

## Unusual association of diseases/symptoms

## Crohn's disease after gastric bypass surgery

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Correspondence to Dr Izabella Janczewska, [izabella.janczewska@ds.se](mailto:izabella.janczewska@ds.se)**Summary**

Bariatric surgery for the treatment of severe obesity has increased dramatically in recent years in the USA and parts of Western Europe. The most commonly used technique is the Roux-en Y gastric bypass (RYGBP). Several nutritional and gastrointestinal complications after bariatric surgery have been described during the last 10 years. The authors present two patients with diarrhoea and malnutrition; one after RYGBP and the other after jejunioleal bypass surgery. These patients were subsequently diagnosed with Crohn's disease.

**BACKGROUND**

Bariatric surgery is an established treatment for a selected group of patients with severe obesity.<sup>1</sup> Bariatric surgery simultaneously achieves weight-loss goals and presents nutritional risks through two mechanisms: restricted intake (of both macronutrients and micronutrients) and the bypass of absorptive and secretory areas of the stomach and small intestine. One of the most commonly performed procedures is the Roux-en Y gastric bypass (RYGBP).<sup>2 3</sup>

The surgery can be performed laparoscopically, and generally results in sustained weight loss. Several complications of gastric bypass may develop at any time.<sup>4 5</sup>

We report here on two patients operated for severe obesity; one with a RYGBP and the other with the older type of jejunioleal bypass. The first patient developed diarrhoea, malnutrition and multiple fistulas in the rectum and vagina. Crohn's disease was suspected and multigene analysis (DiBiCol test)<sup>6</sup> of the colon mucosa showed the pattern compatible to Crohn's disease. The patient responded to treatment with antibiotics and surgical drainage. The second patient also developed diarrhoea and perineal fistula, the colon mucosa was normal in this case. Crohn's disease in the small intestine was suspected, and the DiBiCol test also showed the pattern compatible to Crohn's disease.

**CASE PRESENTATION**

A woman aged 48 years (body mass index 30 kg/m<sup>2</sup>) presented 2 months after laparoscopic RYGBP with watery diarrhoea, fever, vomiting and a weight loss of 16 kg during the 2 months since surgery. There was no family history of inflammatory bowel disease (IBD). The patient underwent laparoscopic surgery in the 1990s for suspected salpingitis, had had an anal abscess, but had no other gastrointestinal symptoms at that time. She had experienced joint and muscle pain since childhood and this was treated with nabumeton (Relifex) in the 1990s, which caused diarrhoea. Medication was changed to meloxicam (Mobic), which then produced no gastrointestinal side effects. Rheumatology investigation in 2007 failed to reveal any rheumatological disease. The patient had diabetes mellitus type 2 treated with insulin since 1991, and severe obesity

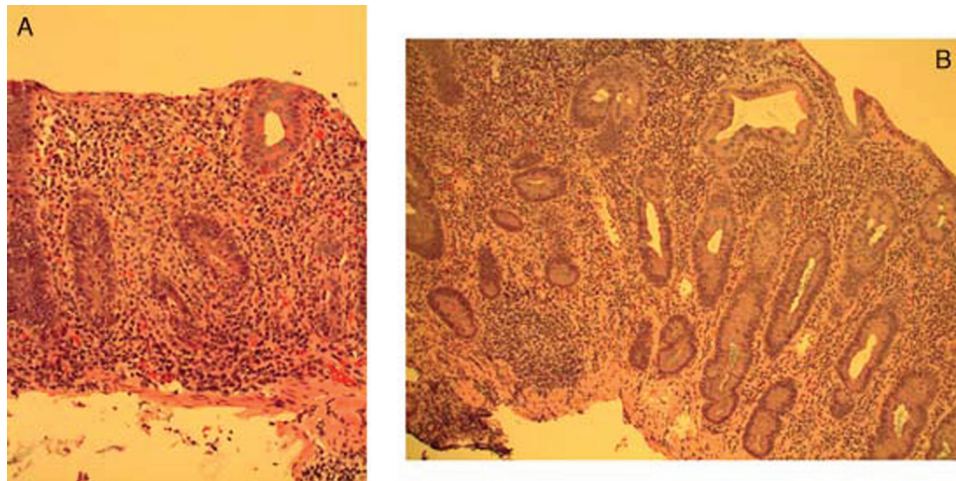
since the beginning of the 1990s. Her body mass index immediately before the bariatric surgery was 38 kg/m<sup>2</sup>.

