Obesity surgery and Ehlers–Danlos syndrome: challenges and considerations based on a case report

IN Gerogiannis¹, ID Gkegkes², NJ Dempster¹, RS Gillies¹, B Sgromo¹

¹Department of Upper Gastrointestinal and Bariatric Surgery, Churchill Hospital, Oxford University Hospitals, Oxford, UK

²Department of Colorectal Surgery, Churchill Hospital, Oxford University Hospitals, Oxford, UK

ABSTRACT

Ehlers–Danlos syndrome is a hereditary connective tissue disorder that has gastrointestinal manifestations in over 50% of its cases. We present the first case of bariatric surgery in a patient with Ehlers–Danlos syndrome and outline management challenges in the context of the relevant literature. A 56-year-old man with type IV Ehlers–Danlos syndrome and a body mass index of 41.8 kg/m² was referred to the bariatric centre of the Churchill Hospital, Oxford, for consideration of surgery for morbid obesity. His comorbidity included type 2 diabetes, hypertension, dyslipidaemia and obstructive sleep apnoea. He underwent a laparoscopic Roux-en-Y gastric bypass. His initial recovery was uneventful and he was discharged on the first postoperative day. Six weeks later, he presented with 43.9% excess weight loss and improved glycaemic control. Three months postoperatively, however, he complained of dysphagia, regurgitation and postprandial pain. A barium meal and gastroscopy suggested the presence of a gastric diverticulum. A surgical exploration was planned. Intraoperative gastroscopy demonstrated an asymmetrical gastric pouch dilatation and the pouch was therefore refashioned laparoscopically. Despite the initial symptomatic relief, two months later he experienced retrosternal pain with progressive dysphagia. Since then, multiple endoscopic dilations of the gastro-oesophageal junction have been performed for recurrence of symptoms. Finally, a laparoscopic hiatus hernia repair and adhesiolysis was performed resulting in complete relief of patient's symptoms. Bariatric management of patients with Ehlers–Danlos syndrome can prove challenging. The bariatric team must implement a careful management plan including a detailed consent process, a tailored surgical intervention and a follow-up focused on potential gastrointestinal manifestations.

KEYWORDS

Ehlers–Danlos syndrome – Bariatric surgery – Gastric bypass, complications

Accepted 30 June 2019

CORRESPONDENCE TO

Ioannis N. Gerogiannis, E: drgerogiannis@gmail.com

Background

Ehlers–Danlos syndrome is a heterogeneous group of heritable disorders affecting the synthesis of collagen, an abundant structural protein found in human and all animals. The biosynthetic pathway of collagen is caused by mutations in structural collagen genes, as well as in genes coding for proteins involved in the processing of the collagen. In the fourth century BCE, Hippocrates had described patients with overly lax joints; although Ehlers–Danlos syndrome was independently described and named by two dermatologists, the Danish Edvard Ehlers and the French Henri-Alexandre Danlos, in 1901 and 1908, respectively.^{1,2} Currently, it is difficult to estimate the overall incidence of the syndrome, because of its phenotypic variability. The worldwide prevalence of all types is about one in 5000 individuals.³ Ehlers–Danlos syndrome affects equally men and women. The variety of clinical syndromes included in Ehlers–Danlos syndrome makes diagnosis and classification difficult.

The principal characteristics of Ehlers–Danlos syndrome, which can be present in the different subtypes, are skin hyperelasticity, joint hypermobility, skin fragility, the presence of characteristic subcutaneous nodules and blood vessel fragility.² Ehlers–Danlos syndrome can clinically be classified into six subtypes: classic, hypermobility, vascular (formerly type IV), kyphoscoliosis, arthrochalasia and dermatosparaxis. Every subtype presents a different clinical identity based on their signs and symptoms, their genetic mutations and their inheritance pattern.⁴ Even though Ehlers–Danlos syndrome is correlated with multiple medical issues, the healing difficulties and friability of the tissues are those of most surgical interest. The main upper gastrointestinal complications are megaesophagus, oesophageal, gastric or small-bowel diverticuli, hiatal hernia, bleeding gastric ulcers, perforation or haematoma of the gastrointestinal tract spontaneously or after oesophagogastroduodenoscopy.²

We present the first case of bariatric surgery in a patient with Ehlers–Danlos syndrome and outline the challenges in the management of patients with this syndrome.

