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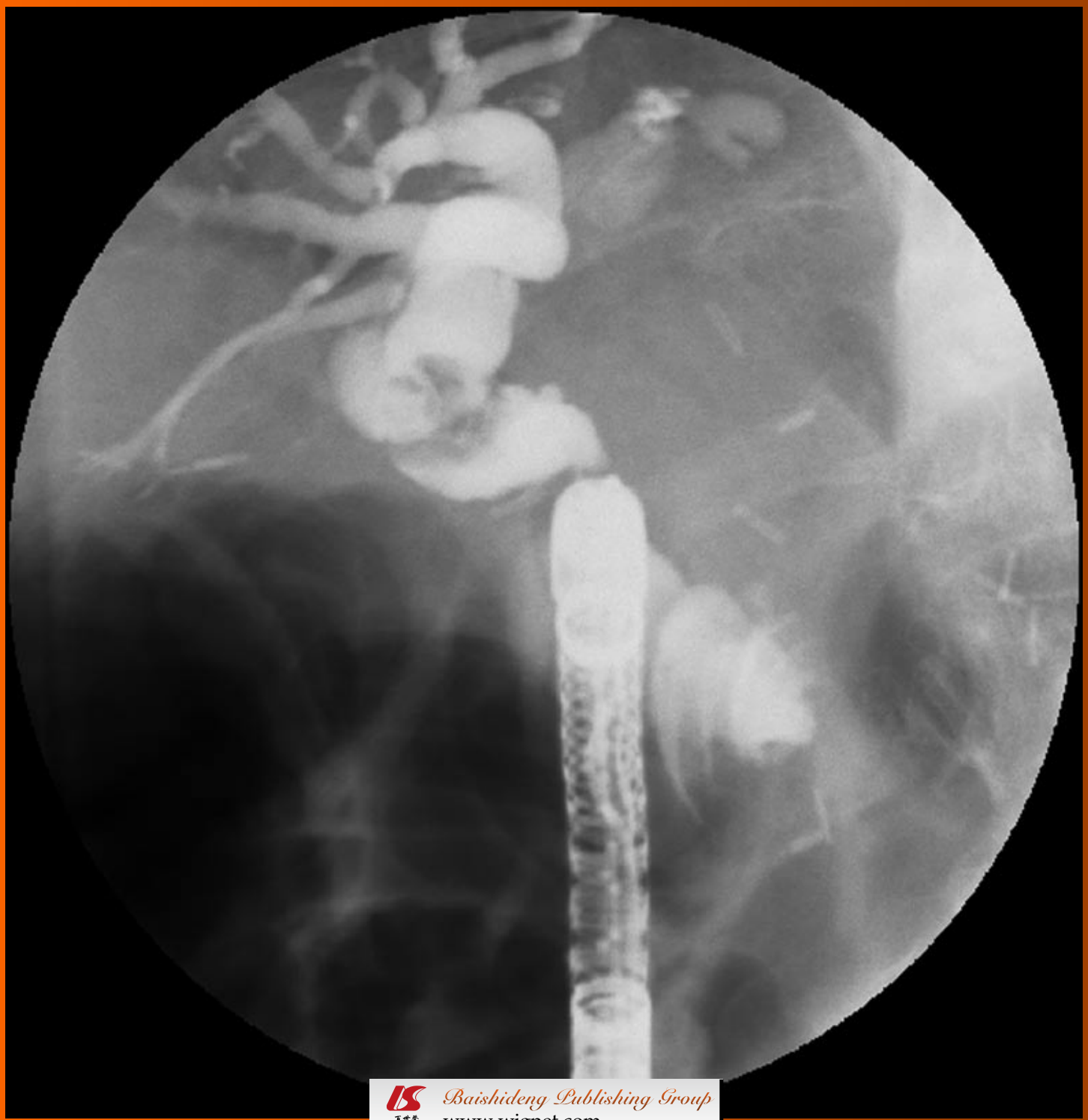

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EDITORIAL

Transoral surgery for morbid obesity

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Abstract

Obesity is a serious health problem in the United States. Although laparoscopic surgical procedures are effective in achieving weight loss and improving obesity-related co-morbidities, they are not without their limitations and consequently there is a growing demand for less invasive approaches. Transoral techniques, as both primary and revisional procedures, are promising in this regard as they may provide a safer and more cost-effective means of achieving meaningful weight loss. The aim of this paper is to review the currently available transoral approaches to weight loss, with a particular focus on those applied in human trials.

Key words: Obesity; Transoral techniques; Humans

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INTRODUCTION

Obesity is a serious public health problem associated with increased morbidity and mortality and decreased quality of life. According to the World Health Organization, in 2005 there were approximately 1.6 billion overweight adults and at least 400 million obese adults worldwide[1]. The prevalence of obesity has increased so rapidly over the last few decades that it is now considered a global epidemic.

In the United States, the National Health and Nutrition Examination Surveys, conducted by the Center for Disease Control, study the prevalence of obesity by using directly measured heights and weights. Studies have shown that currently there are 72 million obese adults [i.e., body mass index (BMI) $\geqslant$ 30 kg/m^2]. Interestingly, while the prevalence has more than doubled over the last four decades (from 13.4% in 1960-1962 to 35.1% in 2005-2006 for adults aged 20-74 years)[2], it seems to have reached a plateau over the last 3 years[3-5]. However, when Ogden *et al*[4] compared the distribution of BMI between 1976-1980 and 2005-2006, they observed that, among adults, the distribution of BMI shifted to the right, reflecting the change in prevalence of super obesity (i.e., BMI $\geqslant$ 50 kg/m^2), which increased from 0.9% in 1960-1962 to 6.2% in 2005-2006 among adults.

Studies have indicated that obesity is responsible for more than 2.5 million deaths worldwide per year[6] due to the increased prevalence of related co-morbidities, including type 2 diabetes, hyperlipidemia, hypertension, obstructive sleep apnea, heart disease, stroke, asthma, back and lower extremity weight-bearing degenerative problems, several forms of cancer and depression[6-8]. Additionally, obesity is an independent risk factor for mortality. A study by Fontaine *et al*[9] demonstrated that,

in comparison with a normal weight individual, a 25-year-old morbidly obese man has a 22% reduction in life expectancy, representing approximately 12 years of life lost. A more recent study examining 10-year mortality rates in more than 500 000 Americans, 50 to 71 years old, demonstrated that in middle aged men and women who were non-smokers and had no pre-existing illnesses, there was a 20%-40% increased mortality in those who were overweight (i.e., BMI 25-30 kg/m^2) and a 2- to 3-fold increased risk of mortality in individuals who were obese (BMI $\geqslant$ 30 kg/m^2)[10].

As is evidenced by the innumerable weight loss programs, most adults attempt to lose weight at some point in their life[11]. However, medically managed weight loss, including diets and pharmaceutical agents, are ineffective in the long-term treatment of obesity[12]. In 1991, the National Institutes of Health established guidelines for the surgical management of morbid obesity (BMI $\geqslant$ 40 kg/m^2 or BMI > 35 kg/m^2 in the presence of significant co-morbidities)[13,14] and, since then, the number of bariatric surgical procedures has dramatically increased. In 2004, approximately 144 000 obese individuals received surgical treatment, compared to the 20 000 procedures performed in 1999[15]. The dramatic increase is most likely the result of refinement in minimally invasive surgical techniques, increased media coverage and increased patient satisfaction. Indeed, of the various available weight-loss strategies, bariatric surgery is the only effective long-term weight-loss therapy for obese patients[16].

Bariatric surgical procedures are divided into restrictive (i.e., adjustable gastric banding, vertical banded gastroplasty, sleeve gastrectomy), malabsorptive (biliopancreatic diversion with/out duodenal switch) or a combination of both (roux-en-y gastric bypass). Of the various procedures, roux-en-y gastric bypass and adjustable gastric banding are the most commonly performed procedures. While bariatric surgery has been shown to be extremely effective for long-term weight loss, the mortality rate, albeit low, is not zero [i.e., 0.28% (95% CI: 0.22-0.34) and 0.35% (95% CI: 0.12-0.58) at $\leqslant$ 30 d and > 30 d respectively[17]]. Additionally, from a morbidity perspective, there are procedure-specific risks[18,19] and shared complications, including incisional hernias, wound infections, fistula and leaks[20].

More recently, there has been emerging interest in transoral techniques for pre-operative, stand-alone or revisional bariatric procedures[21]. Specifically, considering transoral surgery is performed exclusively through the gastrointestinal (GI) tract *via* a flexible endoscope, the value of this approach lies in the possibility of an ambulatory weight loss procedure that may be safer and more cost effective compared with laparoscopic approaches. By extension, this may allow bariatric procedures to be performed in those individuals who are currently precluded due to multiple co-morbidities, older age, super-obesity (BMI $\geqslant$ 50 kg/m^2), mild obesity (BMI 25-30 kg/m^2), atypical anatomy (e.g., adhesions secondary to previous abdominal surgery, a history of gastric resection, or bowel resection) or disease states that affect the bowel (e.g., Crohn's disease). The present paper aims to review currently available transoral techniques with a focus on those applied in human trials.

TRANSORAL DEVICES USED AS PRIMARY PROCEDURES

Primary procedures are divided into restrictive or malabsorptive. Restrictive devices include intragastric balloons, endolumenal suturing, endolumenal stapling and the transoral restrictive implant system. These are designed to mimic restrictive laparoscopic procedures (i.e., adjustable gastric banding, vertical banded gastroplasty, sleeve gastrectomy). Malabsorptive procedures (i.e., biliopancreatic diversion with/out a duodenal switch) induce weight loss by bypassing the absorptive surface of the intestine. The duodenal-jejunal bypass sleeve is a malabsorptive device that mimics such surgical procedures.

Intragastric balloon

One of the earliest transoral devices created to restrict oral intake was the intragastric balloon. Unfortunately, significant complications, premature balloon deflation and failure to achieve meaningful weight loss led to it being abandoned as a weight loss device. However, in 1987, guidelines for development of an appropriate balloon appliance were outlined and the BioEnterics Intragastric Balloon (BIB; Inamed, Santa Barbara CA) was developed[22]. Structurally, the BIB is a small, flexible balloon in the collapsed state and expands into a spherical shape 10 cm in diameter when filled with 500 mL of saline solution. Its shell is made of an inert, nontoxic silicone elastomer that is resistant to gastric acid. The balloon has a radiopaque self-sealing valve that allows volume adjustments from 400 to 800 mL.

Procedurally, under conscious sedation or general anesthesia, a diagnostic endoscopy should be performed to rule out abnormalities that would preclude balloon insertion. The BIB placement assembly, consisting of a sheath with the collapsed balloon and a balloon fill tube, is then inserted into the gastric fundus. A syringe, attached to the balloon fill tube, is then used to fill the balloon under direct visualization with 500-700 mL of saline/methylene blue solution. After filling the balloon, gentle suction exerted by withdrawing the plunger of the syringe creates a vacuum, which seals the valve. The balloon is released by a short pull on the fill tube and this tube with the placement assembly is removed. After placement, the position of the free-floating balloon can be confirmed radiographically (Figure 1)[22]. BIB adjustments, to increase or decrease volume if there is inadequate weight loss or persistent nausea and vomiting respectively, requires endoscopy and a reintubation catheter. Directional arrows at the equator of the balloon assist in identifying the valve and the reintubation catheter is pushed into the valve to add or remove fluid. Finally, to remove the BIB, as much fluid as possible is removed before grasping the balloon with a snare or forceps. The endoscope and the grasped

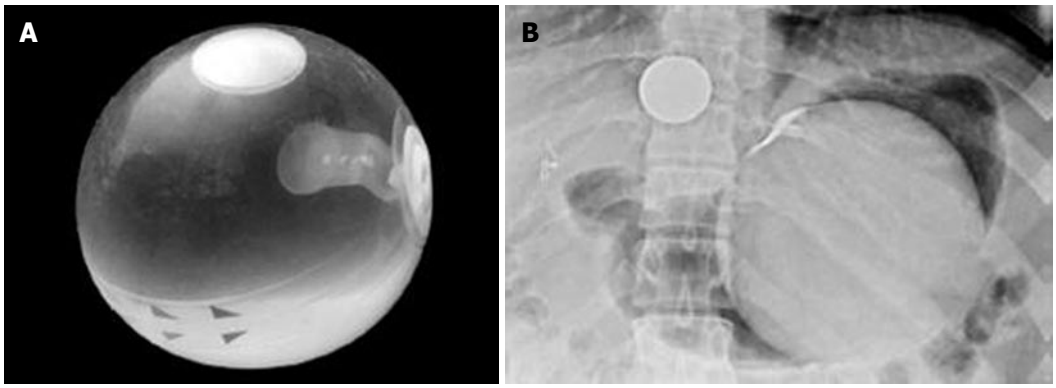

Figure 1 The BioEnterics Intragastric Balloon. A: The balloon is smooth and spherical. The arrows at the equator point toward the valve. The radiopaque self-sealing and repenetrable valve with its Z-shape configuration (visible inside balloon) allows adjustment of the balloon volume from 400 to 800 mL; B: Plain abdominal radiograph showing balloon in body of stomach. A coin taped on the lower sternum permits follow-up comparisons of balloon size to detect premature deflation.

balloon are then gently removed. A needle is available to puncture the balloon in case of unsuccessful reintubation. In terms of morbidity, the major adverse events include nausea and vomiting that in some cases can require early removal, as well as early deflation, gastric ulceration and erosion[22].

Genco *et al*[23] conducted a retrospective analysis to assess the efficacy of the BIB in terms of weight loss and improvement in obesity-related co-morbid states. From 2002-2004, 2515 patients with a mean BMI of (44.8 ± 7.8) kg/m^2 underwent endoscopic placement of the BIB. Positioning of the balloon was successful in all but 2 cases (0.08%), and the overall complication rate was 2.8% (70/2515). Specifically, gastric perforation occurred in 5 patients, 4 of whom had undergone previous gastric surgery, and 2 of whom died. There were 19 gastric obstructions (0.76%) within the first week of insertion and these were remedied by BIB removal. The balloon ruptured in 9 cases (0.36%) and had to be removed. Finally, esophagitis was diagnosed in 32 patients (1.27%) and gastric ulcers developed in 5 patients (0.2%) with a history of peptic disease. Both complications were treated with medical therapy.

Concerning weight loss and improvement in obesity-related co-morbidities, at 6 mo follow-up, the percentage excess weight loss (%EWL) was (33.9 ± 18.7). During this interval, improvement or resolution of diabetes and hypertension was observed in 86.9% and 93.7%, respectively. These results were further supported in a randomized, sham-controlled, crossover study of 32 patients conducted by the same group[24].

Taken together, studies demonstrate that the BIB, in conjunction with the appropriate diet, is a safe, effective *short*-term weight loss procedure in patients that have not had any previous gastric surgery. As such, its role should be relegated to being a bridge to more definitive bariatric interventions. Currently, however, no intragastric balloons are approved for use in the United States.

Endoluminal suturing

Endoluminal vertical gastroplasty (EVG), using the Bard EndoCinch Suturing System (C.R. Bard, Murray Hill, NJ), was first described in the context of treating gastroesophageal reflux disease. Due to lack of repair durability, the role of EVG in control of gastroesophageal reflux disease (GERD) was abandoned[25-27].

In terms of its application for the treatment of obesity, Fogel *et al*[28] first described the use of the EndoCinch in 64 patients. The primary objectives of this study were to determine the safety and technical feasibility of EVG. The secondary aim was assessment of its efficacy with respect to patient weight loss. Technically, the EVG involves configuring one continuous suture running through 5 to 7 stitch points, in a cross-linked fashion from proximal fundus to distal body[28]. The suture is deployed from a capsule attached to the end of a diagnostic gastroscope. Specifically, as described by Fogel *et al*[28], the first stitch is placed proximally in the nearest folds on the anterior face of the gastric fundus (approximately 40-43 cm from the mouth). Subsequently, a second stitch is placed as far down on the anterior face to the most distal fold of the stomach body's rugae, proximal to the antrum, usually 10 to 13 cm from the first stitch (approximately 53 cm from the mouth). A third stitch is then placed 1 to 2 cm proximal to the second stitch but on the posterior face of the stomach (approximately 51 cm from the mouth). Subsequent stitches are placed, working in a proximal direction alternating anterior and posterior faces of the stomach with consecutive stitches separated by approximately 2 cm. The last stitch in the sequence is placed on the posterior face 1 to 2 cm proximal from the first stitch. After all the stitches are placed and visualized, the suture is tightened, bringing the anterior and posterior faces together creating the EVG. The suture is then secured and excess suture is cut.

In terms of outcomes, Fogel *et al*[28] demonstrated that the mean procedure time was 45 min with a recovery time of 1 to 2 h. All patients were discharged on the day of procedure. No patients experienced any serious adverse events. However, minor events included nausea and reflux-like symptoms that resolved within 24 h. Follow-up for up to 12 mo was accomplished in 59 of 64 patients.

Results for secondary outcomes demonstrated a significant reduction in BMI at 12 mo [mean ± SD, BMI (39.9 ± 5.1) kg/m^2 at baseline *vs* (30.6 ± 4.7) kg/m^2 at 12 mo; $P < 0.001$] with mean (%EWL ± SD) of (21.1 ± 6.2), (39.6 ± 11.3), and (58.1 ± 19.9) at 1, 3 and 12 mo post-procedure, respectively. Additionally, repeat endoscopy performed in a non-uniform manner in 14 of 64 patients after reports of feeling hungry or plateauing weight loss, demonstrated 11 patients had intact suture lines but three had disrupted sutures. These were repaired by repeating the suturing procedure.

A newer version of the EVG device was created and tested by Brethauer *et al*[29] in 18 patients in a short term (≤ 24 h) study. They demonstrated that the average procedure time was (125 ± 23) min and there were no serious procedure related complications. Minor complaints included nausea, vomiting and abdominal discomfort.

