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CASE REPORT | ENDOSCOPY

Endoscopic and Pharmacologic Treatment of Obesity in Patients With Hereditary Polyposis Syndromes

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ABSTRACT

Patients with hereditary polyposis syndromes (HPS) are among the highest risk of multiple types of cancer. This risk is further magnified by comorbid obesity; however, HPS present unique risks for bariatric surgery. The advent of endoscopic bariatric and metabolic therapies along with advancements in the realm of antiobesity medications provides potential weight loss alternatives in this vulnerable population. We present 2 cases of patients with obesity and HPS successfully treated with intragastric balloons in combination with antiobesity medications.

KEYWORDS: obesity; bariatric endoscopy; hereditary polyposis; intragastric balloon

INTRODUCTION

Patients with hereditary polyposis syndromes (HPS) have historically been considered poor candidates for bariatric surgery, with concerns regarding potential operative complications and implications in future surveillance strategies. Despite well-documented antioncogenic effects of bariatric surgery in the general populace, data on outcomes in those with HPS are unclear.[1] Furthermore, these patients often require prophylactic gastrointestinal surgery for cancer prevention. Although bariatric surgery is lifesaving and indicated in these patients, it may not be possible to perform in a timely manner before the polyposis-associated surgery and could add to the significant physical and psychosocial costs that these patients already face.[2]

The new emergence of minimally invasive endoscopic bariatric and metabolic therapies (EBMTs) may serve as a novel alternative to treat obesity in patients with HPS. In this case series, we present 2 cases of individuals with a history of obesity and HPS who were successfully treated with EBMTs. We show an effective treatment strategy using endoscopic therapies or EBMTs plus antiobesity medications (AOMs) to manage obesity in patients with hereditary cancers in need of total colectomy or other polyposis-associated surgeries.

CASE REPORT

Case 1: A 45-year-old man with a medical history of obstructive sleep apnea, hypertension, class III obesity, and *MLH1*-variant Lynch syndrome presented for bariatric endoscopy evaluation. Family history was significant for colon cancer (father, paternal grandfather) and pancreatic cancer (paternal grandmother). Previous attempts at lifestyle modifications resulted in a transient loss of 70 lbs, followed by subsequent weight regain. Topiramate was prescribed for weight loss but stopped shortly thereafter due to side effects. He was not interested in bariatric surgery and was referred to bariatric endoscopy.

After thoughtful discussion, the decision was made to proceed with endoscopic intragastric balloon (IGB) placement (Orbera intragastric balloon; Apollo Endosurgery, Austin, TX). On endoscopic examination, the esophagus, stomach, and duodenum appeared normal. The IGB was inflated with 600 cc of sterile saline without evidence of leak or perforation. Postprocedurally, the

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patient was initiated on tirzepatide 2.5 mg/wk and omeprazole 40 mg twice daily. Owing to insurance coverage, the patient switched from tirzepatide to semaglutide 0.25 mg/wk at 3 months after IGB placement.

Before IGB, the patient weighed 315 lbs (body mass index [BMI] 43.4 kg/m^2). One-month post-IGB, he achieved a 7% total body weight loss (TBWL; 290 lbs, BMI 39). By 3 and 5 months post-IGB, he achieved 11% TBWL (281 lbs, BMI 25) and 18% TBWL (257 lbs, BMI 35.84), respectively. The IGB was endoscopically removed after 6 months. Weight loss continued, and at 1-month post-IGB removal, he weighed 243 lbs (BMI 33.89) for a total of 23% TBWL using IGB and AOMs concomitantly. At 9 months post-IGB removal, weight was overall sustained at 249 lbs (BMI 34.74). The patient continues to follow regularly with the bariatric endoscopy multidisciplinary team.

Case 2: A 60-year-old man with a medical history of diabetes, hyperlipidemia, hypertension, obstructive sleep apnea, and *MUTYH*-associated polyposis with a family history of colorectal cancer presented to the bariatric endoscopy clinic. He was planned for a prophylactic total colectomy; however, due to risks of perioperative complications, this could not proceed as planned unless he achieved a target BMI <35. Attempts at lifestyle modifications through diet and exercise resulted in a loss of only 10–20 lbs. He was not interested in bariatric surgery and was referred to bariatric endoscopy.

The decision was made to start pharmacologic therapy (topiramate 25 mg) and proceed with an IGB (Orbera; Apollo Endosurgery). On endoscopic examination, the esophagus and duodenum appeared normal, though several 3–5 mm sessile polyps without high-risk features were found in the gastric body. No ulcers, erosions, or bleeding were observed. The IGB was successfully inflated with 600 cc sterile saline in the gastric body.

