



Digestive Endoscopy

## Non-surgical management of microperforation induced by EMR of the stomach

G. Jeong<sup>1</sup>, J.H. Lee<sup>1</sup>, M.K. Yu, W. Moon, P.-L. Rhee,  
S.W. Paik, J.C. Rhee, J.J. Kim\*

*Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine,  
#50 Irwon-dong, Gangnam-gu, Seoul 135-710, South Korea*

Received 25 October 2005; accepted 27 April 2006

Available online 5 July 2006

### Abstract

**Background.** Perforation and bleeding are major complications associated with gastric endoscopic mucosal resection. Evident perforation during endoscopic mucosal resection can be managed by endoscopic clipping. However, management of microperforation is not well established.

**Patient and method.** From January 2002 to June 2004, 109 early gastric cancers and 300 adenomas were treated with endoscopic mucosal resection. Iatrogenic perforations occurred in 4.16% ( $n = 17$ ) patients. Following exclusion of four evident perforations, microperforation was observed in 3.18% ( $n = 13$ ) patients. The clinical features of microperforation in patients were retrospectively reviewed.

**Results.** In a total of 13 microperforation cases, 2 patients were managed surgically. The remaining patients successfully recovered without surgical management. In the case of 11 patients without surgery, 7 experienced abdominal pain, which required analgesics, 2 patients experienced mild discomfort and 2 patients experienced no symptoms. A body temperature above 37.5 °C was observed in 9.1% ( $n = 1$ ) patients and leucocytosis above 9000  $\mu\text{L}^{-1}$  was in 72.7% ( $n = 8$ ) patients. The mean duration of nasogastric tube drainage was  $2.36 \pm 1.03$  days, of fasting  $4.18 \pm 1.17$  days, of intravenous antibiotics  $5.55 \pm 1.44$  days and of hospitalisation  $7.45 \pm 1.04$  days.

**Conclusion.** Microperforation induced by gastric endoscopic mucosal resection can be managed successfully using a non-surgical approach including fasting, nasogastric tube drainage and intravenous antibiotics.

© 2006 Editrice Gastroenterologica Italiana S.r.l. Published by Elsevier Ltd. All rights reserved.

**Keywords:** Adenoma; Disease; Endoscopy; Gastric carcinoma; Iatrogenic; Intestinal perforation; Stomach; Treatments

### 1. Introduction

Gastric endoscopic mucosal resection (EMR) is widely performed for early gastric cancers and gastric adenomas [1–3]. The most serious complications of EMR are perforation and haemorrhage. Several studies have shown that the rate of perforation is 0.06–5% and that of bleeding is 1.5–25% [3–5]. However, the rates of these complications may change depending on the definition of perforation and bleeding and

the operator's experience also affects the potential rate of complications.

In order to decrease the rate of EMR-induced perforation, several methods have been developed, including submucosal injection of various materials [6], insulated-tip diathermic knife [7], mini snare [8], hooking knife [9] and a small-caliber-tip transparent hood [10].

When a perforation is observed during EMR (evident perforation), it can be closed by application of endoscopic clips [11]. However, there are some other forms of perforation, called 'microperforation', which can only be defined as follows: (1) no perforating defect of the gastric wall is observed during EMR; (2) radiographic evidence of free air

\* Corresponding author. Tel.: +822 3410 3409; fax: +822 3410 3849.

E-mail address: [jjkim@smc.samsung.co.kr](mailto:jjkim@smc.samsung.co.kr) (J.J. Kim).

<sup>1</sup> These authors contributed equally to this paper.

in the abdomen just after EMR. In this study, we describe 11 patients presenting with microperforation, who were successfully treated without additional endoscopic treatment or surgery.

## 2. Material and methods

### 2.1. Patients

A total number of 409 lesions on 399 patients were treated by the EMR-inject, pre-cut and cut method (372 cases) and the EMR-submucosal dissection method (37 cases) at the Samsung Medical Center, Seoul between January 2002 and June 2004. Indications for EMR were adenoma with high-grade dysplasia or early gastric cancer observed during this study. Indications for EMR in early gastric cancer were as follows: (1) well or moderate differentiation in histology; (2) less than 2 cm in elevated lesion or less than 1 cm in depressed lesion; (3) without ulcer. Medical records of selected patients were retrospectively reviewed. The institutional review board approved this study, and we obtained informed consent from each patient.

### 2.2. Methods

The inject, pre-cut and cut method was performed on nine lesions and submucosal dissection method using an insulated-tip diathermic knife was performed on two lesions [7,12].