Issues that still need to be addressed include the long-term durability of the plication procedure given the problems seen with earlier trials focused on the treatment of GERD. Additionally, the ease of repeating interventions to facilitate additional weight loss in refractory or recurrent cases needs to be examined.

Endoluminal stapling

The Transoral Gastroplasty System (TOGA; Satiety Inc., Palo Alto, CA) was the first endoscopic device to use staplers to create full thickness plications along the lesser curve of the stomach, effectively creating a sleeve[30]. The technique entails upper endoscopy and placement of a guide wire over which a 60 Fr bougie is introduced to dilate and test for any resistance prior to device introduction. The TOGA Sleeve Stapler is introduced over the guide wire and the wire removed. A ≤ 8.6 mm endoscope is introduced through a channel in the device, advanced into the stomach and retroflexed for direct viewing of the stapling procedure. In the stomach, the body of the stapler is positioned along the lesser curvature and the jaws opened. A septum with an attached retraction wire is deployed to spread and orient the stomach tissue for capture and stapling. Suction is applied and tissue from the anterior and posterior walls of the stomach is acquired into two vacuum pods in the device. The stapler is closed and fired, delivering three rows of 11 titanium staples. This creates a transmural staple line connecting the anterior and posterior stomach, beginning 1 cm proximal to the Z-line and extending distally 4.5 cm, parallel to the lesser curvature. This process is repeated to add a second staple line, extending the new sleeve distally to create a sleeve approximately 8-9 cm in length. The distal sleeve outlet is then narrowed using the TOGA Restrictor, a single-suction-pod stapler that acquires and staples tissue in pleats. Restrictions are placed until the outlet is less than 20 mm.

Devière *et al*[30] conducted the first human prospective, single-arm trial examining the safety and feasibility of the TOGA system in 21 patients. Primary outcomes focused on safety and appearance of the pouch at 6 mo. Secondary outcomes included %EWL. The study demonstrated that the most common device-related adverse events were vomiting, pain, nausea and transient dysphagia. There were no serious adverse events. Assessment of pouch anatomy at 6 mo demonstrated staple line gaps in 13 patients, incomplete distal sleeves in 3 patients and normal pouch anatomy (i.e., intact sleeves and staple lines) in 5 patients. In terms of secondary outcomes, mean EWL was 16.2%, 22.6%, and 24.4% at 1, 3, and 6 mo and the average BMI decreased from 43.0 pretreatment to 37.8 at 6 mo ($P < 0.0001$).

A follow-up prospective, single-arm study by the same group[31] examined the safety and feasibility of a second generation TOGA stapler that was modified to remedy the staple line gaps. The device was improved by the development of an adjustable septum that allowed closer apposition of the two staple lines. A total of 11 patients were recruited into the trial. No serious adverse events were observed but procedure related problems included transient epigastric pain requiring analgesic treatment, throat pain, esophagitis, nausea and mild dysphagia. At 6 mo, endoscopic examination demonstrated that 4 of 11 patients had a mid-stoma (less than 1cm) indicative of a gap between the first and second staple line. Assessment of %EWL demonstrated a reduction of 19.2 %, 33.7% and 46.0% at 1, 3 and 6 mo, respectively ($P < 0.05$), with a mean BMI reduction from 41.6 kg/m^2 before treatment to 38.1 kg/m^2, 35.4 kg/m^2 and 33.1 kg/m^2 at 1, 3 and 6 mo, respectively ($P < 0.01$).

Taken together, these studies demonstrate that the TOGA system is feasible, safe and can induce significant weight loss in the short-term. Currently the Phase I trials are being validated in multicenter, randomized controlled trials to evaluate the durability and extent of weight loss.

Transoral endoscopic restrictive implant system

The transoral endoscopic restrictive implant system [BaroSense Trans-oral Endoscopic Restrictive Implant System (TERIS), BaroSense, Redwood City, CA] endoscopically implants a prosthetic device at the level of the cardia, creating a small gastric reservoir. The procedure requires formation of 5 gastric plications with insertion of 5 silicone anchors, followed by attachment of the gastric restrictor[32].

Specifically, plications are created at the level of the cardia, 3 cm distal to the gastroesophageal junction. The first plication is created just above the lesser curve of the stomach using an articulating endoscopic circular stapler which, through suction, can acquire a full-thickness gastric plication, compress the tissues and create 2 concentric rings of 3.5 mm staples reinforced by a plastic ring. The stapler also excises the tissues within the ring to create a plication hole. Then using a 2-lumen cannulation guide, the endoscope, silicone anchors and articulated guide with an anchor grasper are inserted. The proximal end of the silicone anchor is pulled under direct visualization through the plication hole and then released. Once all five anchors are placed, they are each attached to

locking anchor graspers using a multiple-lumen guide and a 5mm endoscope. The 5 proximal handles of the anchor graspers are passed through the 5 apertures in the gastric restrictor and are used to guide the gastric restrictor down to the level of the anchors. Under direct visualization, the proximal ends of the silicone anchors are brought inside the gastric restrictor, to lock it in place.

The initial feasibility and safety of the TERIS system is being examined in 20 human subjects by Biertho *et al*[32] using a randomized, uncontrolled, open label, single group Phase I human trial. A published report on their first case demonstrated that there were no intra- or post-operative complications and the patient was discharged home on post-operative day 2 tolerating a soft diet. At 3 and 6 mo, the %EWL was 21% and 26% respectively.

Considering the novelty of the TERIS system, further investigation of the safety and efficacy of the device in both the short and long-term and comparison to controls in a randomized fashion is warranted.

Duodenal-jejunal bypass sleeve

The duodenal-jejunal bypass sleeve (DJBS, The EndoBarrier, GI Dynamics Inc., Lexington, MA, United States) is an endoluminal malabsorptive procedure that effectively bypasses the proximal small intestine using a 60 cm long fluoropolymer liner anchored in the duodenum. Under general anesthesia, the device is delivered using both fluoroscopy and endoscopy. The implant is delivered using an over-the-wire catheter system and is contained within a capsule at the distal end of the catheter. Once the capsule is placed in the duodenum, an inner catheter is pushed and the bowel negotiated with the aid of an atraumatic ball attached to the distal end of the catheter. The sleeve, which is attached to the catheter, is pulled out of the capsule as the catheter is advanced. Once the sleeve is fully deployed, the anchor is deployed from the capsule to sit within the duodenal bulb. The anchor is self-expanding and the barbs engage the tissue to prevent movement. Contrast is flushed to ensure patency of the sleeve and the sleeve and ball are detached from the catheter which is removed from the bowel, leaving the implant in place[33].

Rodriguez-Grunert *et al*[33] reported on the first human experience, delivering and retrieving the DJBS in 12 patients. Primary outcomes measured the incidence and severity of adverse events, with secondary measures focused on %EWL and changes in co-morbid status. The mean implant and explant times were 26.6 and 43.3 min respectively. The device remained in place for 12 wk in 10 of 12 patients, with early retrieval (i.e., 9 d) in 2 patients due to intractable abdominal pain. Most adverse events related to implantation occurred within the first 2 wk and included abdominal pain, nausea and vomiting. During explantation, there was one partial pharyngeal tear and one esophageal tear. All patients had implant site inflammation. In terms of weight loss, at 12 wk, the average %EWL in 10 of 12 patients was 23.6%, with all patients achieving at least a 10% EWL. Finally, of the 4 diabetic patients, all had normal fasting plasma glucose levels for the entire 12 wk without the need for oral hypoglycemics and 3 of 4 patients had decreased HbA1c of $\geqslant$ 0.5% by week 12.

Tarnoff *et al*[34] conducted an open-label, multicenter, prospective randomized control trial comparing the effect of the DJBS with a low fat diet, to a low fat diet alone for 12 wk. The device was implanted in 25 patients and 14 patients comprised the control arm. Both groups received counseling at baseline, consisting of a low calorie diet, with advice on exercise and behavior modification. The study demonstrated that 20 of 25 device subjects maintained the sleeve for 12 wk. The mean EWL was 22% and 5% for the device and control groups, respectively. Five of 25 device subjects had to have the device explanted early due to upper GI bleeding (n = 3), anchor migration (n = 1) and sleeve obstruction (n = 1). At 12 wk, the average %EWL was 22.1% and 5.3% for the device and control group respectively. Concerning diabetes, four patients (i.e. 1 control subject and 3 experimental subjects) had a history of type 2 diabetes. Within 1 wk, all 4 patients had improved HbA1c levels and one diabetic in the device arm had complete resolution of diabetes at 12 wk.

While future studies are needed to elucidate the safety and feasibility of the DJBS in both the short- and long-term, this procedure could potentially be utilized as a non-surgical method for pre-operative weight loss or improvement and/or resolution of type 2 diabetes. Additionally, the DJBS could be utilized as a bridge in those patients whose BMI and/or comorbidities preclude them from undergoing surgery, allowing weight reduction and improvement in co-morbidities to a level that would make a surgical bariatric procedure more safe.

TRANSORAL SURGERY FOR REVISIONAL BARIATRIC PROCEDURES

Transoral procedures are also being investigated in the context of revisional bariatric surgery. Specifically, while roux-en-y gastric bypass remains the gold-standard surgical procedure for weight loss (i.e., %EWL at 2 years of 61.6%[16]; early and late mortality of 0.16% and 0.09%, respectively[17]), inadequate loss and/or weight regain is reported as high as 25%-30% after gastric bypass or other bariatric procedures[35,36]. The etiology of weight regain is multifactorial[37] and includes inadequate long-term management of psychological, dietary or medical issues, as well as anatomical aberrancies.

Focusing on anatomy, initial investigations must include an esophagogastroduodenoscopy (EGD) or upper GI study to evaluate for gastro-gastric fistula, gastric pouch dilatation or anastomotic dilatation. Once a gastro-gastric fistula is ruled out, gastrojejunal anastomosis and/or pouch dilatation may underlie weight regain as patients may lose the feeling of early satiety, leading to overeating. Indeed, upper endoscopy has revealed that, in patients who regain weight, the size of the stoma or anastomosis is twice the immediate post-operative diameter of 1.0-1.5 cm.

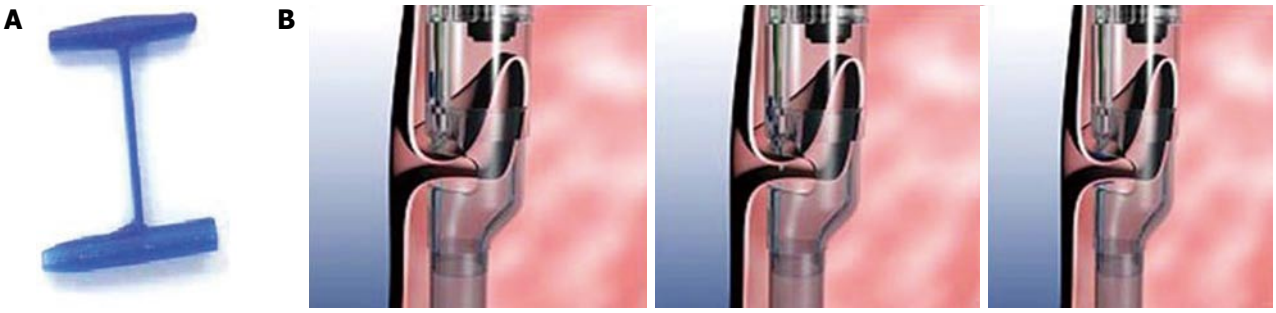

Figure 2 StomaphyX device. A: polypropylene fastener; B: StomaphyX™ mechanism of tissue approximation.

If dilatation of the pouch or gastrojejunal anastomosis is diagnosed, then revisional surgery may be necessary and issues related to feasibility and safety arise. Recent studies estimate a rate of 5%-13% for major complications with re-operative surgery[38], the most serious of which include anastomotic leaks, wound dehiscence, incisional hernias and pulmonary complications.

Given the frequency of weight regain and risk of revisional surgery, Mikami *et al*[39] investigated whether it was possible to restore a dilated gastric pouch to its original inner diameter and/or volume transorally by utilizing the StomaphyX™ device; a natural orifice surgical device that utilizes 7 mm, 3-0 polypropylene H-fasteners to create full-thickness, serosal-to-serosal tissue approximation.

As described by Mikami *et al*[39], under general anesthesia, an EGD is performed to measure the length of the pouch. The gastroscope is then placed through the internal lumen of the StomaphyX™ device and extended approximately 20 cm beyond the device. The apparatus is then passed down the esophagus, through the gastric pouch and the scope is passed into the efferent jejunal limb to allow passage of the StomaphyX™ device through the anastomosis. Using suction, the StomaphyX™ device draws tissue through an opening at its distal end and an H-fastener is deployed. In this manner, a circular pleat of tissue is created 1 cm proximal to the anastomosis, with a second row placed 1 cm proximal to the first row. A total of 12 fasteners are placed at two different levels. Finally, any identified open mucosal areas are fastened (i.e., an additional 3-5 fasteners). Repeat endoscopy is used at the end of the procedure to assess the reduction of the gastric pouch and anastomosis (Figure 2).

A total of 39 patients were enrolled in the trial[39]. The average procedure time was 35 min (16-62 min) and between 12 and 41 H-fasteners were used in each case. In terms of primary safety outcomes, 37 of 39 patients were discharged on the same day with the remaining 2 patients kept overnight due to their procedure being performed late in the day. There were no major adverse events. Minor complications included sore throats lasting less than 48 h [34 of 39 patients (87.1%)] and epigastric pain lasting for a few days [30 of 39 patients (76.9%)]. Interestingly, 3 patients with late dumping syndrome after their original gastric bypass experienced resolution of their postprandial diarrhea. Additionally, at 1 mo follow-up, 8 patients with a history of gastric esophageal reflux noted improvement of their symptoms post-procedure. In terms of weight loss, the average pre-procedure excess body weight was 51.1 kg. Mean weight loss at 2 wk (n = 39) was 3.8 kg (7.4% excess body weight loss, EBWL), at 1 mo (n = 34) was 5.4 kg (10.6% EBWL), at 2 mo (n = 26) was 6.7 kg (13.1% EBWL), at 3 mo (n = 15) was 6.7 kg (13.1% EBWL), at 6 mo (n = 14) was 8.7 kg (17.0% EBWL) and at 1 year (n = 6) was 10.0 kg (19.5% EBWL).

This trial demonstrates that the StomaphyX™ procedure may offer a safe, effective revisional bariatric procedure; however, long-term randomized prospective studies need to be conducted.

CONCLUSION

Currently, laparoscopic surgical therapies for morbid obesity are effective in achieving significant weight loss and improving obesity-related co-morbidities over the long-term. However, as is true of all surgical procedures, laparoscopic approaches to weight loss are not without patient restrictions (e.g., multiple co-morbidities, older age, super-obesity, atypical anatomy) and procedural complications[18,19].

Given the persistence of obesity in the United States and limitations of surgical interventions, there is a growing demand for less-invasive approaches. Transoral techniques, as both primary and revisional procedures, are promising in this regard. However, these therapies need to be rigorously tested in a randomized, controlled fashion, to determine their safety and efficacy in both the short- and long-term. In particular, transoral procedures should not only demonstrate equivalent or lower morbidity and mortality rates compared to the current gold-standard therapy (i.e., roux-en-y gastric bypass) but they should also aim to achieve meaningful weight loss and improvement in co-morbid states.

Currently, several aforementioned techniques are being examined in Phase Ⅱ/Ⅲ trials (Table 1). If these studies demonstrate that transoral procedures can achieve safe, effective and long-term weight loss, then their applicability could be far reaching. Indeed, the major advantages of transoral techniques include: (1) provision of ambulatory weight loss procedures that may be safer and more cost effective compared with laparoscopic approaches; and (2) circumvention of permanent surgical modification. Therefore, those patients who were pre-

Table 1 Summary of developmental phase of transoral procedures

	Endoluminal vertical gastroplasty	Transoral gastroplasty system	Transoral endoscopic restrictive implant system	Duodenal-jejunal bypass sleeve	Stomaphyx
Phase of development	Phase Ⅱ Non-randomized multicenter feasibility studies	Phase Ⅱ Non-randomized multicenter validation trials	Phase Ⅰ Trial still underway - report on first patient	Phase Ⅱ/Ⅲ	Phase Ⅲ
Patients/trials	n = 82 in 2 trials n = 64[28] n = 18[29]	n = 32 in 2 trials n = 21[31] n = 11[30]	n = 20 in 1 trial	n = 37 in 2 trials n = 12[33] n = 25[34]	n = 39 in 1 trial
Short term morbidity	Nausea, vomiting, abdominal pain	Nausea, vomiting, epigastric pain, transient dysphagia	Not reported	Nausea, vomiting, abdominal pain	Sore throat, epigastric pain
Long term morbidity	Disruption of suture lines (n = 3/64[28])	Staple line gaps (n = 13/21[31]) Incomplete distal sleeves (n = 3/21[31])	Not reported	Tissue inflammation at site of anchor	None
Mortality	None	None	None	None	None
Average length of procedure	45 min[28] 125 min[29]	160 min[31] 84 min[30]	195 min	41 min[33] 39 min[34]	35 min
Tested in randomized trials	No	No	No	Yes[34]	Yes
%EWL			Not reported		
1 mo	21.1[28]	16.2[31]; 19.2[30]		16.0[33]; 15.0[34]	10.6
3 mo	39.6[28]	22.6[31]; 33.7[30]	21.0	24.0[33]; 21.0[34]	13.1
6 mo	Not reported	24.4[31]; 46.0[30]	26.0	Not reported	17.0
12 mo	58.1 (n = 59/64)[28]	Not reported	Not reported	Not reported	19.5

%EWL: Percentage excess weight loss.

cluded for pathological/physiological or financial reasons may be candidates for weight loss procedures. Additionally, transoral techniques may also be used as a bridge for more definitive weight loss procedures. Specifically, using these techniques may provide a way of identifying those patients who are committed to a more definitive surgical intervention. Finally, transoral techniques could provide a safer means of revising bariatric procedures in those individuals that have reached their weight-loss plateau or have started regaining weight.

