Management of Bleeding Gastroduodenal Ulcers

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Key Words

Peptic ulcer · Bleeding · Endoscopy · Surgery

Introduction

The management of bleeding peptic ulcers remains a challenging problem. The overall incidence has not dramatically changed over the last 25 years and varies between 10 and 50 per 100,000 person-years [1].

Both NSAIDs and *Helicobacter pylori* infection are important, probably largely independent risk factors for the development of gastroduodenal ulcers. Because discontinuation of NSAIDs and/or *H. pylori* eradication can effectively heal almost all ulcers, the endoscopic and surgical treatment of a bleeding ulcer should be aimed at controlling the hemorrhage, rather than at curing the underlying disease [1, 2].

Over the last two decades endoscopic therapy has superseded surgery as the primary treatment of ulcer bleeding. Endoscopic methods can achieve initial hemostasis in more than 98% of patients in experienced hands [3]. Furthermore, therapy with proton pump inhibitors will heal almost all ulcers and *H. pylori* eradication will prevent recurrent ulcer disease [4] and recurrent ulcer bleeding [5]. Nowadays, surgery is considered a selective

therapeutic option, only to be applied if endoscopic treatment has failed. In these patients timing of the surgical procedure is difficult. The temptation may be to go on with endoscopic therapy, which may however not be wise, especially in elderly patients, because of deterioration of their general condition and subsequent increasing surgical risk.

The fact that endoscopic therapy is the first choice leads to a negative selection of surgical patients with difficult ulcers (large ulcers, frequently located at the posterior duodenal bulb) which are technically demanding even for experienced surgeons [6]. Ideally, such patients are treated in a combined team of medical and surgical gastroenterologists and interventional radiologists.

During this UEGW postgraduate course, a typical difficult case is presented and the literature is reviewed to support clinical decision-making based on the best available evidence. While over the last decade several controlled trials have been performed to refine endoscopic therapy, there is a paucity of data in the recent literature on the surgical management of bleeding ulcers. Multiple-choice questions are asked to the audience and the reported percentages reflect the preferred choices of the audience.

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0253-4886/02/0192-0099\$18.50/0

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Fig. 1. Endoscopic view of the active pulsatile bleeding in a deep ulcer of the posterior duodenal bulb.

Case Report

A 54-year-old woman is admitted to a small community hospital because of abundant hematemesis. In her recent medical history she is complaining of malaise, weight loss, vague abdominal pain and arthralgia for which she has been using NSAIDs over the last 3 months. On physical examination she is pale, with a blood pressure of 110/60 mm Hg and a regular pulse rate of 100/min. On rectal examination typical melena is diagnosed. Hemoglobin level on admission is 4.3 mmol/l.

In this community hospital, diagnostic endoscopy can be performed, but no therapeutic endoscopic experience is available.

Comment

In the seventies and eighties endoscopic therapy was not routinely performed in patients with ulcer bleeding. Only the last two decades it has become obvious that endoscopic therapy improves the outcome of the patient with upper gastrointestinal bleeding [7].

Nowadays, endoscopy should be both diagnostic and therapeutic, if necessary. However, endoscopy in a bleeding patient requires a higher level of skill and is technically more demanding. Important is the availability of a 'bleeding team' with an experienced endoscopist, supported by a trained endoscopy nurse. Early multidisciplinary consultation with the surgeon and radiologist, taking into account the local expertise and the clinical condition of

the individual patient is important and will help in selecting the optimal therapy for the patient.

Case Report (Continued)

After stabilization, the patient is transferred to a secondary referral hospital and an urgent endoscopy is performed. A deep ulcer of 1.5 cm in diameter is identified in the posterior duodenal bulb with an active pulsatile bleeding (Forrest I A; fig. 1).

Question

Which therapeutic endoscopic intervention do you favor?

	Audience's response
A Polidocanol injection	17%
B Epinephrine injection	6%
C Idem plus heater probe	38%
D Endoscopic clip placement	39%

Comment

A meta-analysis showed that endoscopic therapy significantly reduces further bleeding, surgery and mortality rates in patients with ulcers with active bleeding or non-bleeding visible vessels [7]. There is no clear consensus about treating patients with an adherent clot, but further bleeding occurs in 14–36% of patients with these clots, suggesting that endoscopic treatment might also be beneficial in this group as well [8].

