

Pancreatic Abnormalities in Patients with Eating Disorders

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In patients with eating disorders, we evaluated pancreatic abnormalities using serum elastase 1 measurement by RIA and the 50 g oral glucose tolerance test (50 g OGTT). Twenty-one patients had anorexia nervosa (AN) with bulimia and vomiting (AN-B group), 30 had AN without bulimia or vomiting (AN-R group), and 25 had bulimia with normal body weight (B group). The serum elastase 1 level was determined on admission and repeated after body weight gain in 43 anorectic patients. The 50 g OGTT was performed within 2 weeks after admission. The serum elastase 1 level in the AN-B group (363 ± 47 ng/dl, $M \pm SE$), and in the AN-R group (352 ± 37) were significantly higher than that in the B group (242 ± 18) or in the healthy female controls (191 ± 10 ; $n = 13$). A significant decrease of serum elastase 1 was observed before and after body weight gain; however, there was no significant correlation between the serum elastase 1 level and insulin response to the 50 g OGTT. Elevation of the serum elastase 1 level in AN suggests pancreatic abnormalities other than those related to endocrinological events.

INTRODUCTION

A recently developed radioimmunoassay for elastase 1, a pancreatic exocrine enzyme, can stably detect serum elastase 1, the determination of which had been difficult using conventional enzymologic method. Estimation of serum elastase 1 level is a sensitive and specific marker for diagnosis and follow-up of pancreatic diseases such as acute (1) or chronic (2) pancreatitis and pancreatic carcinoma (3). Several authors reported pancreatic involvement in eating disor-

ders such as anorexia nervosa (AN) and bulimia. Most of these were case reports of pancreatitis in patients with eating disorders (4-7). There have been only a few reports on the incidence of pancreatic involvement in patients with eating disorders who had no clinical signs or symptoms of pancreatitis (8-10), and they dealt with only a small number of patients or made use of the serum amylase level, a less sensitive and less specific marker for pancreatitis than is the measurement of serum elastase 1 (2). However, Pichumoni (11) pointed out the histologic change of pancreas such as fibrosis and calcification in the patients with malnutrition. Therefore, we evaluated pancreatic damage using serum elastase 1 measurement in a large number of patients. The serum elastase 1 level was compared with the serum insulin (IRI) response to the 50 g glucose tolerance test (50 g OGTT), the objective being

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TABLE 1. Subjects' Profile

Group	n	Age (years)	BW loss ^a	
AN-B	21	23.3 ± 1.1	31.5 ± 1.5	N.S.
AN-R	30	21.8 ± 1.2	32.2 ± 1.4	
B	25	21.1 ± 0.8	3.2 ± 2.8	N.S.
C	13	20.5 ± 0.7	0 ± 1.8	

^a % of standard body weight.

^bNot significant.

to assess the relationship with pancreatic endocrinologic abnormalities that are apparently altered in patients with eating disorders (12).

SUBJECTS

The subjects were 51 patients with AN and 25 with bulimia and a normal body weight (B group) who met the criteria for AN or bulimia in DSM III (13). Twenty-one with AN had bulimia and vomiting (AN-B group), and 30 were restricters (AN-R group, see Table 1 for details). The frequencies of vomiting in 1 week prior to admission were 1.2 ± 0.4 (mean \pm SEM) times/day in the AN-B and 1.8 ± 0.5 times/day in the B group. All patients denied alcoholic consumption. None had previous or present symptoms or signs of pancreatic disease. Their abdominal x-ray showed no calcification on upper abdominal area, and the ultrasonographic examination in most of the patients revealed no abnormal findings suggesting pancreatitis or pancreatic tumor. No patient had taken any medication prior to testing. Normal healthy controls (C group) included 13 female students at Kyushu University with a normal body weight. They were matched for age and none of them had taken

any medication. Informed consent for the study in accordance with the principles of the Declaration of Helsinki was obtained from each subject.