Physical examination on admission to the hospital in November 2008 showed several deep, suppurative craters of magnitude less than 1 cm on the inside of the thighs and a painful resistance of magnitude approximately 3 cm on the labia minora. Significant laboratory results were Hb 89 g/l (reference interval 117–153), white cell count  $9.3 \times 10^9/l$  (ref 3.5–8.5), C reactive protein 311 (ref <3), potassium 2.5 mmol/l (ref 3.6–4.6), albumin 20 g/l (ref 36–45), faecal calprotectin 11 432 mg/kg (ref <50), vitamin B12 440 pmol/l (ref 100–450), ferritin 487 µg/l (ref 10–130), folic acid 910 mmol/l (ref 330–870).

Gastroscopy revealed a stomal ulceration of magnitude 1×2 cm. Sigmoidoscopy revealed severe deep inflammation with loss of mucosa in 40–50% of circumference of the first 30 cm of the rectum and sigmoideum. There were also several small fistula openings of diameter 0.5–2 cm. The largest fistula was in the anal canal and further investigation showed that it communicated with the vagina. Colonoscopy was performed only to the right flexure and showed no inflammation above 50 cm in the sigmoideum. Biopsies showed findings compatible with discontinuous IBD without established epithelioid granulomas (figure 1).

The patient was initially treated with total parenteral nutrition (TPN), and administration of omeprazol, metronidazol and ciprofloxacin between December 2008 and January 2009. Treatment with metronidazol was continued until March 2009. Surgical investigation under general anaesthesia in December 2008 revealed a rectovaginal fistula and multiple openings on the labia minora. The fistula was drained and setons inserted. MRI showed that the rectum was severely inflamed and revealed a small abscess between the anal sphincter and the introitus. The patient improved with antibiotic treatment. Control sigmoidoscopy in May 2009 showed that the rectal fistula was still present, but no inflammation of the colon mucosa up to right flexure. The calprotectin level had decreased to 74 mg/kg.

Crohn's disease was suspected because of the fistulising disease, inflammation in colon and the absence of any infectious colon disease. The multigene analysis (DiBiCol



**Figure 1** (A, B) The segmental inflammation in the large intestinal mucosa. Moderate crypt distortion and heavy infiltration of plasma cells, lymphocytes and eosinophilic granulocytes across the complete thickness of the lamina propria can be seen. There is also cryptitis with an adjacent granulomatous reaction (H&E staining, magnification 250 times).

test) was performed on colon mucosa and showed the pattern compatible to Crohn's disease.

The second patient reported here was a man aged 69 years with severe obesity (weight 230 kg, height 187 cm). He smoked 20 cigarettes a day and abused alcohol. He was receiving treatment with finasterid (Proscar) due to prostate hyperplasia. He had no inheritance for IBD. Medical treatment and life-style changes failed to reduce his body weight, and he thus underwent a jejunioileal shunt operation in March 1999. Eighteen months later he had lost 63 kg; he now weighed 166 kg. He suffered from watery diarrhoea, which had debuted shortly after the surgery. The diarrhoea was his main problem at this time, and the patient was no longer able to work. He suffered continuously from diarrhoea and developed signs of malabsorption. He was admitted several times to the emergency department during 2007 due to diarrhoea, general muscle weakness and electrolyte disturbances. Blood samples showed severe hypokalemia with a potassium level of 1.7 mmol/l (ref 3.4–4.5), low albumin of 14 g/l (ref 35–45), PK/INR 1.9 (ref <1.2), Hb 90 g/l (ref 135–155). A CT scan showed liver steatosis, while gastroscopy revealed hypertensive gastropathy. Liver cirrhosis was suspected.

He was again admitted in May 2009 due to severe dehydration secondary to diarrhoea. A CT scan showed an air bubble in the urinary bladder, indicating a possible fistula. He had previously had multiple fistulas in the perineum.

The first colonoscopy was performed in 2007 and showed normal mucosa, the second one was performed in June 2009. It showed macroscopically and microscopically normal mucosa. Crohn's disease in the small intestine was suspected and a DiBiCol test on material taken from normal colon mucosa gave a pattern of 100% probability of Mb Crohn. It was decided to carry out surgical reconstruction of his intestine due to the severity of his symptoms and the risk of developing liver cirrhosis.

