

[ CASE REPORT ]

## Pancreatic Exocrine Insufficiency in Intraductal Papillary Mucinous Carcinoma Presenting with Leg Edema Treated with Pancreatic Exocrine Replacement Therapy

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### Abstract:

An 89-year-old woman underwent examinations for leg edema. Blood tests indicated low nutrition and low pancreatic enzymes, and a stool examination indicated fatty stool. Computed tomography showed pleural effusion, ascites, and cystic lesions in the pancreatic head and mural nodules within the cysts. Pancreatic juice cytology revealed adenocarcinoma. The diagnosis was pancreatic exocrine insufficiency caused by intraductal papillary mucinous carcinoma. The patient did not wish to undergo surgery. Therefore, diuretics, component nutrients, and pancreatic exocrine replacement therapy using pancrelipase were initiated. After starting treatment, her leg edema, pleural effusion, and ascites disappeared, and her activities of daily living improved markedly.

**Key words:** intraductal papillary mucinous carcinoma, intraductal papillary mucinous neoplasm, pancreatic exocrine insufficiency, pancreatic cancer, leg edema, pancrelipase

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### Introduction

Intraductal papillary mucinous neoplasm (IPMN) is often found incidentally on ultrasonography or computed tomography (CT) performed during the follow-up of other diseases. There are often no symptoms when IPMN is detected (1). Among patients with symptomatic IPMN, abdominal pain is reported in 69%, weight loss in 38%, pancreatitis in 36%, back pain in 18%, jaundice in 18%, palpable mass in 5%, and postprandial lethargy in 4% (2).

Patients with pancreatic diseases associated with pancreatic duct stenosis or obstruction may have pancreatic exocrine insufficiency (PEI). Edema, ascites, pleural effusion, decreased urine volume, and decreased blood pressure may occur because of malabsorption in patients with PEI. PEI treatment involves treating the causative disease and performing pancreatic exocrine replacement therapy (PERT). Although PEI has been associated with chronic pancreatitis,

pancreatic resection, and pancreatic cancer, there are few reports of PEI associated with IPMN (3, 4).

We herein report an 89-year-old woman who presented to our hospital with a complaint of leg edema and received a diagnosis of PEI associated with intraductal papillary mucinous carcinoma (IPMC).

### Case Report

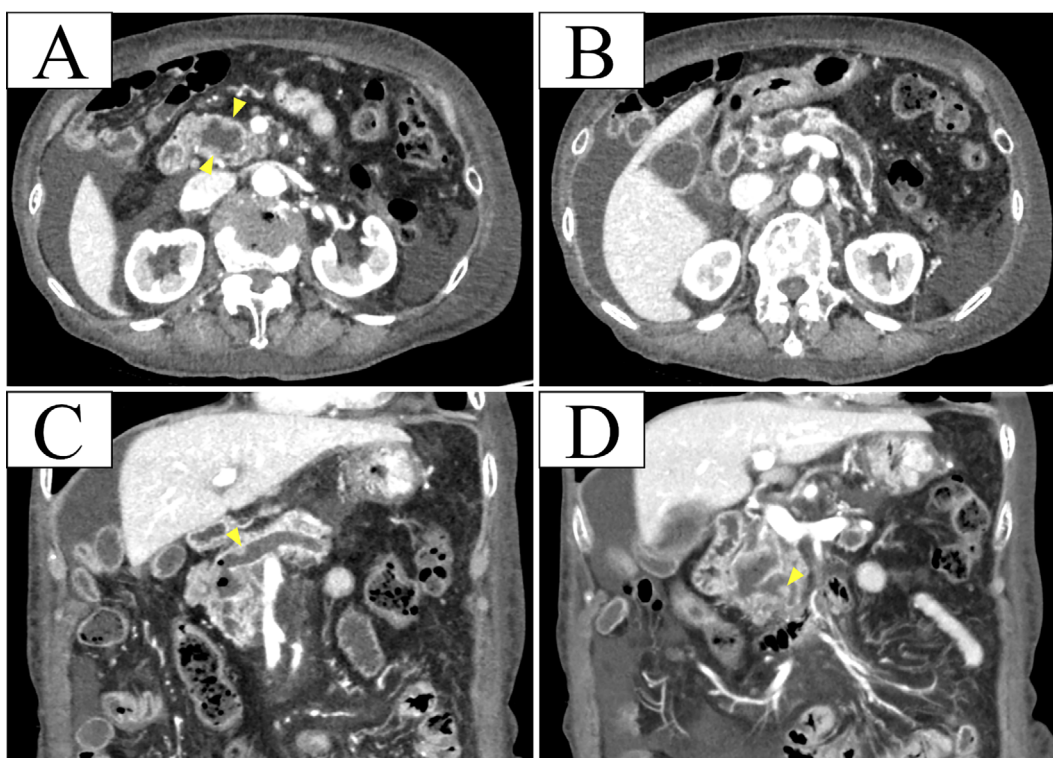
An 89-year-old woman had previously visited a doctor with a chief complaint of severe leg edema for the past 6 months. She did not have diarrhea and had bowel movements once a day but was concerned because her stool had a greasy consistency.

