[Case report]

Usefulness of Fecal Calprotectin Measurement in a Pediatric Patient with Crohn's Disease

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Abstract

Acute pancreatitis in children in Japan is often caused by an anatomical abnormality of the pancreatic and bile duct, resulting in fever, abdominal pain, vomiting, diarrhea, and other symptoms. Crohn's disease, however, is a chronic granulomatous inflammatory bowel disease with ulcerative lesions of the intestinal tract of unknown cause that occurs mainly in young people, with symptoms similar to those of acute pancreatitis. We report a case of acute pancreatitis diagnosed in a patient not only with incomplete fusion of the pancreatic duct but also with Crohn's disease. A 14-year-old girl, healthy by nature, presented to our hospital with complaints of abdominal pain and diarrhea. She was initially diagnosed as having acute pancreatitis due to incomplete pancreas divisum. However, a high level of fecal calprotectin led to endoscopic examination, which resulted in the diagnosis of Crohn's disease. Fecal calprotectin can be useful in the diagnosis of inflammatory bowel disease associated with acute pancreatitis in children. Although the relationship between inflammatory bowel disease and acute pancreatitis has not yet been clarified, we suggest that in the present case, acute pancreatitis may have manifested as a complication of Crohn's disease and an underlying case of incomplete pancreas divisum.

Key words : pancreatitis, incomplete pancreas divisum, pediatric Crohn's disease, calprotectin

Introduction

Acute pancreatitis (AP) in children in Japan is often caused by an anatomical abnormality of the pancreatic and bile duct, resulting in fever, abdominal pain, vomiting, diarrhea, and other symptoms[1]. Crohn's disease (CD), however, is a chronic granulomatous inflammatory bowel disease (IBD) with ulcerative lesions of the intestinal tract of unknown cause that occurs mainly in young people, with symptoms similar to those of AP[2]. As most instances of CD gradually progress with the advancement of clinical symptoms, diagnosing CD in the preclinical stage can be challenging. Recently, fecal calprotectin was shown to be a noninvasive and use-ful biomarker in the diagnosis of IBD[3]. We describe a case of presymptomatic or mild CD that was diagnosed by measurement of fecal calprotectin level soon after the development of AP in a patient with incomplete pancreas divisum.

Case report

A 14-year-old girl had been well until two weeks earlier when she began to experience diarrhea, fever, and abdominal pain. The fever subsided over one day, but the diarrhea and abdominal pain continued.

Her past medical history and family history were not significant. Diarrhea occurred 3-4 times

a day, with watery stools and no gross hematochezia. Her height was 154.8 cm (−0.39 SD), weight was 42.5 kg (−1.15 SD), and her vital signs were stable. Physical examination revealed tenderness in the right lower abdomen and decreased intestinal peristalsis. There were no other findings of ano-rectal lesions or arthralgia. Laboratory results showed a lipase level of 811 U/L, amylase level of 309 U/L, and C-reactive protein (CRP) level of 1.08 mg/dL (Table 1). Contrast-enhanced computed to-mography (CT) scan showed a pancreas of age-ap-propriate size, inflammation not extending beyond the pancreas, and no contrast-enhanced area, but edematous changes were observed in the perirectal wall (Fig. 1a, b). Abdominal echography showed an enlarged pancreatic head measuring 29.8 mm (Fig. 1c). Our patient presented with acute abdominal pain and elevated levels of pancreatic enzymes in the blood. In accordance with Japanese guidelines for the management of AP, a diagnosis of AP was es-tablished, with the severity determined to be mild at hospital admission. Thereafter, abdominal pain and diarrhea became mild by treatment only with bowel rest achieved by nothing per os (NPO), and her pan-creatic enzymes tended to improve. A fat-con-trolled diet was started on day five of hospitalization, after which the amount of fat was gradually increased. Magnetic resonance cholangiopancrea-tography (MRCP) showed unclear delineation of a suspected incomplete pancreas divisum. Her clini-cal symptoms subsided, and she was discharged on hospital day eight on a continued fat-controlled diet. Immediately after discharge, however, the patient experienced recurrent epigastric and back pain after each meal, and diarrhea occurred 2-3 times per day. On day three after discharge, vomiting, epigastric

