Morbid Obesity and Cholangiocarcinoma

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ABSTRACT

The incidence of clinically severe obesity is rapidly escalating in the United States resulting in an increased number of bariatric operations being performed. Morbidly obese patients pose a surgical challenge. First, they often present with obesity related comorbid conditions. Second, when complications occur, it is difficult to perform diagnostic studies in these patients due to their large size (i.e. weight limitations of CT-scanners and poor ultrasound quality limited by the patients' size). Additional challenges are present when incidental findings of malignancy occur at the time of routine bariatric operations. In the present report, we describe the challenging work-up and treatment options of a patient who had cholangiocarcinoma found incidentally during roux-en Y gastric bypass and review reports documenting the presence of occult rare malignancies found at the time of obesity surgery. These cases are similar to the present report in that they occurred in superobese patients (BMI ≥ 50 kg/m^2), all patients were asymptomatic prior to diagnosis, and they had rare forms of cancers (i.e acinar cell carcinoma of the pancreas and schwannoma of the stomach).

INTRODUCTION

Several studies have described a positive correlation between obesity and the overall risk of cancer (1). Cholangiocarcinoma is a rare tumor arising from biliary epithelial cells with an incidence in the United States of 1 to 2 per 100,000 people per year (2). Only 10% of cholangiocarcinomas originate within the intrahepatic biliary tree and present as intrahepatic masses, while most tumors originate from the hepatic duct bifurcation (3). Cholangiocarcinoma typically occurs in patients who are older than 65 years of age (3). Most tumors are sporadic, but several factors confer an increased risk for the development of cholangiocarcinoma including primary sclerosing cholangitis, choledochal cyst, and hepatolithiasis (4). The vast majority of patients with unresectable bile duct cancer die within 6 months to a year following diagnosis, which usually results from liver failure or biliary obstruction (5).

The present report describes a patient who underwent a routine Roux-en-Y gastric bypass (RYGB) for the treatment of morbid obesity. When he presented to our institution, he weighed 193 kg and his body mass index (BMI) was 62 kg/m^2. He underwent an uneventful RYGB, but developed sepsis postoperatively. During a second exploratory laparotomy for suspected anastomotic disruption, a liver mass was detected. Once the diagnosis was established, further surgical intervention for the management of this malignancy was limited due to the patient's large size for CT-Scan, MRI, or even ultrasonography.

Case Report: Cholangiocarcinoma in a morbidly obese patient

The patient is a 37 year-old Caucasian male with a history of morbid obesity present throughout his life. He weighed 144 kg at the time of graduation from high school. He tried several behavioral dietary modifications and pharmacotherapy in attempts to lose weight without success.

The patient's past medical history was unremarkable, but had signs and symptoms consistent with obstructive sleep apnea and osteoarthritis. He had no known history of primary sclerosing cholangitis, choledochal cysts or ulcerative colitis. He had no history of smoking or alcohol intake. He was not taking any medications and had no known allergies. His family history was significant for obesity in mother and daughter. He had no family history of malignancy.

On physical examination, his height was 1.77 m, weight was 193 kg with a BMI of 62 kg/m^2. He had normal vital signs. He was in no acute distress. His heart had a regular rate and rhythm. His lungs were clear to auscultation bilaterally. His abdomen showed extreme obesity without tenderness or scars. Body composition analysis by bioelectrical impedance analysis (BIA) revealed 51 % body fat, basal metabolic rate of 2850 kilocalories per day, fat weight 99.3 kg, lean weight 93.9 kg.

In our institution, we exclusively perform the Roux-en-Y gastric bypass for the treatment of morbid obesity (a one stage operation). However, when a patient is superobese (BMI $\geq$ 50 kg/m^2), a jejunoileal bypass (JIB) is performed, followed by a Roux-en-Y-gastric bypass six months to a year after the JIB (a two stage operation). In our experience, a two stage operation decreases complications in

the superobese patient as the risk of exploring the upper abdomen is eliminated. Surprisingly, in this patient, there was only a minimal amount of mesenteric fat, allowing proper identification of the structures in the upper abdomen. Thus, he underwent a routine Roux-en-Y gastric bypass. There were no complications intraoperatively. On postoperative day number one, he developed tachypnea (with a respiratory rate of 28 breaths per minute) and tachycardia (with a heart rate of 140-150 beats per minute). His oxygen saturation on room air was 90%. An arterial blood gas on 4 liters of oxygen per nasal cannula revealed: pH 7.42, pCO_2 = 36 mmHg, PaO_2 = 48 mmHg, and bicarbonate = 24 mEq/L. He was transferred to the intensive care unit with a possible differential diagnosis of a pulmonary embolism versus early sepsis from an anastomotic leak. He was started on prophylactic intravenous heparin. Lower extremity duplex studies were negative. EKG and cardiac enzymes were within normal limits. On postoperative day number two, he was still tachycardic, tachypneic and had a temperature of 38.5° C. His hemogram revealed a leukocytosis of 20.2 X 10^3 /µL with a normal chest X-ray and negative blood and urine cultures.