CT showed pleural effusion, ascites, and a mass on the pancreatic head. The patient was referred to our hospital under suspicion of pancreatic cancer and cancerous peritonitis. She had a history of type 2 diabetes mellitus and lumbar compression fracture. At the time of her visit, her fasting

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**Figure 1.** Computed tomography (CT) shows that the main pancreatic duct at the pancreatic head is cystically dilated without obstruction (A). The diameter of the main pancreatic duct is 32 mm. The main pancreatic duct is not obstructed, and the pancreatic parenchyma is thinning (B, C). The nodules within the pancreatic duct are stained with contrast (yellow arrowhead) (A, C, D). The branched pancreatic duct at the pancreatic head is also dilated, and the nodule in the branched pancreatic duct (denoted by the yellow arrowhead in picture D), is 8 mm with contrast effect. The branch duct at the pancreatic head is 9 mm in diameter.

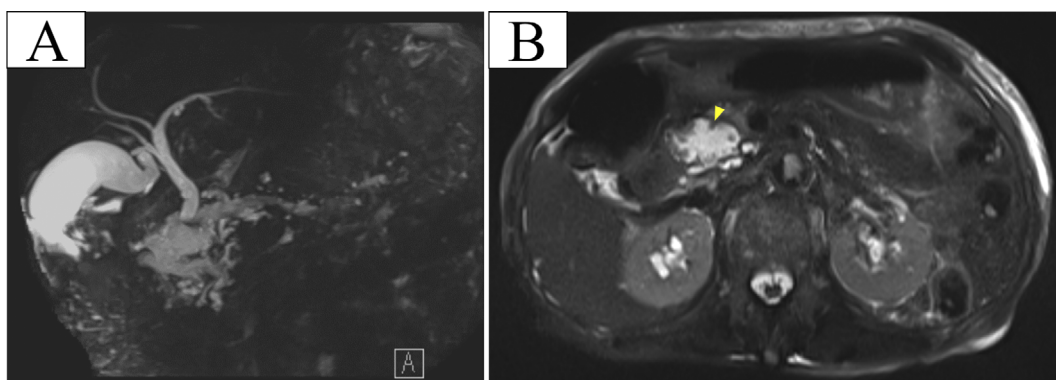
blood glucose was 95 mg/dL, HbA1c was 6.4%, and medical therapy was not required for diabetes. She had no history of drinking or smoking.

