

A Case of Recurrence After Endoscopic Submucosal Dissection for Gastric Neoplasm

Shinsuke Nawa^{1*}, Kiyooki Homma¹, Tamotsu Sugai² and Makoto Eizuka²

¹Department of Therapeutic Endoscopy, Nihonkai General Hospital, Yamagata, Japan

²Department of Molecular Diagnostic Pathology, Iwate Medical University School of Medicine, Iwate, Japan

*Corresponding Author: Shinsuke Nawa, Department of Gastroenterology, Kyoritsu General Hospital, Atsuta-ku, Nagoya, Japan.

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Abstract

We performed endoscopic submucosal dissection in a 67-year-old man with early gastric cancer in August 2012. The lesion was preoperatively diagnosed as a type 0-IIa differentiated adenocarcinoma limited to the mucosa, 20 mm in size, with no ulceration on the anterior wall of the antrum. Pathology revealed a well- to moderately differentiated adenocarcinoma mixed with poorly differentiated adenocarcinoma that was 24.5 × 22 mm in size, negative for lymphovascular invasion or ulceration, and had tumor-free margins. Therefore, this case satisfied the expanded criteria in Japanese guideline for endoscopic submucosal dissection, which was considered a curative resection.

In this case, however, local recurrence and distant metastasis occurred in January 2016. The patient received systemic chemotherapy but died of gastric cancer 6 months after recurrence.

This case seemed to satisfy the expanded criteria for endoscopic submucosal dissection based on routine histological examination, but one of the additional deep-cut sections revealed lymphovascular invasion. Thus, this case did not actually satisfy the criteria. For cases with mixed-type cancer cells, deep-cut sectioning and staining should be performed, preferably with both H&E and D2-40, but there are still practical limitations in detecting lymphovascular invasion.

Keywords: Early Gastric Cancer; Endoscopic Submucosal Dissection; Expanded Pathological Criteria; Local Recurrence; Lymphovascular Invasion

Introduction

Endoscopic submucosal dissection (ESD) has been widely used as a minimally invasive treatment for early gastric cancer (EGC) that has a negligible risk of lymph node metastasis. In Japan, the gastric cancer treatment guidelines (4th edition) specify that the pathological criteria for curative endoscopic resection of EGC are limited to differentiated-type cancer ≤ 2 cm in size without ulceration [1].

Recently, the pathological criteria for curative resection of EGC have been expanded to include other lesions with a negligible risk of lymph node metastasis. These expanded criteria in Japanese guideline include intramucosal differentiated-type cancers > 2 cm in size without ulceration, intramucosal differentiated-type cancers ≤ 3 cm in size with ulceration, intramucosal undifferentiated-type cancers ≤ 2 cm in size without ulceration, and SM1 differentiated-type cancers ≤ 3 cm in size [2,3]. Although the gastric cancer treatment guidelines state that endoscopic resection for these tumors is considered an investigational treatment and ESD should be employed [1], the expanded criteria based on retrospective examinations of surgical resection cases have been accepted.

However, some patients who were diagnosed as having a curative resection by post-ESD pathological examination, ultimately experienced cancer recurrence.

We experienced a case of lymph node and distant metastasis that occurred 3 years and 5 months after ESD. The patient satisfied the expanded criteria in Japanese guideline based on routine histological examination, but had lymphovascular invasion.

Case Report

A 67-year-old man was referred to our hospital for the treatment of EGC in July 2012. There were no abnormalities in the physical examination and no medical history of malignant tumors. Blood test results, including tumor markers, were all within normal limits, with one exception; the lipid value was slightly elevated.

Esophagogastroduodenoscopy (EGD) revealed a slightly elevated lesion, 20 mm in size, on the anterior wall of the antrum, and biopsy indicated moderately differentiated adenocarcinoma (Figure 1a). Endoscopic ultrasonography showed that the tumor was limited to the mucosa and was not surrounded by enlarged lymph nodes (Figure 1b). Computed tomography (CT) revealed no lymph node or distant metastasis.

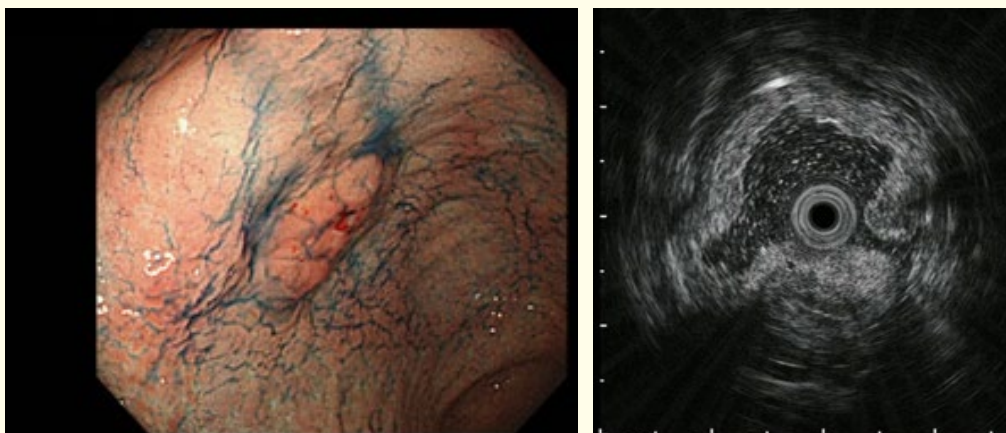


Figure 1: (a) Esophagogastroduodenoscopy reveals a slightly elevated lesion on the anterior wall of the antrum. (b) Endoscopic ultrasonography shows the tumor limited to the mucosa and not surrounded by enlarged lymph nodes.