After demarcating the lesion by topically spraying indigo carmine dye, markings for the incision line were placed 5–10 mm outside the lesion with needle knife (020120, MTW, Germany) and an electrosurgical unit (ICC200, ERBE, Germany).

To lift the mucosal lesion, a hypertonic saline–epinephrine solution was injected, using an injecting needle (0910723123, MTW, Germany), into the submucosa beneath and surrounding the lesion.

After the mucosa had been sufficiently elevated around the lesion, a mucosal incision was made around the lesion with

a needle knife with an endocut mode at 80 W. The elevated lesion was removed using the polypectomy method with a mini-oval snare (SD-12U-1, Olympus, Japan), provided the size of the lesion was appropriate for snaring.

When the lesions appeared too large to encircle with a snare for polypectomy, an insulated-tip diathermic knife (KD-1L, Olympus, Japan) was used to exfoliate the lesion by submucosal dissection with the endocut mode at 80 W.

When bleeding was observed during the procedure, it was controlled by a heat probe, argon plasma coagulation (APC), metal clipping and spraying thrombin. Metal clips were used to control bleeding in six patients during EMR.

During this study, authors performed radiography of the abdomen of all patients who were treated with inject, pre-cut and cut method or EMR with submucosal dissection method. When a patient showed microperforation based on the radiographic evidence of free air in the abdomen, proton pump inhibitor was administered intravenously following nasogastric tube drainage and fasting. Quinolone and metronidazole were also used. Follow-up radiographic examinations were conducted in conjunction with clinical outcome and the results of blood test, if necessary.

## 3. Results

Gastric perforations induced by EMR were encountered in 17 patients. Following a retrospective review of patient medical records and exclusion of evident perforation, a total of 13 patients had microperforations. Eleven out of the 13 patients were treated non-surgically. Two patients, who experienced microperforation with uncontrolled bleeding and with an indefinite resection margin of early gastric cancer due to piecemeal resection, were treated surgically.

Table 1 summarises the clinical characteristics of microperforation in patients who experienced non-surgical management. The mean age of patients was  $64.9 \pm 9.4$  years (10 males and 1 female); 3 patients presented with early gastric cancer and 8 patients presented with adenomas with associated high-grade dysplasia. Of the 3 early gastric

Table 1  
Clinical characteristics of 11 microperforation patients managed non-surgically

Case	Age (year)	Gender	Size (mm)	Method	Diagnosis (type, Diff.)
1	57	M	5	EMR-P	Adenoma (high-grade dysplasia)
2	76	F	30 <sup>a</sup>	EMR-P	EGC (I, moderate)
3	59	M	20	EMR-P	Adenoma (high-grade dysplasia)
4	72	M	20	EMR-P	Adenoma (high-grade dysplasia)
5	60	M	30	EMR-SDM	Adenoma (high-grade dysplasia)
6	62	M	10	EMR-P	Adenoma (high-grade dysplasia)
7	75	M	18	EMR-P	Adenoma (high-grade dysplasia)
8	80	M	15	EMR-P	EGC (IIa + IIc, moderate)
9	64	M	10	EMR-P	Adenoma (high-grade dysplasia)
10	58	M	15	EMR-P	Adenoma (high-grade dysplasia)
11	82	M	10	EMR-SDM	EGC (IIb, Well)

Diff., differentiation; EMR-SDM, EMR with submucosal dissection method; EMR-P, EMR with pre-cut (inject, pre-cut and cut method).

<sup>a</sup> EMR performed as patient had cardiovascular disease.

Table 2  
Clinical features in 11 microperforation patients managed non-surgically

Case	WBC (mm <sup>-3</sup> ) <sup>a</sup>	Nasogastric tube (days)	Fasting (days)	Antibiotics, i.v. (days)	Hospitalisation (days)
1	9200	0	7	7	7
2	9770	2	4	3	5
3	24150	2	5	6	8
4	9300	3	5	5	7
5	10550	3	4	7	8
6	7640	3	3	7	7
7	7420	3	3	4	8
8	13250	4	4	7	8
9	5200	2	4	6	9
10	10860	2	4	5	7
11	9270	2	3	4	8

<sup>a</sup> Highest value after EMR.

cancer cases, 2 lesions were less than 2 cm (Type IIb, IIc); and one lesion was of 3 cm (Type IIa + IIc, high risk of surgery due to serious cardiovascular disease). Histologically, two lesions were moderately differentiated and one lesion was well differentiated. Of the eight adenomas with high-grade dysplasia, five lesions were less than 2 cm; and three lesions were of 2–3 cm. All lesions had no distant metastasis.