Transoral techniques are rapidly becoming a reality in the armamentarium of weight loss procedures and it is our responsibility to ensure that these techniques are safe and effective in the long-term.

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EDITORIAL

Management of abdominal and pelvic abscess in Crohn's disease

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Abstract

Patients with Crohn's disease may develop an abdominal or pelvic abscess during the course of their illness. This process results from transmural inflammation and penetration of the bowel wall, which in turn leads to a contained perforation and subsequent abscess formation. Management of patients with Crohn's related intra-abdominal and pelvic abscesses is challenging and requires the expertise of multiple specialties working in concert. Treatment usually consists of percutaneous abscess drainage (PAD) under guidance of computed tomography in addition to antibiotics. PAD allows for drainage of infection and avoidance of a two-stage surgical procedure in most cases. It is unclear if PAD can be considered a definitive treatment without the need for future surgery. The use of immune suppressive agents such as anti-tumor necrosis factor-α in this setting may be hazardous and their appropriate use is controversial. This article discusses the management of spontaneous abdominal and pelvic abscesses in Crohn's disease.

Key words: Crohn's disease; Abdominal abscess; Psoas abscess; Abscess; Drainage; Computed tomography; Spiral; Infection; Colorectal surgery

EPIDEMIOLOGY AND PATHOGENESIS

Abdominal and pelvic abscesses in Crohn's disease occur spontaneously or as a post-operative complication. This article focuses on the former. Approximately 10% to 30% of patients with Crohn's disease will spontaneously develop an abdominal or pelvic abscess during the course of their illness[1-3]. These abscesses occur from transmural inflammation and microperforation of diseased bowel[4,5]. Fistulas arising from the diseased bowel are often associated with the abscess cavity[6]. In the great majority of cases, the terminal ileum or ileo-cecal region are the foci of Crohn's related activity[1,4,7]. Most commonly, abscesses occur in the abdominal wall, rectus sheath, iliopsoas muscle, gluteus muscle, presacral and subphrenic spaces[1,8]. The majority of abscesses occur on the right side near the diseased bowel and almost always at the site of a prior anastomosis[1].

CLINICAL PRESENTATION AND DIAGNOSIS

Routine history and physical examination will identify most patients suspected of having an abdominal or pelvic abscess[9]. Abdominal pain, fever and a palpable mass are the most common findings[7]. A palpable mass is present

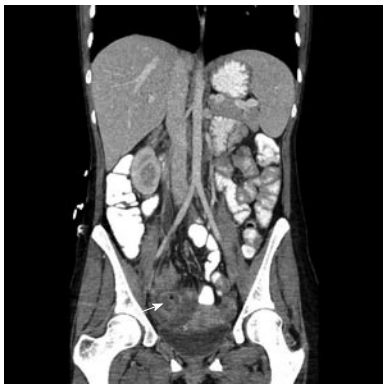

Figure 1 A 33-year-old female patient with a 3 cm pelvic abscess due to Crohn's disease. The computed tomography demonstrates an abscess cavity with a small air bubble within it (arrow) prior to drainage, which was accomplished by placing a drainage catheter via the transgluteal route.

in about 1/3 of patients. Rebound tenderness occurs 30% of the time[10]. Clinicians should be aware that elderly or immune suppressed patients sometimes manifest fewer signs and symptoms[9]. Abscesses involving the psoas muscle can present insidiously as vague flank pain or a new onset limp[11]. Patients with signs and symptoms of abscess should undergo spiral computed tomography (CT) with intravenous and oral contrast (Figure 1). If available, CT enterography with a neutral contrast agent is preferable because it is more likely to demonstrate an associated fistula and also gives valuable information regarding the extent and degree of bowel wall inflammation[12].

The radiological definition of an abscess varies in the literature. An inflammatory mass with ill-defined borders is often referred to as a phlegmon[13]. On the other hand, an abscess has a well-defined border[14]. Most often it is defined as a ring enhancing fluid collection, with or without air[15]. Some authors include the aspiration of pus as a diagnostic inclusion criterion[10].

The next step in management depends on the patient's clinical status. It should be stressed that most abscesses represent contained perforations: free perforations are rare in Crohn's disease[6]. If the patient does not have peritonitis and is hemodynamically stable, a drainage procedure can be delayed for up to 24 h if appropriate antibiotics are given[9]. Acute peritonitis is best treated with surgery rather than percutaneous abscess drainage (PAD), even if imaging demonstrates a drainable collection[9].

COMPUTED TOMOGRAPHY GUIDED PERCUTANEOUS ABSCESS DRAINAGE

PAD has replaced open laparotomy as the initial choice for draining these abscess collections[8]. The benefits of drainage are derived from delaying surgery as long as possible. This will allow the inflammation associated with the septic process to resolve, thereby allowing for a limited resection and a possible one-stage operation at a later date[16]. Delaying surgery also allows time for optimizing nutritional status and reducing or stopping corticosteroids[17,18].

If the abscess is drainable by PAD, the next step is to aspirate the collection in order to demonstrate the nature of the fluid[19]. As much pus as possible should be aspirated[20]. The aspirate should be sent for routine culture and sensitivity. Most abscesses are polymicrobial[21]. Enteric gram-negative bacilli, gram-positive cocci and anaerobes predominate, although a minority of pathogens are identified by routine laboratories[21]. The major pathogens in community-acquired intra-abdominal infections are coliforms (especially *Escherichia coli*) and anaerobes (especially *Bacteroides fragilis*)[9]. Chosen antibiotics should cover these organisms. Also, in choosing the correct antibiotic, it is helpful to know the organisms' resistance pattern in the community and local hospital setting[9,21]. Patients from underdeveloped countries or those who are immune suppressed might have tuberculosis or other opportunistic infections as the causal organism[22]. Abscesses less than 3 cm do not require drainage. They can be managed by antibiotics alone or in combination with simple aspiration[8].

The drainage approach depends on the abscess' location. A transgluteal approach is common for pelvic abscesses and is associated with a low complication rate[6,8]. Transabdominal and perineal approaches are also commonly used[19]. A drainage catheter should be left in place and the quality and quantity of its output should be measured daily. The catheter's diameter should be chosen according to the viscosity of the aspirated material. A large enough diameter is essential to assure success of drainage[23]. The catheter should be flushed with 10-20 mL of saline every 6 h to assure patency[8].

Clinical improvement is usually seen within 48 h of successful drainage[8,19]. If fever persists, a repeat CT is indicated to assure that the catheter is properly positioned. The catheter can be removed when drainage decreases to 10-20 mL per day[3,24]. The mean time for drainage is approximately 7-10 d (range 3 to 23 d)[8,20]. Antibiotics are generally not indicated for more than 7 d or until fever resolves[9].

If an abscess is not accessible by CT, endoscopic ultrasound (EUS) can be employed to drain the cavity by the transrectal or transvaginal approach[19,25,26]. For EUS, the abscess must be within 2 cm of the rectum or left colon[26]. Alternatively if all of these methods fail, a laparoscopic drainage can be performed with minimal invasiveness[27].

SUCCESS OF PERCUTANEOUS ABSCESS DRAINAGE

The definition of success varies across studies. Generally, success is defined as resolution of symptoms with collapse of the abscess cavity and avoidance of early surgery (within 30-60 d)[3,5,10,20,28,29]. With this definition in mind, success rates vary from 50%-95%[3,5,8,19,23]. Multiple or multi-locular abscesses and those associated with a fistula are more often prone to failure[3,8,29]. Also, spontaneous

abscesses have a poorer prognosis than post-operative ones. Golfieri *et al*[8] found that spontaneous abscesses were associated with a lower success rate than post-operative abscesses (77% *vs* for 84.3% respectively), although this was not statistically different. Failure of PAD is usually heralded by continued drainage of > 20 mL/d (with continued thick viscosity). If this happens, a sinogram should be performed and will usually demonstrate a fistula to bowel, indicating a need for prompt surgical repair[8].

TIMING OF SURGERY

The timing of surgery after successful PAD is controversial. Poritz *et al*[15] successfully performed a one-stage surgery in 84% of 19 patients after only 7 d of drainage. da Luz Moreira *et al*[5] performed surgery on 48 patients at a median of 43 d (range 8 to 220 d) after PAD. Twenty-three percent of these patients required a stoma; therefore, successful PAD does not guarantee a one-stage operation. Others wait 6-8 wk to perform elective surgery after drainage[30]. The timing of surgery is also influenced by other factors such as nutritional status and prior steroid use[6]. There is a high risk of surgical dehiscence if steroids are used for more than 3 mo[4].

Whether or not all patients require surgery after successful PAD is unknown. One argument favoring elective surgery is that diseased bowel left intact is a focus for future abscess recurrence, perhaps requiring emergency surgery at a later date. In one study, only 23% of patients avoided a definitive operation after a mean follow-up of 7.2 years[3]. In another study, 6 of 7 patients that did not have elective surgery had a severe recurrence within 3 years[1]. On the other hand, some studies have shown the majority of patients do well after PAD without definitive surgery and that the recurrence rate is acceptably low[10]. Golfieri *et al*[8] found that only 12.6% of 70 patients developed a recurrent abscess after a mean follow-up of 39 mo and that only 5/11 of these patients required urgent surgery. As mentioned, patients with fistula are likely to recur and should undergo surgery[18].

THE USE OF BIOLOGICS AFTER PERCUTANEOUS ABSCESS DRAINAGE

Anti-tumor necrosis factor (TNF)-α drugs such as adalimumab are approved for use in patients with inflammatory Crohn's and fistulizing disease and are contraindicated in patients with abscess or active infection[31]. Their safety after PAD drainage has not been formally evaluated and is therefore not known[32].

Anti-TNF-α drugs may potentially benefit patients after PAD by decreasing inflammation and closing fistulas, thereby limiting surgery or avoiding it altogether. Their use is probably safe if all infection has been successfully drained. However, undrained collections (which may be undetectable) represent a problem. Eighteen patients underwent a planned one-stage surgical procedure after successful PAD in one study: in 2 of these 18 patients, residual pus was found at the time of surgery[15]. Therefore, they should be used with extreme caution in this setting and only after a thorough discussion with the patient of the potential risks and benefits. Also, there is a concern that they may increase post-operative complications; however, this aspect is controversial[17,18].

CONCLUSION

Spontaneous abdominal and pelvic abscess occur in 10%-30% of Crohn's patients over the lifetime of their disease. Successful management depends on a highly skilled team of surgeons, gastroenterologists and interventional radiologists who have experience with this complication. PAD (in conjunction with IV antibiotics) should be done whenever possible until the infection has subsided. Fistulas and multiple abscesses predict a poor response to PAD. After successful PAD, patients should be offered the option of elective surgery, which can be done soon after successful drainage. If patients are poorly nourished or have been on steroids for more than 3 mo, it is best to wait in order to optimize their medical condition. Anti-TNF-α drugs can be used after successfully draining all infected fluid collections. Their safety and efficacy in this setting is not currently known and should be used with caution.

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BRIEF ARTICLE

Endoscopic and retrograde cholangiographic appearance of hepaticojejunostomy strictures: A practical classification

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Abstract

AIM: To study the endoscopic and radiological characteristics of patients with hepaticojejunostomy (HJ) and propose a practical HJ stricture classification.

METHODS: In a retrospective observational study, a balloon-assisted enteroscopy (BAE)-endoscopic retrograde cholangiography was performed 44 times in 32 patients with surgically-altered gastrointestinal (GI) anatomy. BAE-endoscopic retrograde cholangio pancreatography (ERCP) was performed 23 times in 18 patients with HJ. The HJ was carefully studied with the endoscope and using cholangiography.

RESULTS: The authors observed that the hepaticojejunostomies have characteristics that may allow these to be classified based on endoscopic and cholangiographic appearances: the HJ orifice aspect may appear as small (type A) or large (type B) and the stricture may be short (type 1), long (type 2) and type 3, intrahepatic biliary strictures not associated with anastomotic stenosis. In total, 7 patients had type A1, 4 patients A2, one patient had B1, one patient had B (large orifice without stenosis) and one patient had type B3.

CONCLUSION: This practical classification allows for an accurate initial assessment of the HJ, thus potentially allowing for adequate therapeutic planning, as the shape, length and complexity of the HJ and biliary tree choice may mandate the type of diagnostic and therapeutic accessories to be used. Of additional importance, a standardized classification may allow for better comparison of studies of patients undergoing BAE-ERCP in the setting of altered upper GI anatomy.

Key words: Endoscopic retrograde cholangio pancreatography; Roux en Y anastomosis; Hepaticojejunostomy; Biliary strictures; Bile duct strictures; Double balloon enteroscopy

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INTRODUCTION

Occasionally, patients with previous complex upper gastrointestinal (GI) surgery and hepaticojejunostomy (HJ) present with pancreatobiliary problems[1-5]. HJ is a common curative and palliative procedure performed for benign and malignant biliary obstruction. The incidence of anastomotic stricture following HJ in experienced centers is 4%-10%[1-3]. Because re-operation carries a significant morbidity, endoscopic or radiological approaches to treat these strictures are now preferred[1-3]. Nevertheless, performing an endoscopic retrograde cholangio pancreatography (ERCP) in these patients is technically very challenging or impossible, frequently mandating an operative intervention. However, the advent of balloon-assisted enteroscopy (BAE)[4] has increased our ability to reach the HJ located in the excluded limb and perform diagnostic and therapeutic endoscopic retrograde cholangiography (ERC)[3-18]. During BAE-ERC, we have observed that the HJ and biliary tree have specific appearances (i.e., patterns).

The aims of this study were to assess the endoscopic and radiological characteristics of the HJ of patients with Roux-en-Y anastomosis presenting with biliary problems undergoing BAE-ERC and propose a practical HJ stricture classification.

MATERIALS AND METHODS

Patients

Over a period of 4 years, we performed 44 BAE-ERCPs in 32 patients with various types of complex post-surgical upper GI anatomy and pancreatobiliary problems. In the present study, we focused on the endoscopic and radiological findings of hepaticojejunostomies. Patients without HJ or with intact papilla were excluded. The procedures were performed at the University of Magdeburg Medical Center and Marienhospital, Bottrop, Germany. All patients provided written informed consent before the endoscopy. The study was approved by the institutional review board and conducted according to the guidelines of Helsinki.

Procedure description

The patients were placed in the prone position and the endoscopy was performed using conscious sedation with midazolam and propofol with constant monitoring of vital signs. ERC was performed with the therapeutic DBE (DBE-EN-450T5, Fujinon, Saitama, Japan) with a working channel of 2.8 mm diameter and a 140 cm long, 13.5 mm diameter overtube (TS Fujinon, 13.5 mm, Saitama, Japan). The ERC was performed either with balloons mounted on both the enteroscope and overtube or only on the overtube. The details of the procedure have been described in detail elsewhere[6-10]. BAE-ERC was performed under fluoroscopic control using a C-arm (Philips, Holland). Cannulation of the biliary tract was achieved with a tapered tip biliary catheter (F3CTPK1810250M, Fujinon, Japan) and two types of guidewires: Jagwire (Boston Scientific, Miami, United States) or the FTE-Wildcat nitinol exchange guide wire (650 cm long, F3LQPK0850650X-S) Fujinon Europe, GmbH). The following stents were used: 7 Fr 5 cm long (Wilson Cook, Ireland). These stents were pushed with the biliary catheter or the customized pusher tube for the DBE system (Fujinon FPU7270: this pusher pushes 7 Fr stents and has a length of 270 cm). These additional accessories were used to accomplish the various interventional procedures: balloon dilation of the anastomosis was performed using a constant radial expansion (CRE) wire-guided balloon dilatation catheter (Wire-guided 240 cm, CRE™ Balloon Dilator, Boston Scientific Medizintechnik GmbH, Ratingen, Germany).

Descriptive statistics were employed to describe the patient's demographics and clinical characteristics, presenting means and ranges.

RESULTS

ERCP using the DBE was performed on 44 occasions in 32 patients (10 female and 22 male, mean age 62.5, range 25 to 78) with altered upper GI anatomy. Twenty three BAE-ERCPs were performed in 18 patients with Roux-en-Y type of reconstruction with HJ and represent the study group. In fourteen patients (3 female, and 11 male), the HJ could be clearly visualized and cannulated. In five patients, multiple procedures (2 to 3) were performed (e.g., follow-up to remove or place new stents). Thus, a total of 19 out of 23 (82%) procedures were successful (Table 1). The mean follow-up has been 18 mo (range 6 to 40 mo). Table 1 summarizes the demographic, clinical, endoscopic findings, procedures and interventions of the study group. Indications for ERC included biliary obstruction and cholestasis in all patients. The procedure lasted a mean time of 70 min (range 35 to 240 min).

We observed that the HJ does not have a uniform appearance but rather a few key characteristics that may allow the stenosis to be stratified based on endoscopic (letter classification, i.e., A, B, C and D) and cholangiographic appearance (numbers, i.e. 0, 1, 2 and 3) (Table 2). Endoscopically, the HJ orifice can appear as small (type A) (Figure 1), large (type B) (Figure 2), normal (C) and double (i.e., separate anastomosis for the left and right hepatic ducts) (D)[17]. Of note, the endoscopic appearance allows classification of the HJ-orifice at the level of the lumen or above it. In Figure 2, a case of a suprastenotic stricture is seen, i.e. the anastomosis at the luminal level is wide open or normal, whereas there is a clear stricture a few millimeters above it (i.e., proximal) (Figure 2). This is a supra-anastomotic stricture (S) (Table 2).