METHODS

All patients were hospitalized at Kyushu University Hospital and were given no drugs. At hospitalization, the serum elastase 1 concentration was determined using blood samples collected after an overnight fast along with the individual clinical profile such as body weight and period of illness. After weight gain, serum elastase 1 measurements were repeated for 43 anorectic patients who obtained body weight gain during treatment (19 in AN-B group and 24 in AN-R group). The 50 g OGTT was performed within 2 weeks after admission to assess the relationship between the serum elastase 1 level and endocrine function, as described (12). Briefly, after an overnight fast, an indwelling needle was inserted in the antecubital vein, and blood samples to determine serum glucose and insulin (IRI) levels were obtained at 0, 30, 60, 90, 120, and 180 min after oral ingestion of 50 g glucose. Individuals in the C group were subjected to the same procedures. Both serum elastase 1 and IRI levels were determined in duplicate, using highly specific commercial radioimmunoassay kits (Dainabot, Tokyo, Japan [12] and Dainabot, Tokyo, Japan [14]). The blood glucose concentration was determined by the glucose oxidase method (15). Statistical analyses were carried out using analysis of variance, one-way layout (between group comparisons), or two-tailed paired *t* test (longitudinal comparisons of the same patients). Correlations were examined with linear-regression analysis. All data were expressed as mean \pm SEM.

RESULTS

Serum Elastase 1

Serum elastase 1 concentration in all patients with eating disorders on admission was 319 ± 21 ng/dl; that is a significant elevation compared with findings in the control group (191 ± 10 ng/dl, $p < 0.001$). Twelve had a high serum elastase 1 level (above 400 ng/dl, four of AN-B, seven

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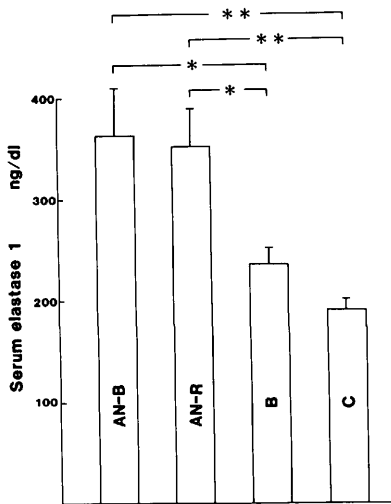


Fig. 1. Serum elastase 1 concentration in patients with eating disorders before treatment, and in healthy women. Body weight losses in each group were as follows (mean ± SEM, % of standard body weight and % of pre-morbid weight in parentheses): AN-B: 31.5 ± 1.5 (28.4 ± 1.3), n = 21; AN-R: 32.2 ± 1.4 (28.9 ± 1.4), n = 30; B: 3.2 ± 2.8 (2.0 ± 1.9), n = 25; C: 0 ± 1.8, n = 13. *p < 0.05, **p < 0.01.

of AN-R, and one of B group). The AN-B (363 ± 47 ng/dl) and AN-R (352 ± 37 ng/dl) groups had a significantly higher serum elastase 1 level than did the B group (242 ± 18 ng/dl) or C group. The serum elastase 1 level in the B group tended to be elevated, albeit not significantly (Fig. 1). There were significant correlations between serum elastase 1 levels on admission and % of body weight loss from standard body weight (% of BW loss, $p < 0.001$, Fig. 2A) or period of illness ($p < 0.05$, Fig. 2B). A significant decrease in serum elastase 1 con-

centration was observed after body weight gain in the 43 anorectics (Fig. 3).

50 g OGTT (Fig. 4)

The fasting blood glucose level of the anorectics tended to be lower than that of the B or C groups, although only the AN-B group showed a significantly lower blood glucose level than the C group (Fig. 4A). The peak blood glucose level in the 50 g OGTT in both anorectic and bulimic patients was similar to that in the C group. The B group showed a significantly higher peak blood glucose level than did the AN-B group (Fig. 4B).

The fasting IRI levels in anorectic patients (both AN-B and AN-R groups) were significantly lower than that of the C group (Fig. 4C) and showed a significant correlation with % of BW loss (data are not shown, $p < 0.05$). IRI response after 50 g oral glucose ingestion in patients with eating disorders showed no consistent tendency. As a whole, no significant differences in peak IRI levels were observed between groups with eating disorders or the control group (Fig. 4D).

Relationship Between Serum Elastase 1 Level and IRI Response in 50 g OGTT

There was no significant correlation between serum elastase 1 level and peak IRI concentration in the 50 g OGTT.