He was then taken back to the operating room with a presumptive diagnosis of an anastomotic leak. During exploratory laparotomy, an intra-abdominal hematoma and a small proximal anastomotic leak were identified. The hematoma was evacuated and the leak repaired. During peritoneal irrigation, a 10 cm X 6 cm X 6 cm necrotic, poorly perfused liver mass was identified beginning at the falciform ligament extending into the left lobe. Biopsies of the

mass were obtained and sent for pathological analysis. His liver function tests revealed a total bilirubin of 0.3 mg/dL, albumin 2.9 g/dL, alkaline phosphatase 88 U/L, AST 25 U/L, and ALT 25 U/L.

Pathological testing revealed the following: the tumor was positive for CEA with focal cytoplasmic staining but no canalicular staining. The tumor was also positive for cytokeratins 19, and 7 as well as galactin 3. The tumor was negative for Bcl-2. Microscopically, the specimen was an invasive, well to moderately differentiated adenocarcinoma. The tumor was composed of infiltrating, small to large, irregular neoplastic glands within a dense fibrous stromal background with focal necrosis. The neoplastic glands were lined by cuboidal to columnar cells with hyperchromatic, irregular nuclei. These findings were most consistent with cholangiocarcinoma.

Following surgery the patient was informed of the pathological diagnosis but awaited further testing (i.e CT-Scan of the abdomen) to delineate tumor involvement and surgical options, which was still limited by his obesity. At five months follow up, he still had no symptoms of carcinogenesis. His weight was 150 kg and his BMI 48 kg/m^2.

DISCUSSION

In the present report, we describe a patient with an unusual malignancy found during bariatric surgery. This case is unusual for several reasons: First, intrahepatic cholangiocarcinoma is a rare malignancy, accounting for only a small percentage of cholangiocarcinomas. Second, the age of onset in this patient was much younger than expected with cholangiocarcinoma. Additionally, cholangiocarcinoma in an obese patient is contrary to the expected weight loss typically seen with cancer. It is unclear; however, whether obesity was a contributing risk factor or this was a sporadic case of cholangiocarcinoma.

In support of a possible relationship between obesity and carcinogeneis, we have previously reported a case of acinar cell carcinoma of the pancreas in a superobese patient (BMI = 116 kg/m^2) (6), which was found incidentally following a routine Roux-en-Y gastric bypass for the treatment of obesity. Another group has described incidental gastric schawannomas in a superobese (58 kg/m^2) female patient found during bariatric surgery (7). The characteristics of these patients and their cancer types are depicted in table 1.

These three cases are similar in that they all occurred as incidental findings during bariatric surgery and were found in young patients. All of these patients were superobese (BMI ≥ 50 kg/m^2), and they all had relatively rare tumors.

In two of these cases, which have been encountered by our group, the initial plan had been to perform a staged operation consisting of a jenunoileal bypass (JI) followed by a Roux-en-Y gastric bypass after some weight loss to avoid injury to vital structures in the upper abdomen resulting from superobesity.

However, in both cases, there was minimal mesenteric fat resulting in proper identification of the anatomy to perform a routine Roux-en-Y gastric bypass. It is possible that the process of carcinogenesis resulted in mesenteric fat reduction with minimal decrease in subcutaneous fat.

In our experience of over 1000 bariatric operations we have encountered four incidental cases of cancer (acinar cell carcinoma of the pancreas, sarcoma of the stomach, gall bladder carcinoma, and cholangiocarcinoma). These patients represent a diagnostic challenge for our current scanners due to their large size and, in many cases, surgical intervention must be delayed as in the present case. It is important to be aware of these cases so that a diagnostic plan and appropriate management can be established for these patients.

References

(1) Albanes D. Energy balance, body size, and cancer. Crit Rev Oncol Hematol 1990; 10(3):283-303.

(2) Carriaga MT, Henson DE. Liver, gallbladder, extrahepatic bile ducts, and pancreas. Cancer 1995; 75(1 Suppl):171-190.

(3) Burke EC, Jarnagin WR, Hochwald SN, Pisters PW, Fong Y, Blumgart LH. Hilar Cholangiocarcinoma: patterns of spread, the importance of hepatic resection for curative operation, and a presurgical clinical staging system. Ann Surg 1998; 228(3):385-394.

(4) Broome U, Olsson R, Loof L, Bodemar G, Hultcrantz R, Danielsson A et al. Natural history and prognostic factors in 305 Swedish patients with primary sclerosing cholangitis. Gut 1996; 38(4):610-615.

(5) Jarnagin WR. Cholangiocarcinoma of the extrahepatic bile ducts. Semin Surg Oncol 2000; 19(2):156-176.

(6) Huerta S, Arteaga J, Li Z, Livingston EH. Morbid Obesity and Acinar Cell Carcinoma of the Pancreas. Pancreas 2002; 25(4): 414-415.

(7) Godziashvili Z, Paramesh A, Chahin F, Chahin C, Hares M. Gastric schwannomas: Incidental tumors found during gastric surgery. Surgical Rounds 2001; 24(9):465-467.

TABLE 1. Patient characteristics of two patients previously reported (6, 7) and the present case: their gender, age, body mass index, and their types of cancers. All patients are superobese (BMI $\geq$ 50 Kg/m^2).

Gender	Age	BMI (Kg/m^2)	Cancer Type
Male	44	116	Acinar Cell Carcinoma of the Pancreas (6)
Male	37	62	Cholangiocarcinoma
Female	44	58	Gastric Schwannoma (7)