Injection therapy, thermal contact methods and laser therapy are all similarly effective [7, 9]. Injection therapy is easy to use, portable, cheap and safe and for these reasons the one most likely to use first in daily practice. Addition of a sclerosant (such as polidocanol) to epinephrine injection therapy does not give a benefit in outcome [9], and because of the potential risk of perforation we do not advise to use a sclerosant. Combination therapy is getting more attention and for a selected group of patients with spurting bleeding combination therapy with epinephrine injection and thermal contact might be beneficial. The endoscopic hemoclip is an attractive alternative in individual cases, but further studies should be performed before this method can be recommended as standard therapy.

In vitro studies have shown that platelet aggregation and blood coagulation become abnormal when the pH falls <6.8. To achieve an optimal coagulation, the intragastric pH should therefore be >6. To reach such a high intragastric pH level, a high-dose proton pump inhibitor should be administered intravenously (80-mg bolus injection, followed by 8 mg/h continuous infusion because of the short half-life time) [10].

A recent randomized trial showed that high-dose intravenous omeprazol for patients with peptic ulcer hemor-

rhage with high-risk stigmata (active bleeding, nonbleeding visible vessel and adherent clot) significantly reduced the rebleeding rate compared to the placebo group. Surgery and mortality rate did not differ between the two groups [11].

The large majority of (bleeding) ulcers is caused by NSAIDs or by *H. pylori* infection. The intake of NSAIDs should of course be discontinued, if possible. *H. pylori* status should be determined. However, most endoscopists are reluctant to take antral biopsies at the emergency endoscopy in patients with bleeding ulcers. Unfortunately, many of these patients leave the hospital without antimicrobial eradication therapy and carry the unnecessary risk of ulcer persistence/recurrence. It is our strong advice to take antral biopsies during the first endoscopy and to start eradication of *H. pylori*, if present, as soon as possible.

Case Report (Continued)

The ulcer bleeding is effectively stopped by the endoscopic injection of 15 cm³ of epinephrine (1:10,000). NSAIDs are discontinued and intravenous proton pump inhibitor therapy is started immediately. After adequate blood transfusion the hemodynamic condition remains stable over the next few days.

Patient's recent complaints, including malaise, arthralgia and abdominal pain plus the apparent renal failure (creatinine 425 µmol/l, urea 29.2 mmol/l, proteinuria) are further analyzed. Erythrocyte sedimentation rate is markedly elevated (140 mm in first hour) and various autoimmune antibodies (ANCA, ANA, anti-PR-3) are positive. A selective angiography of the mesenteric arteries shows multiple non-atherosclerotic stenoses and microaneurysms, confirming the diagnosis of polyarteritis nodosa. Treatment with prednisolone is started.

After 6 days an abundant rebleeding occurs (hematemesis, melena, hypotension). At repeated urgent endoscopy, the duodenal ulcer does not show an active bleeding, but a visible vessel is identified (Forrest II A).

Question

What is your next therapeutic step?

	Audience's response
A No intervention (no bleeding)	44%
B Endoscopic retreatment	51%
C Surgery	5%

Comment

A recent randomized trial indicated that in patients with recurrent peptic ulcer bleeding after initial endoscopic control, repeat endoscopic therapy reduced the need for surgery without increasing mortality. There were significantly less complications in the group with repeat endoscopic therapy compared to the group with surgery [3]. In the present case, repeat endoscopy was the treatment of first choice. For patients with larger ulcers (>2 cm) and hypotension, indicating a more severe bleed-

ing, it is suggested in literature that surgery might be a better choice than repeat endoscopic therapy.

Case Report (Continued)

One day after the second successful endoscopic treatment, rebleeding occurs with imminent shock and markedly increased abdominal pain. It is decided to perform an urgent laparotomy.

Question

Which operation would you perform?

	Audience's response
A Duodenotomy with intraluminal stitch ligatures	65%
B Ibidem plus extraluminal vasoligation	21%
C Partial gastric resection with ulcer excision/exteriorization	6%
D Ibidem plus vagotomy	8%

Comment

Timing of Surgery

The optimal timing of surgical intervention for significant ulcer bleeding remains a difficult clinical decision. Massive, life-threatening hemorrhage, uncontrollable by endoscopic therapy, is a clear indication for emergency surgery. Three randomized trials have been performed to address the timing of semielective surgery. The first study was performed in the early eighties and randomized 142 patients [12]. Patients with a visible vessel, the persistence of bleeding or the recurrence of bleeding were randomized to early aggressive or delayed surgery. The type of operation was decided by the surgeon. All patients received intravenous cimetidine. Only for a subgroup of patients aged >60 was an early aggressive surgical policy associated with a significant reduction in mortality.