Eleven of the 13 microperforation patients were treated in a conservative, non-surgical manner. These 11 patients successfully recovered with non-surgical management, such as fasting, nasogastric tube drainage and intravenous antibiotics. No additional endoscopic management was needed to treat microperforation.

In the group containing the 11 patients without surgery, 7 patients experienced abdominal pain, which required analgesics more than once, 2 patients experienced mild discomfort, which required no analgesics and 2 patients complained of no abdominal discomfort when microperforation occurred. No sign of severe peritonitis or rebound tenderness was present.

Table 2 summarises the clinical features of microperforation patients who had non-surgical management. On the first day after perforation, a rise in body temperature above 37.5 °C was observed in 1 patient (9.1%) out of 11 microperforation patients, who resumed normal body temperature the following day. On the second day, all patients presented with normal body temperature. On the first day following perforation, a leucocytosis higher than 9000 μL<sup>-1</sup> was observed in eight patients (72.7%). On the second day following perforation, leucocytosis was observed in four patients (36.4%), however, leucocytosis was absent in all patients on the third day following perforation.

The mean duration of fasting ( $n = 11$ ) was  $4.18 \pm 1.17$  days in the microperforation cases. The mean duration of nasogastric tube drainage was  $2.36 \pm 1.03$  days. The patients began to eat food regardless of the presence of free air, if peritonitis was absent. There were no complications after resuming oral intake. The mean duration of hospitalisation was  $7.45 \pm 1.04$  days. The mean duration of intravenous antibiotics used was  $5.73 \pm 1.49$  days. Of the total patients, 11 were found to have

free air in the abdominal cavity according to radiography taken just after EMR. Ten out of 11 patients experienced radiographic evidence of free air in the abdomen before diet initiation and discharge. All patients successfully recovered using non-surgical approach without further endoscopic treatment. Presently, all patients are healthy with no complaints relating to the incident.

#### 4. Discussion

The most serious complications of EMR are perforation and haemorrhage. To decrease the rate of EMR-induced complications, several methods have been developed. Despite the development of several safe methods, major complications such as perforation and bleeding cannot be avoided.

Evidently, patients who have a large perforation or severe haemorrhage, which cannot be controlled with endoscopic management, should be treated surgically. However, non-surgical management has attempted to manage perforations in the stomach and colon following EMR and resulted in successful treatment and recovery in many institutions [4,13–16].

During this study we experienced a different type of perforation. Several perforations remain unnoticed during EMR, however, these perforations can be observed with radiographic evidence of free air in the abdomen following EMR. These perforations are referred to as 'microperforation'. The cause of microperforation is presumed to be a tiny perforation, which cannot be observed using endoscopy and which can be easily sealed. High pressure present in the stomach during EMR causes radiographic evidence of free air as observed in abdomen. Microperforation cannot be managed using endoscopic metal clipping because perforation is not suspected during the EMR. Therefore, non-surgical management may be attempted with care.

The clinical features of microperforation in patients such as mild leucocytosis and elevation of body temperature are observed, however, it does not last more than 1 day in most cases. If peritonitis is absent following nasogastric tube

drainage and fasting, patients can resume eating with initial sips of water and subsequently, a liquid diet. In the absence of clinical exacerbation, patients can be discharged in spite of free air observed in abdomen.

The inject, precut and cut method was performed in 10 lesions and the submucosal dissection method was performed in 3 lesions, in a total number of 13 microperforation patients, who participated in this study. This discrepancy in the number of patients may be due to preference of the inject, precut and cut method used in our hospital.

Two patients with microperforation were treated using surgical management for reasons previously mentioned. However, after discovering non-surgical management for microperforation, no more patients were treated surgically. Two management options of gastric perforations induced by EMR ought to be addressed. Firstly, if perforation is suspected during EMR, metal clip placement can immediately be applied using an endoscopic approach for closure of the perforation. Subsequently, conservative non-surgical management or surgical management should be considered. Secondly, if perforation is not suspected during EMR and radiographic evidence of free air in the abdomen following EMR is observed, no further endoscopic management is required and conservative non-surgical management is sufficient to manage the perforation and microperforation.

