

Liver failure in an obese middle-aged woman after biliointestinal bypass

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Abstract

Obesity is considered an emerging epidemic that is often associated with non-alcoholic fatty liver disease. Among the therapeutic options for morbid obesity, bariatric surgery plays an important role when conventional therapies fail. The effects of bariatric surgery on liver function and morphology are controversial in the literature. Liver failure has been reported after jejunoileal bypass (JIB), biliopancreatic diversion and gastric bypass. Biliointestinal bypass (BIB) is considered an effective procedure among recently introduced bariatric surgery techniques. It is a clinically safe, purely malabsorptive operation in which the blind intestinal loop of the JIB is anastomosed to the gallbladder, allowing a portion of bile to transit into excluded intestinal tract. BIB is the only procedure, to our knowledge, to have

no liver side effects reported in the literature. We report the case of a young obese woman who developed liver failure 8 mo after BIB. She had a rapid weight loss (70 kg) with a reduction in body mass index of 41% from January to September 2012. Because of a severe hepatic decompensation, she was referred to a transplantation centre. We strongly believe that the most important pathogenetic mechanism involved in the development of liver injury is the rapid weight loss that produced a significant fatty liver infiltration.

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Key words: Bariatric surgery; Biliointestinal bypass; Liver failure; Non-alcoholic fatty liver disease; Obesity; Rapid weight loss

Core tip: Biliointestinal bypass (BIB) is considered an effective procedure among recently introduced bariatric surgery techniques. Liver failure has been described after jejunoileal bypass, biliopancreatic diversion and gastric bypass; however, no case of liver injury has been reported after BIB in the literature, to our knowledge. We present a case of liver failure that developed 8 mo after biliointestinal derivation in a young obese patient, who subsequently required a liver transplantation.

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INTRODUCTION

Currently, obesity is considered an emerging epidemic,

often associated with non-alcoholic fatty liver disease (NAFLD)^[1]. A wide spectrum of conditions ranging from fatty liver to non-alcoholic steatohepatitis (NASH) is included in NAFLD. Conventional therapies often do not induce significant, life-changing weight loss, so alternative surgical approaches have been developed for the treatment of morbid obesity. New therapeutic surgical procedures include restrictive bowel surgery, aimed at reducing oral intake by limiting gastric volume, and surgery that promotes malabsorption, such as the Fobi-Cappella gastric bypass (GB) and the Scopinaro biliopancreatic diversion (BPD) operations and biliointestinal bypass (BIB). There are also mixed procedures that apply both techniques simultaneously, such as sleeve gastrectomy with duodenal switch. A laparoscopic approach has been described in the literature for the surgical treatment of morbid obesity, and this approach has been associated with a reduction in surgical site infection rate by 70%-80%, compared with open surgery, across general abdominal surgical procedures^[2]. The jejunoileal bypass (JIB) was abandoned in the 1980s due to a high rate of early and late liver complications, ranging from acute hepatic failure to cirrhosis^[3]. Among recently introduced bariatric surgeries, BIB is the only procedure in which no liver side effects have been described in the literature. This procedure is a clinically safe, purely malabsorptive operation in which the blind intestinal loop of the JIB is anastomosed to the gallbladder, allowing a portion of bile to transit into excluded intestinal tract. The cholecystojejunal anastomosis eliminates stasis in the bypassed bowel and reduces the amount of bile salts malabsorbed compared with the JIB. We report the case of a young obese woman who developed liver failure 8 mo after BIB. Due to severe hepatic decompensation, she was referred to a transplantation centre.