The patient's initial weight at the time of presentation was 254 lbs (BMI 40). One-month post-IGB, he achieved 11.6% TBWL (220 lbs, BMI 34.4). At this time, he stopped requiring metformin due to normalization of glycemic control. By 3 months post-IGB, he achieved 18% TBWL (205 lbs, BMI 31). The IGB was removed at the 3-month mark, and with an additional month of topiramate and lifestyle modifications, he reached a weight of 195 lbs (23% TBWL, BMI 29.65). He proceeded to undergo an uncomplicated total colectomy 2 months later, which along with treatment of his obesity significantly reduces his lifetime risk of malignancy. At 12 months post-IGB removal, again weight remained stable at 197 lbs (BMI 30.85) (Figure 1). He continues to adhere to lifestyle modifications and follows with the bariatric endoscopy multidisciplinary team.

DISCUSSION

HPS represent a heterogeneous group of genetic disorders that predispose individuals to certain tumors at an early age. Obesity itself is thought to have strong genetic underpinnings.[3] There is a close association between cancer and obesity: 4%–8% of cancers are attributed to obesity, including postmenopausal breast, endometrial, kidney, liver, pancreatic, and colorectal cancer.[4,5] Bariatric surgery is the most effective treatment for obesity, leading to long-term weight loss and remission of obesity-related comorbidities, and a growing pool of literature supports bariatric surgery as an invaluable tool in reducing the overall incidence of cancer, obesity-related cancer, and cancer-associated mortality.[6]

A complex interplay between genetics, biology, and environmental factors exists in individuals with both obesity and HPS. However, few studies have sought to explain the relationship between obesity and cancer risk in this population. In a meta-analysis investigating the risk of colorectal cancer in patients with obesity and Lynch syndrome, investigators report a significantly increased risk (~2-fold) in men with obesity compared with those without, which was further potentiated in the presence of an *MLH1* mutation.[7] These results suggest that patients with HPS may benefit even more from bariatric

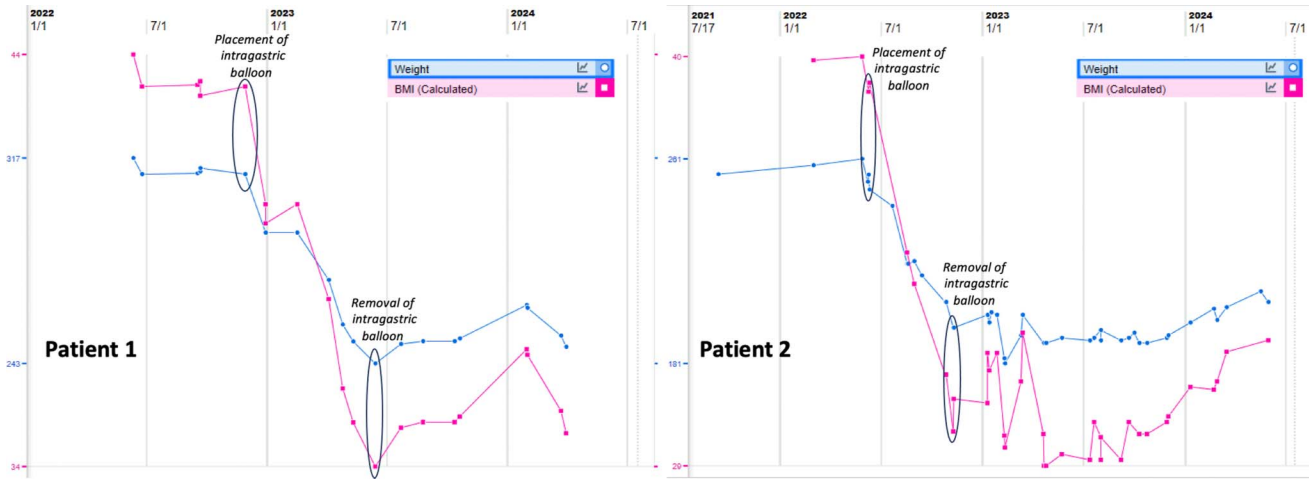

Figure 1. Trends in weight and BMI for patients 1 (left) and 2 (right). BMI, body mass index.

surgery. However, limited reports demonstrate the potential for increased complications in patients with polyposis syndromes who undergo bariatric surgery.[8] Furthermore, the altered surgical anatomy may greatly impair the ability to perform guideline-recommended endoscopic surveillance.

In this series, we present 2 successful examples of using IGBs in concert with AOMs to treat obesity in individuals with HPS. To our knowledge, this is the first series describing the feasibility and effectiveness of EMBTs in this population. These techniques are minimally invasive, safe, and effective at reducing not only the burden of obesity but also potentially cancer in those patients at highest risk.

DISCLOSURES

Author contributions: M. Iyer, SA Firkins, R. Patel, B. Flora, E. Staneff, R. Simons-Linares conceptualized the study. M. Iyer, SA Firkins contributed to the writing (original draft) of the manuscript. M. Iyer, SA Firkins, R. Patel, B. Flora, E. Staneff, R. Simons-Linares contributed to the writing (review and editing) of the manuscript. SA Firkins, R. Patel, R. Simons-Linares supervised the study. We certify that all authors have read and approved the submission of the manuscript. R. Simons-Linares is the article guarantor.

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