DISCUSSION

This seems to be the first report on the serum elastase 1 level in patients with eating disorders. At present, the actual mechanism related to the serum elastase 1 elevation is not clear, except for that with

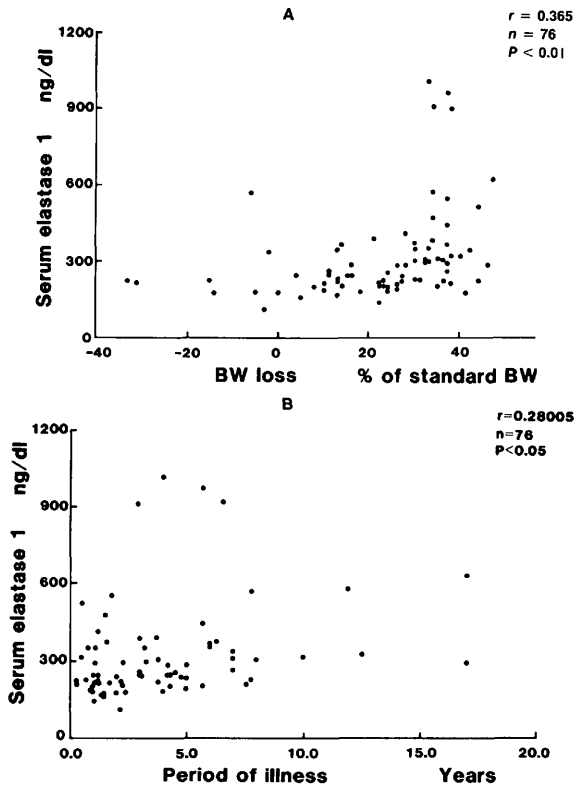


Fig. 2. Correlation between serum elastase 1 level and body weight loss (A) or period of illness (B) in all patients with eating disorders.

an acute pancreatitis (16). However, it seems reasonable that some pancreatic damage evokes the serum elastase 1 elevation even in patients with eating disorders.

In the present study, the serum elastase 1 level was elevated in anorectic patients, and this elevation showed a good corre-

lation with weight loss and was reversed with weight gain. A significant correlation between the serum elastase 1 level and period of illness showed that long-term body weight loss accelerated the pancreatic abnormalities. These findings are consistent with reported data that pancreatic exocrine dysfunction or histologic changes

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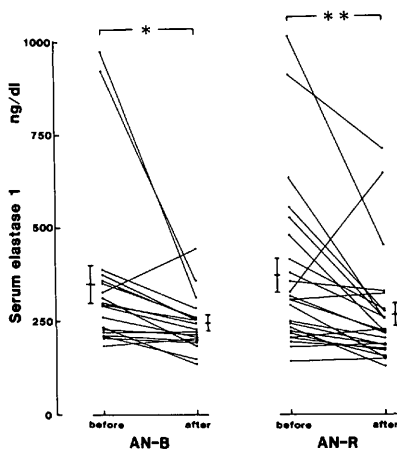


Fig. 3. Effects of body weight gain on serum elastase 1 concentration in anorectic patients who obtained body weight gain during treatment. The lines link the values in each patients before and after body weight gain. Short horizontal bars indicate mean (middle bar) \pm SEM (upper and lower bars) of serum elastase 1 concentration in each stages. Body weight losses in each stages were as follows (mean \pm SEM, % of standart body weight and % of premorbid weight in parentheses). AN-B: before 31.2 ± 1.7 (28.3 ± 1.6), after 15.2 ± 1.6 (13.5 ± 1.6), $n = 19$; AN-R: before 33.3 ± 1.4 (30.3 ± 1.3), after 17.2 ± 1.9 (15.7 ± 1.9), $n = 24$. Statistical analyses were performed using Student's t test. * $p < 0.05$, ** $p < 0.01$.

developed in patients with malnutrition (11, 17).

There seem to be only three reports on hyperamylasemia or pancreatic involvement in patients with eating disorders in whom clinical evidence of pancreatitis was only tenuous. Cox et al. (8) examined 10 patients with AN for pancreatic abnormalities; three had an elevated amylase

value, seven an elevated amylase creatinine clearance ratio, and three a reduced echogenesity of the pancreas. Mitchell and associates (9) reported that 30 out of 108 consecutive out-patients seen in their clinic for eating disorders had elevated amylase activity. However, these two reports lack clear evidence of pancreatic involvement because the amylase isozyme was not measured. Humphries et al. (10) reported that six out of 17 consecutive patients with eating disorders had hyperamylasemia and five of these six had an isolated increase in salivary isoamylase activity. However, the existence of pancreatic abnormalities could not be ruled out, because in one of their patients there was an increase in pancreatic isoamylase activity and lipase activity; hence, a pancreatic abnormality may have been present. In our study, abnormalities in serum pancreatic enzyme concentration were more frequent. Serum elastase 1 measurement is thought to be a more sensitive marker for pancreatitis than is measurement of serum amylase (2). Disappearance time of serum elastase 1 after endoscopic retrograde pancreatography is said to be longer than that of serum amylase (18).

