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CASE REPORT

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Exocrine Pancreatic Insufficiency: Postoperative Complication Emerging Decades after Surgery?

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ABSTRACT

Exocrine pancreatic insufficiency (EPI) arises from a deficiency in pancreatic enzymes, leading to malabsorption and varied symptoms such as gastrointestinal discomfort, weight loss and steatorrhea. Though EPI commonly follows chronic pancreatitis or pancreatic surgery, its delayed onset is rarely discussed. We report a unique case of EPI manifesting 29 years after pancreaticoduodenectomy. A 71-year-old female, who underwent pancreaticoduodenectomy for carcinoma in 1992, presented with fatigue, weight loss, edema, diarrhea and paresthesias. Physical examination revealed mucocutaneous pallor, ascites, lower limb edema and brittle hair. Laboratory results indicated anemia, hypoproteinemia, vitamin deficiencies and severe fecal elastase reduction. After excluding other possible etiologies such as malignancy, autoimmune and infectious, the diagnosis of EPI was established. Treatment included enzyme replacement, vitamin supplementation and diuretics, leading to symptom resolution and normalization of laboratory parameters over a 12-month period. This case underscores the prolonged latency of post-surgical EPI, presenting diagnostic challenges. Exocrine pancreatic insufficiency can severely impair nutrient absorption, causing significant morbidity. In our patient, timely enzyme supplementation and nutritional management reversed the symptoms and deficiencies. The 29-year delay in symptom onset is among the longest documented, emphasizing the need for long-term vigilance in post-pancreatic surgery patients.

Keywords: exocrine pancreatic insufficiency, steatorrhea, hypoalbuminemia, malabsorption, enzyme replacement therapy.

INTRODUCTION

Exocrine pancreatic insufficiency (EPI) is a complex condition stemming from decreased production or activity of pancreatic enzymes and/or bicarbonate. This deficiency often manifests in a spectrum of symptoms, ranging from subtle gastrointestinal discomfort to more pronounced issues such as weight loss, abdominal pain and steatorrhea, which can significantly impact an individual's quality of life (1, 2). In more severe cases, neurological deficits and bone disease may occur due to vitamin deficiencies (1, 3).

Exocrine pancreatic insufficiency is also linked to a higher likelihood of death among individuals with chronic pancreatitis (CP) because it can contribute to complications such as infections, cardiovascular disease and malignancy (4, 5).

The prevalence of EPI in the general population remains unknown. However, it is primarily

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linked with advanced stages of chronic pancreatitis, where a pathological process occurs in which pancreatic parenchyma is replaced by fibrotic tissue due to a repeated inflammatory insult (6, 7).

On the other hand, post-surgical exocrine pancreatic insufficiency is a common complication. Its prevalence varies with the type of intervention. The Whipple technique is associated with higher prevalence, afflicting up to 95% of patients (8).

Despite being a well-documented surgical complication, the timeframe when symptoms arise is yet poorly understood and sparsely recorded in the literature.

We present the case of a patient whose diagnosis of EPI emerged 29 years after duodenopancreatectomy, prompting a reassessment of our understanding of this condition's latent manifestations. ❑

CASE REPORT

A 71-year-old woman, who underwent pancreaticoduodenectomy for pancreatic carcinoma in 1992, with no other relevant history, presented to the Emergency Department with ongoing weight loss, mucocutaneous pallor, dyspnea, peripheral edema, progressive fatigue with minimal exertion and lower limb paresthesias. These symptoms had been worsening over the past month. Additionally, she also experienced occasional diarrhea.

The patient's physical examination revealed brittle hair and nails, xerophthalmia, reduced breathing sounds in both lungs, ascites, edema of the lower limbs extending from the groin to the malleolar region bilaterally with positive Godet sign and steatorrhea. Her neurological exam revealed no deficits asides from complaints of paresthesias on both legs. Her vitals were unremarkable aside from a peripheral oxygen saturation of 90%.

The laboratory data (Table 1) revealed several abnormalities, including normocytic and normochromic anemia, hypoproteinemia with hypoalbuminemia and hypolipidemia, as well as vitamin A, D and E deficiencies. Her stool sample showed a significant decrease in fecal elastase (confirmed in a second sample).

A computed tomography (CT) scan of the chest, abdomen and pelvis (Figure 1) revealed bilateral pleural effusion with passive collapse of adjacent basal segments as well as a large amount of ascites in all peritoneal recesses, with no signs of malignancy or other abnormalities.

