CASE REPORT

A Case of Myocardial Infarction Occurred after Endoscopic Submucosal Dissection under Bridging Therapy with Low Molecular Weight Heparin

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Myocardial infarction (MI) is a complication that can occur after endoscopic submucosal dissection (ESD). However, very few reports are available about this complication. A 71-year-old male, who had two drug eluting stents inserted due to ischemic heart disease, was referred to the Division of Gastroenterology for ESD of a lesion suspicious of early gastric cancer. ESD was performed after dual antiplatelet agents were discontinued and bridging therapy with low molecular weight heparin (LMWH) was initiated. However, MI occurred immediately after the ESD procedure. A coronary angiogram did not show any significant stent thrombosis or restenosis. The patient recovered spontaneously. Here, we report a case of MI that occurred after ESD under bridging therapy with LMWH. (Korean J Helicobacter Up Gastrointest Res 2015;15:258-263)

Key Words: Stomach neoplasms; Myocardial infarction; Heparin

INTRODUCTION

Endoscopic submucosal dissection (ESD) is a minimally invasive treatment modality for early gastric cancer. More ESD procedures are being performed as detection of early gastric cancer has increased. Gastroenterologists are confronted with complications, such as bleeding, perforation, stenosis, and rarely myocardial infarction (MI). In addition, the number of patients with cardiovascular disease has been increasing, making management of antiplatelet agents and anticoagulants during ESD particularly difficult in patients with high risk for thromboembolism. Many institutions have reported management strategies for patients with coronary stents who are undergoing dual antiplatelet therapy and require a high bleeding risk procedure.1,2 However, no guidelines have been established. The American Society for Gastrointestinal Endoscopy (ASGE) recommends that patients with a high thromboembolic risk, taking dual antiplatelet therapy, and who need a high bleeding risk procedure such as ESD should consider continuing aspirin during the procedure. Some institutions including the Japanese Circulation Society (JCS) agree with aspirin use, but they remark that heparin bridging can be considered if dual antiplatelet therapy is discontinued.3-6 Bridging therapy with heparin has been used as perioperative anticoagulation after discontinuation of oral anticoagulants and has been used in clinical practice after discontinuing antiplatelet therapy.7 Here, we report a case of MI that occurred after ESD using bridging therapy with low molecular weight heparin (LMWH).

CASE REPORT

A 71-year-old male visited the Division of Gastroenterology for treatment of gastric adenoma. He had a history of ischemic heart disease, diabetes mellitus, hypertension, and Parkinson’s disease. He underwent a percutaneous coronary intervention and had two drug eluting stents coated with paclitaxel and cilostazol inserted about 3 months ago. After implantation of the coronary stents, he began taking aspirin and clopidogrel as dual antiplatelet therapy, and was kept under observation in the cardiology outpatient department. A screening endoscopy re-
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revealed a 1.8×1.2 cm lesion suspicious of early gastric cancer on the posterior side of the gastric angle and a 2.0×2.0 cm lesion suspicious of gastric adenoma on the posterior side of the lower body. A biopsy confirmed high grade dysplasia (HGD) and low grade dysplasia (LGD) of the two lesions, respectively (Fig. 1).

No extension into the gastric wall, adherence to surrounding tissue, or enlarged lymph nodes were detected on abdominopelvic computed tomography. We planned to delay the ESD 6–12 months after the stents were implanted considering his thromboembolic risk. However, the patient wanted treatment immediately considering cancer progression. First, we planned ESD for the HGD lesion suspected to be early gastric cancer, and decided to delay the ESD for the LGD lesion until 12 months after the coronary stent implantation. We consulted with cardiology about managing the antiplatelet agents during ESD. Cardiology recommended that aspirin should be used continuously during ESD, and that discontinuing the antiplatelet agents and using heparin bridging was an appropriate alternative plan. Because we had more experience with heparin bridging therapy after discontinuing anticoagulants, we decided to use heparin bridging therapy after discontinuing dual antiplatelet therapy. We continued aspirin and clopidogrel 7 days before the procedure and administered 1 mg/kg LMWH until 12 hours before the procedure. The patient’s vital signs were stable on the day of ESD. The baseline electrocardiogram (ECG) showed no interval change and his cardiac enzyme levels were normal (Fig. 2).