We found that basal blood glucose level in the AN-B group was lower than that in the C group, and also peak blood glucose level in the AN-B group was lower than that in the B group. Usually, basal blood glucose level in AN was low compared with control group (12). However, we cannot make sure the reason why peak blood glucose level in the AN-B group was lower than that in the B group.

We also noted the relationship between the serum elastase 1 level and IRI response in 50 g OGTT but found no significant correlation. This suggests that the abnormal serum elastase 1 level in patients with eating disorders is not associated with en-

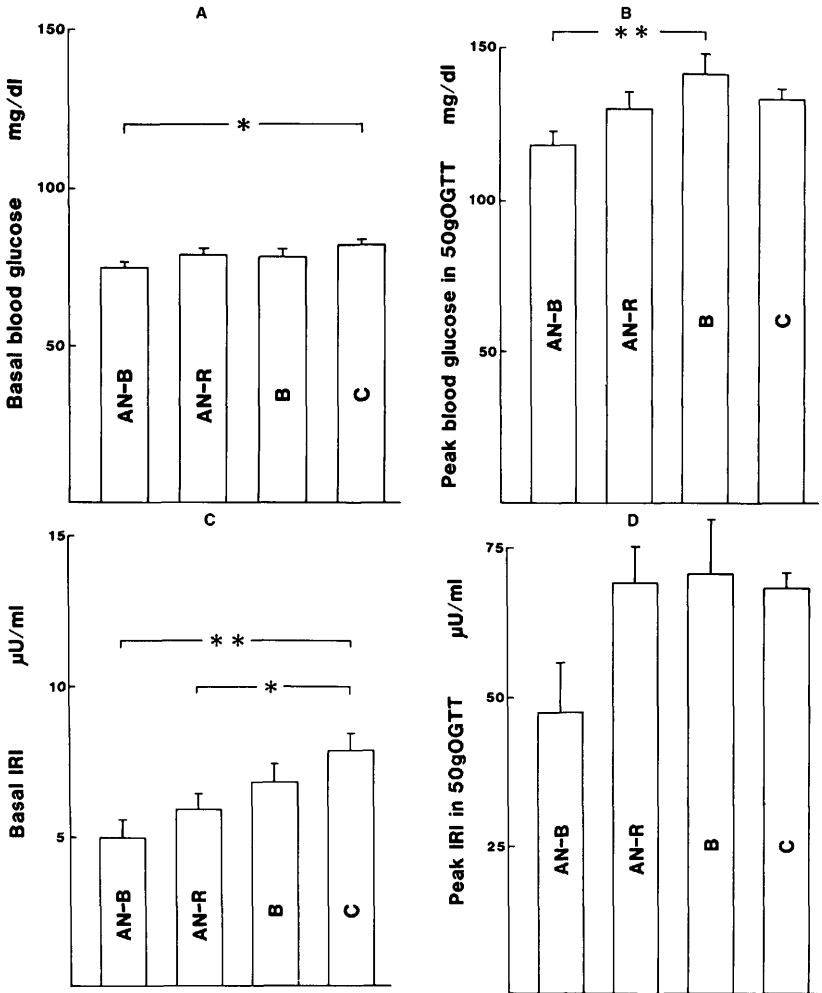


Fig. 4. Results of 50 g OGTT in patients with eating disorders on admission. (A) Basal blood glucose level; (B) peak blood glucose level in 50 g OGTT; (C) basal IRI level; (D) peak IRI level in 50 g OGTT. Body weight losses in each group were as follows (% of standard body weight and % of premorbid weight in parentheses). AN-B: 31.2 ± 1.5 (28.1 ± 1.3), AN-R: 31.9 ± 1.5 (28.6 ± 1.4); B: 3.2 ± 2.8 (2.0 ± 1.9). Each characters and number of patients were same as in Figure 1.

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doctrinologic abnormalities. However, further studies are necessary to clarify this association, because the IRI response in the 50 g OGTT is altered by factors such as gastric emptying in patients with eating disorders (19–21).