After the cholangiogram was performed, the biliary tract was depicted and a stricture was verified, which was short (type 1) (Figure 3), long (type 2) (Figure 4) and type 3, intrahepatic biliary strictures not associated with anastomosis, i.e., non-anastomotic, e.g., sclerosing cholangitis) (Figure 5). In the theoretical case of absence of cholangigraphic stricture, the classification would be type 0. In total, 7 patients had type A1 (Figure 6A-D), 4 patients A2 (Figure 7A and B), one patient had B1 (Figure 8A-C), one patient had B3 and one patient had large orifice HJ without stenosis (type B0, Figure 9A and B). The types of HJ

Table 1 Demographic, clinical and endoscopic data in patients undergoing endoscopic retrograde cholangio pancreatography with the double balloon enteroscopy

No	Sex	Age (yr)	Indication	Post surgical anatomy	Findings	Intervention
1	Male	55	Jaundice	s/p Whipple with Roux-en-Y HJ	A1	Stenting Stent extraction and new stent (× 2) Balloon dilation
2	Male	55	Cholestasis, jaundice	s/p Whipple with Roux-en-Y HJ	A1	Cannulation with Jagwire Cholangiogram Stenting
3	Female	78	Upper GI-bleeding, melena, suspicious bleeding from the afferent loop	s/p Roux-en-Y HJ after complicated CCE	B	Direct endoscopic cholangiogram APC-therapy of angiodysplasias at the HJ
4	Male	36	Cholestasis, recurrent cholangitis	s/p Whipple with Roux-en-Y HJ	A2	Cholangiogram Stent placement Stone extraction
5	Male	69	Jaundice, suspicious relapse of Klatskin-Tumor	s/p partial CBD resection with hepaticojejunostomy	NA	Tumor biopsies at the HJ Cannulation failed => PTCD
6	Male	70	Cholestasis	s/p Whipple's operation, Roux-en-Y HJ	A1	Cholangiogram Stent insertion
7	Male	77	Cholestasis	s/p partial gastric resection with Roux-en-Y HJ s/p PTCD	A2	Cannulation with Jagwire Cholangiogram DHC-stenosis No stent
8	Male	72	Cholangitis	s/p Roux-en-Y HJ	NA	Failed (adhesions)
9	F	36	Cholestasis, chronic abdominal pain	s/p Roux-en-Y HJ	A1	Cholangiogram Balloon dilatation Perforation
10	Male	36	Cholestasis	s/p at age of 17 with Roux-en-Y HJ Late onset ulcerative colitis	B3	Referred for OLT
11	Male	65	Choledocolithiasis, abdominal pain, cholestasis	s/p Whipple's operation, Roux-en-Y HJ	A1	Balloon dilation and stenting Stent and stone extraction
12	Female	25	Cholangitis	s/p at age of 3 resection of a choledococele with Roux-en-Y HJ	A1	Bougienage of CBD stenosis and stent (× 2) insertion Stent retrieval and balloon dilation of CBD stenosis
13	Female	75	Choledocolithiasis	s/p Roux-en-Y HJ after complicated CCE (iatrogenic bile duct injury)	NA	Failed, adhesions, afferent limb intubated but proximal end not reached and HJ not found
14	Male	70	Cholestasis	s/p Whipple's operation, Roux-en-Y HJ	B1	Failed, oxygen desaturation Cholangiogram, biliary stent insertion
15	Male	72	Cholangitis	s/p Roux-en-Y with HJ after a complicated CCE (gangrenous cholecystitis)	A2	Dilation of CBD stenosis Biliary stent insertion
16	Male	54	Choledocolithiasis	s/p partial gastric resection with Roux-en-Y HJ	A2	Dilation of CBD stenosis, stent insertion Stone extraction
17	Female	58	Choledocolithiasis	s/p Whipple's operation, Roux-en Y HJ	NA	Failed, adhesions, afferent limb intubated but proximal end not reached and HJ not found
18	Male		Jaundice	s/p Whipple's operation, Roux-en Y HJ	A1	Dilatation Stenting

HJ: Hepaticojejunostomy; GI: Gastrointestinal; CBD: Common bile duct; CCE: cholecystectomyPTCD: Percutaneous transhepatic cholangiography drainage; DHC: ductus hepaticus communis; OLT: Orthotopic liver transplantation; s/p: Status post; NA: Not applicable.

found in each patient are depicted in Table 1. Interestingly, when observing a large opening of the HJ, a stenosis cannot be completely excluded as this can be located in the supra-anastomotic segment of the bile duct (type B, Figure 8A). In these cases, the stricture may be either short (type 1) or long (type 2). In other cases of type B or D HJ orifice (wide opening), a direct cholangiography using the thin enteroscope can be accomplished (Figures 9A and B). In occasional cases, unexpectedly, strictures may not be directly related to the HJ operation at all and affect the biliary tract diffusely, such as in a case of primary sclerosing cholangitis (type 3, Figure 5). The proposed classification and various types of HJ strictures are depicted in Figure 10. In addition, the proposed classification is summarized in Table 2.

In three patients, we were unable to deeply intubate the afferent limb. In another patient, the HJ was infiltrated with a recurrent Klatskin tumor impeding cannulation of the bile duct (Patient No. 5). The overall diagnostic success was 93% (13/14) and the endoscopic therapeutic

Table 2 Endoscopic-cholangiographic classification of hepaticojejunostomies

Type	Endoscopic findings
A	Small opening
B	Large opening
C	Normal opening
D	Double opening (i.e., double anastomosis)
S	Supra-anastomotic stricture[1]
	Cholangiographic findings
0	No stricture
1	Short stricture
2	Long stricture
3	Intrahepatic strictures

Letters refer to endoscopic appearance and numerals refer to cholangiographic characteristics. [1]In cases of normal (B) or large opening (C) a supra-anastomotic stricture can be present. This is separately indicated by S.

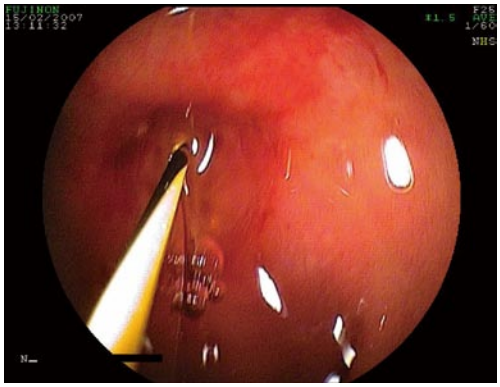

Figure 1 Small hepaticojejunostomy opening. A guidewire barely traverses it. This is a type A hepaticojejunostomy.

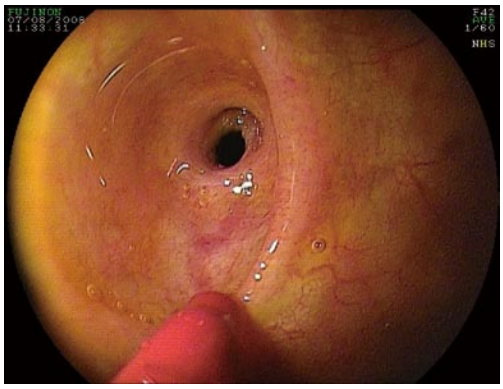

Figure 2 Wide opening hepaticojejunostomy (type B). The tip of the catheter shows the lower rim of the large hepaticojejunostomy opening. Above the hepaticojejunostomy there is a visible stenosis, which is clearly supra-anastomotic (type S). The length of the stenosis will be determined with a cholangiography (e.g., type 1 short or type 2 long).

success was 75% (9/13, in one patient no therapeutic intervention was attempted as he had sclerosing cholangitis and was referred for liver transplantation). Therapeutic interventions included biliary stent insertion (n = 8), dilation of common bile duct stenosis with a balloon (n = 5), stone removal with Dormia basket (n = 3) and stent

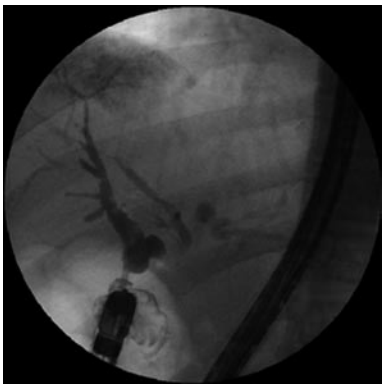

Figure 3 Short stricture of the distal bile duct at the level of the hepaticojejunostomy (type 1).

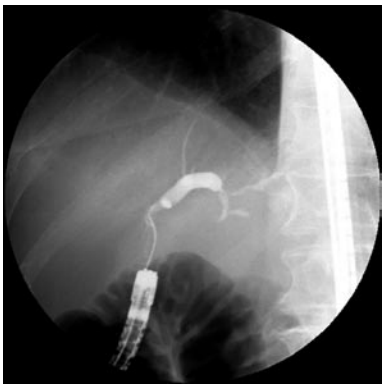

Figure 4 Long stricture of the hepaticojejunostomy (type 2).

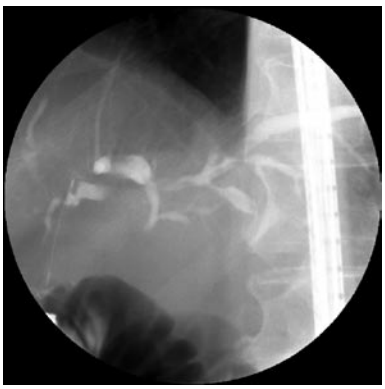

Figure 5 Intrahepatic bile duct strictures not affecting the hepaticojejunostomy in a patient with primary sclerosing cholangitis (type 3).

retrieval (n = 5) (therapeutic interventions exceeds the number of patients as in some patients more than one procedure was done). One complication occurred. This was a perforation of a HJ during balloon dilation (Table 1, Case No. 9). The patient was taken to the operating room immediately and a new surgical HJ was performed after extracting multiple stones from the biliary tract.

DISCUSSION

We and others have demonstrated that diagnostic and

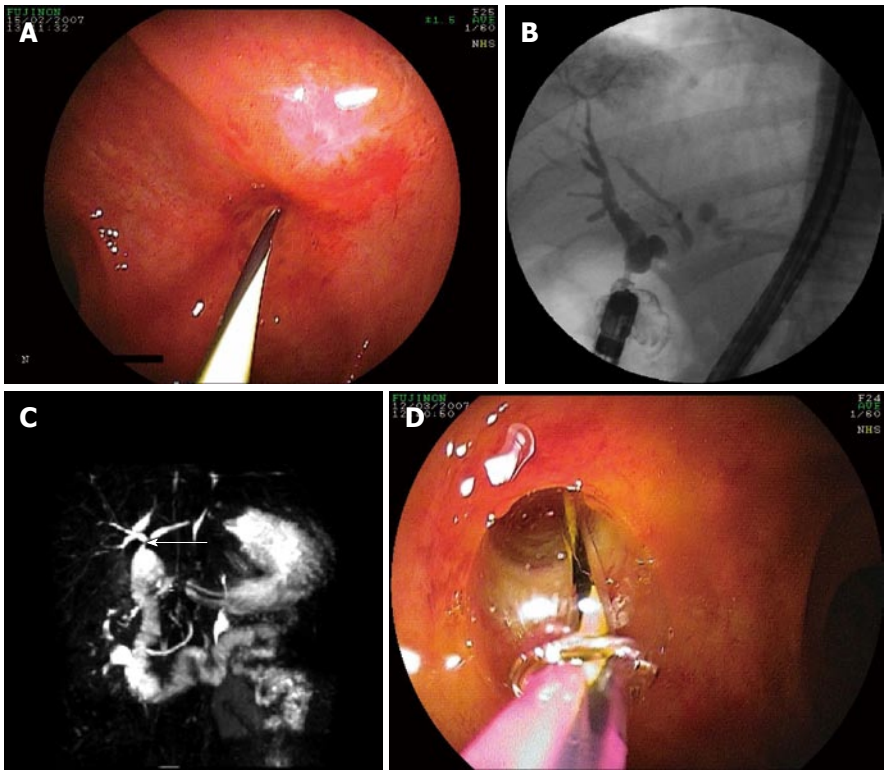

Figure 6 The small hepaticojejunostomy orifice (type A) barely permits the passage of a 0.035 inch wire (A), short stricture (type 1) on the cholangiogram (B), corresponding MRC image (C) and dilation with constant radial expansion-through the scope balloon (D). This is an example of a type A1 hepaticojejunostomy stricture.

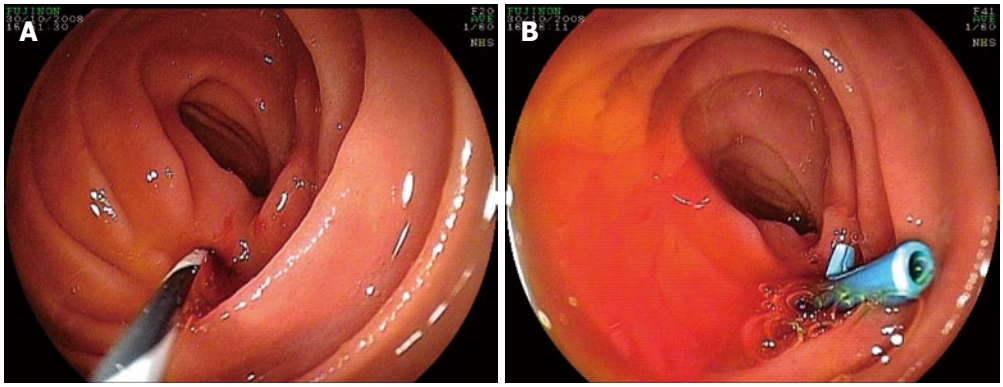

Figure 7 Small hepaticojejunostomy orifice (type A) (A). The 7 Fr plastic stent is seen in the small bowel lumen (B). This is an example of a type A2 hepaticojejunostomy stricture.

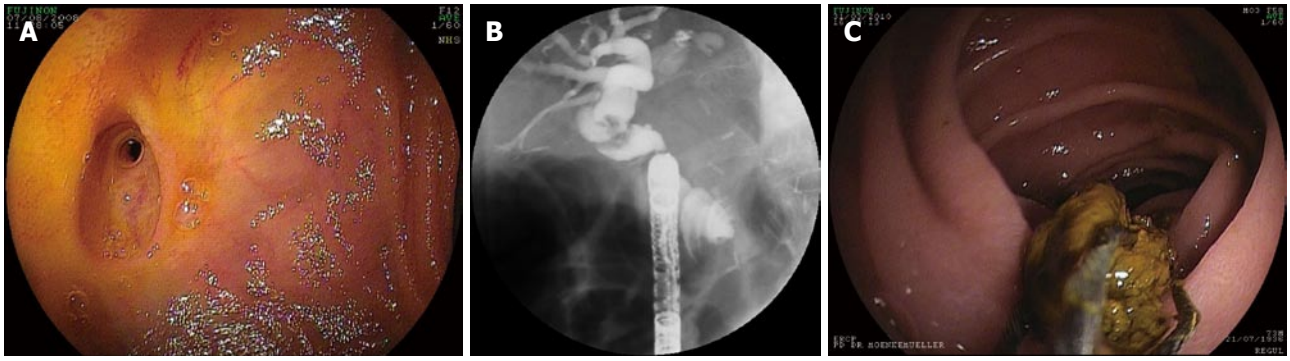

Figure 8 Wide opening of the hepaticojejunostomy (type B) (A) accompanied with short (cholangiographic type 1), supra-anastomotic stricture (type S) with dilated proximal bile duct and visible stone (B). After dilation of the stricture with a constant radial expansion-through the scope balloon, the stones were extracted with Dormia basket (C). This is an example of a B1 hepaticojejunostomy stricture.

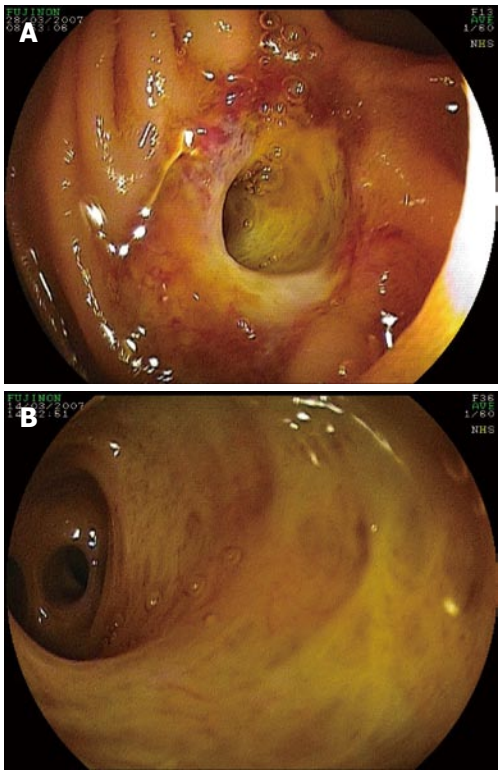

Figure 9 This patient had an exceptionally large hepaticojejunostomy (type C) (A), permitting the careful insertion of tip of the scope to perform a direct cholangioscopy (B). This is a type C hepaticojejunostomy without strictures (type 0).

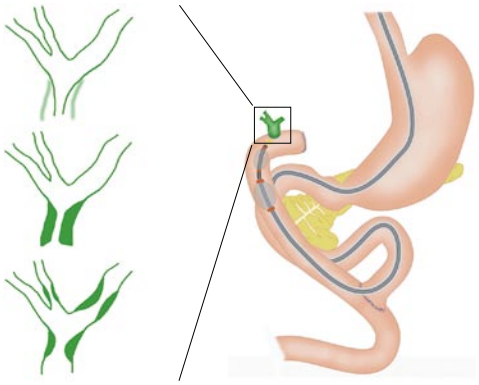

Figure 10 This figure exemplifies the proposed classification (adapted from[18]).

therapeutic ERCP with the BAE in patients with altered bowel anatomy is feasible, allowing for the localization of the afferent limb, visualization of the HJ or papilla of Vater and demonstration of anastomotic strictures or bile duct stones of the choledochojejunostomy[5-17,19]. Besides diagnostic capabilities, BAE-ERCP also permits therapeutic interventions such as sphincterotomy, biliary stent placement, biliary balloon dilation and stent extraction[5-18]. Anastomotic strictures account for the majority of secondary long-term complications of hepaticojejunostomies such as hepaticolithiasis (stones in the hepatic duct), liver abscess and secondary biliary cirrhosis if left untreated[2,3]. Almost 50% of the strictures develop within the first 5 years after surgery whereas the remaining occur at later intervals[2,3]. Recurrences requiring further treatment occur in about 20%-25% of cases[2,3,20,21].

