CASE REPORT

Exocrine pancreatic insufficiency following bariatric surgery: unveiling alternative aetiology—case report and short review

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Bariatric surgery (BS) is currently the most effective treatment for severe obesity, requiring ongoing multidisciplinary follow-up to ensure proper progress and nutrition post-procedure. Despite its favourable safety profile, it is not exempt from complications, one of which being exocrine pancreatic insufficiency (EPI). The underlying pathophysiological mechanisms of EPI after BS are multifactorial, including poorly synchronized pancreatic enzyme secretion with the passage of nutrients (pancreaticocibal or postcibal asynchrony), insufficient pancreatic stimulation and bacterial overgrowth. We conducted a short literature review of the topic through a case of a patient who underwent BS in our centre and subsequently developed EPI and severe malnutrition. EPI initially was attributed to the surgery, but after a comprehensive evaluation, an unexpected cause was revealed.

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CASE DESCRIPTION

A 27-year-old woman, an active smoker with severe obesity (BMI: 42 kg/m^2) and recent cholecystectomy due to recurrent abdominal pain and biliary sludge, was referred to our obesity unit for bariatric surgery (BS). Elective gastric bypass (GBP) was performed successfully but persistent abdominal pain ensued.

Two months later she was admitted for acute pancreatitis with mild pancreatic edema along with elevated pancreatic enzymes, yet magnetic resonance cholangiopancreatography revealed no underlying cause. Following discharge, sporadic abdominal pain persisted.

One year after BS, she was admitted due to steatorrhea and excessive weight loss (WL) (40 kg/Total weight loss: 37.7%). Computed tomography (CT) showed pancreatic atrophy (Fig. 1B). Infectious diarrhoea and celiac disease were ruled out. Faecal elastase (FE1) was undetectable, and secretin-enhanced magnetic resonance cholangiopancreatography(S-MRCP) confirmed EPI diagnosis. Introduction of pancreatic enzyme replacement therapy (PERT) initially improved abdominal symptoms, but the patient discontinued the treatment because tolerance.

Despite persistent WL, she refused repeatedly hospital admission for nutritional support. After 18 months of BS, the patient was admitted with severe malnutrition, septic shock and multiorgan failure because of bacterial translocation and distal intestinal obstruction syndrome (DIOS), requiring multiple amputations due to finger ischemia. She remained hospitalized for three months, receiving total parenteral nutrition (PN). A percutaneous gastrostomy was placed into the bypassed stomach to wean the patient from PN through combined oral and enteral nutritional support. Genetic study was performed to explore alternative causes of EPI. Two pathogenic CFTR mutations (F508del [c.1521_1523delCTT] and G126D [c.337 G > A]) were identified, and a pathological chloride sweet test result (Cl^-: 65 mmol/L) confirmed the diagnosis of cystic fibrosis (CF). CFTR modulator therapy elexacaftor/tezacaftor/ivacaftor-Kaftrio® (Dublin, Ireland) was initiated, PERT tolerance improved and the gastrostomy tube could be removed after a year of the CF diagnosis. Despite recommendations, the patient continued smoking.

DISCUSSION

EPI is characterized by maldigestion and impaired nutrient absorption, caused by inadequate pancreatic production, activity and/or limited enzyme activation into the gut [1]. It is worth mentioning that tobacco worsens pancreatic function even without prior disease [2]. Abdominal complaints after BS are frequent in the long-term, EPI being one significant cause. Even when the mechanisms behind EPI in BS are not fully understood, they are most likely to be secondary to postcibal pancreatic asynchrony when neurohormonal signalling fails to coordinate [1, 3].

The prevalence of EPI after BS isn't well-established. In a cohort of 188 patients followed for 2 years after GBP, the prevalence was 31% [4]. Other studies reported higher rates after GBP compared to sleeve gastrectomy (SG) [3, 5]. The disruption of enteric homeostasis may partially explain the higher rates after GBP. Nonetheless, gastrointestinal disturbances in postprandial

