Original

Pancreatic Dysfunction and Imaging Abnormalities in Patients with Inflammatory Bowel Disease

Junichi NISHIKAWA, Fumihiko NOZU, Ken SATOYOSHI,
Masashi SAKAMOTO, Akifumi IKEGAMI, Yasushi AKITA,
Nozomi YOSHIKAWA and Keiji MITAMURA

Abstract : Background : Although patients with inflammatory bowel disease (IBD) frequently exhibit various extraintestinal manifestations, pancreatic disorder is not generally considered as an extraintestinal complication of IBD. We investigated pancreatic dysfunction and imaging abnormalities in patients with IBD. We estimated serum and urinary pancreatic enzyme levels for evaluation of pancreatic function in 42 patients with IBD, including 29 patients with ulcerative colitis (UC) and 13 patients with Crohn's disease (CD). In addition, some of the patients were examined by ultrasonography, abdominal computed tomography, and endoscopic retrograde pancreatography (ERP) for evaluation of pancreatic imaging. Elevation of serum or urinary pancreatic enzyme concentrations was observed in 23.8 % of patients, and abnormal pancreatic imaging, in 26.7 %. In 4 patients, the pancreatic enzyme concentrations decreased or normalized during remission of IBD. In one patient initial ERP showed irregularity of the main pancreatic duct, and follow-up ERP indicated normal appearances of the duct after remission of IBD. Our observations suggest that pancreatic dysfunction and imaging abnormalities develop in patients with IBD ; moreover, these may relate to the activity of disease and resolve when colonic inflammation is brought into remission.

Key words : inflammatory bowel disease, pancreatic disorder

Introduction

Various pancreatic manifestations of inflammatory bowel disease (IBD) and a number of pancreatic insufficiencies with IBD have been described since initial report of Ball *et al.*¹⁾

However, pancreatic disorder is not yet widely considered as an extraintestinal manifestation of IBD. We investigated pancreatic dysfunction and pancreatic imaging abnormalities in patients with IBD.

Methods

Forty-two patients with IBD admitted to our hospital were studied. Twenty-nine patients,

Table 1. Frequency of pancreatic dysfunction and image abnormalities with inflammatory bowel disease

	UC	CD	Total
Elevation of pancreatic enzymes	20.7 % (6/29)	30.8 % (3/13)	23.8 % (10/42)
Serum amylase	10.6 % (3/29)	23.1 % (3/13)	14.3 % (6/42)
Urine amylase	13.8 % (3/29)	30.8 % (4/13)	19.0 % (8/42)
Lipase	13.8 % (4/29)	15.4 % (2/13)	14.3 % (6/42)
Elastase 1	13.8 % (4/29)	15.4 % (2/13)	14.3 % (6/42)
Abnormalities of pancreatic imaging	33.3 % (6/18)	16.7 % (2/12)	26.7 % (8/30)

UC: ulcerative colitis

CD: Crohn's disease

performance of pancreatic enzyme examination: all cases

performance of pancreatic imaging examination: UC-18 cases, CD-12 cases

16 males and 13 females, with ulcerative colitis (UC) had a mean age of 35.0 (range 13–77). The extent of their disease was determined by barium enema or complete colonoscopy.

UC involved the entire colon in 18 patients, the left colon in 9, and the rectum in 2. Thirteen patients, 8 males and 5 females, with Crohn's disease (CD) had a mean age of 37.2 (range 21–53). Both the small intestine and the colon were involved in 5 patients, and the colon alone in 8 patients. We performed serum and urinary pancreatic enzyme examinations for all patients, abdominal ultrasonography (US) for 30, abdominal computed tomography scans (CT) for 13, and endoscopic retrograde pancreatography (ERP) for 16 patients. Evaluation of imaging abnormalities was based on criteria proposed by the International Workshop at Cambridge²⁾. We obtained informed consent for the study of pancreatic disorder from all patients.

Results

Elevations of serum or urine amylase, lipase, and elastase I values were observed in 10 (23.8 %) out of 42 patients with IBD, including 6 patients with UC (20.7 %) and 4 patients with CD (30.8 %) (Table 1). Elevated amylase concentrations in serum or urine included the pancreatic type isoenzyme.

Pancreatic imaging showed chronic pancreatitis in 8 (26.7 %) out of 30 patients examined, including 6 with UC (33.3 %) and 2 with CD (16.7 %) (Table 1). All pancreatic imaging abnormalities on US or CT were detected by ERP. ERP was particularly useful (Table 2). In all patients diagnosed by ERP, as having pancreatic duct abnormalities, mild or moderate pancreatitis was confirmed.