Case history

A 56-year-old man with type IV Ehlers–Danlos syndrome and a body mass index (BMI) of 41.8 kg/m^2 (137 kg) was referred to the bariatric centre of the Churchill Hospital, Oxford, for consideration of surgery for morbid obesity. His comorbidity included type 2 diabetes mellitus, on insulin for more than 10 years, hypertension, dyslipidaemia, non-alcoholic fatty liver disease and obstructive sleep apnoea requiring continuous positive airway pressure.

In the two years prior to referral to our unit, he had been thoroughly investigated for mild dysphagia and retrosternal pain; computed tomography (CT) of the chest, abdomen and pelvis was normal. The oesophagogastroduodenoscopy was also normal. A 24-hour pH and manometry study revealed non-propagated contractions of the lower oesophagus and a subsequent barium swallow scan showed dysmotility with very slow oesophageal transit and tertiary contractions of the lower oesophagus and a small hiatal hernia.

The preoperative assessment, after discussion in our multidisciplinary team meeting, was to proceed with an oesophagogastroduodenoscopy, which confirmed gastritis and absence of *Helicobacter pylori*. However, during consultations with the bariatric team at the outpatient clinic, he complained of occasional dysphagia. Hence, a barium swallow scan and a gastric emptying study were requested, which again revealed oesophageal dysmotility and a small hiatal hernia. Preoperatively, he attended all outpatient appointments with the bariatric team. He managed to lose 12 kg from the initial referral date (a period of eight months) and his BMI was 38.2 kg/m^2 on the day of the planned operation.

The patient underwent a laparoscopic Roux-en-Y gastric bypass and liver biopsy. His initial recovery was uneventful and he was discharged on the first postoperative day. He presented to our clinic six weeks later with 43.9% excess weight loss, with a weight of 112 kg (BMI 34.4 kg/m^2) and improved glycaemic control. Three months postoperatively, however, he complained of dysphagia, regurgitation and postprandial pain. A further barium swallow scan and oesophagogastroduodenoscopy showed a tight gastro-oesophageal junction and suggested the presence of a gastric diverticulum (Figures 1 and 2). A surgical exploration was planned; laparoscopy and intraoperative oesophagogastroduodenoscopy demonstrated an asymmetrical gastric pouch dilatation, so the pouch was refashioned laparoscopically. He recovered well with complete relief of his symptoms, a weight of 93.1 kg and controlling his diabetes without administration of insulin.

Two months later, he returned to clinic experiencing retrosternal pain and progressive dysphagia to solid foods. Proton pump inhibitors were prescribed, but there was no improvement, and an oesophagogastroduodenoscopy was

requested. Despite the trial of proton pump inhibitors, the patient presented to endoscopy with the same symptomatology. The oesophagogastroduodenoscopy showed no abnormality other than a tight gastro-oesophageal junction. A dilatation of the gastro-oesophageal junction with a 20-mm balloon resolved his symptoms for one week. Subsequently, four dilatations were performed for recurrence of symptoms in two- to three-week intervals.

Figure 1 Endoscopic appearance of the gastric diverticulum.

Figure 2 Barium swallow study confirming the gastric pouch dilatation.

The barium swallow scan following those dilatations showed marked oesophageal dysmotility but no anatomical abnormality of the Roux-en-Y gastric bypass.

Seven months after the second laparoscopic operation, still suffering from dysphagia and postprandial pain, the patient required admission to our unit and insertion of a nasojejun tube for feeding. His weight at that point was 88 kg (BMI 26.9 kg/m² and excess weight loss 88.9 k). Our multidisciplinary team meeting recommended a diagnostic laparoscopy and intraoperative oesophagogastrroduodenoscopy, to proceed as required.