## DISCUSSION

Bariatric surgery procedures in Stockholm County have risen from 1000 operations in 2008 to almost 4000 in 2009. At Danderyds Sjukhus, 450 operations were performed

in 2009 (L Granström, personal communication). Gastric bypass surgery (often referred to in American literature as the 'Roux-Y' gastric bypass) is the most modern bariatric surgery, but several gastrointestinal adverse effects have been described. These include nausea, vomiting and diarrhoea.<sup>7</sup> Postbariatric surgery diarrhoea may be a physiological response to the procedure itself as a result of malabsorption/maldigestion, bile salt diarrhoea or dumping syndrome. Most of the patients will experience the side effects within the first 18 months. The incidence of chronic dumping syndrome is 5–10% and is frequently accompanied by abdominal pain and diarrhoea. These symptoms usually arise in those who ingest a high-sugar liquid meal. Other possible causes of diarrhoea include irritable bowel syndrome (IBS) exacerbated by surgery and pre-existing or de novo food intolerances that developed after surgery. Diarrhoea due to small bowel bacterial overgrowth may be a consequence of the change in anatomy, lack of gastric acidity and/or stasis in the afferent loop. The empiric therapy with antibiotics/probiotics for bacterial overgrowth, dietary modification to prevent dumping syndrome and the avoidance of foods to which the patient is known to be intolerant usually resolves the symptoms.<sup>8</sup> Persistent symptoms despite dietary compliance or symptoms accompanied by abdominal pain, excessive weight loss or malnutrition should raise the suspicion of an underlying disease or structural complication of surgery. Our first patient experienced severe diarrhoea directly after surgery and developed several fistulas and severe inflammation in rectum and sigmoideum. Crohn's disease was suspected when we excluded all infectious factors. Surgical treatment of the fistulas and abscesses, followed by with the administration of TPN and antibiotics, was successful. The calprotectin level which was very high at the presentation normalised after the treatment. Although the faecal calprotectin is a non-specific inflammatory marker, it is regarded as a useful screening method for identifying patients who need endoscopy for suspected IBD.<sup>9</sup> The diagnosis of Crohn's disease was confirmed by a multigene analysis (DiBiCol test) of inflamed colon mucosa. In this new test seven marker genes with dysregulated expression

in inflamed biopsy samples have been identified. These marker genes are used to differentiate between Crohn's disease and ulcerative colitis or IBS. The first report was very promising but additional studies on larger number of patients are required. The value of this test in normal colon mucosa for diagnosing Crohn's disease in the small intestine has not yet been evaluated (P v Stein, personal communication). This patient will be a candidate for biological drug treatment after the surgical treatment is complete, and she is free from abscesses.

The surgical procedure used for the second patient was an old type of obesity surgery – the jejunoileal bypass. This is now no longer used because of the high risk of severe complications. Death from liver cirrhosis after this kind of surgery has been observed.<sup>2</sup>

Three cases of Crohn's disease after RYGBP surgery have recently been reported in the USA.<sup>10</sup> These patients had endoscopic and histological findings consistent with Crohn's disease, with no gastrointestinal symptoms before surgery or family history of IBD. We speculate that the anatomic changes after gastric bypass surgery promotes a bacterial milieu in genetically predisposed patients that triggers chronic intestinal inflammation, resulting in Crohn's disease. These cases show that a potential association between Crohn's disease and RYGBP should not be overlooked in patients with postoperative abdominal pain, diarrhoea and/or unanticipated weight loss. Even if it is too early to speculate about an association between gastric bypass surgery and Crohn's disease, we recommend that this kind of surgery should be avoided in patients with known Crohn's disease. Risk patients with an anamnesis of diarrhoea and/or anal abscess should be evaluated during the preoperative investigation by determining the calprotectin level and performing an endoscopic investigation. The role of the DiBiCol test should be evaluated.

### Learning points

- ▶ Gastric bypass surgery should be avoided in patients with Crohn's disease.
- ▶ Risk patients with anamnesis of diarrhoea and/or anal abscess should be evaluated during the preoperative investigation by determining the faeces calprotectin level and endoscopic investigation.

**Competing interests** None.

**Patient consent** Obtained.

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