CASE REPORT

A 42-year-old woman was admitted to our hepatology unit for jaundice, asthenia and diarrhoea. She underwent BIB for severe obesity: body mass index (BMI) 54 in January 2012. Abdominal ultrasound (US) performed before the surgery revealed a bright liver pattern (slight NAFLD), and no evidence of liver cytolysis or abnormal functional tests were detected. Serum markers for hepatitis B virus, hepatitis C virus and other causes of liver damage (AMA, ANA, ASMA, anti-LKM1, α 1-AT, copper, ceruloplasmin, iron and transferrin) were negative. No alcohol abuse was reported. Her lipid profile was characterised by high levels of total cholesterol (2.45 g/L, normal values 0.60-2.00 g/L) and triglycerides (2.00 g/L, normal values 0.20-1.75 g/L). No paracetamol or other drug consumption was detected. She was not under total parenteral nutrition. A liver biopsy was not performed during the surgical procedure. After the operation, the patient underwent periodic nutritional controls, and the intake of vitamins and proteins was recommended. She experienced a rapid weight loss (70 kg) with a reduction

in BMI of 41% from January to September 2012. During this period, she had only diarrhoea, a well-known side effect of bariatric malabsorptive operations. In September 2012, she presented with jaundice and severe asthenia and was admitted to the surgery unit where she had received the previous operation. Upon admission, a physical examination revealed jaundice, pale mucosae and splenomegaly. The laboratory data revealed: anaemia [hemoglobin (Hb) 72 g/L, normal values 126-160 g/L; red blood cell (RBC) $2.23 \times 10^6/\text{mm}^3$, normal values $4.20\text{-}5.40 \times 10^6/\text{mm}^3$; mean corpuscular volume (MCV) 102 fL, normal values 81.0-99.0 fL], a low platelet (PLT) count (54 000/ μL , normal values 13 000-400 000/ μL), clotting alterations [international normalized ratio (INR) 1.90, normal values 0.8-1.2], hyperbilirubinemia (total bilirubin 0.14 g/L, normal values < 0.01 g/L, with a direct bilirubin of 0.06 g/L, normal values < 0.002 g/L), hypoalbuminemia (31 g/L, normal value 35-55 g/L), hepatocytolysis [aspartate aminotransferase (AST) 135 U/L, normal values 5-32 U/L; alanine aminotransferase (ALT) 150 U/L, normal values 5-33 U/L], a low cholinesterase value (3220 U/L, normal values 5320-12 920 U/L), and negative for markers of viral hepatitis. D-Dimer, antithrombin III and fibrinogen values excluded a disseminated intravascular coagulation. Hemocultures for aerobic and anaerobic pathogens were repeatedly negative. Therefore, due to the severe anaemia, a blood transfusion was performed. Abdominal US showed: hepatomegaly with a bright liver pattern (mild steatosis), 20 mm portal vein diameter, and splenomegaly (lateral diameter 20 cm). Abdominal computed tomography confirmed the US findings. Endoscopic exams (esophagogastroduodenoscopy and colonoscopy) produced negative results. The patient also underwent a bone marrow biopsy that revealed non-specific low dysplasia. Clinical, laboratory and imaging data might have suggested that the patient had Banti Syndrome (*i.e.*, congestive splenomegaly with hypersplenism secondary to liver cirrhosis, portal or spleen venous thrombosis). Doppler ultrasonography (USG) of the portal system might have helped in the diagnosis. There are several studies demonstrating that changes in the hepatic artery resistance index, phasicity of right hepatic vein blood flow, or velocity of portal vein blood flow are inversely related to the degree of fatty infiltration of the liver. However, Doppler USG was not performed. As an alternative, transient or dynamic elastography might have helped in detecting hepatic fibrosis, but this procedure was also not performed. Thirty days after the admission to the surgery division, she was moved to our hepatology unit. Upon admission, a physical examination, similar to the one performed at the surgery division, was performed. The laboratory data were as follows: white blood cell (WBC) $6.03 \times 10^3/\text{mm}^3$ (normal values $4.20\text{-}10.80 \times 10^3/\text{mm}^3$), Hb 96 g/L, RBC $3.08 \times 10^6/\text{mm}^3$, MCV 95 fL, PLT 75 000/ μL , INR 1.89, total bilirubin 0.07 g/L with a direct bilirubin of 0.03 g/L, albumin 37 g/L, AST 31 U/L, ALT 45 U/L, cholinesterase 3018 U/L, alkaline phosphatase (ALP) 61 U/L (normal values 35-108 U/L), γ -glutamyltransferase (GGT)