In conclusion, the serum elastase 1 level was elevated in patients with eating disorders, especially AN, and correlated with

body weight loss but not IRI response in the 50 g OGTT. These findings suggest that pancreatic abnormalities other than endocrinologic abnormalities are present in patients with eating disorders but with no clinical evidence for pancreatitis.

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REFERENCES

1. Murata A, Ogawa M, Fujimoto K, Kitahara T, Kosaki G: Changes in serum immunoreactive pancreatic elastase 1 in acute pancreatitis. *Hepatogastroenterol.* 29:278–280, 1982
2. Malfertheiner P, Biichler M, Stanescu A, Uhl W, Ditschuneit H: Serum elastase 1 in inflammatory pancreas and gastrointestinal diseases and in renal insufficiency. A comparison with other serum pancreatic enzymes. *Int J Pancreatol* 2:159–170, 1987
3. Hamano H, Hayakawa T, Kondo T: Serum immunoreactive elastase in diagnosis of pancreatic diseases, a sensitive marker for pancreatic cancer. *Dig Dis Sci* 32:50–56, 1987
4. Nordgren L, Von Scheele C: Hepatic and pancreatic dysfunction in anorexia nervosa: A report of two cases. *Biol Psychiatry* 12:681–686, 1977
5. Keane FB, Fennell JS, Tomkin GH: Acute pancreatitis, acute gastric dilatation, duodenal ileus, following refeeding in anorexia nervosa. *Ir J Med Sci* 147:191–192, 1978
6. Gryboski J, Hillemeier C, Kocoshis S: Refeeding pancreatitis in malnourished children. *J Pediatr* 97:441–443, 1980
7. Backett SA: Acute pancreatitis and gastric dilatation in a patient with anorexia nervosa. *Postgrad Med J* 61:39–40, 1985
8. Cox KL, Cannon RA, Amrent ME, Phillips HE, Schaffer CB: Biochemical and ultrasonic abnormalities of the pancreas in anorexia nervosa. *Dig Dis Sci* 28:225–229, 1983
9. Mitchell JE, Pyle RL, Eckert ED, Hatsukami D, Lentz R: Electrolyte and other physiological abnormalities in patients with bulimia. *Psychol Med* 13:273–278, 1983
10. Humphries LL, Adams LJ, Eckfeldt JH, Levitt MD, McClain CJ: Hyperamylasemia in patients with eating disorders. *Ann Int Med* 106:50–52, 1987
11. Pitchumoni CS: Pancreas in primary malnutrition disorders. *Am J Clin Nutr* 26:374–379, 1973
12. Kumai M, Tamai H, Fujii S, Nakagawa T, Aoki TT: Glucagon secretion in anorexia nervosa. *Am J Clin Nutr* 47:239–242, 1988
13. American Psychiatric Association Task Force on Nomenclature and Statistics. *Diagnostic and Statistical Manual of Mental Disorders*, 3rd ed. Washington, D.C.: American Psychiatric Association, 1980
14. Hayakawa T, Noda A, Kondo T, Okumura N, Sakakibara A, Kameya A, Katada N, Nagai K: Diagnostic significance of serum elastase determination by RIA kit. *J Adult Dis (in Japanese)* 11:1295–1299, 1981
15. Cawley LP, Spear FE, Kendal R: Ultramicro chemical analysis of blood glucose oxidase. *Am J Clin Pathol* 32:195–200, 1959
16. Geokas MC, Murphy R, McKennea RD: The role of elastase in acute pancreatitis. *Arch Pathol* 86:117–126, 1968
17. Barbezat GO, Hansen JDL: The exocrine pancreas and protein-calorie malnutrition. *Pediatrics* 42:77–92, 1968
18. Okuno M, Himeno S, Kurokawa M, Shinomura Y, Kuroshima T, Kanayama S, Tsuji K, Higashimoto Y, Tarui S: Changes in serum levels of pancreatic isoamylase, lipase, trypsin and elastase 1 after endoscopic retrograde pancreatography. *Hepatogastroenterol* 32:87–90, 1985

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19. Saleh JW, Lebwohl P: Metoclopramide-induced gastric emptying in patients with anorexia nervosa. *Am J Gastroenterol* 74:127–132, 1980
20. Holt S, Ford MJ, Grant S: Abnormal gastric emptying in primary anorexia nervosa. *Br J Psychiat* 139:550–552, 1981
21. McCallum RW, Grill BB, Lange R: Definition of gastric emptying abnormality in patients with anorexia nervosa. *Dig Dis Sci* 30:713–722, 1985