Combining biochemical tests and imaging examinations, 14 patients had pancreatic dysfunction or imaging abnormalities (Tables 3 and 4). Pancreatic disorder was not associated with age or sex, and there was no relationship between pancreatic enzyme concentrations and severity of imaging abnormalities. In 4 patients pancreatic imaging examinations showed chronic pancreatitis despite normal enzyme concentrations, and 4 patients with normal pancreatic imaging revealed elevation of pancreatic enzyme concentrations. Pancreatic disorder was often observed in patients with UC involving the entire

Table 2. Frequency of abnormality on pancreatice imaging in patients with inflammatory bowel disease

	UC	CD	Total
US	5.6 % (1/18)	8.3 % (1/12)	6.7 % (2/30)
CT	0 % (0/ 7)	16.7 % (1/ 6)	7.7 % (1/13)
ERP	54.5 % (6/11)	40 % (2/ 5)	50.0 % (8/16)

UC : ulcerative colitis

CD : Crohn's disease

US : ultrasonography

CT : computed tomography

ERP : endoscopic retrograde pancreatography

Table 3. Pancreatic dysfunction and imaging abnormalities in patients with uncerative colitis

case, age, sex	1.44, M	2.39, M	3.63, F	4.77, F	5.42, F	6.65, M	7.37, M	8.38, M	9.20, M
type	Total	Left-C	Total	Total	Total	Left-C	Total	Left-C	Left-C
severity of disease	moderate	mild	mild	severe	moderate	moderate	severe	severe	mild
therapy for UC	SASP, PSL	SASP	PSL	SASP	SASP	SASP, PSL	SASP	SASP, PSL	SASP
alcohol intake	(-)	(-)	(-)	(-)	(-)	(+)	(+)	(+)	(+)
cholelithiasis	(-)	(-)	(-)	(-)	(+)	(-)	(-)	(-)	(-)
symptoms of pancreatitis	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
duration of disease	1 M	30 M	1 M	2.5 M	1 M	18 M	1 M	60 M	7 W
max S-Amylase (isozyme) (IU/I)	823 (P) ↑	85	220	355 (P) ↑	127	92	279 (P) ↑	183	122
max U-Amylase (isozyme) (IU/I)	6924 (P) ↑	430	nt	nt	nt	nt	902 ↑	950 (P) ↑	1269 ↑
max Lipase (IU/I)	3093 ↑	54	359 ↑	801 ↑	81	100	287 ↑	193	nt
max Elastase-1 (ng/dl)	3267 ↑	161	523 ↑	693 ↑	nt	289	1182 ↑	nt	nt
exocrine function (PS test, PFD)	mild dysfunction	nt	nt	nt	nt	nt	nt	nt	nt
abdominal US	chronic pancreatitis	normal	normal	normal	normal	normal	normal	normal	normal
abdominal CT	normal	nt	normal	nt	normal	nt	normal	normal	normal
ERP	MIP	MIP	MIP	MIP	MIP	MIP	normal	normal	nt

Total : total colitis Left-C: left-sided colitis SASP : salazosulfapyridine PSL : prednisolone

MIP : mild pancreatitis MOP : moderate pancreatitis nt : not tested

colon or the left colon. Incidence of pancreatic dysfunction also increased in patients with CD involving both the small intestine and the colon; however, the incidence did not correlate with the activity of disease.

Table 4. Pancreatic dysfunction and imaging abnormalities in patients with Crihn's disease

case, age, sex	10.35, M	11.53, F	12.28, M	13.38, M	14.25, M
type	small int-colon	colon	small int-colon	small int-colon	small int-colon
severity of disease (IOIBD score)	5	7	3	3	3
therapy for UC	Metronidazole, Tranilast	SASP	(—)	SASP, PSL	SASP
alcohol intake	(+)	(—)	(—)	(—)	(—)
cholelithiasis	(—)	(—)	(—)	(—)	(—)
duodenal lesion	(—)	(—)	(—)	(—)	(—)
symptoms of pancreatitis	(—)	epigastric pain	(—)	(—)	(—)
duration of disease	39 M	3 W	7 M	9 Y	6 M
max S-Amylase (isozyme) (IU/I)	81	1927 (P) ↑	139	290 (P) ↑	288 ↑
max U-Amylase (isozyme) (IU/I)	159	12460 (P) ↑	1357 (P) ↑	2582 (P) ↑	1236 ↑
max Lipase (IU/I)	nt	5360 (P) ↑	nt	393 (P) ↑	10
max Elastase-1 (ng/dl)	140	3715 (P) ↑	nt	763 (P) ↑	nt
exocrine function (PS test, PFD)	nt	mild dysfunction	nt	nt	nt
abdominal US	normal	chronic pancreatitis	nt	normal	normal
abdominal CT	normal	pancreatitis	nt	normal	normal
ERP	MIP	MOP	nt	normal	normal

small int-colon: small intestine and colon type colon: colon type SASP: salazosulfapyridine

IOIBD: International Organization for the Study of Inflammatory Bowel Disease

PSL: prednisolone nt: not tested MIP: mild pancreatitis MOP: moderate pancreatitis

None of 14 patients had pancreatic disorder due to drugs. Five patients were habitual ethanol drinkers, and one patient had a gallstone. No patient had a duodenal lesion observed in CD, and none had a metabolic disease associated with pancreatic disorder.

