

Resolving bile reflux by lanreotide in patients with Roux-en-Y gastrojejunostomy

K. Moubax, F. Mana, D. Urbain

UZ Brussel, VUB (Vrije Universiteit Brussel), België.

Abstract

Reflux into the esophagus after partial or total gastrectomy is a well known problem. Even a Roux-en-Y reconstruction is not always a definitive solution. Bile reflux might occur and cause disabling symptoms, unresponsive to the classic anti-acid or anti-reflux therapy. Endoscopy and a Tc-99m-BrIDA hepatobiliary (HIDA) scan can be used to make the diagnosis. Clinical studies have shown that lanreotide (somatuline), which strongly inhibits many gastro-intestinal hormones, reduces the bile salts outputs.

We present a case of a patient with bile reflux after Roux-en-Y. After administration of lanreotide he had a good clinical improvement and mucosal healing on endoscopy. Lanreotide can be a good treatment option for bile reflux when classic treatment fails, but clinical trials with more patients will have to confirm this. (*Acta gastroenterol. belg.*, 2014, 77, 377-378).

Key words : somatostatine analogue, HIDA scan, lanreotide, bile reflux.

Introduction

Bile reflux after gastric surgery is a difficult to treat complication, not responding to classic anti-acid treatment. For several decades, Roux-en-Y (RY) reconstruction has been used to prevent bile and pancreatic secretions from reaching the remnant stomach or esophagus after total or distal gastrectomy (1). It has been reported that alkaline reflux oesophagitis occurs in less than three percent of patients with RY, far less than in patients with alternative reconstructions like Billroth I, Billroth II (2-3). Symptoms are often atypical and medical treatment can be challenging since response to classic anti-reflux therapy is unsure. Patients, resistant to medical treatment, are in general re-operated with lengthening of the alimentary limb (4).

Somatostatin, a hypothalamic hormone present in a variety of organs including central nervous system, pancreas and gastrointestinal tract, strongly inhibits the secretion of neurotransmitters, exocrine enzymes and many gastro-intestinal hormones (5). A long-acting analogue of native somatostatin, lanreotide (Somatuline), is currently used in patients with carcinoid syndrome and acromegaly (6). Lanreotide induces a dose-dependent reduction of postprandial plasma cholecystokinin (CCK) secretion with a concomitant inhibition of postprandial gallbladder contraction (7). In that way lanreotide almost completely abolishes bile salts output from the gallbladder (8).

Therefore, it might be a good option to use somatuline in patients with difficult to treat bile reflux after gastric bypass.

Case report

A 63-year-old man presented to our consultation five months after a total gastrectomy followed by Roux-en-Y reconstruction for adenocarcinoma of the cardia, pT-1N0M0. He complains of vomiting, dysphagia and a weight loss of 28 kg.

On physical examination, he had mild epigastric pain and his laboratory values were unremarkable.

Upper gastrointestinal (GI) endoscopy revealed oesophagitis Los Angeles (LA) classification grade D (Fig. 1A). A CT scan of the abdomen showed no other explanation for his symptoms. Therapy with antacids, alginates, proton pump inhibitors, histamine-2 blockers and cholestyramine were administered sequentially, but without clinical success. The patient refused an additional impedance pH monitoring to confirm the diagnosis of persistent bile reflux.

A Tc-99m-BrIDA hepatobiliary (HIDA) scan was then performed (9). Hereby, scintigraphic images and time/activity curves from the distal esophagus showed the appearance of the radiocompound, indicating a 99mTc-HIDA-tagged bile gastroesophageal reflux (Fig. 1C), confirming the suspected diagnosis of important bile reflux (10).

Since all other available drug therapies were not efficient, the patient was given 120 mg of lanreotide subcutaneously. One week later, the complaints of the patient were almost completely over. A new HIDA scan after eight weeks showed a decrease of the bile reflux (Fig. 1D) and a new upper GI endoscopy showed a net amelioration of the oesophagitis, now LA grade A (Fig. 1B).

Treatment was continued with one injection every month. The patient is still asymptomatic after four months of treatment. No side effects were noted.

Discussion

Reflux into the esophagus after total gastrectomy is a well known problem (1-2). A Roux-en-Y reconstruction can decrease this complication (1-2). However, as in our

Correspondence to : Kim Moubax, UZ Brussels, department of Gastro-Enterology, Laarbeeklaan 101, 1090 Brussel, België.
E-mail : kimmoubax970@hotmail.com

Submission date : ??????????

Acceptance date : ??????????

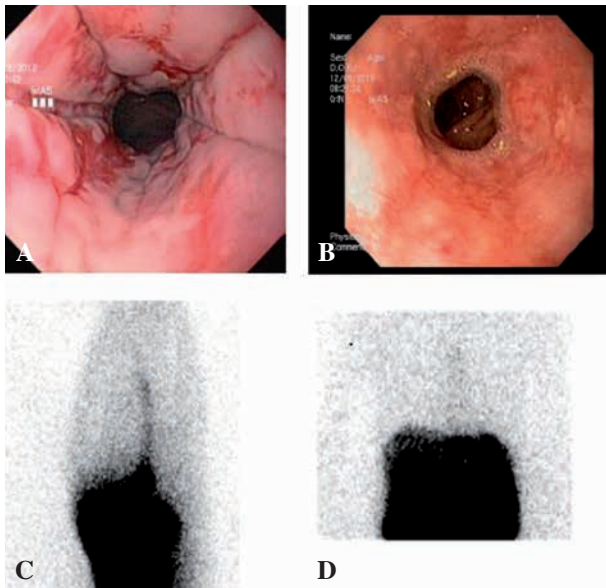


Fig. 1. — Initial oesophagitis LA grade D on upper GI endoscopy (A), oesophagitis grade A on upper GI endoscopy after treatment with lanreotide (B). Important gastroesophageal bile reflux on initial HIDA scan (C). Almost complete disappearance of bile reflux on HIDA scan after treatment with lanreotide (D).

patient, bile reflux might occur and cause disabling symptoms, unresponsive to the classic anti-acid or anti-reflux therapy (4).