At the time of the visit, the patient's height was 150 cm, weight was 40 kg, and body mass index was 17.7, and bilateral leg indentation edema was prominent. Blood tests showed normal liver, kidney, and thyroid functions, but an assessment of the nutritional system showed hypoalbuminemia (1.5 g/dL) and low total cholesterol (87 mg/dL). The levels of serum pancreatic enzymes were significantly decreased: pancreatic amylase, 2 U/L and lipase, 9 U/L. Tumor markers showed no elevation: carcinoembryonic antigen, 3.0 ng/mL; carbohydrate antigen 19-9, 8 U/mL; elastase-1, <80 ng/dL. A urinalysis did not detect any urinary protein. A stool examination showed 3+ fecal fat globules (stool was stained with Sudan III, and more than 20 adipocytes were detected in the high-power field).

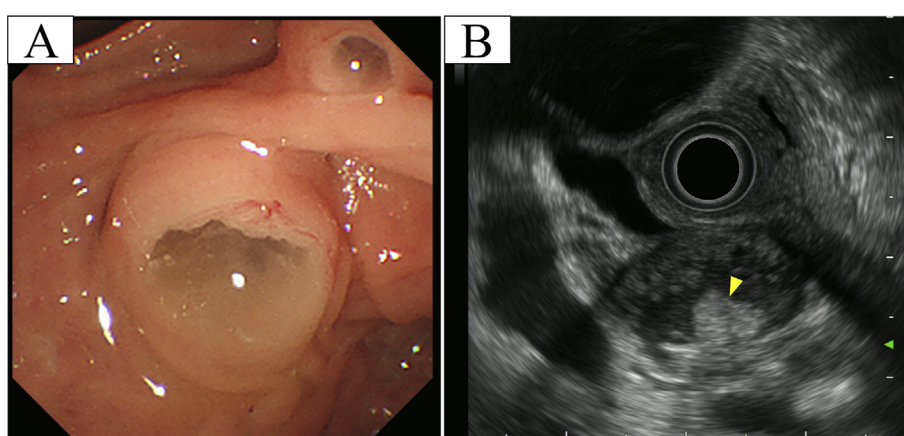
No obvious cardiac enlargement was observed on chest radiography. Dynamic CT showed a cystic lesion with markedly dilated main pancreatic duct (MPD) at the head of the pancreas, a mural nodule with contrast enhancement, and an atrophic pancreatic parenchyma (Fig. 1A-D). No stenosis or irregularity in the MPD, suggesting pancreatic ductal cancer, was noted, nor were there any obvious disseminated nodules in the abdominal cavity. Magnetic resonance imaging (MRI)

showed diffuse pancreatic duct dilatation without obstruction along with a nodular defect in the MPD, and the branch ducts of the pancreatic head were dilated (Fig. 2). Endoscopy showed that both the major and minor duodenal papillae were dilated with a fish-eye-like appearance and were discharging mucus (Fig. 3A). Endoscopic ultrasonography revealed a nodule in the lumen of the MPD at the head of the pancreas (Fig. 3B). A pancreatic duct biopsy revealed IPMN, and pancreatic juice cytology showed adenocarcinoma. Thus, the pancreatic mass was diagnosed as IPMC. The cause of the leg edema was suspected to be malabsorption syndrome due to PEI associated with IPMC.

We recommended surgery for IPMC, but the patient did not want to undergo surgery and instead wished to be monitored through follow-up due to her advanced age. During hospitalization, the patient received supplemental fluids, PERT (pancrelipase 1,800 mg/day), peroral diuretics (furosemide 20 mg/day), and oral component nutrition (elemental diet 300 kcal/day). Her albumin level gradually increased, and her activities of daily living (ADLs) improved markedly. Four months after the start of treatment, the albumin level had improved (3.6 g/dL), fat globules in the stool were 1+ (approximately 4-5 adipocytes detected per high-power field), and the leg edema and ascites had completely disappeared (Fig. 4A-D, 5).



**Figure 2.** Magnetic resonance imaging (MRI) shows diffuse pancreatic duct dilatation without pancreatic duct obstruction, and the branch ducts of the pancreatic head are dilated (A). The horizontal section shows deflection by nodules in the highly dilated main pancreatic duct (yellow arrowhead) (B).