Table 1.　Laboratory Results

Test		Admission	Re-Admission	3 months after discharge
WBC		5,800	4,120	6,200 /μL
	Stab	3.0	3.5	%
	Seg	64.0	57.5	69.0 %
	Lymph	23.0	26.5	23.5 %
	Baso	0.5	2.0	1.0 %
	Eosino	4.0	2.0	1.0 %
	Mono	5.5	8.5	5.0 %
Hb		13.4	13.3	12.0 g/dL
Plt		501	368	399 $\times10^3$/μL
Na		139	152	140 mEq/L
K		4.0	4.6	3.8 mEq/L
Cl		102	103	105 mEq/L
Ca		9.2	9.9	9.6 mg/dL
Alb		3.4	3.5	3.8 mg/dl
T-Bil		0.33	0.48	0.51 mg/dL
AST		15	13	18 IU/L
ALT		12	8	13 IU/L
BUN		8	7	12 mg/dL
Cre		0.46	0.42	0.55 mg/dL
Amylase		309	521	134 U/L
Lipase		811	1649	103 U/L
CRP		1.08	2.46	0.06 mg/dL
IgG		1077		mg/dL
IgG4		21		mg/dL
Fecal calprotectin			>6,000	270 mg/kg
ANA		(−)		
FIT		(−)		

WBC : white blood cell, Hb : hemoglobin, Plt : platelet, Alb : albumin, T-Bil : total bilirubin, AST : aspartate aminotransferase, ALT : alanine, BUN : blood urea nitro-gen, Cre : creatinine, CRP : C-reactive protein transaminase, IgG : immunoglobulin G, ANA : antinuclear antibody, FIT : fecal immunochemical test.
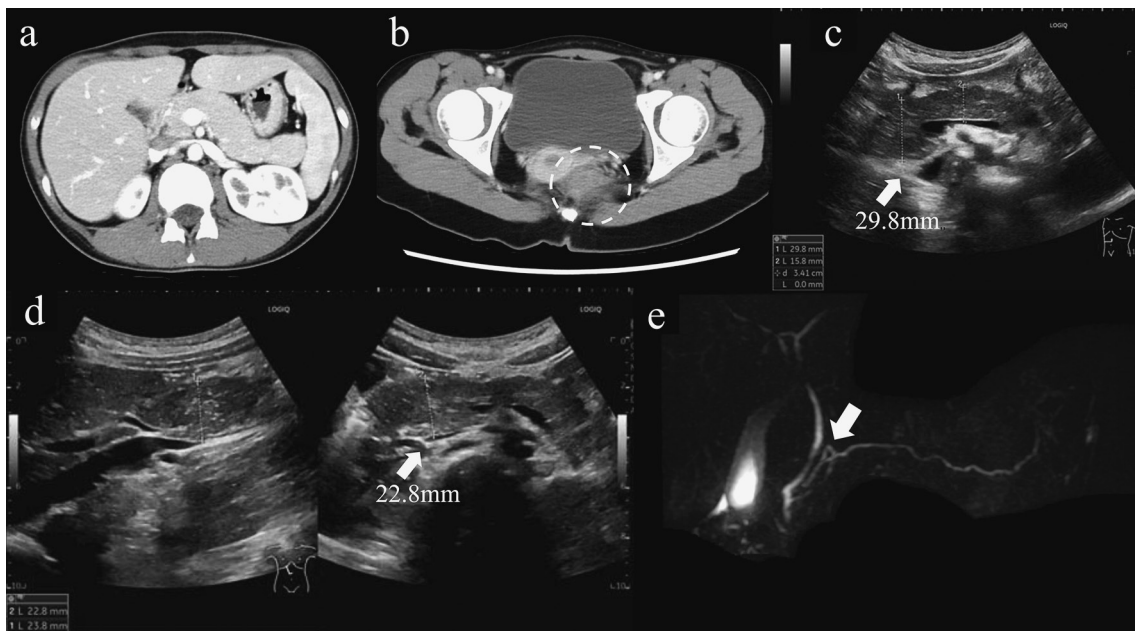
Fig. 1.   Computed tomographic (CT), abdominal echographic, and magnetic resonance (MR) cholangiopancreato-
graphic findings.
  (a) Contrast-enhanced CT scan of the abdomen on first admission.   The pancreas was of an age-appropriate
size and showed no contrast-enhanced area.   Inflammation did not extend beyond the pancreas.   (b) Contrast-
enhanced CT of the abdomen on first admission.   Edematous changes in the perirectal wall were observed (*white
dashed circle*).   (c) Abdominal echography on first admission.   The pancreatic head was enlarged to 29.8 mm
(*white arrow*).   (d) Abdominal echography after relief of symptoms.   The pancreatic head had shrunk to 22.8
mm, clearly smaller than in (c) (*white arrow*).   (e) Magnetic resonance cholangiopancreatography showed that
the dorsal pancreatic duct joins the main ventral pancreatic duct (*white arrow*).