A hiatal hernia was repaired laparoscopically with adhesiolysis, blunt and sharp dissection of the right and left crus of the diaphragm, extensive adhesiolysis around the oesophagus and the gastric pouch and finally primary closure of the crural defect. The postoperative course was uneventful. On review in clinic two and six months after the last procedure, he remained asymptomatic, with good glycaemic control and an excess weight loss of 107.1% (78 kg, BMI 23.8 kg/m²).

Discussion

The wide phenotypic variability of Ehlers–Danlos syndrome presents difficulties in diagnosis. A key component in making the diagnosis in a bariatric patient, is both the surgical and family history. Patients with a history of numerous failed surgical procedures, most often abdominal hernias, as well as presence of recurrent surgical failures in members of the same family should raise the index of suspicion for Ehlers–Danlos syndrome.² Physical findings such as joint hyperelasticity, paper thin scars and skin hyperelasticity are further suggestion of an underlying connective tissue disorder.⁵ Nevertheless, the diagnosis of Ehlers–Danlos syndrome is confirmed by geneticists, through genetic testing.

Most patients with Ehlers–Danlos syndrome present with gastrointestinal symptoms including severe chronic constipation (17%), irritable bowel syndrome (12%), acid reflux or gastroesophageal reflux disease (14%) and/or chronic abdominal pain (22%). Gastroparesis has also been described.⁶ Zeitoun *et al* described dysphagia, epigastric pain, nausea, postprandial fullness and belching in the majority of patients with Ehlers–Danlos syndrome.⁷ Our patient, prior to his referral and during the preoperative period, was thoroughly investigated for mild dysphagia and retrosternal pain, revealing lower oesophageal dysmotility with tertiary contractions and a small hiatal hernia.

Surgical intervention on patients with Ehlers–Danlos syndrome is challenging. A high frequency of surgical complications has been described, especially the Vascular type.⁵ Early postoperative complications, described in the literature, are anastomotic dehiscence and anastomotic bleeding in colorectal surgeries.⁸ Iatrogenic oesophageal perforation secondary to endoscopy is also reported, with a 10% risk of perforation in Vascular Ehlers–Danlos syndrome, but probably safer in the remaining subtypes.⁹ In our patient, despite having multiple

oesophagogastrroduodenoscopies before and after surgery with gastro-oesophageal junction dilatations, no complication occurred.

Regarding late complications, spontaneous oesophageal perforation in connection with vomiting has been described at least twice in the literature.¹⁰ Oesophageal diverticula, megaoesophagus, gastric atony, megaduodenum, small bowel dilatation, megacolon and delayed gastric emptying are described as surgical complications in patients with Ehlers–Danlos syndrome.^{5,10,11} The lack of perivascular structural integrity may predispose to increased bleeding from the gastric mucosa.¹² Spontaneous intramural haematoma of the small bowel wall is seen in patients with Ehlers–Danlos syndrome. It increases the risk of focal necrosis of the intestinal wall, which could potentially lead to perforation.¹² Altered gut motility, spontaneous cases of megaduodenum with bacterial overgrowth and spontaneous dilatation of the small intestine from the Treitz ligament to the terminal ileum are also mentioned in international literature.^{13–15} Our patient developed asymmetrical gastric pouch dilatation, which was refashioned laparoscopically. Moreover, the gastro-oesophageal junction was found to be tight, with lower oesophageal dysmotility, a finding that existed preoperatively, but became more intense postoperatively. Both of those postoperative conditions are similar to those described in literature.^{16–17}

The anaesthetic management of bariatric patients and especially of those with Ehlers–Danlos syndrome can also be challenging. According to the literature, there are recommendations regarding the position, the intubation and the ventilation of bariatric patients with Ehlers–Danlos syndrome, to avoid possible complications. The positioning of the patient on the surgical bed is important to avoid any joint dislocations, as well as cutaneous injuries from mechanical stress, traction or pressure increase.^{18,19} Furthermore, as most bariatric patients are diabetic with a degree of peripheral neuropathy, the vulnerability of peripheral nerves must be always taken in consideration whilst positioning or transferring. Ohshita *et al* managed the potential problems by using a low rebounding mattress to reduce pressure.²⁰ It is possible to cause lesions at the skin, the oropharynx and the larynx of the patient during endotracheal intubation.