Based on these findings, ESD was performed on this gastric 0-IIa lesion in August 2012. The procedure was completed without any complications, resulting in an en bloc resection.

Routine histopathological examination with hematoxylin and eosin (H&E) staining of the resected specimen, which was 24.5 mm × 22 mm in size and sectioned at 2-mm intervals according to the Japanese classification of gastric carcinoma, revealed well- to moderately-differentiated tubular adenocarcinoma mixed with poorly differentiated adenocarcinoma in some lesions (Figure 2). The cancer cells were limited to the mucosa, with negative lymphovascular invasion and ulceration. Both the lateral and vertical margins were negative for cancer invasion. These findings satisfied the expanded pathological criteria in Japanese guideline for ESD, and this was considered a curative resection.

After ESD, the patient was followed up with EGD every 6 months. For 3 years, no finding of local recurrence was detected. However, in January 2016 (3 years and 5 months after ESD), the patient felt abdominal discomfort and underwent EGD to evaluate his symptoms. The EGD revealed irregular ulceration with surrounding wall thickness on the lesser curvature from the angle to the antrum, involving the location of the original ESD scar (Figure 3a). A biopsy specimen from the ulcerative tumor revealed moderately to poorly differentiated adenocarcinoma. CT showed a thickened gastric wall, multiple enlarged lymph nodes, including those near the lesser curvature, and multiple liver metastases (Figure 3b). Blood tests revealed increased tumor markers, including CEA: 7.8 ng/ml (normal: < 3.4 ng/ml), and

CA19-9: 472.5 U/ml (normal: < 37 U/ml). These findings suggested local recurrence and distant metastasis, which is considered inoperable. The patient received systemic chemotherapy but died of gastric cancer 6 months after the recurrence.

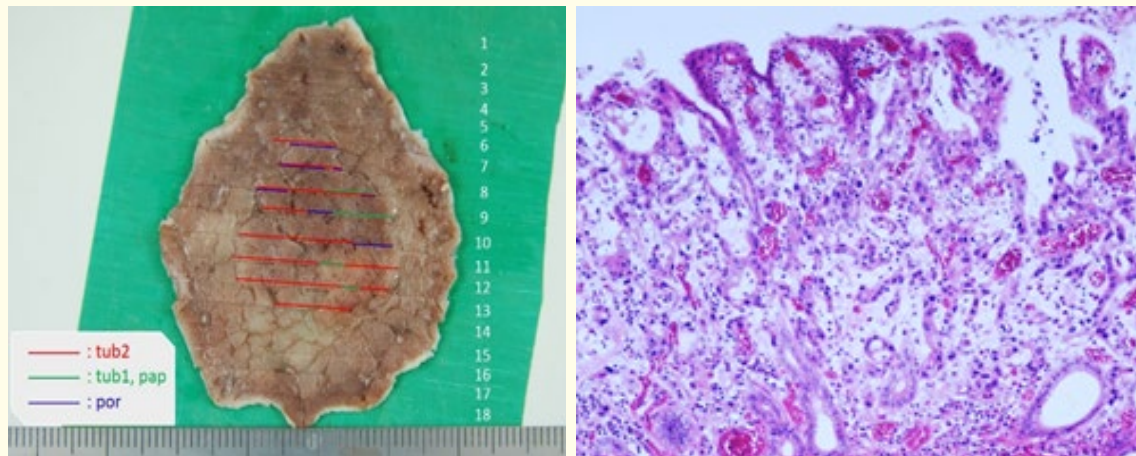


Figure 2: (a) The resected specimen was 24.5 mm × 22 mm in size. (b) Pathologic findings reveals well- to moderately differentiated tubular adenocarcinoma, mixed with poorly differentiated adenocarcinoma in some lesions.