A paracentesis was performed and did not reveal any concerning findings. Additionally, thoracocentesis findings were compatible with a transudate. To exclude serositis of autoimmune etiology, an autoimmune screening panel was ordered, which returned normal results.

Parameter	Value	Normal range	Parameter	Value	Normal range
WBC	4.90x10^9/L	4.50–11.50	**T-bil**	1.4 mg/dL	0.2–1.1
RBC	2.86x10^{12}/L	4.00–5.40	**CRP**	5.1 mg/dL	0.00–0.50
HgB	7.6 g/dL	12–15	**Vitamin A**	3 µg/dL	30–80
PLT	159 x10^9/L	150–450	**Vitamin B$_{12}$**	300 pg/mL	179–1130
Glu	87 mg/dL	74–106	**Vitamin D$_3$**	16.6 ng/mL	30.0–95.0
Creat	1.6 mg/dL	0.5–1.2	**Vitamin E**	135 µg/dL	500–1800
TSP	4.2 g/dL	6.6–8.7	**Vitamin K**	0.71 µg/dL	0.10–2.12
Alb	1.8 g/dL	3.5–5.0	**Folic acid**	7.2 ng/mL	1.0–20.0
ALT	64 UI/L	3–31	**TC**	52.0 mg/dL	150–200
AST	38 UI/L	3–31	**TSH**	4.16 mUI/L	0.55–4.78
ALP	93 UI/L	25–100	**NT-proBNP**	222 pg/mL	0.00–125.00
GGT	27 UI/L	0–38	**tTG IgA**	0.60 AU/mL	0.00–10.00
LDH	412 UI/L	120–246	**IgA**	325 mg/dL	40–350
AMY	2 UI/L	13–53	**UTP**	7.3 mg/dL	1–14
Fecal elastase	1st sample	<10 µg/g	Severe insufficiency < 100		
	2nd sample	>15 µg/g			

TABLE 1. Laboratory data on admission

WBC=white blood count; RBC=red blood count; HgB=hemoglobulin; PLT=platelet count; Glu=glucose; Creat=creatinine; TSP=total serum proteins; Alb=albumin; ALT=alanine transaminase; AST=aspartate aminotransferase; ALP=alkaline phosphatase; GGT=gamma-glutamyl transpeptidase; LDH=lactate dehydrogenase; AMY=amylase; T-bil=total bilirubin; CRP=C-reactive protein; TC=total cholesterol; TSH=thyroid-stimulating hormone; NT-proBNP=N-terminal prohormone of brain natriuretic peptide; tTg IgA-tissue transglutaminase IgA; IgA=immunoglobulin A; UTP=urinary total protein.

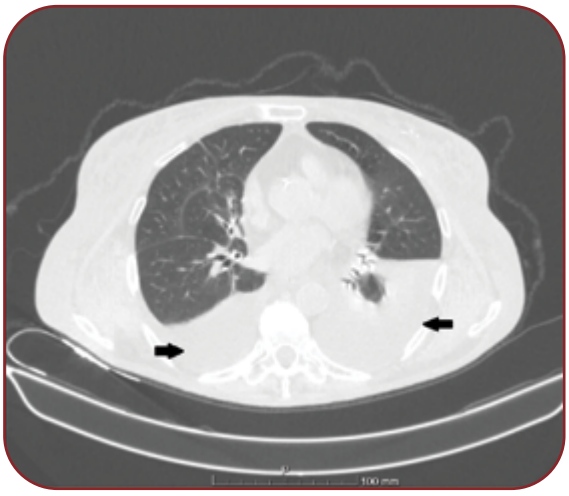

FIGURE 1. Computed tomography (CT) scan of the chest, with the black arrows showing the bilateral effusion

A transthoracic cardiac ultrasound showed mild left ventricular wall hypertrophy but normal biventricular function.

A 24-hour urine collection ruled out nephrotic syndrome. Upper gastrointestinal endoscopy showed no lesions or relevant alterations other than subtotal gastrectomy with a Billroth II reconstruction. Jejunal biopsies ruled out Celiac disease.

After excluding other potential causes, such as infections, hypothyroidism, congestive heart failure or liver disease and considering the personal history, analytical evidence of malabsorption and the reduced fecal elastase levels the diagnosis of exocrine pancreatic insufficiency was established.

In a primary phase, treatment involved loop diuretics and intravenous albumin replacement to manage fluid buildup, as well as supplementation of pancreatic enzymes with pancrelipase. We initiated treatment with a daily dose of 1 800 mg. Subsequently, a specialized diet rich in fat-soluble vitamins was developed in collaboration with the Nutrition and Dietetics Department to address nutritional deficiencies.