Table 1 Laboratory data

Date	WBC ¹ (/mm ³)	RBC (/mm ³)	Hb (g/L)	PLT (/μL)	INR	Total bilirubin (g/L)	Albumin (g/L)	ALP (U/L)	GGT (U/L)
September 27	5.30	2.23	72	54	1.90	0.14	31	56	22
October 24	3.60	2.64	82 ²	42	2.06	0.07	36	62	30
November 06	6.30	3.08	96 ²	75	1.89	0.07	37	61	28
November 20	3.24	3.04	94 ²	63	2.13	0.06	29	52	18

¹The differential was normal; ²The patient received blood transfusions. RBC: Red blood cell; WBC: White blood cell; Hb: Hemoglobin; PLT: Platelet; INR: International normalized ratio; ALP: Alkaline phosphatase; GGT: γ-glutamyltransferase.

28 U/L (normal values 5–36 U/L), total cholesterol 0.71 g/L [high density lipoprotein (HDL) 0.37 g/L, normal values > 0.45 g/L; low density lipoprotein (LDL) 0.21 g/L, normal values < 1.29 g/L] and triglycerides 0.49 g/L. Arterial blood gas analysis showed mixed metabolic and respiratory acid-base disturbances (pH 7.478, pCO₂ 33.0 mmHg, pO₂ 72.2 mmHg, HCO₃⁻ 25.4 mmol/L, Na⁺ 136.6 mmol/L, K⁺ 1.83 mmol/L, Cl⁻ 107 mmol/L).

She underwent abdominal US at our USG section, which confirmed the bright liver pattern, with posterior acoustic attenuation and poor visualisation of vascular structures (mild-high steatosis) with splenomegaly (lateral diameter 24 cm) and a dilated spleno-portal axis. Because cirrhosis has been described in these patients, a liver biopsy might have been important for diagnosis. However, we neither performed a percutaneous liver biopsy due to the severe coagulative injury nor performed a transjugular liver biopsy even though this procedure has been reported to be potentially well tolerated in this setting. During hospitalisation, liver function worsened, and 7 d after admission, the laboratory data were as follows: WBC $3.24 \times 10^3/\text{mm}^3$, Hb 94 g/L, RBC $3.04 \times 10^6/\text{mm}^3$, MCV 96.2 fL, PLT 63 000/μL, INR 2.13, albumin 29 g/L, cholinesterase 2052 U/L, bilirubin 0.15 g/L, ALP 52 U/L, GGT 18 U/L, total cholesterol 0.55 g/L (HDL 0.32 g/L, LDL 0.14 g/L), and triglycerides 0.49 g/L. Changes in the laboratory data are presented in Table 1. Due to the rapid liver decompensation, we sent the patient to a transplantation unit. She underwent orthotopic liver transplantation with a reversal of the bariatric surgery. Her subsequent condition was characterised by a satisfactory clinical improvement. Unfortunately, we have no data concerning hepatic histological findings.

DISCUSSION

The prevalence of obesity has increased dramatically over the last decades with NASH becoming more frequent. Among therapeutic options for morbid obesity, bariatric surgery plays an important role when conventional therapies fail. The effects of bariatric surgery on liver function are controversial in the literature. Moreover, the progression and/or regression of hepatic steatosis after bariatric surgery is poorly understood^[4].

Several trials suggest that bariatric surgery improves liver morphology in patients with pre-existing histological liver alterations such as steatosis or steatohepatitis.