**Figure 3.** Endoscopy reveals that both the major and minor duodenal papillae are dilated with a fish-eye-like appearance and discharging mucus (A), and endoscopic ultrasonography (EUS) reveals a nodule in the highly dilated main pancreatic duct at the pancreatic head (yellow arrowhead). The nodule shown is approximately 6 mm in length. (B).

## Discussion

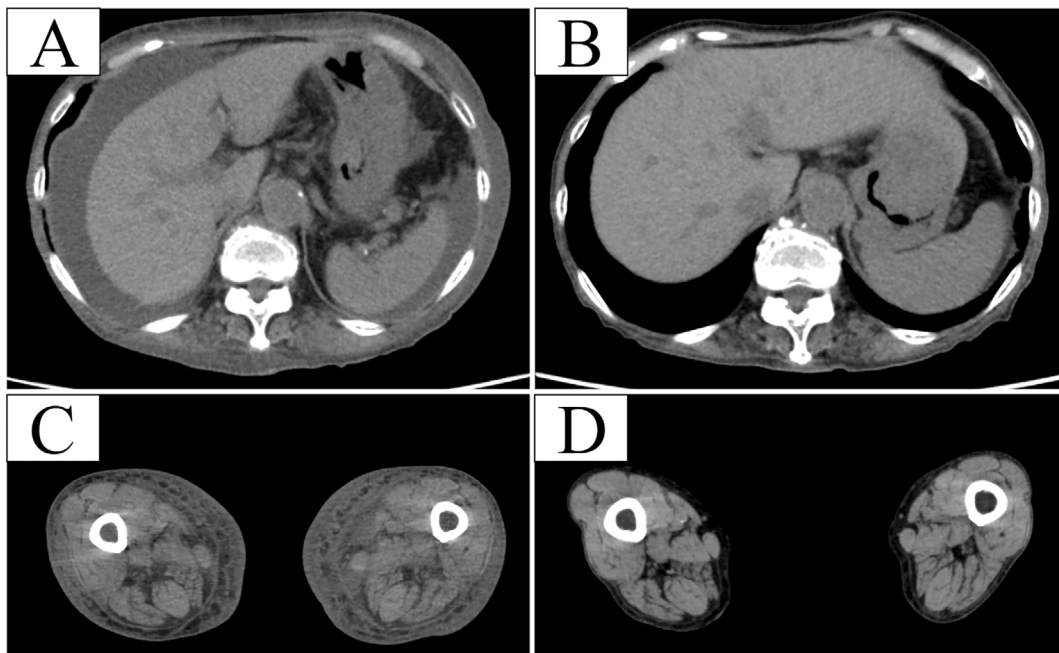
PEI has been reportedly associated with chronic pancreatitis, pancreatic resection, and pancreatic cancer. It is suggested to be caused by obstruction of the main pancreatic duct by pancreatic cancer or chronic pancreatitis. However, there are few reports of PEI associated with IPMN (3, 4). When mucus retention and pancreatic juice stasis occur due to the presence of IPMN, as in the present case, pancreatic atrophy may occur over time, leading to malabsorption syndrome caused by PEI (5). Therefore, as a differential disease of leg edema, malabsorption syndrome due to PEI should be considered, and the presence of pancreatic disease should be investigated.