The patient's nutritional condition steadily improved, leading to the resolution of steatorrhea and eventual weight gain. Additionally, her laboratory test results returned to normal, including her albumin levels, which remained within the healthy range. The patient has been symptom-free for over 12 months. ❑

DISCUSSION

Exocrine pancreatic insufficiency can manifest through a myriad of nonspecific gastrointestinal symptoms such as chronic diarrhea, persistent weight loss and recurrent episodes of abdominal pain (9). This complexity was evident in the case of our 71-year-old patient who presented with a constellation of symptoms suggestive of EPI nearly three decades after pancreaticoduodenectomy.

Despite being acknowledged as a well-documented surgical complication, the literature surrounding the temporal evolution of symptoms post-intervention onset remains surprisingly sparse, leaving a notable gap in our understanding of the condition (10). The prolonged latency period between surgery and symptom onset underscores the diagnostic challenge posed by this condition.

In more severe and protracted cases of EPI, characterized by lipase levels plummeting to less than 10% of normal values, patients may experience profound alterations in nutrient absorption, resulting in debilitating nutritional deficiencies, extensive bone demineralization and a notable deficit of essential fat-soluble vitamins (9, 11). Moreover, the ramifications of malabsorption predispose individuals to an array of adverse health outcomes, including an elevated risk of cardiovascular complications, heightened susceptibility to infectious pathogens and an increased likelihood of both short-term and long-term morbidity and mortality (5).

Our patient exhibited signs of debilitating nutritional deficiencies, including normocytic and normochromic anemia, hypoalbuminemia and hypolipidemia, indicative of impaired nutrient uptake. This associated with severe decreased fecal elastase levels corroborated the diagnosis of EPI. Additionally, our patient showed signs of neurological impairment in the form of paresthesias, as well as brittle hair and nails, consistent with vitamin deficiency that completely resolved after supplementation with pancreatic enzymes and appropriate diet.

Imaging studies revealed additional complications associated with EPI. A CT scan identified bilateral pleural effusion and ascites, suggestive of fluid accumulation secondary to diminished oncotic pressure, consequence of malabsorption. A near normal transthoracic ultrasound as well as an only slightly elevated NT-proBNP assisted in the exclusion of congestive heart failure. A urine analysis ruled out the presence of proteinuria thus eliminating the hypothesis of nephrotic syndrome. No manifestations of malignancy were found in both imaging and endoscopic investigations.

Other possible etiologies such as autoimmune involvement, Celiac disease, or liver disfunction were also excluded through the blood work. There were no signs of infection.

Treatment strategies aimed to address both the underlying pancreatic insufficiency and associated nutritional deficiencies. Pancreatic enzyme supplementation was initiated to ensure adequate digestion and absorption of nutrients, while a specialized diet rich in fat-soluble vitamins was prescribed to replenish depleted stores. Additionally, loop diuretics and intravenous albumin replacement were utilized to manage fluid overload and correct hypoalbuminemia.

Remarkably, the patient under review remained largely asymptomatic for nearly three decades after the initial surgical procedure, thereby presenting an intriguing diagnostic puzzle for the medical team.

The patient's response to treatment was promising, with resolution of symptoms, normalization of laboratory parameters, and improved nutritional status observed over time. This underscores the importance of early recognition and intervention in managing EPI-associated complications and improving patient outcomes. ❑

CONCLUSION

This case highlights the implications of exocrine pancreatic insufficiency that may arise even decades after surgical intervention, underscoring the need for vigilance in long-term postoperative follow-ups.

Our findings emphasize the multifaceted nature of EPI, ranging from gastrointestinal disturbances to debilitating nutritional deficiencies and neurological impairments. This underlines the importance of early recognition and targeted intervention in mitigating the morbidity associated with EPI. In our case, symptom resolution was achieved with the supplementation of pancreatic enzymes and nutritional support.

Overall, this case reinforces the diagnostic challenges of EPI, particularly in the context of delayed symptom development. To the best of our knowledge, this represents the most chronologically delayed onset ever documented in the medical literature, thus reinforcing the importance of continued vigilance in long-term patient care. ❑

Conflicts of interest: none declared.

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Statement of human and animal rights: Authors certificate that all procedures and experiments done for this work meet the ethical standards in the Helsinki Declaration of 1975, as revised in 2000 (5), as well as the national law.

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