Japanese) 32: 1292—1303, 1977.
27) Whittingham S, Youngchaiyud U, Mackay IR, Buckley JD, Morris PJ: Thyrogastric autoimmune disease. Clin Exp Immunol 19: 289—299, 1975.

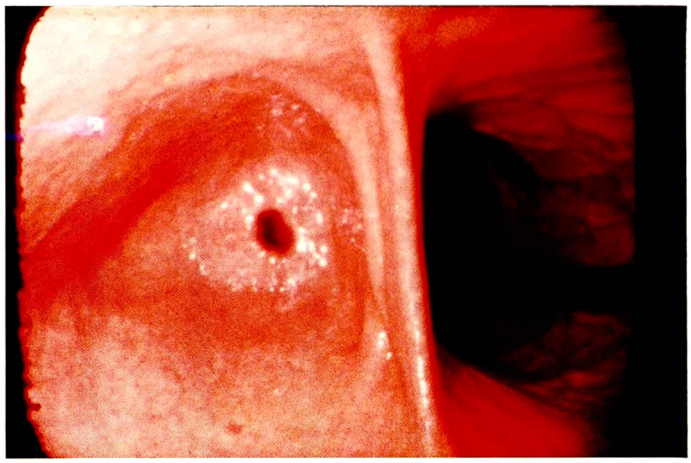
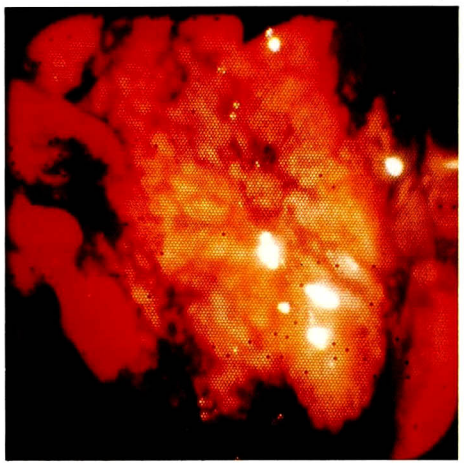


Fig. 1 Endoscopic picture of the stomach in a patient with juvenile atrophy.



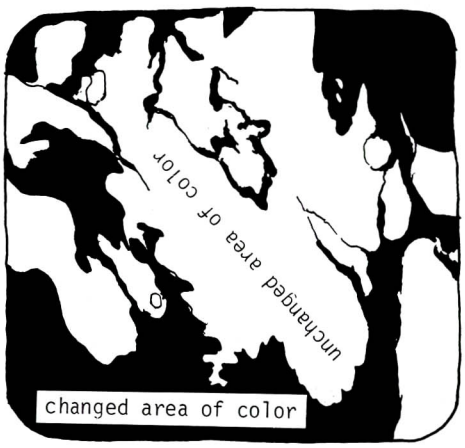


Fig. 2 Endoscopic congo-red picture of the stomach in a patient with juvenile atrophy.