ESD was performed under moderate sedation with 2 mg midazolam and 25 mg meperidine. No additional sedatives were used. The submucosal injection fluid consisted of a mixture of saline and 1:1,000 epinephrine and indigocarmine. A dual knife (KD-650L; Olympus, Tokyo, Japan) and an insulation-tipped knife (KD-611L; Olympus) were used to make the mucosal incision and for the submucosal dissection, respectively. Endocut and an electrosurgical unit (VIO 300D; ERBE Elektromedizin GmbH, Tübingen, Germany) set on forced coagulation mode were used for dissection and bleeding control. Total procedure time was 49 minutes, and vital signs were stable during

Fig. 1. Initial gastroscopy. (A) Approximate 1.8×1.2 cm, type IIa+IIc early gastric cancer was observed on the posterior side of the angle. (B) Approximate 2.0×2.0 cm, type IIa adenoma was observed on the posterior side of the lower body.

Fig. 2. Baseline electrocardiogram shows poor R progression and changes in Q waves on leads II, III, aVF, and changes in ST segment on leads V1~V4 due to previous myocardial infarction.
the procedure. As the patient complained of chest pain immediately after the procedure, ECG, CK-MB, and troponin T were checked. The ECG showed >2 mm ST segment elevation in leads V1 - V4 compared to that before the procedure (Fig. 3).

CK-MB and troponin T levels had increased to 199.5 ng/mL (normal: 0.1 ∼ 1.5 ng/mL) and 3.33 ng/mL (normal: 0 ∼ 0.1 ng/mL), respectively. A portable echocardiogram showed regional wall motion abnormalities on territories supplied by the left anterior descending and right circumflex arteries but no apical ballooning suggesting stress-induced cardiomyopathy and no significant changes compared to the last examination. A coronary angiogram showed no stent thrombosis or stent restenosis, and no definite visible thrombus in the coronary artery (Fig. 4).

The cardiologist remarked that MI thought to be caused by coronary artery vasospasm near the stent implantation site. The patient recovered spontaneously, and the ECG and cardiac enzymes normalized. Second look endoscopy revealed no bleeding on the dissection plane. Therefore, dual antiplatelet therapy was started immediately. The pathological result of the ESD specimen was well differentiated adenocarcinoma confined to the lamina propria. The resection margin was clear, and no lymphovascular invasion was observed. We performed a follow-up endoscopic examination 3 months after ESD and a 3×3 cm adenoma on the posterior side of the lower body had increased in size compared to that at the last examination. A biopsy confirmed tubular adenoma with LGD. We planned to perform an endoscopic procedure 12 months after the stents were inserted due to the previous MI. The second ESD was performed with LMWH bridging using the same method. The pathological result of the ESD specimen was well differentiated tubular adenocarcinoma confined to the muscularis mucosa with curative resection. No adverse events occurred during the second ESD.

We found a 3.5×3.0 cm, lateral spreading tumor on the ascending colon during follow-up assessments. A bi-
opsy confirmed tubulovillous adenoma. ESD was performed successfully with bridging therapy, and the patient was followed-up regularly at the outpatient department.

**DISCUSSION**

National Cancer Screening Programs are implemented in Korea and Japan because of the high incidence of gastric cancer. As a result, early detection of gastric cancer as well as endoscopic treatment have increased. The major complications of gastric ESD include bleeding, perforation, stenosis, and aspiration pneumonia, but rarely MI. Only three cases of MI after ESD have been reported in Korea.