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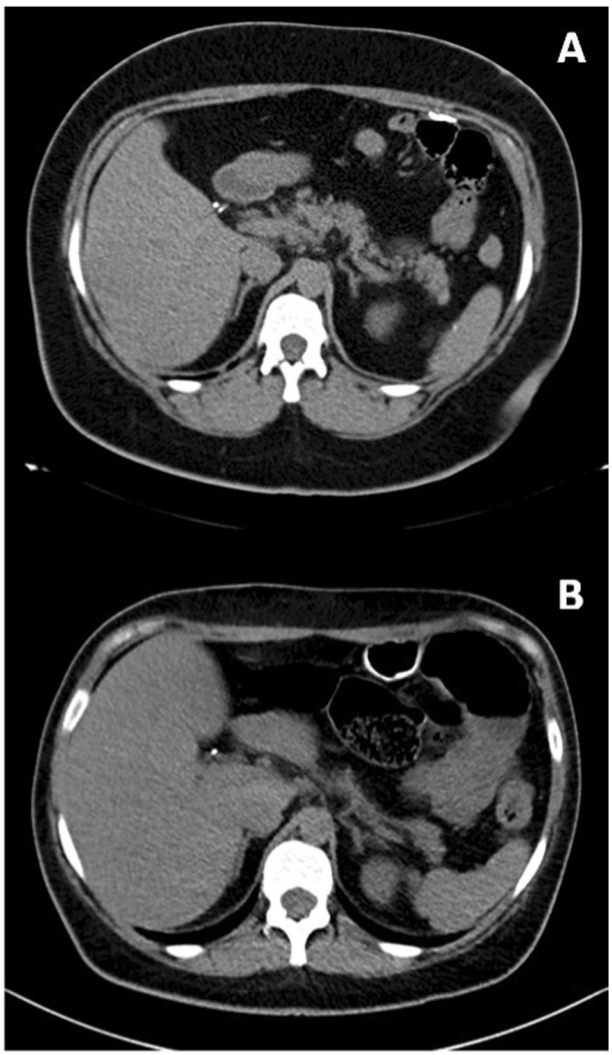

Fig. 1 Abdominal Computed Tomography. A 2 months after bariatric surgery. **B** 8 months after bariatric surgery.

parasympathetic neural stimulation after SG might worsen pancreatic function, potentially also causing EPI [1, 3, 5].

Typical clinical manifestations include fatty stool, weight loss and lipid malabsorption, occurring when pancreatic lipase secretion or action decreases by <10%. In mild to moderate cases a range of symptoms can be observed, from noor flatulence [3, 6].

The gold standard for diagnosing steatorrhea is the coefficient of fat absorption (CFA), but it has limited specificity and low sensitivity in mild and moderate cases for EPI diagnosis [6]. FE1 is the simplest and most widely used test to diagnose EPI, showing a 100% sensitivity in severe cases and 54–75% in mild to moderate ones. Nonetheless, specificity of FE1 decreases following BS and there is very little evidence for using it as a screening tool after BS [3, 7]. The 13C-mixed triglyceride breath test (13C-MTG-BT) offers an alternative to FE1 but is not extensively available and it is not specific of EPI and has low sensitivity for mild cases [1, 8]. The S-MRCP provides insights into ductal morphological changes and offers semi-quantitative data on functional alterations. It is highly suitable morphological test for evaluating pancreatic exocrine function [6, 8].

CF is caused by mutations in the CFTR gene with 85% of patients presenting pancreatic insufficiency early in life. Severity and presence of EPI are linked to specific CFTR mutations. CF can also be diagnosed in adulthood in close to 15% of cases [7]. The CF population has seen an increase in overweight and obesity attributed to treatment advancements, implementation of CFTR modulator therapies, improved life expectancy and multifactorial factors akin to those affecting the general population [9, 10].

Achieving WL in CF patients with overweight or obesity can be challenging due to the delicate balance between its risks on lung function and the health benefits of maintaining a "normal" weight. In this context, the Australia and New Zealand CF Nutrition guidelines recommend a threshold of ≤27 kg/m² for CF patients [9].

We have only found one previously reported case of BS (SG) in a patient with cystic fibrosis (CF) who had F508del/3272–26A- > *G* genotype. In this case, the patient progressed with expected and sustained WL two years and a half after the surgery without CF worsening [10]. To our knowledge, our case is the first reported GBP in a patient with CF.

PERT is the cornerstone for EPI treatment. In bariatric patients, higher doses may be needed, and due to reduced acid secretion, open capsules improve absorption [3, 8]. Our patient's poor adherence to PERT resulted in noteworthy nutritional complications. We suspect that the patient may have had an asymptomatic form of CF and the GBP could have potentially triggered subsequent CF symptoms. The patient's noncompliance worsened nutritional issues. Initially, our main challenge in this case was to distinguish the underlying causes of EPI, from those stemming post-BS of other causes.

CONCLUSIONS

The mechanisms of EPI development after BS are not fully understood, potentially underestimating its incidence compounded by the absence of diagnostic tools in this population. Performing BS on patients with CF or asymptomatic CFTR mutations could pose risks to pancreatic dysfunction, requiring careful assessment and follow-up. Early detection and treatment are vital to prevent complications, especially in patients with additional EPI risk factors like smoking, alcohol use and previous pancreatitis.

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AUTHOR CONTRIBUTIONS

CM, ADH and JLN have written the paper; AI, MC, PL, EV, VM, AJ and XM have critically reviewed and contributed to the paper´s intellectual content. All authors have reviewed and approved the final version of the paper.

COMPETING INTERESTS

The authors declare no competing interests.

INFORMED CONSENT

Informed Patient consent have been obtained.

ADDITIONAL INFORMATION

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