According to Dixon *et al*^[5] who examined the effects of weight loss on NAFLD in 36 selected obese patients, steatosis, lobular inflammation, centrolobular fibrosis and ballooning degeneration improved significantly after bariatric surgery. Moreover, a significant reduction in the prevalence of metabolic syndrome (from 70% to 40%) and a marked improvement in liver steatosis, inflammation and fibrosis after GB were described by Mattar *et al*^[6]. Concerning the effects of bariatric surgery on cardiometabolic risk factors and weight loss, BIB seems to produce, for a longer period, marked improvements in HOMA I, Tot-C/HDL-C ratio and body composition compared to restrictive bariatric surgery procedures^[7]. However, several authors highlight the occurrence of hepatic complications after bariatric surgery. In particular, the risk of liver decompensation or cirrhosis is one of the reasons JIB has been abandoned. Piringer *et al*^[8] described the case of an obese woman who developed severe NAFLD 23 years after JIB. A multicentre Belgian survey reported that 10 patients were listed for liver transplantation due to severe hepatocellular failure after bariatric surgery. Nine of the patients had undergone a Scopinaro operation, and one had a JIB; the hepatic failure was observed after a median time of 5 years following surgery^[9].

Several cases of early hepatic failure after bariatric surgery are described in the literature. D'Albuquerque *et al*^[4] studied three patients, 20 to 38 years old, with no history suggestive of liver failure, who developed liver decompensation for which transplantation was considered, 7 to 24 mo after GB or BPD. Castillo *et al*^[10] reported a case of morbid obesity in a patient who developed subacute hepatitis resulting in hepatic failure 1 year after BPD. A patient, who developed steatohepatitis and, subsequently, died of fatal hepatic failure after BPD, has been described by Grimm *et al*^[11]. More recently, Sagredo *et al*^[12] described a 28-year-old obese woman who developed acute liver failure 11 mo after gastroplasty with intestinal resection and a gastro-jejunal anastomosis. A liver biopsy performed after the surgery revealed severe steatohepatitis and fibrosis.

No cases of liver decompensation after BIB have been described in the literature, to our knowledge. We report the case of a young obese woman who developed liver failure 8 mo after BIB. We hypothesise that multiple factors might have contributed to liver damage after bariatric surgery, such as hormonal, autoimmune and/or inflammatory factors. First, the non use of the intestinal loop

may lead to bacterial overgrowth with the production of toxic polymers and inflammatory cytokines. The excluded mucosal barrier can be damaged and these molecules may be absorbed into the portal venous system, facilitating hepatic injury. However, bacterial overgrowth is observed less in BIB than in other surgical bariatric procedures because of the transit of bile salts into the excluded intestinal loop. Nyhlin *et al*^[13] observed that patients with BIB had a significantly lower elimination time of bile acid than those with JIB. Moreover, the authors suggest that BIB surgery to treat obesity seems to be advantageous over JIB in reducing the postoperative loss of bile acid and choleretic diarrhoea, without influencing weight loss. Secondly, when a long jejunoileal loop is excluded by intestinal transit, several nutritional supplements are not absorbed, and this condition has a negative impact on liver function. Moreover, because of the rapid weight loss that occasionally follows bariatric surgery, a surplus of fatty acids reaches the liver, exceeding the liver's ability to metabolise them. Thus, we also hypothesise that liver failure after bariatric surgery may be the consequence of an acute or subacute fatty liver infiltration.

In the case we described, the actual liver damage mechanism is not clear because a liver biopsy was not performed due to the severe coagulative injury. However, while all of the mechanisms described above may have played a role in the development of hepatic decompensation, the rapid weight loss could represent the most important pathogenetic mechanism in our case. In fact, the BMI was 54 kg/m² before the surgery and 34 kg/m² 8 mo after, and our patient lost approximately 70 kg during the same period.

In conclusion, we suggest strict monitoring of liver function in the management of obese patients before and after bariatric surgery, including adequate supplementation with specific nutrients to prevent rapid weight loss and consequent liver injury.

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