The risk of cervical atlantoaxial subluxation is always present in patients with Ehlers–Danlos syndrome as a consequence of the laxity of the cervical ligaments, while temporomandibular dislocation is an eventuality that the anaesthetist should always have in mind during endotracheal intubation.^{19,20} Higher positive inspiratory pressures during mechanical ventilation, especially in obese patients, where are necessary, may cause barotrauma in the context of Ehlers–Danlos syndrome. The anaesthetist should therefore always have in mind that any increase of airway resistance could also be the result of a pneumothorax. In our case, there were no complications from the anaesthetic point of view.

There are important aspects that the bariatric surgeon should take into consideration before proceeding with

surgery (Box 1). Minimal invasive technique is encouraged. Small incisions and reduced traction of the abdominal wall can decrease the probability of incisional hernia. However, in the case of open surgery, synthetic mesh placement is recommended at all abdominal incisions.² If the surgery is considered either clean-contaminated or contaminated, Peppas *et al* suggest the application of biological mesh to avoid any postoperative wound complications.²¹ It is also advisable that tissue dissection and the application of lateral force on the tissues should be minimal, to avoid intraoperative bleeding and unnecessary tissue damage.¹ Wound closure should be performed in two layers with no tension. The aponeurosis of the muscular sheath should always be closed with deep sutures. We suggest closing the skin with adhesive agents such as skin glue until adequate healing of the underlying tissues is reached. However, if non-absorbable sutures are used for skin closure they should be left twice as long as is usually recommended.¹

Postoperatively, Fogel *et al* recommend that prevention of constipation is crucial for all patients with

Ehlers–Danlos syndrome, as this is the inciting event in cases of colonic perforation.² In bariatric patients, constipation secondary to dehydration is a common condition, especially during the early post-operative period. Postoperative instructions for the use of oral fluids, diet, opioids and laxatives should always be considered in patients with Ehlers–Danlos syndrome. In our case, there is a question whether a Roux-en-Y gastric bypass was the appropriate bariatric procedure for this patient with Ehlers–Danlos syndrome or even whether surgical intervention was contraindicated. Fogel *et al* recommend that surgical intervention in patients with Ehlers–Danlos syndrome should be avoided if possible.² However, our patient was referred to our specialist obesity service with a BMI of 41.8 kg/m², a 10-year history of difficult to control type 2 diabetes on insulin, non-alcoholic fatty liver disease with deranged liver functions tests, hypertension and obstructive sleep apnoea on continuous positive airway pressure. Furthermore, the patient had tried but had failed to achieve clinically beneficial weight loss for at least six months, he was fit for anaesthesia and surgery and showed commitment to the need for long-term follow-up, also managing to reach the 5% preoperative weight loss target. According to guidelines from the National Institute for Health and Care Excellence, our patient fulfilled the selection criteria for bariatric surgery.²²

Retrospectively, we could say that a less invasive procedure would be more suitable to patients with Ehlers–Danlos syndrome. Sleeve gastrectomy is less invasive than Roux-en-Y gastric bypass. Laparoscopic adjustable gastric band surgery should be avoided, as it can lead to dysmotility and increase in lower oesophageal pressure.²³ As patients with Ehlers–Danlos syndrome are more prone to developing dilatation of the lower oesophagus or diverticula formation (oesophageal or gastric), it seems reasonable to avoid laparoscopic adjustable gastric band surgery. Furthermore, sleeve gastrectomy could be potentially safer than Roux-en-Y gastric bypass in bariatric patients with Ehlers–Danlos syndrome, as it involves less tissue handling and no anastomoses. Indeed, Roux-en-Y gastric bypass should be performed in cases where there are contraindications for sleeve gastrectomy, such as the presence of a hiatal hernia, severe gastroesophageal reflux disease or any other gastric pathology that can increase the risk of failure and complications. It is known that Roux-en-Y gastric bypass leads to an improvement of the symptoms of gastroesophageal reflux disease and the preservation of oesophageal motility.