The second study was performed in the mid-eighties and randomized 69 patients [13]. Patients with a Forrest I B, II B or II C ulcer were randomized to either immediate surgery or expectant management with surgery reserved only for rebleeders. Patients were treated with intravenous cimetidine. Mortality in patients submitted to early surgery was 5 times higher than that in those allocated to expectant therapy (15 vs. 3%). It should be noted, however, that the majority of patients included in this study (Forrest I B, II B, II C) carried a relatively low risk of recurrent bleeding.

Combining the outcome of both trials, it was concluded at that time that early surgery should not be undertaken before bleeding has recurred, but is mandatory once that has taken place.

This last conclusion should be revised based on the third, recently published, randomized trial by Lau et al.

[3], who showed that in patients with recurrent bleeding, endoscopic retreatment reduces the need for surgery without increasing the risk of death and is associated with fewer complications than surgery.

In conclusion, endoscopic treatment is the therapy of first choice in patients with active bleeding (Forrest I A and I B), a visible vessel (Forrest II A) or an adherent clot (Forrest II B). Furthermore, in patients with rebleeding after initial endoscopic control, endoscopic retreatment should be preferred over surgery. Subgroup analysis of the literature indicates that for patients with larger ulcers (> 2 cm) and hypotension, surgery may be a better choice than endoscopic retreatment. An approach in patients with larger bleeding ulcers could be to perform semielective surgery even before bleeding recurs. The substantial complications of emergency salvage surgery might be prevented by semielective surgery.

Type of Surgery

Two randomized trials have studied the optimal type of operation for bleeding (duodenal) ulcers. The first study randomized 137 patients either to conservative intraluminal stitch ligatures (> 4) in combination with H₂-receptor blockade or to conventional surgery (i.e. intraluminal stitch ligatures plus truncal vagotomy or partial gastrectomy) [14].

Fatal rebleeding occurred more frequently in the conservatively managed group. The clinical relevance of this conclusion might nowadays be questioned, ever since the introduction of highly effective proton pump inhibitors which result in a 'chemical vagotomy'.

A second study, which was performed in 22 different institutes, randomized only 120 (60%) out of the 202 eligible patients either to oversewing plus vagotomy or to gastric resection for bleeding duodenal ulcers [15]. The more aggressive approach of gastric resection with ulcer excision was accompanied by a lower rebleeding rate (3 vs. 17%). The duodenal leak rate was higher after gastric resection than after oversewing (13 vs. 3%), but was not different when the morbidity of reoperations for bleeding recurrence after oversewing was considered on an 'intention-to-treat' basis (12 vs. 13%). Overall mortality was high and similar: 23% after gastrectomy and 22% after oversewing plus vagotomy. The two major problems in this study are the slow inclusion rate (12 patients per year, i.e. less than 1 patient per participating center per year) and the significant escape rate (40% dropout of eligible patients).

The available evidence of randomized trials indicates a slight preference for a relatively aggressive surgical procedure, once an operation is deemed inevitable. One should

realize, however, that the main conclusions of the available randomized trials might be outdated, because over the last decade the knowledge about the etiology of 'peptic' ulcer disease has tremendously increased, effective medical therapy for healing of ulcer diathesis has become available (i.e. proton pump inhibition and *H. pylori* eradication) and endoscopic therapy for ulcer bleeding has been refined.

Although more based on theoretical arguments and less on solid data from randomized studies, intraluminal underrunning and extraluminal vasoligation seems to be preferable over a more radical surgical procedure for bleeding duodenal ulcers, provided that gastric acid output is effectively blocked with intravenous proton pump inhibitors [1]. An exception to this guideline might be the giant ulcers that penetrate into the pancreas and carry a relatively high risk for rebleeding even after surgical therapy [2].

Case Report (Continued)

At laparotomy and longitudinal duodenotomy, four quadrant intraluminal stitch ligatures are placed to exclude the gastroduodenal artery complex. The duodenum is closed transversely.

