The feasibility of endoscopic submucosal dissection for superficial esophageal cancer in patients with cirrhosis (with video)

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Endoscopic submucosal dissection (ESD) was initially developed for gastric cancer and is currently accepted as an established procedure for superficial cancer of the esophagus. The most important advantage of ESD compared with EMR is that it can provide a high en bloc resection rate and precise histologic assessment even for large lesions.[1] On the other hand, the disadvantage of ESD is a higher risk of bleeding and perforation than for EMR.[2] Previous reports described that esophageal ESD-related adverse events, such as postoperative bleeding and perforation, are considerably serious risks.[3-6] However, ESD for patients with cirrhosis may carry a higher risk of these adverse events because of the low platelet count, coagulopathy, and portal hypertensive gastroenteropathy, including esophageal varices, in these patients. As a result, endoscopists have been hesitant to apply ESD for the treatment of esophageal cancer in patients with cirrhosis.

Abbreviations: EIS, endoscopic injection sclerotherapy; ESD, endoscopic submucosal dissection; EVL, endoscopic variceal ligation; SCC, squamous cell carcinoma.

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Although several reports described the feasibility of ESD for superficial gastric neoplastic lesions in patients with cirrhosis,[1,7] the feasibility of ESD for superficial esophageal cancer in patients with cirrhosis has been uncertain. Therefore, we assessed the efficacy and safety of ESD for superficial esophageal cancer in patients with cirrhosis accompanied by esophageal varices.

CASE SERIES

Participants

Between January 2004 and June 2013, a total of 355 esophageal ESD procedures were performed in the Department of Gastroenterology, Akita University Hospital. Among them, 7 patients (9 lesions) had cirrhosis with esophageal varices and were enrolled in this study. These patients were diagnosed to have cirrhosis based on the radiology findings, clinical data with laboratory investigation, and the presence of esophageal varices. All cases were regarded as compensated cirrhosis.

Table 1 summarizes the clinical characteristics of the patients. The pathologic diagnosis of all of esophageal lesions was squamous cell carcinoma (SCC). The average age of the patients was 67 years (range 55-73 years). We evaluated the severity of esophageal varices based on the endoscopic findings according to the classification defined by the Japanese Research Society of Portal Hypertension.[8,9] Namely, the form and fundamental color of varices and the presence or absence of the red wale marking were evaluated. With respect to red color signs, no other signs, including cherry red spots or hematocystic spots, were observed in any of the patients in this study, so we described only the presence or absence of the red wale marking in Table 1.

ESD procedure

Written informed consent was obtained from all patients before ESD. This study was carried out in accordance with the Declaration of Helsinki. During the procedure, patients were maintained under conscious sedation via intravenous propofol or flunitrazepam, and their blood pressure, electrocardiogram, and SpO_2 saturation values

TABLE 1. Clinical characteristics of 7 male patients with cirrhosis who underwent ESD for superficial esophageal SCC

Case	Age	Etiology of cirrhosis	Child-Pugh class[14]	Platelet count ($\times 10^3/\mu L$)	INR	Severity of esophageal varices			SCC located on the varices
1	55	Alcohol	A	134	1.33	F_1,	Cb,	RWM(−)	Yes*
2	67	Alcohol	A	156	1.17	F_1,	Cb,	RWM(−)	No
3	70	HCV	C	59	1.25	F_1,	Cw,	RWM(−)	No
4	70	Alcohol	A	178	1.01	F_1,	Cb,	RWM(−)	No
5	68	Alcohol	A	143	1.01	F_2,	Cb,	RWM(+)	No
6	69	Alcohol	A	155	1.02	F_1,	Cb,	RWM(−)	Yes*
7	73	Alcohol	B	175	1.28	F_1,	Cb,	RWM(−)	No

ESD, Endoscopic submucosal dissection; *SCC,* squamous cell carcinoma; *INR,* international normalized ratio; F_1, straight varices; *Cb,* blue varices; *RWM,* red wale marking; *HCV,* hepatitis C virus; *Cw,* white varices; F_2, enlarged, tortuous varices.
*EVL was done before ESD.

were monitored. The ESD procedure was typically performed by using GIF-H260Z and Q260J endoscopes (Olympus Optical, Tokyo, Japan) with a transparent hood F-03 (Top Corporation, Tokyo, Japan) attached to the tip. The electrosurgical generator used in the ESD was an ICC 200 device (ERBE, Tubingen, Germany) or a VIO300D device (ERBE). Esophageal SCCs were detected by Lugol staining solution and magnified endoscopy with narrow-band imaging and were marked by making spots with a needle-knife (Olympus) approximately 5 mm outside the lesion. Then, a mixture of 30% hyaluronic acid, 70% saline solution, and a small amount of indigo carmine was injected into the submucosal layer to lift the lesion. This injection was repeated if necessary during ESD to keep the lesion lifted. A circumferential incision was made just outside the marked spots with a needle-knife. Then, submucosal dissection was carried out with a needle-knife, a hook-knife, an insulated tip knife 2, or an insulated tip knife nano (Olympus) as described in Table 2, concomitantly using hemostatic instruments such as the coagulation forceps Coagrasper (Olympus) and/or metal clips (Olympus) to treat spurring or oozing hemorrhage. When esophageal SCC was located on an esophageal varix, endoscopic variceal ligation (EVL) was carried out at the distal side of the SCC by using an EVL device (Sumitomo Bakelite, Tokyo, Japan) before the ESD during the same procedure.

Histopathologic assessment

The resected ESD specimens were cut into 2-mm slices, stained with hematoxylin and eosin, and evaluated by a pathologist. The depth of vertical SCC invasion and the presence or absence of lateral margins and lymphovascular SCC involvement were evaluated. When both the vertical and horizontal margins of the specimens resected en bloc were free of SCC, the procedure was defined as complete resection. The curability of the resected specimens was defined according to the current Japanese consensus of the curability of endoscopic treatment for esophageal cancer.[10] Namely, when the vertical depth of SCC invasion was limited to the muscularis mucosa without lymphovascular tumor involvement in complete resection cases, the procedure was defined as a curative resection.

Post-ESD management and follow-up

Intravenous administration of a full dose of a proton pump inhibitor (omeprazole or lansoprazole) for 2 days and antibiotics (cefazolin sodium hydrate) for 3 days was started on the day of the ESD procedure. The proton pump inhibitor was administered orally for 2 months thereafter. In order to check the patients for hepatic failure and infections, blood tests including blood cell counts, liver enzyme levels, bilirubin and albumin levels, international normalized ratio, and C-reactive protein level were performed twice during the first week after the ESD. Follow-up endoscopy was performed 2 months after the ESD. The examinations were conducted every 6 months or every year thereafter. The latest follow-up examination was conducted in July 2013.

RESULTS

Table 2 summarizes the outcomes of ESD. No adverse events such as uncontrollable or delayed bleeding, perforation, post-ESD cicatricial luminal stenosis, or hepatic failure occurred. The average length of the procedure was 63 minutes (range 19-152 minutes), and the average major axis length of the resected specimens was 34 mm (range 16-49 mm). EVL was required before the ESD procedure in 2 cases (cases 1 and 6, Table 1) because the SCC was located on the esophageal varices in both cases. The patients were treated successfully endoscopically, and their postoperative courses were uneventful. Consequently, the en bloc resection rate was 100% (9/9 lesions). However,