PEI is generally diagnosed using the N-benzoyl-L-tyrosyl-p-aminobenzoic acid test while measuring the level of fecal elastase-1 and chymotrypsin (6-8). However, in the present case, the diagnosis was made comprehensively based on the decrease in nutritional parameters, such as serum total protein, albumin, and total cholesterol; low levels of pancreatic

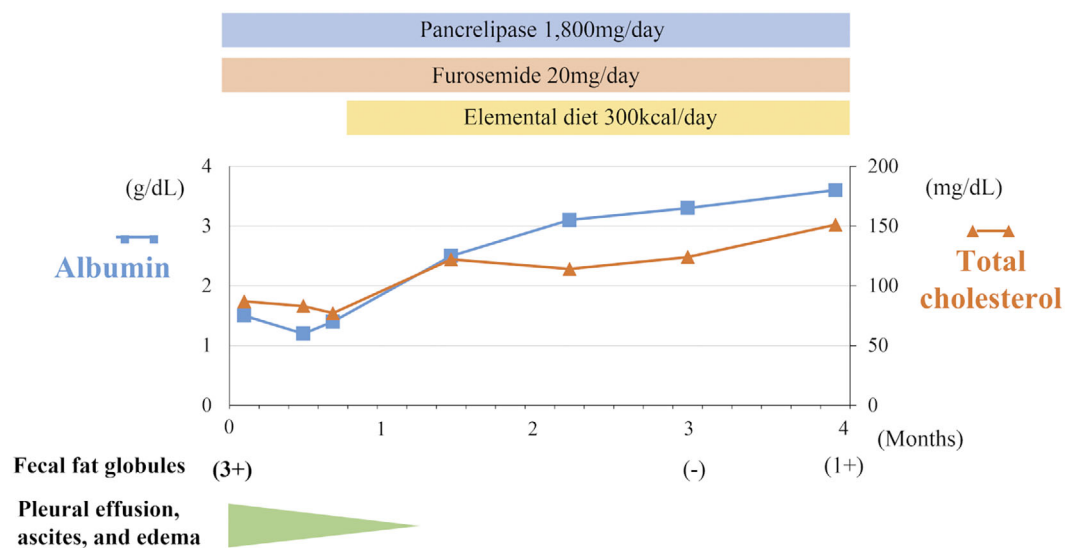
enzymes, such as lipase and pancreatic type amylase; detection of fatty stools; and severe atrophy of the pancreatic parenchyma observed with CT.

Along with causing symptoms of indigestion, PEI leads to osteoporosis, low traumatic fracture, sarcopenia, and increased mortality. This suggests that when PEI is diagnosed, PERT can directly improve patients' ADLs, quality of life (QOL), and survival rate (9, 10). In the present case, pancrelipase was effective at improving the PEI because the serum albumin level and edema improved markedly, and the greasiness in the stool decreased on administering pancrelipase as PERT along with diuretics and component nutrition.

With respect to the prognosis of IPMNs, when high-risk stigmata (HRS) (MPD diameter  $\geq 10$  mm, enhancing mural nodule  $\geq 5$  mm, and cystic lesion at the head of the pancreas with obstructive jaundice), considered an indication for surgery, are present, the 5-year survival rate with follow-up is 74%, and the disease-specific survival rate is 91% (11). This is a better prognosis than that in cases of pancreatic cancer. The present patient met the HRS criteria and was deemed eligible for surgery. However, she did not wish to undergo



**Figure 4.** Four months after the start of pancrelipase, diuretics, and component nutrition administration, the severity of the ascites and leg edema are significantly improved (B, D) compared to before treatment (A, C).



**Figure 5.** With pancreatic exocrine replacement therapy and the administration of diuretics and component nutrition, the patient's blood albumin and total cholesterol levels are improved. Her fecal adipocyte level is also improved, changing from 3+ at the beginning of treatment to 1+ after four months of treatment.

surgery because of her advanced age. In addition, it has been reported that 56% of cancers of the pancreatic head and 32% of cancers of the pancreatic body and tail are associated with PEI. Furthermore, previous studies showed that the survival time was prolonged to 189 days in the group treated with PERT and 95 days in the group not treated with replacement therapy for unresectable pancreatic cancer (12, 13). These reports suggest that it is important to maintain the long-term improvement of the ADLs/QOL using PERT in patients with PEI caused by IPMN as well as

pancreatic cancer.

The authors state that they have no Conflict of Interest (COI).

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