At careful inspection of the small and large bowel, multiple ischemic patches are identified, compatible with visceral polyarteritis nodosa. A 10-cm ischemic jejunal segment is resected with ETE anastomosis. During second- and third-look laparotomies multiple resections are needed, leaving 200 cm of small bowel in situ.

Two days later significant rebleeding occurs. Endoscopy confirms oozing from the duodenal ulcer (Forrest I B).

Question

Which therapy do you prefer?

	Audience's response
A Duodenotomy with intraluminal ligatures	30%
B Ibidem plus extraluminal vasoligation	5%
C Partial gastric resection	28%
D Angiographic embolization	37%

Case Report (Continued)

At laparotomy the remaining small bowel looks vital. The duodenum is reopened again and new intraluminal stitches are placed. Moreover, extraluminal vasoligation is performed of the (proximal) gastroduodenal artery. Due to massive edema the right gastroepiploic and superior pancreaticoduodenal arteries cannot easily be identified near the duodenum.

When after 3 days rebleeding occurs, angiographic embolization is preferred over a fifth laparotomy with partial gastric resection and duodenal ulcer excision. Via the right femoral artery and the celiac trunk, the catheter is advanced into the origin of the gastroduodenal artery. Extravasation of contrast into the duodenum is visualized from a side branch of the gastroduodenal artery (fig. 2a). The gastroduodenal artery is clearly open, but the right gastric artery is not visualized. Apparently, during the previous laparotomy the right gastric artery has been ligated erroneously and not the gastroduodenal

Fig. 2. a The tip of the catheter has been advanced into the origin of the gastroduodenal artery. Extravasation of contrast into the duodenum is visualized from a side branch of the gastroduodenal artery. b The gastroduodenal artery complex has been occluded completely by eleven fiber coils.

artery. The catheter tip is advanced into the right gastroepiploic artery and on pulling back the catheter the gastroduodenal artery complex is completely occluded by eleven fiber coils (fig. 2b). After this radiological intervention, definite hemostasis has been accomplished.

Comment

Angiographic transcatheter embolization in patients with upper (and lower) gastrointestinal hemorrhage of various origins has long been known as a therapeutic option in patients who do not respond to conservative, endoscopic, or surgical treatment. The first report of transcatheter embolization of a bleeding duodenal ulcer appeared in 1974 using autologous blood clot as embolization material [16]. As autologous blood is quickly lysed by the fibrinolytic system, this treatment did not prove durable and transcatheter intra-arterial infusion of vasopressin was introduced as an alternative method of embolization. The effect of this treatment was not durable either and was accompanied by significant ischemic complications.

Catheter and guidewire technology have improved dramatically over the last two decades and safe and reliable superselective catheterization of small vessels can currently be achieved, using 3- to 5-French catheter sys-

tems. Moreover, new and safer embolization materials have become available. (Micro)coils, which produce permanent vessel occlusion and minimize the risk of bowel ischemia and infarction, have become the preferred embolic agent in most institutions. When used in the duodenal circulation, care should be taken to occlude the vessel both proximal and distal to the site of bleeding to avoid retrograde filling of the vessel. This means that in many cases the gastroduodenal or pancreaticoduodenal vessels have to be catheterized and embolized from a celiac axis approach as well as from a superior mesenteric approach.

A few studies have selectively addressed embolization of duodenal ulcer hemorrhages [17–20]. Several other series consist of patients with upper gastrointestinal hemorrhage due to a variety of causes including gastric and duodenal ulcers [21, 22]. These series have shown angiographic transcatheter embolization to be effective with bleeding control being achieved in 48–90% of patients. Rebleeding rates in these series are reported between 0 and 40% and repeat embolization was often possible in these patients. Significant ischemia/necrosis of bowel or pancreas have been encountered in 0–15% of patients. It has been claimed in literature that such complications are almost never encountered when using coils.

In spite of these promising results, angiographic embolization in duodenal hemorrhage has as yet not been widely accepted within the surgical and gastroenterological community. This may be caused by a variety of factors including unfamiliarity with the technique, fear of isch-

emic complications, dating back from older publications and the limited availability of appropriate equipment and skilled interventional radiologists in many general hospitals. Randomized data are needed to define the true value of this semi-invasive intervention.

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