During BAE-ERC we observed that the HJ and biliary tree have specific appearances that may allow it to be classified based on endoscopic and cholangiographic appearances. In almost half of our cases, the opening of the HJ was very small, barely permitting the passage of a 0.035 inch wire or a tapered 5 Fr catheter (type A), suggestive of a stenosis at the level of anastomosis. However, the cholangiographic appearance was vital in determining the length of the stricture, as in some cases the stricture was short and in others long. Short strictures are classified as type 1 and long strictures as type 2. Thus, a small HJ orifice (type A) with a short stricture (type 1) is classified as A1. The therapeutic approach to this type of stricture may be different from one that has a wide HJ orifice (type B). From our own experience, in cases of type A1 HJ stricture, it is advisable to place a stent into the bile duct in order to enlarge and "soften" the small HJ and, in a second session, proceed with balloon dilation of the HJ stricture, a lesson we learned from our case of balloon-induced perforation (Patient No. 9, Table 1). In the same vein, long strictures may fare better with bougienage and/or previous stenting and subsequent balloon dilation. However, our study was not designed to evaluate whether this classification has implications in therapeutic outcomes. We mainly wanted to describe the types of hepaticojejunostomies that can be found and propose a potential classification or basis for future standardized classifications. Whether our classification will have wide applicability is unknown at present. However, we strongly believe that describing the different appearances of the HJ has practical consequences. We also believe that this classification may lead to a better understanding of the post-surgical changes of the HJ and a better appreciation of the diagnostic and therapeutic success of endoscopic interventions. Therefore, other endoscopists interested in treating patients with biliopancreatic disorders after major surgical interventions with altered upper GI anatomy may apply the presented information. We truly expect that our results should be reproducible. Indeed, upon reviewing the reported literature, we find that the reported endoscopic and cholangiographic pictures could fall into the classification presented herein.

A potential limitation of the study is its retrospective design. Nevertheless, the immense collection of endoscopic and cholangiographic images, coupled with the careful, prospective collected database of our centers, has allowed us to make these careful observations. Indeed, our series has the advantage of providing an extensive and detailed endoscopic and cholangiographic description of the HJ.

In summary, this endoscopic-radiological description and the proposed classification is practical as it provides a quick and accurate initial endoscopic assessment of the HJ, potentially allowing for adequate therapeutic planning, as the shape, length and complexity of the HJ and biliary tree may mandate the type of diagnostic and ther-

apeutic accessories to be used to treat the stricture (e.g., balloon *vs* bougie dilatation, Soehendra screw-type stent extractor or 3.3F peripheral angioplasty balloon over a 0.018 inch guidewire). Furthermore, such a practical classification method to characterize the HJ stenosis may be reproducible and thus allow better comparison of the diagnostic and therapeutic results of BAE-ERC in patients with Roux-en-Y anastomosis and HJ.

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COMMENTS

Background

Performing an endoscopic retrograde cholangio pancreatography (ERCP) in patients with Roux-en-Y and hepaticojejunostomy (HJ) anastomosis is technically very challenging or impossible, frequently mandating an operative intervention. The advent of balloon-assisted enteroscopy (BAE) has increased the authors' ability to reach the HJ and perform ERCP.

Research frontiers

Although there are various types of hepaticojejunostomies, there have been no focused attempts to categorize these endoscopically. In this study, the authors describe the endoscopic and radiological characteristics of the hepaticojejunal anastomosis of patients with HJ and propose a practical HJ stricture classification.

Innovations and breakthroughs

The authors observed that the hepaticojejunostomies have characteristics that may allow the stenosis to be classified based on endoscopic and cholangiographic appearances: the HJ orifice aspect may appear small (type A) or large (type B), normal (C), double (i.e. separate anastomosis for the left and right hepatic ducts) (D). The stricture may be short (type 1), long (type 2) and type 3, intrahepatic biliary strictures not associated with anastomotic stenosis. In addition, the anastomosis may not be strictured (0) or the stricture may be above the anastomosis, i.e. supra-anstomotic stricture (S).

Applications

By understanding the anatomy of hepaticojejunostomies, this classification potentially allows for adequate therapeutic planning, as the shape, length and complexity of the HJ and biliary tree choice may dictate the type of diagnostic and therapeutic accessories to be used.

Terminology

A standardized classification may allow for better understanding and comparison of studies of patients undergoing BAE-ERCP in the setting of altered upper gastrointestinal anatomy.

Peer review

The authors present a combined endoscopic and radiological classification of HJ as visualized by balloon-assisted endoscopic retrograde cholangiopancreatography. While the clinical implications of such a scoring system are not known nor validated in other reports, it does provide a framework for other investigators to use, modify or refute.

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BRIEF ARTICLE

Role of needle knife assisted ampullary biopsy in the diagnosis of periampullary carcinoma

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Abstract

AIM: To study the role of needle knife assisted ampullary biopsy in the diagnosis of periampullary carcinoma.

METHODS: In this study the authors retrospectively analyzed clinical records of patients with periampullary tumors diagnosed by ampullary biopsy taken after needle knife papillotomy in whom surface ampullary biopsies were non contributory.

RESULTS: Between January 2008 and December 2010, 38 patients with periampullary tumors were seen by us and initial side viewing endoscopy with surface biopsy from the papilla was positive for malignancy in 25 patients. Thirteen patients with a negative surface biopsy for malignancy underwent a repeat ampullary biopsy following needle knife papillotomy. There were 8 (61.5%) males and 5 (38.5%) females. The most common presenting symptom was jaundice (100%), followed by fever (46.2%), melena (38.5%), abdominal pain (30.8%) and weight loss (30.8%). All the patients had hyperbilirubinemia with a mean ± SD serum bilirubin of (11.2 ± 1.9) mg/dL (normal value < 1 mg%) and the mean ± SD serum alkaline phosphatase was (288.0 ± 94.3) IU/L (normal value < 129 IU/L). Serum CA 19.9 level estimation was done in 11 patients; it was elevated (cut off value > 70.5 IU/L) in all of them with a median of 1200 IU/L (inter quartile range 274-3500). Side viewing endoscopy showed a bulky papilla in all of them. Adequate tissue was obtained in all of the 13 patients for histological evaluation; 12 of the 13 patients were reported to have adenocarcinoma while one patient had adenoma. There were no complications from the needle knife papillotomy in any of the patients.

CONCLUSION: Needle knife assisted ampullary biopsy appears to be a safe and effective diagnostic modality for periampullary carcinoma.

Key words: Carcinoma; Periampullary; Papillotomy; Needle knife; Endoscopic ultrasound; Endoscopy

Peer reviewers: John A Karagiannis, Associate Professor, Gastroenterology Unit, "Konstantopoulio" Hospital, 3-5 Agias Olgas Street, N.Ionia, Athens 14233, Greece; Tony Chiew Keong Tham, MD, Consultant Gastroenterologist, Ulster Hospital, Dundonald, Belfast BT16 1RH, Northern Ireland, United Kingdom

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INTRODUCTION

Periampullary tumors are defined as those arising within 2 cm of the major papilla. They include tumors of the ampulla of Vater, the distal common bile duct (CBD), duodenal tumors involving the papilla and tumors of

the pancreatic head involving the papilla[1]. They are considered collectively because of their similar clinical presentation and difficulty in distinguishing them without examination of the resected specimen. Early and accurate diagnosis of periampullary carcinoma is important because the prognosis is generally much more favorable than pancreatic carcinoma after radical resection[2].

The mainstay of diagnosis of periampullary carcinoma is side viewing endoscopy with ampullary biopsy but only a few studies have assessed the role of endoscopic biopsy for the diagnosis of periampullary carcinoma[3-6]. The reported yield of endoscopic biopsies is limited[3-6]. A major reason for negative biopsies is the submucosal location of some of the tumors with no infiltration of the overlying mucosa. Surface biopsies with conventional forceps fail to get the desired tissue in such patients. Yamaguchi *et al*[4] have described three macroscopic types of ampullary tumors: intramural protruding, exposed protruding and ulcerating. In the intramural protruding variety, the yield of forceps biopsies is the least. It has been suggested that a prior sphincterotomy can help expose the submucosal tumor in such patients[6,7]. Using the same logic, we used needle knife papillotomy to take biopsies from intramural protruding periampullary tumors. Moreover, in some cases the carcinoma is within an adenoma and the surface biopsy may diagnose only the benign lesion. Few studies have shown increased diagnostic yield with post sphincterotomy deeper papillary biopsies[6,7]. The aim of the present study is to report our experience of papillary biopsy taken after needle knife incision.

MATERIALS AND METHODS

Between January 2008 and December 2010, all patients with extrahepatic biliary obstruction referred to our hospital were subjected to detailed evaluation in the form of liver function tests, tumor marker (CA 19.9), ultrasound abdomen and contrast enhanced computed tomography (CECT) of the abdomen. Detailed clinical profile was noted. Cut off value for serum CA 19.9 was 70.5 U/mL[8]. Coagulation parameters including prothrombin index and platelet count were checked in all the patients. Patients suspected of having periampullary carcinoma underwent side viewing endoscopy and ampullary biopsy using standard biopsy forceps (RBF-2.4-160, Olympus Corp, Tokyo, Japan). Patients with negative surface biopsy of papilla for malignancy underwent a repeat endoscopic biopsy from the papilla following needle knife incision of the papilla. The incision was made either from the ampullary orifice upwards towards 12 o'clock or from the most prominent part of ampulla along the 12 o'clock position downwards towards the opening. As the incision was made and the superficial tissue retracted, the underlying tissue was exposed. The depth of the incision was increased until the tumor was clearly visible. In patients who already had a biliary stent *in situ*, the stent was used to guide the incision starting at the ampullary orifice and the incision was extended depth wise till the stent was exposed. In patients with jaundice and without a stent *in situ*, the needle knife incision was extended to assess the bile duct and a flexible 0.035" guidewire (Hydra Jag, Boston Scientific Co., Marlborough, Mass, United States) was placed under fluoroscopic guidance. A biliary stent was placed over the guidewire in such patients. All the side viewing endoscopies with surface as well as needle knife assisted biopsies were obtained by a single experienced endoscopist using Fujinon duodenoscope (ED 4400, Fujinon Co., Saitama, Japan) and the needle knife incision was made by using a triple lumen needle knife sphincterotome (Micro-knife XL®, Boston Scientific Co., Marlborough, Mass, United States). Patients with gastric outlet obstruction and those who did not consent for the procedure were excluded. All the patients were observed for 6 h in the hospital for bleeding, pain, tenderness and drop in blood pressure. They were reviewed the next day in the outpatient department and those with any complications were admitted. The formalin-fixed tissue was embedded in paraffin and sections were stained with hematoxylin-eosin. Histological interpretation of the biopsy specimen was done by a single experienced histopathologist (Vaiphei K). Informed written consent was obtained from each patient and the study was approved by the Institute Ethics committee.

Statistical analysis

Parametric quantitative variables were expressed as mean ± SD and non parametric quantitative variables were expressed as median with inter quartile range (IQR). Categorical variables were expressed as percentages. Statistical analysis was performed using the statistical software package SPSS version 17.0 (SPSS, Chicago, Illinois, United States).

RESULTS

Between January 2009 and December 2010, 38 patients were suspected to have periampullary carcinoma on the basis of initial work up. Initial side viewing endoscopy with surface biopsy from the papilla was positive for malignancy in 25 patients. Thirteen patients with negative surface papillary biopsy for malignancy underwent repeat ampullary biopsy following needle knife papillotomy, which was positive in 12 of them.

Clinical profile

Details of the patients who underwent needle knife assisted papillary biopsy are given in Table 1. Mean ± SD age of the patients was (62.3 ± 9.6) years. There were 8 (61.5%) males and 5 (38.5%) females. All the patients (100%) presented with jaundice, 6 (46.2%) had a history of fever, 5 (38.5%) had melena, 4 (30.8%) had abdominal pain and 4 (30.8%) had significant weight loss. Nine (69.2%) patients were anemic with hemoglobin < 12 gm/dL. All the patients had hyperbilirubinemia with a mean ± SD serum bilirubin of (11.2 ± 1.9) mg/dL

Table 1 Clinical profile and laboratory data of 13 patients diagnosed by needle knife assisted ampullary biopsy

Case	Age (yr)/ gender	Presentation	GB mass	Hb (gm/dL)	TLC (/mm^3)	Serum bilirubin (mg/dL)	ALP (IU/L)	CA 19.9 (U/mL)	Post needle knife biopsy	Stent
1	75/female	Jaundice,weight loss	+	11.0	8800	11.0	312	NA	Adeno CA	+
2	54/male	Jaundice, melena	-	12.0	7400	8.0	274	274	Adeno CA	-
3	42/male	Jaundice, pain abdomen	+	11.2	9400	12.5	310	430	Adeno CA	+
4	65/female	Jaundice, fever	+	11.5	12100	15.5	471	780	Adeno CA	-
5	58/male	Jaundice, weight loss	-	13.0	9400	10.5	321	1408	Adeno CA	-
6	71/male	Jaundice, melena	+	9.2	12000	9.2	475	2900	Adeno CA	-
7	54/male	Jaundice, fever	+	9.5	13400	11.2	274	1451	Adeno CA	-
8	61/female	Jaundice, pain abdomen, fever	+	7.8	11400	9.5	183	714	Adeno CA	-
9	63/male	Jaundice, pain abdomen, melena	+	8.1	12400	9.9	274	1121	Adeno CA	+
10	68/male	Jaundice, pain abdomen,weight loss	-	12.2	7800	11.5	210	3500	Adeno CA	+
11	63/female	Jaundice, fever, weight loss	+	11.5	8500	12.5	194	1200	Adenoma	-
12	58/male	Jaundice, fever, melena	+	12.5	9900	11.2	248	NA	Adeno CA	-
13	75/female	Jaundice, fever, melena	-	7.5	13500	13.0	198	3400	Adeno CA	+

GB: Gall bladder; Hb: Hemoglobin; TLC: Total leukocyte count; ALP: Alkaline phosphatase; CA: Carcinoma; EUS: Endoscopic ultrasound; +: Present; -: Absent.

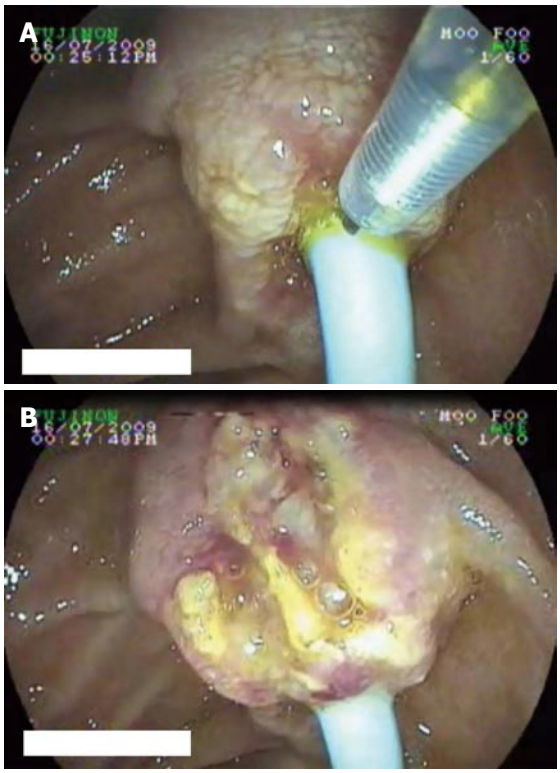

Figure 1 Duodenoscopy showing a periampullary mass with stent *in situ* and needle knife coming out of endoscope (A) and endoscopic image after needle knife papillotomy showing exposed tumor tissue (B).

(normal value < 1 mg%) and mean ± SD serum alkaline phosphatase was (288.0 ± 94.3) IU/L (normal value < 129 IU/L). Serum CA 19.9 level estimation was done in 11 patients and was elevated (>70.5 U/mL) in all of them with a median of 1200 IU/L (IQR 274-3500). Ultrasound of the abdomen showed a dilated CBD and main pancreatic duct (MPD) in 9 (69.2%) and only dilated CBD in 4 (30.8%). Side viewing endoscopy in all of them showed a bulky papilla fitting the description of intramural protruding type of tumor as per Yamaguchi's classification[4]. In 5 patients, the stent was already *in situ*, while in 8 patients the stent was placed after needle knife incision (Figure 1). A CECT abdomen was available in all the patients and it showed dilated CBD and MPD in 10 (76.9%) patients and only dilated CBD in 3 (23.1%) patients; a definite mass was demonstrated in 10 patients (76.9%) (Figure 2). The tumor was resectable in 9 (69.2%) patients and it was unresectable in 4 (30.8%) patients. Endoscopic ultrasonography was done in the last 3 (23.1%) patients, showing a small periampullary mass in all of them (Figure 3). Adequate tissue was obtained in all 13 patients for histological evaluation; 12 of the 13 patients were reported to have adenocarcinoma (Figure 4) and one had adenoma. The diagnosis of adenocarcinoma was confirmed at histopathological examination of the resected specimen or fine needle aspiration cytology from the metastasis. There were no complications from the needle knife papillotomy in any of the patients.

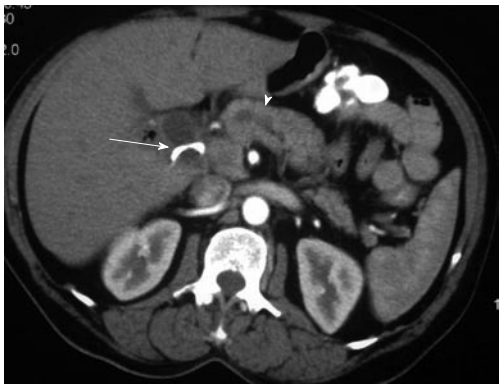

Figure 2 Computed tomography showing dilated common bile duct with stent in it (arrow) and dilated main pancreatic duct (arrowhead); no definite mass could be visualized.