pain, and back pain worsened, and the patient re-
turned to the hospital the next day.   Laboratory re-
sults showed lipase at 1649 U/L, amylase at 521 U/L,
CRP at 2.46 mg/dL, and fecal calprotectin >6,000
mg/kg (Table 1).   The patient was diagnosed as
having a relapse of AP and was readmitted to
hospital.   As before, clinical symptoms subsided af-
ter she was placed on NPO status.   After the symp-
toms became mild, abdominal echography showed
no enlargement of the pancreatic head, and re-eval-
uation with MRCP showed delineation of the dorsal
pancreatic duct and a meandering ventral pancreatic
duct, which led to the diagnosis of incomplete pan-
creas divisum (Fig. 1d, e).   Thereafter, the patient
was started on a fat-controlled elemental diet, camo-
stat mesilate, and Sanactase.   Although there was
no relapse of symptoms after increasing the fat dose,
the pancreatic enzymes showed no tendency to de-
crease.

    The patient's high fecal calprotectin level and
edematous wall thickening on CT raised the possi-
bility that the IBD itself might have either coexisted
with or caused the AP.   Colonoscopy showed an ul-
cer on the lower lip of the ileocecal valve and defor-
mity due to scarring of a recurrent ulceration along

with circular shallow ulcers in the descending colon,
sigmoid colon, and rectum (Fig. 2a-c).   Upper gas-
trointestinal endoscopy revealed a bamboo sign from
the curvature of the stomach to the cardia (Fig. 2d),
but there was no gross lesion in the duodenum.
Histological examination revealed noncaseating
granulomas in the colon, stomach, and duodenum
(Fig. 2e, f).   Magnetic resonance enterography
showed no abnormal dilation or stricture within the
small intestine on hospital day 30.   Thus, the pa-
tient met Japanese diagnostic criteria for CD and
was diagnosed as having CD of mild-to-moderate
activity.   Prednisolone was administered with an in-
duction dose of 20 mg.   Her pancreatic enzymes
improved, and she was discharged on hospital day
43.   The prednisolone was tapered, a 5-ASA drug
was introduced without symptom relapse, and her
symptoms remained controlled.   At 3 months from
discharge, her abnormal pancreatic enzyme levels
showed improvement (Table 1).

Discussion

    We encountered a case of pediatric AP with in-
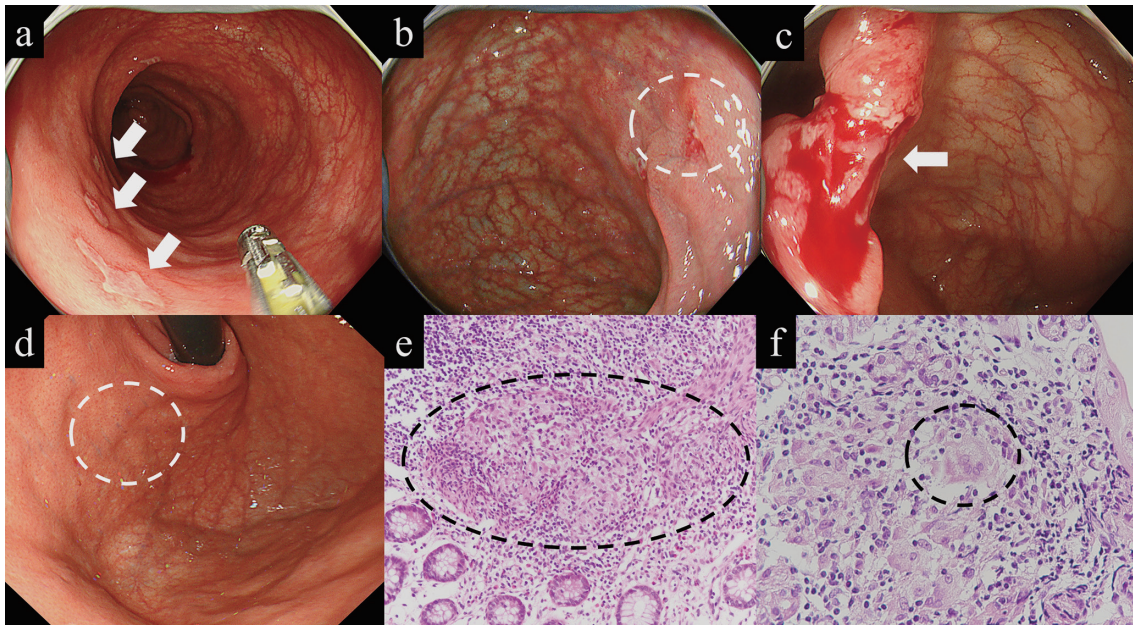complete pancreas divisum and presymptomatic or