Despite all the above challenges and difficulties, the long-term physiological outcomes of bariatric surgery in our patient with Ehlers–Danlos syndrome were very satisfactory, as follow-up revealed that he was symptom free with good glycaemic control and a BMI of 23.8 kg/m².

Finally, it is crucial to understand the necessity for a detailed initial consultation by the bariatric team, following the referral of patient to the bariatric clinic. The attempt to add the described considerations to the process of counselling of patients with Ehlers–Danlos syndrome for

Box 1 Issues to consider in the management of bariatric patients with Ehlers–Danlos syndrome.

- > Identify the type of Ehlers–Danlos syndrome and underline the complications that are observed in literature.
- > A detailed past medical and family history should be taken highlighting symptoms suggestive of gastrointestinal manifestations pathology.
- > Inform the patient about the risk and benefits of the surgery and complications in detail. The specific potential complications secondary to Ehlers–Danlos syndrome should be highlighted in the written consent form.
- > Avoid bariatric surgery if required criteria are not optimally met.^{2,22}
- > Choose minimally invasive technique with less tissue handling, careful surgical dissection and fewer anastomoses if possible.²
- > The anaesthetic team should be aware of possible positional injuries (joint dislocations, cutaneous injuries), intubation and mechanical ventilation related complications.^{18–20}
- > In case of conversion to open surgery, mesh placement is suggested to avoid incisional hernias. The abdominal wall should be closed without tension and with deep stitches and skin glue and Steri-Strips™ are recommended for skin closure.¹
- > Any non-absorbable sutures should be left in place for twice the usual length of time before removal.¹
- > There should be frequent follow-up appointments at the bariatric clinic with the surgeon and a dietitian.
- > There should be a low threshold for requesting imaging in the case of postoperative symptomatology.

bariatric surgery could be challenging. Further research is therefore needed on the management of the patient with Ehlers–Danlos syndrome requiring bariatric surgery.

Conclusion

Bariatric management of patients with Ehlers–Danlos syndrome can prove challenging. Consultation of a new patient presenting to the bariatric centre with morbid obesity and known Ehlers–Danlos syndrome should be meticulous. The bariatric multidisciplinary team must be vigilant for symptoms suggestive of gastrointestinal manifestations pathology to ensure prompt investigation and appropriate intervention. If an intervention is necessary, unless contraindicated, a minimally invasive technique with less tissue handling and fewer anastomoses should be chosen. It is equally important that patients are informed of these risks so that they are able to provide informed consent for bariatric surgery. The anaesthetist should be aware of the potential difficulties that can arise before and during anaesthesia and how they can be managed. Follow-up in the bariatric clinic should be arranged at frequent intervals with the bariatric surgeon and dietitian to identify postoperative complications that can lead to malnutrition and rapid deterioration as early as possible.