DISCUSSION

We have described the role of needle knife assisted

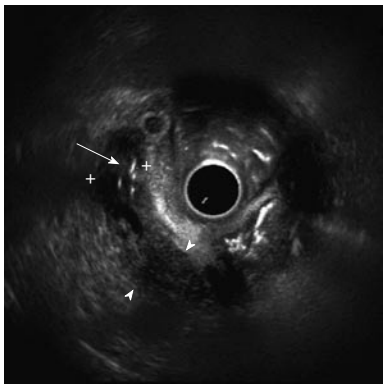

Figure 3 Endoscopic ultrasound image of the same patient as in Figure 2, showing dilated common bile duct measuring 11.8 mm with stent *in situ* (arrow); a mass is seen in the periampullary region measuring 1.2 cm × 1.8 cm (arrowheads).

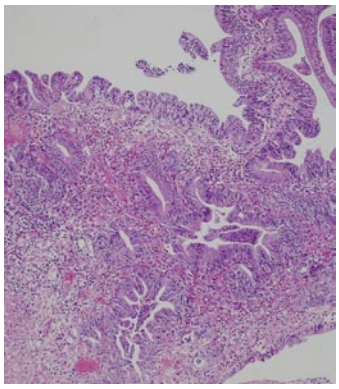

Figure 4 Photomicrograph showing papillary adenocarcinoma; tumor cells are arranged in both papillary fronds and glands (HE, × 240).

ampullary biopsies in the diagnosis of periampullary carcinoma. A positive diagnosis of adenocarcinoma was obtained in 12 of the 13 patients who had a negative surface biopsy earlier. There were no procedure related complications in any patients. The sensitivity of forceps biopsies for the diagnosis of periampullary carcinoma ranges from 21 to 81% in different studies[3,4,9,10]. The sensitivity of ampullary biopsy depends on the gross appearance of the tumor; Yamaguchi *et al*[4] reported biopsy positivity of 50% in intramural protruding type, 64% in the exposed protruding type and 88% in the ulcerating type.

As the yield of ampullary surface biopsy in the diagnosis of periampullary carcinoma is limited, different techniques have been used to take a deeper biopsy. A tumor arising inside the ampulla can produce a bulge with normal overlying duodenal mucosa which can mimic an impacted stone. Huibregtse *et al*[9] reported that snare biopsy improved the tissue quality and improved the diagnostic yield from 60% to 83% in such patients. Other studies have suggested an increase in sensitivity following sphincterotomy. Menzel *et al*[6] reported improvement in the accuracy of ampullary biopsy following sphincterotomy in the diagnosis of ampullary tumors from 63% to 70% overall and from 21% to 37% for carcinoma. In their series, 12 out of 19 carcinomas were missed even after sphincterotomy. Ponchon *et al*[7] also reported increased yield of ampullary biopsy after sphincterotomy; biopsies were taken on the day of sphincterotomy in 9 patients and 10 d to 4 wk later in 22 patients. In 4 patients whose biopsies were normal or non interpretable at the time of sphincterotomy, it was observed that biopsies taken 10 d later showed an ampullary tumor in all of them. They suggested that endoscopic sphincterotomy makes interpretation of biopsy specimens difficult as a result of the thermal effect on tissue, often leading to negative results. So they recommended that a biopsy should be taken 2 to 10 d after sphincterotomy[7,10].

Needle knife papillotomy is an improvement over previous techniques. A smooth bulky papilla can be incised and the tumor exposed. In contrast to a sphincterotomy, needle knife incision of the papilla only cuts the superficial layers of papilla and leads to a minimal thermal effect on deeper tissue so biopsies can be taken at the same time. There were no procedure-related complications recorded in any of our patients, suggesting that needle knife assisted biopsy is a safe technique in expert hands. In addition to a biopsy, needle knife papillotomy also helps to gain access to the bile duct to provide endoscopic biliary drainage. Surface biopsy diagnosis of adenoma does not rule out the possibility of underlying carcinoma, as reported by Seifert *et al*[11] in 30% of their patients with papillary adenoma. Needle knife assisted biopsy rules out this possibility by sampling a deeper tissue specimen.

Endoscopic ultrasound (EUS) is an important recent diagnostic modality in the detection of small periampullary tumors. Shoup *et al*[12] found EUS to be more sensitive although less specific than computed tomography (CT) in the detection of periampullary tumors; EUS was 90% accurate for detecting tumors smaller than 2 cm compared with 70% for CT scan. EUS images of periampullary tumors correspond well with the histological findings[13]. EUS guided fine needle aspiration can be used to take cytological samples in periampullary tumors but it is technically demanding as positioning the scope and needle insertion are difficult.

To conclude, needle knife assisted ampullary biopsy appears to be a safe and effective diagnostic modality in the diagnosis of periampullary tumors, particularly in those patients who have an intramural protruding type of tumor as per Yamaguchi's classification[4]. A prospective study to validate the role of needle knife assisted ampullary biopsy in different morphological types of periampullary masses is needed to establish its role on a larger scale.

COMMENTS

Background

Endoscopic biopsy is the mainstay of diagnosis of periampullary carcinoma but the yield of surface ampullary biopsy is limited. This study was conducted to evaluate the role of needle knife assisted ampullary biopsy in the diagnosis of periampullary carcinoma.

Research frontiers

In view of the limited yield of surface ampullary biopsy, different techniques have been applied in an effort to increase the yield of ampullary biopsy in the diagnosis of periampullary carcinoma.

Innovations and breakthroughs

In the present study, the authors studied the role of needle knife assisted ampullary biopsy in the diagnosis of periampullary carcinoma.

Applications

The study results suggest that needle knife assisted ampullary biopsy is a useful technique for increasing the yield of ampullary biopsy in the diagnosis of periampullary carcinoma.

Peer review

This paper describes an alternative approach to obtain deep biopsy specimens from papillary tumors, substantially increasing the diagnostic accuracy, according to the data described in the paper.

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CASE REPORT

A simplified method for stent placement in the distal duodenum: Enteroscopy overtube

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Abstract

The treatment of choice for patients with unresectable neoplastic obstruction of the small intestine is the placement of expandable metal stents. However, endoscopic delivery from the distal duodenum can be more difficult. This case, shows the usefulness and technical advantages of the overtube and single balloon enteroscopy in the treatment of neoplastic stenosis affecting the small intestine.

Key words: Neoplastic obstruction; Small intestine; Neoplasm of the pancreas; Enteral stent; Enteroscopy; Single balloon enteroscope; Overtube

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INTRODUCTION

Obstruction of the small intestine may be due to malignant neoplasms of adjacent organs. In neoplastic stenosis affecting the gastric exit and the proximal duodenum, palliative treatment with self-expanding metallic stents employing endoscopes of large working channel is a widely used and generally simple option[1,2]. However, when the neoplastic stenosis is more distal (distal duodenum), serious technical limitations related to the endoscopes and the stent make placement challenging.

We present a case of malignant neoplastic obstruction of the distal duodenum-angle of treitz, treated palliatively with placement of an enteral stent, using a single balloon enteroscope.

CASE REPORT

The patients was a 73-year-old man with clinical signs of intestinal obstruction. An abdominal computed tomography scan revealed inoperable neoplasm of the pancreas infiltrating the third duodenal section (angle of Treitz). Placement of a palliative enteral stent was requested.

With the patient under general anaesthesia, the stenosis was accessed with a single balloon enteroscope (Olympus SIF Q180) with overtube (ST-SB1). A contrast medium was injected in order to delimit the stenosis (Figure 1). A 0.35-mm guide (Jagwire®, Boston sc) was passed through the stenosis leaving the overtube (OT), and the enteroscope was then withdrawn. Under fluoroscopic control, an enteral stent (22 mm × 90 mm - Wallflex®, Boston) was advanced over the guide and through the OT until it passed through the stenosis (Figure 2A and B). Then, the OT was removed and the stent was released in

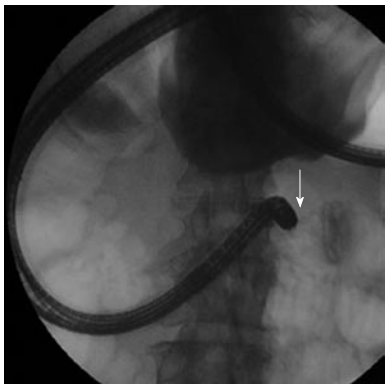

Figure 1 Neoplastic stenosis of the distal duodenum (arrow).

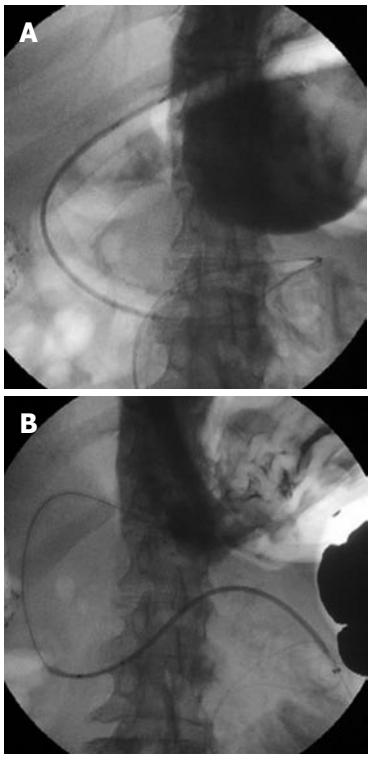

Figure 2 Stent placement. A: Advance of the enteral stent through the overtube, over the guide wire; B: Stent placed through the distal duodenal stenosis.

the stenosis (Figure 3A and B).

The patient tolerated a liquid diet after 24 h, and was subsequently discharged.

DISCUSSION

The OT is a semi-rigid plastic device designed to facilitate the performance of endoscopy. Its purpose is to protect the gastrointestinal mucosa from trauma and reduce the risk of aspiration. It also facilitates access in patients with difficult anatomy, increases the depth of insertion and maintains access for repeated entry and withdrawal of the endoscope. Potential indications for the use of an OT during upper digestive tract endoscopy are: extraction of foreign bodies orally (prevention of damage to the oesophageal mucosa and aspiration), facilitation of endoscopic intubation (mucosal resection, variceal ligation), protection of altered anatomy (Zenker's diverticulum), the incorporation of specialized endoscopies (single or double balloon enteroscope, therapeutic endoscopic retrograde cholangiopancreatography in patients with surgically altered anatomy, for cholangioscopy), reduction of infection or neoplastic seeding during placement of a percutaneous endoscopic gastrostomy. In the case of enteroscopy, use of OT can to reduce looping, allowing the most distal sections of the intestine to be reached[3]. To our knowledge, use of the OT in the placement of enteral stents is exceptionally well received[4,5] and this is the first detailed case of the use of an OT with simple balloon enteroscopy for this indication. There is interest in the technique in that the OT permits access to a constricted section of the distal duodenum, and the enteral stent can be rapidly and easily released under fluoroscopic control.

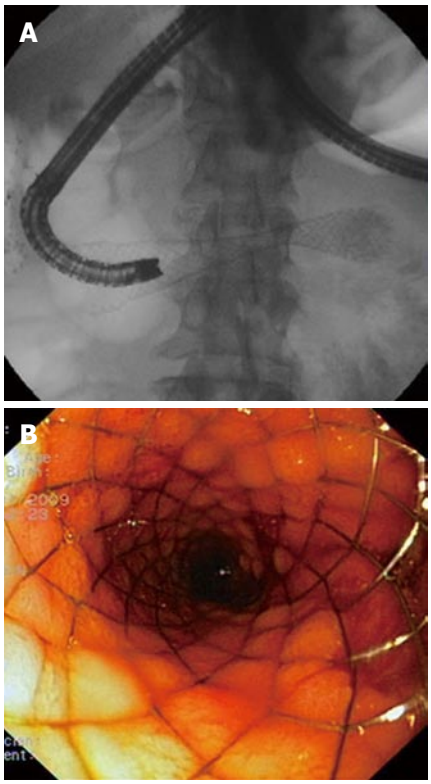

Figure 3 Released enteral stent. A: Radiological image; B: Endoscopic image.

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CASE REPORT

An incidentaloma at ileal intubation

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Abstract

The authors report the case of a primary small bowel lymphoma discovered incidentally in a 33-year-old male following ileal intubation at colonoscopy. The patient subsequently underwent curative treatment with chemotherapy. This case not only highlights the importance of routine ileoscopy but also the successful use of chemotherapy in a disease for which the optimal treatment modality has not been well characterized.

Key words: Primary intestinal lymphoma; Ileal intubation; Chemotherapy

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Donnellan F, Moran S, Patchett SE. An incidentaloma at ileal intubation. *World J Gastrointest Endosc* 2011; 3(11): 228-230 Available from: URL: http://www.wjgnet.com/1948-5190/full/v3/i11/228.htm DOI: http://dx.doi.org/10.4253/wjge.v3.i11.228

INTRODUCTION

Primary small bowel lymphoma is uncommon. It usually presents as a surgical emergency, including obstruction or perforation. While surgery is the mainstay of management, other treatment modalities have been used successfully. We report a case of lymphoma involving the terminal ileum discovered at routine ileal intubation and successfully treated with chemotherapy.

CASE REPORT

A 33-year-old male with an unremarkable medical history presented to the outpatient department with a 3 mo history of left iliac fosse discomfort and intermittent rectal bleeding. The patient denied nausea, vomiting or a change in bowel habit. The patient underwent colonoscopy which demonstrated unremarkable colonic mucosa. However, intubation of the terminal ileum revealed a 4 cm non-obstructing mass lesion just proximal to the ileocecal valve (Figure 1).

The histology from the ileal mass, with immunohistochemical staining positive for the markers L26, Bcl-6 and CD10, revealed a large diffuse B-cell non-Hodgkin's lymphoma (Figure 2). The patient was diagnosed with a primary gastrointestinal lymphoma confined to the terminal ileum following positron emission tomography computed tomography (PET CT) scanning and a bone marrow examination. The lactate dehydrogenase level was elevated at 805 IU/L (110-300). The patient underwent chemotherapy with a 6-cycle regimen of Cyclophosphamide 750 mg/m^2 intravenously (IV) day 1, Adriamycin 50 mg/m^2 IV day 1, Vincristine 1.4 mg/m^2 IV day 1, Prednisolone 50 mg twice daily orally days 1-5 (CHOP) and Rituximab 375 mg/m^2 IV day 1. Colonoscopy performed 3 mo post-treatment demonstrated a normal terminal ileum (Figure 3). Subsequent biopsies from the terminal ileum were also unremarkable. A PET CT scan was also normal. On the basis of the endoscopic and radiological responses, the patient was not considered for radiotherapy.

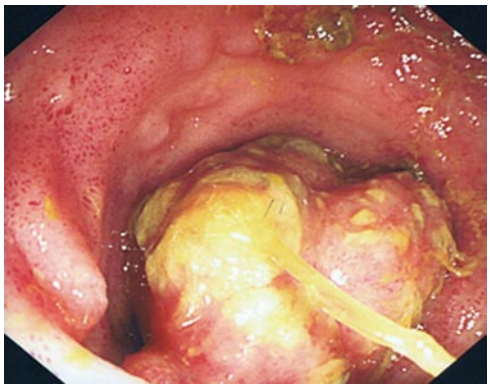

Figure 1 Endoscopic image demonstrating a mass lesion in the terminal ileum.

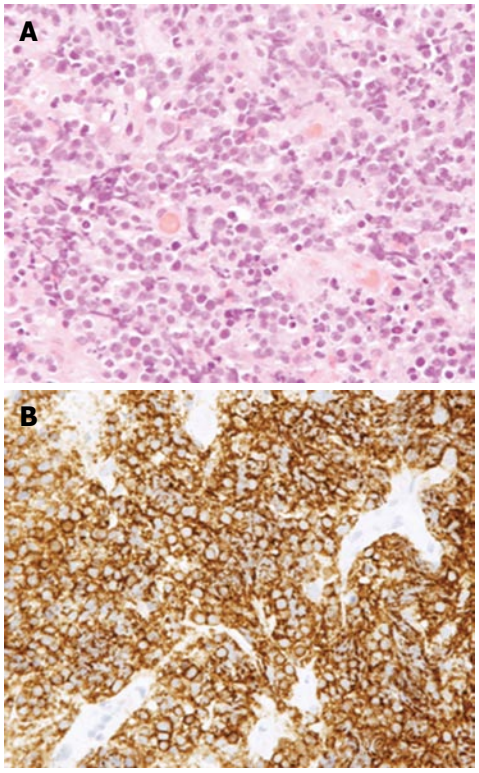

Figure 2 Histological image demonstrating HE staining (A) and immunohistochemical staining positive for the L26 marker (B) confirming a large diffuse B-cell non-Hodgkin's lymphoma.

DISCUSSION

The gastrointestinal tract, accounting for up to 40% of all extranodal disease, is the most commonly involved site for primary extranodal non-Hodgkin's lymphoma. The most frequent primary sites are the stomach and small intestine, accounting for 60% and 20% respectively[1]. While the lymphoma in our patient was discovered as an incidental finding following routine ileal intubation, small intestinal lymphoma typically presents with abdominal pain, weight loss or acute surgical conditions such as obstruction and perforation[2,3].

In contrast to gastric lymphoma, the optimal treatment modality for primary small bowel lymphoma has not been well characterized. Surgery alone[4,5], or in combination with chemotherapy[6,7], is considered the mainstay of treatment for localized disease. However, some reports have demonstrated benefit from sole treatment with either chemo- or radiotherapy in localized disease[8,9].