Although the mechanism of MI after ESD is unclear, it is thought to be caused by three factors. First, the mixed epinephrine solution could be absorbed into the submucosa, and could cause MI. It has reported that epinephrine causes coronary artery vasospasm and potentiates platelet aggregation by increasing adenosine diphosphate and arachidonate-induced thromboxane B2 production. Second, a large volume of submucosal injection solution can induce hemodynamic stress. Third, the stressful condition induced by ESD escalates sympathetic tone and stimulates the hypothalamic-pituitary-adrenocortical axis. The corticotrophin-releasing hormone and cortisol released can facilitate MI and arrhythmia. We suggest that MI in our case may have been caused by coronary vasospasm induced by epinephrine and increased sympathetic tone. However, we cannot completely exclude other reasons, such as an earlier timing of ESD, premature discontinuation of antiplatelet agents, unclear efficacy of heparin bridging therapy, or a hemodynamic effect of sedatives.

Management of antplatelet and antithrombotic agents for endoscopic procedures has been reported in many institutions. However, no guidelines have been established. The ASGE and the European Society for Gastrointestinal Endoscopy recommend that patients at high thromboembolic risk who are taking dual antiplatelet therapy and need a high bleeding risk procedure such as ESD, should consider continuing aspirin during the procedure. However, continuous aspirin use can increase the risk for post-ESD bleeding (relative risk, 4.49) and decrease the en-bloc resection rate. Therefore, an alternative plan, such as bridging therapy, is used in clinical practice. The JCS, the Cardiac Society of Australia/New Zealand, the French Task Force, and the American College of Chest Physicians agree to aspirin use. However, they remarked that it can be considered a bridge with heparin if dual antiplatelet therapy is discontinued. Bridging therapy is traditional management for perioperative anticoagulation using unfractionated heparin or LMWH after discontinuation of oral anticoagulants. Unlike aspirin, heparin has a short half-life and there is an antidote to reverse the antithrombotic effect. In this respect, heparin bridging in a patient taking dual antiplatelet therapy is empirically conducted in many institutions. However, our patient suffered MI after ESD despite bridging therapy with LMWH. Therefore, the efficacy of bridging therapy should be further investigated.

Lee et al. reported a discrepancy of clinical practice patterns to manage anticoagulation and antiplatelet therapy between Eastern and Western endoscopists. Eastern endoscopists are more concerned with the risk of bleeding, whereas Western endoscopists are more concerned about the risk of thromboembolism. This discrepancy is based on racial differences in bleeding and thromboembolism between Asians and Caucasians which is thought to cause the low dispersal of Western guidelines. Therefore, consistent guidelines are needed for managing anticoagulation and antplatelet medications during endoscopic procedures.

The American Heart Association and JCS Guidelines for percutaneous coronary intervention recommend that elective surgery or high bleeding risk procedures should be postponed 4~6 weeks after implantation of a bare metal stent and for 6~12 months after implantation of a drug eluting stent. According to these guidelines, ESD should be postponed at least 6~12 months after insertion of a drug eluting stent. In our case, we considered the thromboembolic risk and recommended postponing ESD by 6~12 months after implantation of coronary stents. The natural course of early gastric cancer is unclear, but rapid disease progression over 3~9 months would be rare. In contrast, Jeong et al. reported that one-fourth
of untreated patients with early gastric cancer develop to advanced gastric cancer within 5–12 months. Thus, we discussed the issue with the patient and decided to perform the ESD procedure within the recommended period because the patient was afraid of disease progression during observation. However, we should have considered timing the ESD and discontinuation of antiplatelet agents because the patient suffered a MI. A short-term follow-up of at least 6 months might be necessary after inserting coronary artery stents rather than performing a procedure immediately. We delayed the second ESD procedure by 12 months after stent insertion. However, the pathological result of the ESD specimen was tubular adenocarcinoma confined to the muscularis mucosa. This lesion could have advanced more with an additional delay.

In conclusion, MI is a rare, but fatal complication of ESD. Thus, use of local epinephrine injections, antithrombotic agents, and sedatives should be considered carefully in older patients with cardiovascular disease. Bridging therapy with heparin is a good option to prevent bleeding and thromboembolic events before an ESD procedure, but efficacy should be further investigated. Elective high bleeding risk procedures, such as ESD, should be delayed 6–12 months after insertion of coronary stents. The timing of the ESD procedure should be determined cautiously considering both cancer progression and thromboembolic risk, particularly in patients with cancer who had a coronary artery stent inserted.

REFERENCES