In 4 of 10 patients with elevated pancreatic enzyme levels in the active phase of IBD, the elevated pancreatic enzyme concentrations decreased or normalized during remission of IBD (Cases 1, 4, 11, 14). Follow-up ERP was done on one patient (Case 11); she experienced epigastric pain and elevation of pancreatic enzyme concentrations in the active phase of CD.

Initial ERP performed in the active phase showed the irregular main pancreatic duct (MPD); however, follow-up ERP showed a normal appearance of the MPD after remission of IBD (Fig. 1).

Discussion

Pancreatic disorder associated with UC

Patients with UC occasionally manifest pancreatic disorder. Ball *et al.*¹⁾ found interstitial pancreatitis in 46 of 86 autopsied cases of UC (53%), and parenchymal fibrosis and atrophy in 11 cases. Chapin *et al.*³⁾ also reported that abnormal pancreatic histology was frequent in UC. Angelini *et al.*⁴⁾ reported that exocrine pancreatic dysfunction was found in 30% of patients with UC.

We evaluated that none of our subjects had drug-related etiologies or metabolic disease.

Fig. 1A, Initial ERP showed the irregular main pancreatic duct

Fig. 1B, Follow-up ERP after remission of IBD showed normal appearance of the main pancreatic duct

Four of our patients were habitual ethanol drinkers. Only one had a gallstone. These conditions were not considered related to pancreatic disorder. We considered other well-known etiologies of pancreatic disorder.

Possible mechanisms of pancreatic disorder associated with UC include activation of trypsinogen by bacterial infection, nutritional compromise, and disordered microcirculation due to irritation of autonomic nerves⁵⁾. Other potential mechanisms include hyperamylasemia induced by stress via adrenal cortical hormones, irritation of the pancreatic parenchyma and interstitium by proteases and cytokines produced in the colonic mucosa, and increased viscosity of secretions arising by dehydration from intestinal motor paralysis⁶⁾. None of these hypotheses is favored over the others by the present study.

Two patients in our study revealed decreases or normalization of pancreatic enzyme levels

after remission of UC. This result suggests that pancreatic dysfunction in patients with UC may relate to the activity of disease. Pancreatic imaging abnormalities, especially on ERP, were found in some patients with UC. However, pancreatic imaging abnormalities in our patients were minimal changes.

Pancreatic disorder associated with CD

There are several prior reports of pancreatic disorder associated with CD. Chapin *et al.*³⁾ reported that fibrosis of the interstitium or surrounding pancreatic ducts were seen in 15 of 39 autopsied patients. Seidman *et al.*⁷⁾ reported a case of pancreatitis in which inflammation of surrounding pancreatic ducts and interstitial fibrosis were seen in a pancreatectomy specimen. Dreiling⁸⁾ observed exocrine dysfunction in 18 % of patients by the secretin test, and Angelini *et al.*⁴⁾ found the same dysfunction in 35 % of patients by secretin and caerulein tests.

In our study one patient was a habitual ethanol drinker. However, there were no other well-known etiologies of pancreatic disorder such as drug use, gallstones, or metabolic disease.

With regard to the mechanism of pancreatic disorder in patients with CD, Altman *et al.*⁹⁾ reported that a reflux of duodenal contents into the pancreatic duct had been proved in cases of CD having a duodenal lesion. Recently, a case of duodenal Crohn's disease involving the ampulla of Vater¹⁰⁾ and a case showing histologically granulomatous inflammation consistent with Crohn's disease involving the stomach, duodenum, and head of the pancreas¹¹⁾ have been reported. The notion of reflux or mechanical obstruction of the pancreatic duct is attractive; however, we found no patient with CD having duodenal lesions in our study. In 2 patients with CD, similar to UC, pancreatic enzyme levels improved with remission of CD in our study. ERP was performed for one patient with CD in both active and inactive phases. Initial ERP showed chronic moderate pancreatitis; however, follow-up ERP found no abnormality. Therefore, we assume that pancreatic dysfunction and imaging abnormalities in patients with IBD may relate to the activity of disease.

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