Diagnosis is mostly based on endoscopy and the history of upper GI surgery. Impedance pH monitoring and HIDA scan can be used to visualize the reflux and semi-quantify the amount of reflux.

Treatment can be challenging, because classical medications like antacids, alginates, proton pump inhibitors and histamine-2 blockers often do not give enough clinical improvement (11-12). Theoretically, somatostatine could be used for treating bile reflux since it reduces bile salt output from the gallbladder and inhibits intragastric acid secretion (7). However the use of somatostatine is impractical because of its short acting effect so that it must be administrated three times daily subcutaneously. Therefore we preferred a long acting somatostatine analogue, lanreotide.

After treatment, the complaints of our patient improved and upper GI endoscopy confirmed the mucosal healing. The decrease of reflux volume by somatostatine was demonstrated by HIDA scan.

To the best of our knowledge, this is the first patient with bile reflux after Roux-en-Y gastrectomy to be treated successfully with lanreotide.

A potential long term problem due to the reduction of gall bladder emptying could be the formation of gall stones, although the proportion of patients with symptomatic gall stones is likely to remain small (13). Another side effect after long-term somatostatin analogue treatment might be the deficiency of fat-soluble vitamins (14).

To conclude, oesophagitis caused by bile reflux in patients with gastrectomy and Roux-en-Y reconstruction can be a difficult and cumbersome clinical problem. Lanreotide can be a good treatment option when classic treatment fails, but clinical trials with more patients will have to confirm this.

References

1. ISHIKAWA M., KITAYAMA J., KAIZAKI S., NAKAYAMA H., ISHIGAMI H., FUJII S. *et al.* Prospective randomized trial comparing Bilroth I and Roux-en-Y procedures after distal gastrectomy for gastric carcinoma. *World J. Surg.*, 2005, **29** : 1415-1420.
2. MONTESANI C., D'AMATO A., SANTELLA S., PRONIO A., GIOVANNINI C., CRISTALDI M. *et al.* Bilroth I versus Bilroth II versus Roux-en-Y after subtotal gastrectomy. Prospective randomized study. *Hepatogastroenterology*, 2002, **49** : 1469-1473.
3. GERARD PS., GERCZUK P., FINESTONE H. Bile Reflux in the Esophagus Demonstrated by HIDA Scintigraphy. *Clinical Nuclear Medicine*, 2007, **32** : 224-225.
4. SWARTZ D.E., MOBLEY E., FELIX E.L. Bile reflux after Roux-en-Y gastric bypass : an unrecognized cause of postoperative pain. *Surg. Obes. Relat. Dis.*, 2009, **5** : 27-30.
5. GANS S.L., VAN WESTREENEN H.L., KIEWIET J.J., RAUWS E.A., GOUMA D.J., BOERMEESTER MA. Systematic review and meta-analysis of somatostatin analogues for the treatment of pancreatic fistula. *Br. J. Surg.*, 2012, **99** : 754-760.
6. LUDLAM W.H., ANTHONY L. Safety review : dose optimization of somatostatin analogs in patients with acromegaly and neuroendocrine tumors. *Adv. Ther.*, 2011, **28** : 825-841.
7. DREWE J., SIEBER C., MOTTET C., WULLSCHLEGER C., LARSEN F., BEGLINGER C. Dose-dependent gastrointestinal effects of the somatostatin analog lanreotide in healthy volunteers. *Clin. Pharmacol. Ther.*, 1999, **65** : 413-419.
8. LAMRANI A., VIDON N., SOGNI P., NEPVEUX P., CATUS F., BLUMBERG J. *et al.* Effects of lanreotide, a somatostatin analogue, on postprandial gastric functions and biliopancreatic secretions in humans. *Br. J. Pharmacol.*, 1997, **43** : 65-70.
9. ERIKSSON B., EMÁS S., JACOBSSON H., LARSSON S.A., SAMUELSSON K. Comparison of gastric aspiration and HIDA scintigraphy in detecting fasting duodenogastric bile reflux. *Scand. J. Gastroenterol.*, 1988, **23** : 607-610.
10. BORTOLOTTI M., ABBATI A., TURBA E., POZZATO R., BERSANI G., LABÒ G. 99mTc-HIDA dynamic scintigraphy for the diagnosis of gastroesophageal reflux of bile. *Eur. J. Nucl. Med.*, 1985, **10** : 549-550.
11. SIFRIM D., ZERDIP F. Diagnosis and management of patients with reflux symptoms refractory to proton pump inhibitors. *Gut*, 2012, **61** : 1340-1354.
12. TODD J.A., BASU K.K., DE CAESTECKER J.S. Normalization of oesophageal pH does not guarantee control of duodenogastro-oesophageal reflux in Barrett's esophagus. *Aliment. Pharmacol. Ther.*, 2005, **21** : 969-975.
13. TURNER H.E., LINDSELL D., VADIVALE A., THILLAINAYAGAM A.V., WASS J.A. Differing effects on gall-bladder motility of lanreotide SR and octreotide LAR for treatment of acromegaly. *European Journal of endocrinology*, 1999, **141** : 590-594.
14. FIEBRICH H.B., VAN DEN BERG G., KEMA I.P., LINKS T.P., KLEIBEUKER J.H., VAN BEEK A.P. Deficiencies in fat-soluble vitamins in long-term users of somatostatin analogue. *Aliment. Pharmacol. Ther.*, 2010, **32** : 1398-1404.