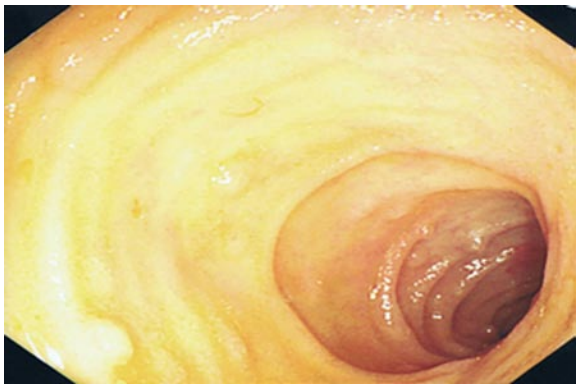

Figure 3 Endoscopic image demonstrating a normal terminal ileum following treatment with chemotherapy.

Ileal intubation as part of the colonoscopic examination is a topic of great debate. It has been demonstrated that performing routine ileal intubation, when not indicated, is of little diagnostic value[10,11]. However, mastering this technique is an important part of colonoscopic training. Furthermore, visualization of ileal mucosa is the most definitive landmark that the colonoscopy has been successfully completed.

This case highlights the benefit of performing routine ileal intubation, which is a topic of great debate, and curative treatment of primary localized small bowel lymphoma with chemotherapy.

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CASE REPORT

New cannulation method for pancreatic duct cannulation-bile duct guidewire-indwelling method

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Abstract

The patient was a 58-year-old male with symptomatic alcoholic chronic pancreatitis. Since a 10 mm calculus was observed in the pancreatic body and abdominal pain occurred due to congestion of pancreatic juice, endoscopic retrograde cholangiopancreatography was conducted for assessment of the pancreatic duct and treatment of pancreatic calculus. Pancreatogram was slightly and insufficiently obtained by injecting the contrast media *via* the common channel of the duodenal main papilla. We tried to cannulate selectively into the pancreatic duct for a clear image. However, the selective cannulation of the pancreatic duct was difficult because of instability of the papilla. On the other hand, selective cannulation of the bile duct was relatively easily achieved. Therefore, after the imaging of the bile duct, a guidewire was retained in the bile duct to immobilize the duodenal papilla and cannulation of the pancreatic duct was attempted. As a result, selective pancreatic duct cannulation became possible. It is considered that the bile duct guidewire-indwelling method may serve as one of the useful techniques for cases whose selective pancreatic duct cannulation is difficult ("selective pancreatic duct difficult cannulation case").

Key words: Endoscopic retrograde cholangiopancreatography; Bile duct guidewire-indwelling method; Selective pancreatic duct cannulation; Endoscopic pancreatic sphincterotomy; Pancreatic duct guidewire-indwelling method

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INTRODUCTION

Endoscopic retrograde cholangiopancreatography (ERCP) is a technique that plays an important role in the diagnosis and treatment of cholangio-pancreatic diseases. Including the drainage, the approach to the bile duct rather than the pancreatic duct becomes necessary in many cases when ERCP is performed. To this end, various approaches are available for selective pancreatic duct difficult cannulation cases. These approaches, or methods, include the guidewire method[1], two-devices-in-one-channel method[2], flexible tip method[3], pre-cut papillotomy[1,4-14], wire-guid-

ed cannulation[15,16], pancreatic duct guidewire-indwelling method (P-GW)[1,17-20], *etc*. From the empirical viewpoint, the endoscopic approach to the pancreatic duct is easier and causes less difficulty in cannulation in comparison with that to the bile duct. Furthermore, since pancreatography is a risk factor for pancreatitis, cases of the pancreatic duct approach are limited. Accordingly, hardly any reports have been made on the approach to selective pancreatic duct difficult cannulation cases. In this regard, we found that the bile duct guidewire-indwelling method was useful in a selective pancreatic duct difficult cannulation case. The case is reported in the following.

CASE REPORT

The patient was a 58-year-old male with alcoholic chronic pancreatitis. Since a 10 mm calculus was detected in the pancreatic body and abdominal pain occurred frequently due to congestion of pancreatic juice, ERCP was conducted for assessment of the pancreatic duct and for treatment of pancreatic calculus. The procedures were carried out using side-viewing duodenoscopes (JF260V: Olympus Co., Tokyo, Japan). A catheter PR-104Q was used for cannulation (Olympus Co.). Two guidewires were employed in the procedure (Jagwire: Microvasive, Boston Scientific Co., Natick, MA, Revo Wave: Olympus Co.). After the start, the pancreatic duct was imaged to some extent from the common duct but the image was not clear enough and the catheter was dislodged from the papillary region due to the strong mobility of the duodenal papilla (Figure 1). The second attempt at pancreatography was not successful. However, despite the strong mobility of the duodenal papilla, imaging of the bile duct was possible. Therefore, after the imaging of the bile duct, a guidewire was retained in the bile duct to immobilize the papilla and cannulation of the pancreatic duct was attempted. As a result, selective pancreatic duct cannulation became possible (Figures 2A, 2B and 3). Subsequently, the guidewire was inserted up to the pancreatic tail (Figure 4) and endoscopic pancreatic sphincterotomy (EPST), a technique to provide separate openings for the pancreatic duct and the bile duct, was performed so as to conduct an Extracorporeal Shock Wave Lithotripter later on to remove pancreatic calculus. It is reported that EPST and difficult cannulation cases constitute a risk factor of post-ERCP pancreatitis because they induce edema in the papilla that leads to the stasis of pancreatic juice[21]. Accordingly, the procedure was completed by retaining a 5 Fr. Three centimeters unilateral-flapped pancreatic duct stent (Geenen, Pancreatic Stent: Wilson-Cook Medical Inc., Winston-Salem, NC)[22,23] that might prevent pancreatitis by securing the outlet for the congestion of pancreatic juice. Although post-operative hyperamylasemia was observed, no problematic incidental disease occurred. No substantial problem with the pancreatic duct stent occurred and the X-ray that was taken the next day confirmed the spontaneous dislodgement.

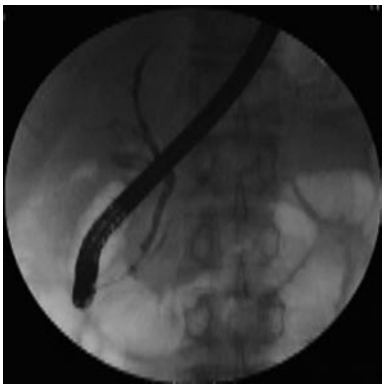

Figure 1 Pancreatic calculus is observed in the pancreatic body. Although the pancreatic duct was imaged to some extent by endoscopic retrograde cholangiopancreatography, the catheter was dislodged due to the strong mobility of the duodenal papilla, after which only the bile duct was imaged.

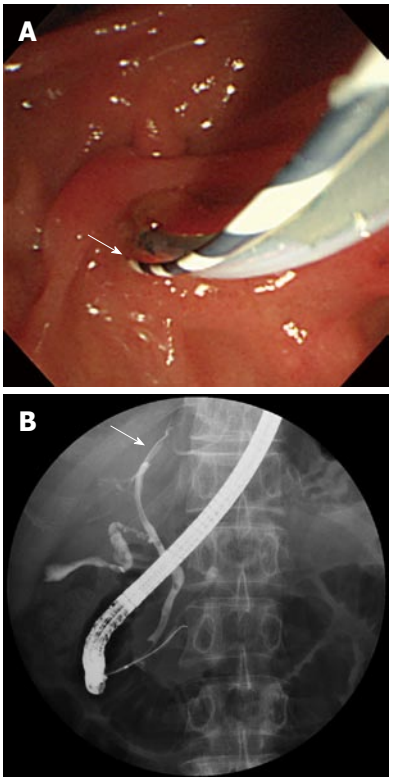

Figure 2 A guidewire in the bile duct and catheter. Because the papilla was very mobile, a guidewire was retained in the bile duct and the catheter is pressed to the duodenal papilla while the pancreatic duct direction is probed with the guidewire inserted into the catheter. Arrows indicate bile duct guidewire-indwelling. A: Endoscopic image of duodenal papilla; B: X-ray image.

DISCUSSION

Thanks to the recent progress of imaging diagnosis, including magnetic resonance cholangiopancreatography and endoscopic ultrasound in regard to cholangio-pancreatic diseases[24-27], other imaging methods are employed as much as possible in many cases and ERCP, with a risk of inducing serious incidental diseases, is used only when the diagnosis is still difficult or when treatment becomes necessary[27]. However, ERCP is still an essential technique

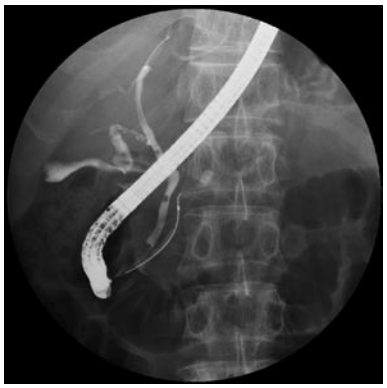

Figure 3 The guidewire went ahead in the direction of pancreatic duct.

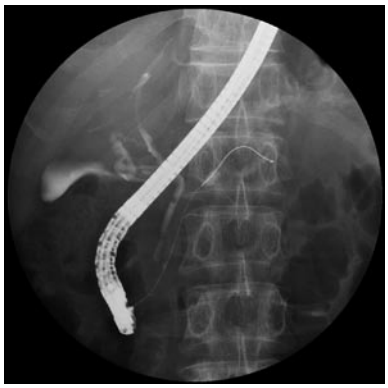

Figure 4 The guidewire was retained across the calculus to the pancreatic tail.

for the diagnosis and treatment of cholangio-pancreatic diseases. The use of various methods has been reported in selective bile duct difficult cannulation cases. On the other hand, the endoscopic approach to the pancreatic duct is easier from the anatomical viewpoint and causes less difficulty in cannulation in comparison with that to the bile duct. Furthermore, since pancreatography is a risk factor of pancreatitis[21], cases of the pancreatic duct approach are limited. Accordingly, hardly any report has been made on the approach to selective pancreatic duct difficult cannulation cases. However, sometimes there are cases such as ours that require selective pancreatic duct cannulation. Since the selective pancreatic duct cannulation was difficult by the usual catheterization in our case, we made use of the pancreatic duct guidewire-indwelling method, applicable to selective bile duct difficult cannulation cases, and retained the guidewire in the bile duct for selective pancreatic duct cannulation. P-GW for selective biliary cannulation in a patient with surgically altered anatomy was first reported by Dumonceau *et al*[17]. Gotoh *et al*[18] reported a second case of successful biliary cannulation with P-GW in a patient with a tortuous common channel. The method which was subsequently employed by Maeda *et al*[19] and Ito *et al*[20] in a substantial number of cases is reported to increase the bile duct cannulation rate in selective bile duct difficult cannulation cases by reducing, linearizing and fixing the sphincter muscle of papilla, and is useful in cases with parapapillary diverticulum, deviated papilla and with strong papillary mobility, and those with a tortuous and long papillary sphincter muscle. Although pancreatic duct cannulation was necessary, our case demonstrated strong papillary mobility. The imaging of the pancreatic duct was difficult because the ordinary catheter was easily dislodged from the papilla. However, since imaging of the bile duct was possible, the papilla could be firmly fixed by retaining a guidewire in the bile duct, thereby making selective pancreatic duct cannulation possible. It may be difficult to investigate this method in a large number of cases because selective pancreatic duct cannulation is required infrequently. As in the case of the pancreatic duct guidewire-indwelling method, the bile duct guidewire-indwelling method is considered useful for those who require selective pancreatic duct cannulation, cases with parapapillary diverticulum, with deviated papilla and papillary mobility, and for those with a tortuous and long papillary sphincter muscle. We plan to perform the bile duct guidewire-indwelling method and to re-investigate the procedure after accumulating corresponding cases in the future.

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CASE REPORT

Primary intestinal lymphangiectasia diagnosed by capsule endoscopy and double balloon enteroscopy

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Abstract

Primary intestinal lymphangiectasia (PIL) is a rare disorder characterized by dilated intestinal lymphatics and the development of protein-losing enteropathy. Patients with PIL develop hypoalbuminemia, hypocalcemia, lymphopenia and hypogammaglobulinemia, and present with bilateral lower limb edema, fatigue, abdominal pain and diarrhea. Endoscopy reveals diffusely elongated, circumferential and polypoid mucosae covered with whitish enlarged villi, all of which indicate intestinal lymphangiectasia. Diagnosis is confirmed by characteristic tissue pathology, which includes dilated intestinal lymphatics with diffusely swollen mucosa and enlarged villi. The prevalence of PIL has increased since the introduction of capsule endoscopy. The etiology and prevalence of PIL remain unknown. Some studies have reported that several genes and regulatory molecules for lymphangiogenesis are related to PIL. We report the case of a patient with PIL involving the entire small bowel that was confirmed by capsule endoscopy and double-balloon enteroscopy-guided tissue pathology who carried a deletion on chromosome 4q25. The relationship between this deletion on chromosome 4 and PIL remains to be investigated.

Key words: Capsule endoscopy; Double balloon enteroscopy; Chromosome deletion; Chromosome 4q25; Primary intestinal lymphangiectasia

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Oh TG, Chung JW, Kim HM, Han SJ, Lee JS, Park JY, Song SY. Primary intestinal lymphangiectasia diagnosed by capsule endoscopy and double balloon enteroscopy. *World J Gastrointest Endosc* 2011; 3(11): 235-240 Available from: URL: http://www.wjgnet.com/1948-5190/full/v3/i11/235.htm DOI: http://dx.doi.org/10.4253/wjge.v3.i11.235

INTRODUCTION

Primary intestinal lymphangiectasia (PIL) was first described by Waldmann *et al*[1] in 1961. In PIL, impaired lymphatic drainage causes lymph leakage into the bowel

lumen, which results in protein-losing enteropathy. Hypoalbuminemia, lymphocytopenia, hypogamma-globulinemia and fat-soluble vitamin deficiency anemia are common laboratory findings in PIL[2]. Patients complain of persistent diarrhea, abdominal pain, malabsorption, peripheral edema and chylous effusion. Obstructive ileus of the small intestine may develop, requiring partial jejunectomy[3]. In this condition, a sudden blockade of lymphatic drainage occurs in the affected area, followed by the massive dilation of submucosal channels and possible obstructive ileus. Congenital lymphedema is also associated with a selective deficit of naive CD4+ T lymphocytes. PIL with very low CD4+ counts and immunoglobulin G levels is related to recurrent and opportunistic infections and associated with increased morbidity and mortality[4].

The diagnosis of PIL is based on histological analysis of surgical specimens or endoscopic biopsies that reveal lacteal juice and dilated mucosal and submucosal lymphatic vessels. Typical mucosal findings upon endoscopy include diffuse swelling and enlarged whitish villi. Esophagogastroduodenoscopy and colonoscopy can be used to visualize parts of the small bowel, duodenum and terminal ileum, but capsule endoscopy is more useful to explore the entire small bowel mucosa[5]. Double-balloon enteroscopy can localize lesions and small bowel tissue can be obtained for pathological confirmation[6].

Only a few reports describe the diagnosis of PIL using capsule endoscopy and double-balloon enteroscopy[7]. No prior cases were similar to the case described in the present study, in which a deletion was found on chromosome 4. We present clinical, radiological, endoscopic and histological findings for a patient with PIL who was diagnosed using these techniques. Genetic analysis was also performed because the patient's protein-losing enteropathy occurred at a very young age.

CASE REPORT

An 18-year-old male was transferred from the pediatrics department for endoscopic evaluation. He had been diagnosed with protein-losing enteropathy 15 d after birth based on laboratory findings and symptoms, but no cause was identified. Recurrent abdominal pain, diarrhea, hypoalbuminemia and malnutrition led to frequent hospitalization throughout his childhood. At the age of 11 years, the patient underwent a Denver shunt operation to control chylous ascites. He adhered to a low-fat diet supplemented with medium chain triglycerides (MCT) to avoid lacteal engorgement and to prevent lymphatic rupture with ensuing protein loss.

At the age of 18 years, he presented with a 3 wk history of abdominal pain, diarrhea over 20 times a day, general weakness and poor oral intake. He had short stature due to malnutrition. The physical examination showed edema in his ankles and legs. Total protein and albumin were low (3.2 and 1.8 g/dL). Sodium and potassium were within normal ranges (141 and 4.3 mmol/L), whereas ionized calcium was lower than normal (3.90 mg/dL). Urinalysis did not show proteinuria. The indicator levels of thyroid function, T3 and free T4, were low (76.31 and 0.66 ng/dL). His pituitary function and mental capacity were normal.

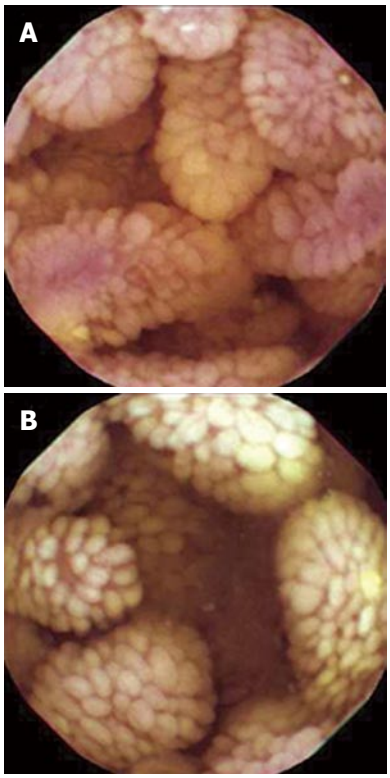

Figure 1 Capsule endoscopy shows diffuse edematous mucosae covered with enlarged and swollen villi in the jejunum (A), and diffuse finger-like elongated mucosa covered with enlarged whitish villi in the ileum (B).