References

- Burcharth J, Rosenberg J. Gastrointestinal surgery and related complications in patients with Ehlers–Danlos syndrome: a systematic review. *Dig Surg* 2012; **29**(4): 349–357.
- Fogel S. Surgical failures: is it the surgeon or the patient? The all too often missed diagnosis of Ehlers–Danlos syndrome. *Am Surg* 2013; **79**(6): 608–613.
- Byers PH, Murray ML. Heritable collagen disorders: the paradigm of the Ehlers–Danlos syndrome. *J Invest Dermatol* 2012; **132**(E1): E6–E11.
- US National Library of Medicine. Genetics Home Reference. Ehlers–Danlos syndrome. <https://ghr.nlm.nih.gov/condition/ehlers-danlos-syndrome#genes> (cited August 2019).
- Beighton P, De Paepe A, Steinmann B *et al*. Ehlers–Danlos syndromes: revised nosology, Villefranche, 1997. Ehlers–Danlos National Foundation (USA) and Ehlers–Danlos Support Group (UK). *Am J Med Genet* 1998; **77**(1): 31–37.
- Gustafson A., Griswold BF, Sloper L *et al*. Gastrointestinal disorders in patients with hypermobile or classical ehlers–danlos syndromes. (Program Nr: 11076). Presented at the 56th Annual Meeting of the American Society of Human Genetics, October 23–27, 2007, San Diego, CA, USA.
- Zeitoun JD, Lefèvre JH, de Parades V *et al*. Functional digestive symptoms and quality of life in patients with Ehlers–Danlos syndromes: results of a national cohort study on 134 patients. *PLoS One* 2013; **8**(11): e80321.
- Freeman RK, Swegle J, Sise MJ. The surgical complications of Ehlers–Danlos syndrome. *Am Surg* 1996; **62**(10): 869–873.
- Kilaru SM, Oza SS, Gautam S, Wolf LJ. Su1098 colonoscopies are not safe in patients with type 4 Ehlers–Danlos syndrome but appear to be safe with minimally increased rate of perforation in patients with other types of Ehlers–Danlos or Marfan syndrome. *Gastroenterology* 2015; **148**(4 Suppl 1): S-407.
- Reis ED, Martinet OD, Mosimann F. Spontaneous rupture of the oesophagus in an adolescent with type IV Ehlers–Danlos syndrome: Ehlers–Danlos and spontaneous oesophageal rupture. *Eur J Surg* 1998; **164**(4): 313–316.
- McEntyre RL, Raffensperger JG. Surgical complications of Ehlers–Danlos syndrome in children. *J Pediatr Surg* 1977; **12**(4): 531–535.
- Byard RW, Keeley FW, Smith CR. Type IV Ehlers–Danlos syndrome presenting as sudden infant death. *Am J Clin Pathol* 1990; **93**(4): 579–582.
- Harris RD. Small bowel dilatation in Ehlers–Danlos syndrome: an unreported gastrointestinal manifestation. *Br J Radiol* 1974; **47**(561): 623–627.
- Hines C Jr, Davis WD Jr. Ehlers–Danlos syndrome with megaduodenum and malabsorption syndrome secondary to bacterial overgrowth: a report of the first case. *Am J Med* 1973; **54**(4): 539–543.
- Sigurdson E, Stern HS, Houpt J *et al*. The Ehlers–Danlos syndrome and colonic perforation: report of a case and physiologic assessment of underlying motility disorder. *Dis Colon Rectum* 1985; **28**(12): 962–926.
- Fikree A, Chelimsky G, Collins H *et al*. Gastrointestinal involvement in the Ehlers–Danlos syndromes. *Am J Med Genet Part C Semin Med Genet* 2017; **175C**: 181–187.
- Nelson AD, Mouchli MA, Valentin N *et al*. Ehlers–Danlos syndrome and gastrointestinal manifestations: A 20-year experience at Mayo Clinic. *Neurogastroenterol Motil* 2015; **27**(11): 1,657–1,666.
- Castori M, Voermans NC. Neurological manifestations of Ehlers–Danlos syndrome(s): a review. *Iran J Neurol* 2014; **13**(4): 190–208.
- Lane D. Anaesthetic implications of vascular type Ehlers–Danlos syndrome. *Anaesth Intensive Care* 2006; **34**(4): 501–505.
- Ohshita N, Kanazumi M, Tsuji K *et al*. Anesthetic management of a patient with Ehlers–Danlos syndrome. *Anesth Prog* 2016; **63**(4): 204–207.
- Peppas G, Gkegkes ID, Makris MC, Falagas ME. Biological mesh in hernia repair, abdominal wall defects, and reconstruction and treatment of pelvic organ prolapse: a review of the clinical evidence. *Am Surg* 2010; **76**(11): 1,290–1,299.
- National Institute for Health and Care Excellence. *Obesity: Identification, Assessment and Management of Overweight and Obesity in Children, Young People and Adults*. Clinical Guideline CG189. London: NICE; 2014.
- Naik RD, Choksi YA, Vaezi MF. Consequences of bariatric surgery on oesophageal function in health and disease. *Nat Rev Gastroenterol Hepatol* 2016; **13**(2): 111–119.