Owing to a lack of experience in performing EMR procedure, including precutting technique, authors performed radiographic examination for every patient who underwent EMR at the time when this study was conducted. As a result, 11 patients were found to have a microperforation although two of them did not complain abdominal pain, which is considered a reliable sign of perforation. However, the study has a limitation as it failed to suggest any clinical features that can be used for the criteria for first radiographic examination.

Non-surgical management of patients with microperforation is constantly evolving. The duration of non-surgical management is gradually decreasing as experience of microperforation is accumulated. Our result also suggests that the presence of free air does not affect management or clinical outcome. We anticipate that this report contributes to establishing the guideline of non-surgical management for microperforation of the stomach induced by EMR.

#### Conflict of interest statement

None declared.

#### References

- [1] Kojima T, Parra-Blanco A, Takahashi H, Fujita R. Outcome of endoscopic mucosal resection for early gastric cancer: review of the Japanese literature. *Gastrointest Endosc* 1998;48:550–4 [discussion 4–5].
- [2] Ono H, Kondo H, Gotoda T, Shirao K, Yamaguchi H, Saito D, et al. Endoscopic mucosal resection for treatment of early gastric cancer. *Gut* 2001;48:225–9.
- [3] Soetikno RM, Gotoda T, Nakanishi Y, Soehendra N. Endoscopic mucosal resection. *Gastrointest Endosc* 2003;57:567–79.
- [4] Rembacken BJ, Gotoda T, Fujii T, Axon AT. Endoscopic mucosal resection. *Endoscopy* 2001;33:709–18.
- [5] Kato M, Shimizu Y, Nakagawa S, Sugiyama T, Asaka M. The results of questionnaire about endoscopic mucosal resection in the stomach. *Digest Endosc* 2003;15:S2–7.
- [6] Fujishiro M, Yahagi N, Kashimura K, Mizushima Y, Oka M, Enomoto S, et al. Comparison of various submucosal injection solutions for maintaining mucosal elevation during endoscopic mucosal resection. *Endoscopy* 2004;36:579–83.
- [7] Ohkuwa M, Hosokawa K, Boku N, Ohtu A, Tajiri H, Yoshida S. New endoscopic treatment for intramucosal gastric tumors using an insulated-tip diathermic knife. *Endoscopy* 2001;33:221–6.
- [8] Yahagi N, Fujishiro M, Kakushima N, Kobayashi K, Hashimoto T, Oka M, et al. Endoscopic submucosal dissection for early gastric cancer using the tip of an electro-surgical snare (thin type). *Digest Endosc* 2004;16:34–8.
- [9] Oyama T, Kikuchi Y, Shimaya S, Tomori AKH. Endoscopic mucosal resection using a hooking knife (hooking EMR). *Stomach Intest* 2003;37:1155–61.
- [10] Yamamoto H, Kawata H, Sunada K, Sasaki A, Nakazawa K, Miyata T, et al. Successful en-bloc resection of large superficial tumors in the stomach and colon using sodium hyaluronate and small-caliber-tip transparent hood. *Endoscopy* 2003;35:690–4.
- [11] Tsunada S, Ogata S, Ohyama T, Ootani H, Oda K, Kikkawa A, et al. Endoscopic closure of perforations caused by EMR in the stomach by application of metallic clips. *Gastrointest Endosc* 2003;57:948–51.
- [12] Hiraio M, Masuda K, Asanuma T, Naka H, Noda K, Matsuura K, et al. Endoscopic resection of early gastric cancer and other tumors with local injection of hypertonic saline-epinephrine. *Gastrointest Endosc* 1988;34:264–9.
- [13] Binmoeller KF, Grimm H, Soehendra N. Endoscopic closure of a perforation using metallic clips after snare excision of a gastric leiomyoma. *Gastrointest Endosc* 1993;39:172–4.
- [14] Yoshikane H, Hidano H, Sakakibara A, Niwa Y, Goto H. Feasibility study on endoscopic suture with the combination of a distal attachment and a rotatable clip for complications of endoscopic resection in the large intestine. *Endoscopy* 2000;32:477–80.
- [15] Kaneko T, Akamatsu T, Shimodaira K, Ueno T, Gotoh A, Mukawa K, et al. Nonsurgical treatment of duodenal perforation by endoscopic repair using a clipping device. *Gastrointest Endosc* 1999;50:410–3.
- [16] Kim HS, Lee DK, Jeong YS, Kim KH, Baik SK, Kwon SO, et al. Successful endoscopic management of a perforated gastric dysplastic lesion after endoscopic mucosal resection. *Gastrointest Endosc* 2000;51:613–5.