Fig. 2. Colonoscopy and pathological findings.
 (a) Colonoscopy. Circular shallow ulcers are scattered over the sigmoid colon (*white arrow*s). (b) Colonoscopy. Circular shallow ulceration of the descending colon (*white dashed circle*). (c) Colonoscopy. Ulceration and deformity due to scarring suspected to be from recurrent ulceration of the inferior lip of the ileocecal valve (*white arrow*). (d) Upper gastrointestinal endoscopy. A bamboo sign is present from the curvature of the stomach to the cardia (*white dashed circle*). (e) Pathological findings from the colon (H & E stain, ×200). The histopathological image depicts noncaseating granulomas (*black dashed circle*). (f) Pathological findings from the stomach (H & E stain, ×400). The histopathological image similarly depicts noncaseating granulomas (*black dashed circle*).

mild CD. Although the diagnosis of presymptomatic or mild CD is challenging, as pediatricians, we should consider the coexistence of IBD in pediatric AP. Fecal calprotectin measurement offers the potential to diagnose and evaluate complications of IBD.

Pediatric AP results from multiple factors such as genetic causes, pancreatic anomalies, gallstones and microlithiasis, medications, and additional risk factors of trauma, metabolic disorders, infections, systemic disease, and autoimmune pancreatitis[4]. Our patient's pancreatic anomaly had the potential to cause development of AP. A large study found a 1.5- to 4-fold increased risk of AP in patients with IBD compared with healthy controls, although the pathophysiology for this remains unknown[5-8]. In the present case, the exact relationship between her AP and CD remained unclear.

Calprotectin is a calcium-binding protein component of neutrophils and is released in the presence of inflammation. Calprotectin in stool correlates with neutrophil infiltration in the intestinal tract[9]. Fecal calprotectin is a useful tool with which to diagnose IBD along with endoscopic evaluation of disease activity in IBD[3,10]. In general, the gold standard for the diagnosis and evaluation of CD is endoscopy and histopathology, but these are invasive, expensive tests, and general anesthesia is sometimes required in children, making such tests not easily performed[3]. As most instances of CD gradually progress with the appearance of clinical symptoms, diagnosing CD in the preclinical stage can be challenging. In fact, it was difficult to determine the indication for endoscopy in our patient because her symptoms could be explained as the course of AP due to incomplete pancreas divisum. The diagnostic utility of fecal calprotectin showed excellent negative predictive value in ruling out IBD in symptomatic undiagnosed patients[11]. While only scattered data are present on optimal calprotectin threshold values in pediatric patients, the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition has reported a level of >250 mg/kg as being predictive of mucosal inflammation[12]. High fecal calprotectin levels and abnormal CT findings of edematous changes in the perirectal wall suggest the possibility of coexisting IBD. Because of the difficulty in diagnosing CD in the asymptomatic or early clinical stage, fecal calprotectin measurement in the screening of patients suspected of having IBD offers the potential to establish the coexistence of IBD accurately and quickly.

Informed consent

Written informed consent was obtained from the patient's parents for publication of this case report.

Conflict of interest

The authors declare no conflict of interest.

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Author contributions

S.I. wrote the manuscript. K.I., K.Z., Y.Y., Y.S., and Y.K. supervised the manuscript. All authors read and approved the final manuscript.

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