Double-contrast small bowel series with barium revealed diffuse mucosal fold thickening and increased granularity in the duodenum, jejunum and ileum; however, barium transit time was within the normal range. Abdominal ultrasonography showed diffuse small bowel wall thickening with a small amount of ascites. Abdominopelvic computerized tomography (CT) showed markedly thickened and enhanced mucosal layers of the jejunum and ileum. Capsule endoscopy (MiroCam®, Intromedic Co., Korea) revealed diffusely elongated, circumferential and polypoid mucosae covered with enlarged whitish villi involving the entire small bowel. These findings suggested intestinal lymphangiectasia (Figure 1), which was confirmed by double-balloon enteroscopy (Fujinon Inc., Japan). PIL involved the duodenum (A), jejunum (B) and ileum (C) (Figure 2). Multiple polypoid lesions throughout the small bowel were observed by enteroscopy and were consistent with the capsule endoscopic findings. The intestinal mucosa was slightly atrophic and covered with enlarged whitish villi and numerous lymphangitic follicles (Figure 3). Endoscopic biopsies using forceps were performed on the proximal jejunum. Histological examination demonstrated dilated lymphatic vessels with positive immune reaction of the lymphatic endothelium, compatible with lymphangiectasia (Figure 4).

To evaluate the possibility of a genetic cause, a chro-

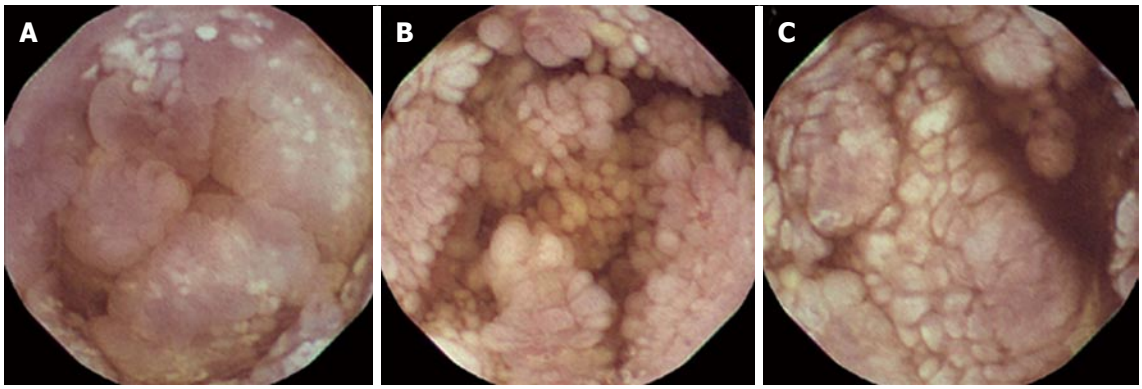

Figure 2 Capsule endoscopic findings in the duodenum (A), jejunum (B) and ileum (C).

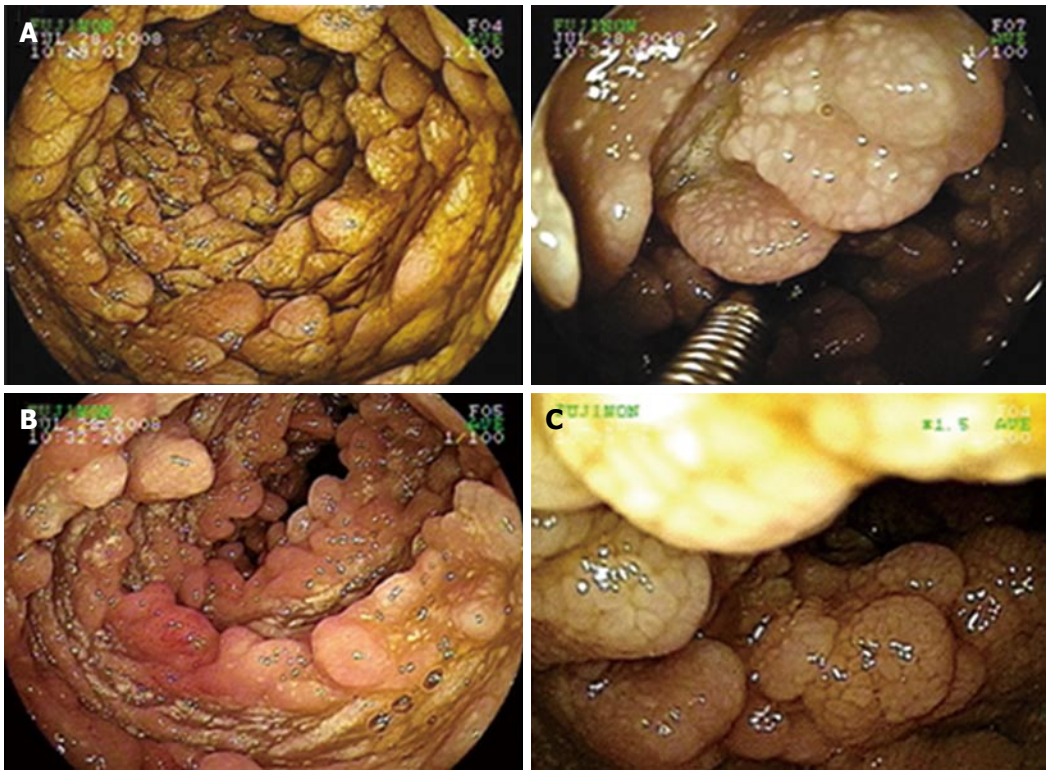

Figure 3 Double balloon enteroscopy was performed with biopsy forceps to obtain a small bowel specimen of polypoid mucosa covered with enlarged whitish villi (A); and additional double balloon enteroscopic findings (B, C).

mosomal study was performed which revealed a normal male karyotype (46, XY) with a deletion of chromosome 4q25 (Figure 5). A chromosomal study of the patient's father revealed a normal male karyotype (46, XY).

During hospitalization, the patient underwent conservative treatment that included a high protein, high calcium diet with intravenous electrolytes and albumin replacement. He has had regular check-ups and received conservative care such as albumin replacement since being discharged.

DISCUSSION

PIL is a rare congenital disorder caused by abnormal lymphatic function. Intestinal lymphangiectasis can also occur as a secondary effect of tuberculosis, sarcoidosis, Crohn's disease, Budd-Chiari syndrome, lymphoma, congestive heart failure, constrictive pericarditis, systemic lupus erythematosus and retroperitoneal fibrosis[8]. A rare, previous case of intestinal lymphangiectasia caused by multiple myeloma involved the mesenteric lymph nodes[9]. PIL was suggested because there was no evidence of pancreatic disease, systemic lupus erythematosus, Menetrier's disease, other intestinal disorders, other disorders of intestinal lymphatics or intestinal lymphoma[10]. Ruptured lymphatic vessels resulting from inflammatory diseases of the small intestine or malrotation were reported to be mechanisms of secondary intestinal lymphangiectasis. Lymph leakage into the bowel lumen, which leads to hypoalbuminemia and lymphopenia, is a basic mechanism

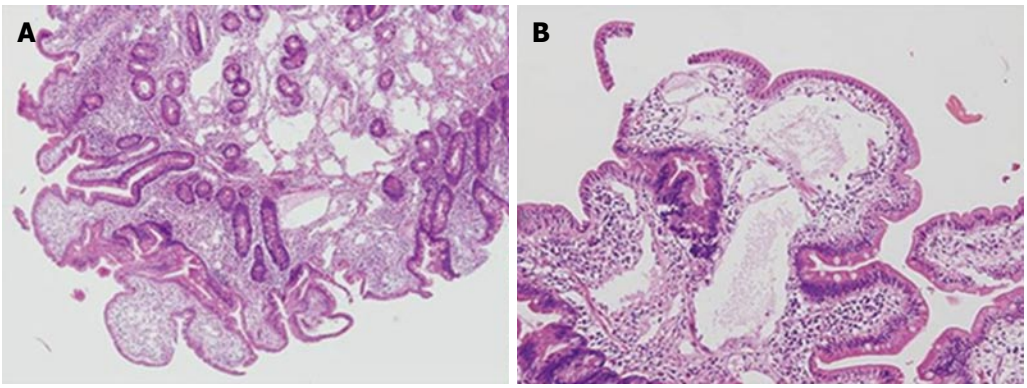

Figure 4 Histology of mucosal tissue in the jejunum shows multiple dilated lymphatics. A: HE, × 40; B: HE, × 100.

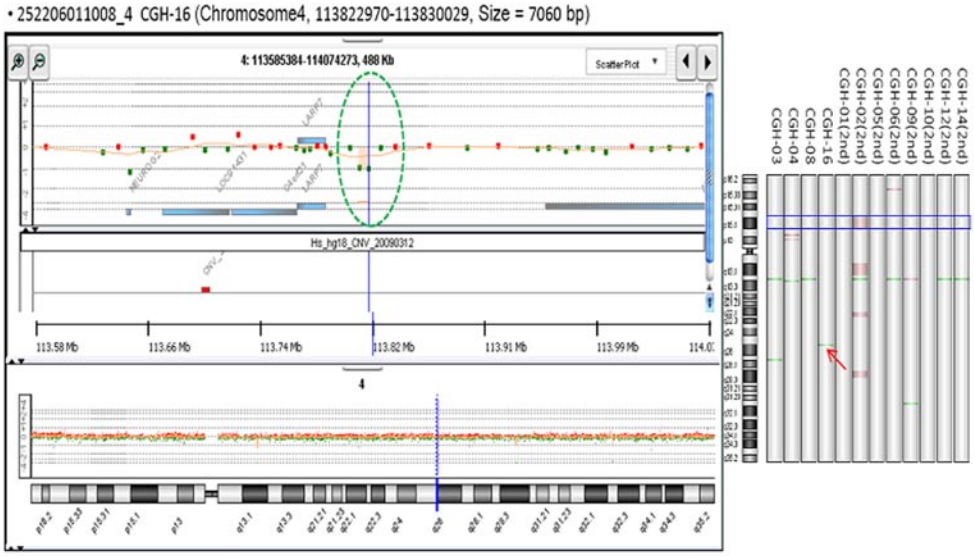

Figure 5 The deletion on chromosome 4q25.

of intestinal lymphangiectasis[11]. In PIL, the etiology of lymphatic dysfunction is unknown. Some studies point to genetic factors in hereditary lymphatic disorders, while other data suggest that regulatory signals involved in lymphangiogenesis, such as vascular endothelial growth factor receptor 3 and LYVE-1, are associated with intestinal lymphagiectasia[12]. Vascular endothelial growth factors-C and -D may also stimulate lymphangiogenesis[13]. Mutations in the FOXC2 (MFH-1) gene or deletion of the pik3r1 gene may result in lymphangiectasia, arrested lymphatic sprouting and maturation defects[14,15]. Defects in chromosome 4 may be related to Rieger syndrome, head and neck squamous cell carcinoma and postoperative atrial fibrillation[16-18]. However, the present case is unique because a deletion was found on chromosome 4. We hypothesized that the deletion of 4q25 and PIL were related because a recent study identified a chromosome 4q25 variant that was associated with diseases such as atrial fibrillation[18]. However, the relationship between deletions on chromosome 4q25 and lymphatic disorders such as PIL remains to be investigated. Mutations related to PIL have never previously been reported.

Diagnoses of PIL are typically confirmed by the presence of intestinal lymphangiectasia based on endoscopic findings and the corresponding histology in intestinal biopsy specimens[11]. Intestinal tissue is acquired through double balloon enteroscopy if a suspicious lesion is observed in the small intestine. Abdominal ultrasonography and CT show diffuse wall thickening and mesenteric edema[19]. Typical mucosal lesions can be identified using endoscopy. Donzelli *et al*[20] described two types of lymphangiectatic plaques on the surface of the duodenal mucosa that were detected *via* duodenoscopy. One type had a diameter of less than 1 mm, while the other exceeded 3 mm in diameter. Asakura *et al*[21] reported three cardinal endoscopic findings in protein-losing enteropathy: scattered white spots, white villi and chyle-like substances covering the mucosa in the jejunum. In cases of sustained protein-losing enteropathy, capsule endoscopy may assist diagnosis. Chamouard *et al*[22] described a case of PIL that was detected using Given M2A video capsule endoscopy. Fang *et al*[10] reported the case of a female patient who

was diagnosed with PIL by M2A capsule endoscopy and was confirmed by pathological examination. In our case, we were able to examine the patient's small bowel completely and detect these typical findings *via* capsule endoscopy following accurate pathological diagnosis according to double balloon enteroscopy. However, the roles of capsule endoscopy and double balloon enteroscopy as prognosticators have not been reported.

Outcomes of PIL may be predicted according to whether complications, such as infection, malignancy (lymphoma) and serous effusion (pleural or pericardic), occur. There is no gold standard treatment for PIL. A low-fat diet with supplemental MCT forms the cornerstone of management in PIL[23]. MCT are directly absorbed into the portal venous system, which prevents lacteal engorgement[24]. Dietary intervention is more effective in children than in adults, therefore early diagnosis of intestinal lymphangiectasia and consistent attention to diet are very important for early nutrition and growth[25]. Small bowel resection may be helpful to treat localized disease[26]. Antiplasmin, octreotide and corticosteroids are treatment options, but their efficacies are variable and insufficient[11]. In our patient, the course of disease apparently stabilized after treatment; however, he has reported episodes of protein-losing enteropathy during occasional periods of dietary therapy cessation. Antiplasmin, octreotide and corticosteroids may be future options if his symptoms progress despite dietary therapy.

We report the case of a patient with PIL involving the entire small bowel, which we confirmed using capsule endoscopy and double-balloon enteroscopy-guided tissue pathology. Capsule endoscopy showed diffusely swollen mucosae and enlarged whitish villi, and genetic analysis revealed a deletion on chromosome 4. However, we did not identify the specific gene associated with chromosome 4q25 that may be related to PIL. The LARP7 gene, which is located near chromosome 4q25, may be involved. The possible relationship between the deletion at chromosome 4q25 and PIL warrants further study.

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Events Calendar 2011

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AGA Clinical Congress of Gastroenterology and Hepatology: Best Practices in 2011
Miami, FL 33101, United States

January 20-22, 2011
Gastrointestinal Cancers Symposium 2011
San Francisco, CA 94143, United States

January 28-29, 2011
9. Gastro Forum München
Munich, Germany

February 04-05, 2011
13th Duesseldorf International Endoscopy Symposium
Duesseldorf, Germany

February 13-27, 2011
Gastroenterology: New Zealand CME Cruise Conference
Sydney, NSW, Australia

February 24-26, 2011
Inflammatory Bowel Diseases 2011-6th Congress of the European Crohn's and Colitis Organisation
Dublin, Ireland

February 24-26, 2011
2nd International Congress on Abdominal Obesity
Buenos Aires, Brazil

February 26-March 1, 2011
Canadian Digestive Diseases Week
Westin Bayshore, Vancouver
British Columbia, Canada

March 03-05, 2011
42nd Annual Topics in Internal Medicine
Gainesville, FL 32614, United States

March 14-17, 2011
British Society of Gastroenterology Annual Meeting 2011
Birmingham, England, United Kingdom

March 17-19, 2011
41. Kongress der Deutschen Gesellschaft für Endoskopie und Bildgebende Verfahren e.V.
Munich, Germany

March 17-20, 2011
Mayo Clinic Gastroenterology & Hepatology 2011
Jacksonville, FL 34234, United States

March 25-27, 2011
MedicReS IC 2011 Good Medical Research
Istanbul, Turkey

April 07-09, 2011
International and Interdisciplinary Conference Excellence in Female Surgery
Florence, Italy

April 15-16, 2011
Falk Symposium 177, Endoscopy Live Berlin 2011 Intestinal Disease Meeting, Stauffenbergstr. 26
Berlin 10785, Germany

April 18-22, 2011
Pediatric Emergency Medicine: Detection, Diagnosis and Developing Treatment Plans
Sarasota, FL 34234, United States

April 20-23, 2011
9th International Gastric Cancer Congress, COEX, World Trade Center, Samseong-dong
Seoul 135-731, South Korea

April 25-27, 2011
The Second International Conference of the Saudi Society of Pediatric Gastroenterology, Hepatology & Nutrition
Riyadh, Saudi Arabia

April 28-30, 2011
4th Central European Congress of Surgery
Budapest, Hungary

May 07-10, 2011
Digestive Disease Week
Chicago, IL 60446, United States

May 12-13, 2011
2nd National Conference Clinical Advances in Cystic Fibrosis
London, England, United Kingdom

May 21-24, 2011
22nd European Society of Gastrointestinal and Abdominal Radiology Annual Meeting and Postgraduate Course
Venise, Italy

May 25-28, 2011
4th Congress of the Gastroenterology Association of Bosnia and Herzegovina with international participation, Hotel Holiday Inn
Sarajevo, Bosnia and Herzegovina

June 11-12, 2011
The International Digestive Disease Forum 2011
Hong Kong, China

June 13-16, 2011
Surgery and Disillusion XXIV Spigc II ESYS, Napoli, Italy

June 22-25, 2011
ESMO Conference: 13th World Congress on Gastrointestinal Cancer
Barcelona, Spain

September 10-11, 2011
New Advances in Inflammatory Bowel Disease
La Jolla, CA 92093, United States

September 10-14, 2011
ICE 2011-International Congress of Endoscopy, Los Angeles Convention Center, 1201 South Figueroa Street
Los Angeles, CA 90015, United States

September 30-October 1, 2011
Falk Symposium 179, Revisiting IBD Management: Dogmas to be Challenged, Sheraton Brussels Hotel
Brussels 1210, Belgium

October 19-29, 2011
Cardiology & Gastroenterology Tahiti 10 night CME Cruise
Papeete, French Polynesia

October 22-26, 2011
19th United European Gastroenterology Week
Stockholm, Sweden

October 28-November 02, 2011
ACG Annual Scientific Meeting & Postgraduate Course
Washington, DC 20001, United States

November 11-12, 2011
Falk Symposium 180, IBD 2011: Progress and Future for Lifelong Management, ANA Interconti Hotel, 1-12-33 Akasaka, Minato-ku
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15 Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis serial online, 1995-01-03, cited 1996-06-05; 1(1): 24 screens. Available from: URL: http://www.cdc.gov/ncidod/eid/index.htm

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16 **Pagedas AC**, inventor; Ancel Surgical R&D Inc., assignee. Flexible endoscopic grasping and cutting device and positioning tool assembly. United States patent US 20020103498. 2002 Aug 1

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