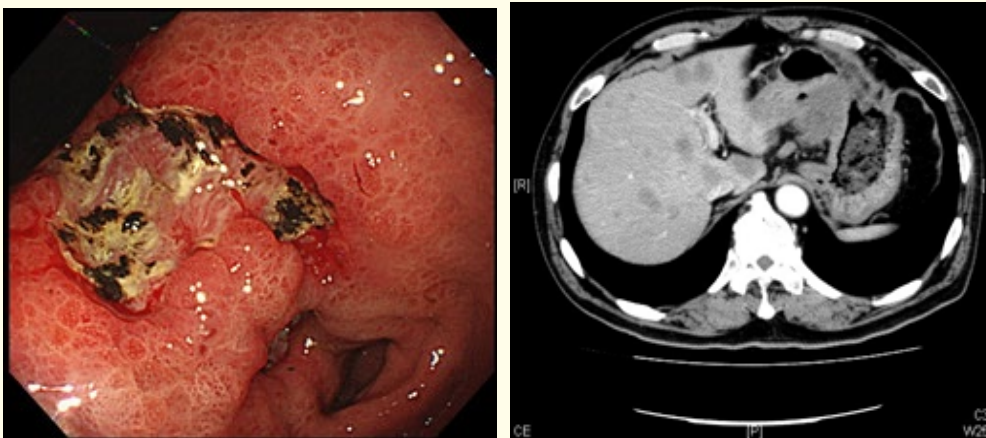


Figure 3: (a) In January 2016, esophagogastroduodenoscopy reveals irregular ulceration on the lesser curvature from the angle to the antrum, involving the location of the original endoscopic submucosal dissection scar. (b) Computed tomography shows a thickened gastric wall, multiple enlarged lymph nodes, including those near the lesser curvature, and multiple liver metastases.

This case was so unusual that we decided to conduct additional staining of the deep-cut sections of the original resected specimen with H&E and D2-40. One of the additional deep-cut sections stained with D2-40 showed lymphovascular invasion (Figure 4). Therefore, this case actually did not satisfy the criteria for ESD.

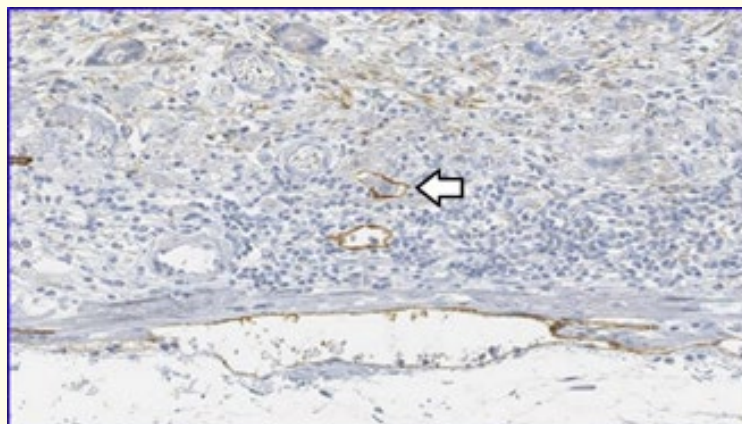


Figure 4: One of the additional deep-cut sections stained with D2-40 shows lymphovascular invasion.

Discussion and Conclusion

We identified two important clinical issues. First, there is a possibility for recurrence with histological mixed-type EGC that satisfies the expanded criteria in Japanese guideline. Second, for cases that meet the expanded criteria, an evaluation of deep-cut sections from the original resected specimen might reveal lymphovascular invasion.

Histological mixed-type EGC has a possibility of recurrence even if it satisfies the expanded criteria for ESD and ESD is considered a curative resection. In patients with differentiated-type EGC who underwent gastrectomy with lymph node dissection, lymph node metastasis was not found in the intramucosal cancer when the lesions were ≤ 3 cm in size, regardless of ulceration or when there was no ulceration regardless of tumor size [2]. These results developed into the current expanded pathological criteria for curative endoscopic resection of EGC. However, the mixture of adenocarcinoma is considered a risk factor for lymph node metastasis and poor outcomes [4-6]. In case of histological mixed-type EGC, the gastric cancer treatment guidelines recommend ultrasonography (US) or CT, in addition to EGD every 6 to 12 months, to detect lymph node or distant metastasis [1]. Hamada, *et al.* reported a case of undifferentiated-type EGC with lymph node metastasis, but it was 10 mm in size. In that case, in addition to surgery, the expanded criteria consider CT necessary at 6 and 12 months after ESD and then on an annual basis, with careful follow-up for at least 5 years [7].

Our study also suggests that in cases that satisfy the expanded criteria, the evaluation of deep-cut sections from the original resected specimen might reveal lymphovascular invasion. A similar case of lymph node metastasis following ESD was reported that involves such a mixed-type adenocarcinoma, and the patient subsequently died of liver metastasis 33 months after ESD [8]. In our case, one of the additional deep-cut sections showed lymphovascular invasion. An undifferentiated type tumor that satisfies the expanded criteria does have the possibility of lymph node metastasis, and histological criteria have practical limitations.

In conclusion, histological mixed-type EGC has a possibility of recurrence even if it satisfies the expanded criteria in Japanese guideline for ESD, and the evaluation of deep-cut sections from the original resected specimen might reveal lymphovascular invasion. We should consider the possibility of recurrence and follow up carefully. In cases of histological mixed-type EGC, it is necessary to carefully conduct additional deep-cut sections with H&E and D2-40 staining to evaluate the possibility of lymphovascular invasion, and to perform imaging examinations such as US or CT in addition to annual EGD.

Conflicts of Interest

No financial interest or any conflict of interest exists.

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