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Salvage endoscopic submucosal dissection for the esophagus-localized recurrence of esophageal squamous cell cancer after definitive chemoradiotherapy

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Abbreviations: CRT, chemoradiotherapy; dCRT, definitive chemoradiotherapy; ESD, endoscopic submucosal dissection; SCC, squamous cell carcinoma.

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Reprint requests: Mario Jin, MD, PhD, Department of Gastroenterology, Akita University Graduate School of Medicine, 1-1-1 Hondo, Akita City, Akita 010-8543, Japan. The incidence of esophageal cancer is increasing worldwide, and its prognosis is still poor.¹ Although surgery is the best treatment, two thirds of cases of esophageal cancer are inoperable at the time of diagnosis because of advanced clinical stages and/or patient comorbidities.¹ Thus, chemoradiotherapy (CRT) has been applied as a definitive treatment for inoperable locally advanced esophageal squamous cell carcinoma (SCC)²⁻⁴ because it can induce the complete remission. The use of definitive CRT (dCRT) has been increasing the 5-year survival rate of SCC by 13% to 27%.²⁻⁴ However, the relatively high incidence of local recurrence after dCRT is a major problem that needs to be resolved.²

Salvage surgery is generally considered for the treatment of a recurrence of esophageal cancer after dCRT. However, its morbidity and surgical risk are high,⁵ with postoperative mortality rates reported to be 12% to 25% even in recent reports.^{6,7} In this study, we applied endoscopic submucosal dissection (ESD) for the treatment of esophagus-localized superficial recurrence of esophageal SCC after dCRT. We examined the efficacy and safety of the salvage ESD and assessed its feasibility as a treatment option for recurrent esophageal SCC after dCRT.

PATIENTS AND METHODS

Patients

Between January 2004 and December 2011, a total of 234 patients with esophageal SCC underwent dCRT. The protocol for the CRT was 2 cycles of cisplatin at 40 mg/m² (days 1 and 8) and fluorouracil at 400 mg/m² (days 1-5 and 8-12). Concurrently, patients underwent radiation therapy with a daily 2-Gy fractional dose 5 days a week for a final dose of 60 Gy. Complete remission was achieved in 36 of these patients with the dCRT. After the confirmation of the complete remission by endoscopy and CT, these patients were carefully followed with repeat endoscopy and CT. During the follow-up period, esophagus-localized superficial recurrence was observed in 12 patients without any extraesophageal recurrence, and these patients underwent salvage ESD.

ESD

Written informed consent was obtained from all patients before ESD. This study was conducted in accordance with the Declaration of Helsinki. ESD was performed by M.J. in patients 2, 3, and 7 (Tables 1 and 2) and by T.M. in patients 1, 4 through 6, and 8 through 12. During ESD, patients were sedated with intravenous administration of 2,6diisopropylphenol or flunitrazepam with blood pressure, electrocardiographic, and SpO₂ saturation monitoring. ESD was typically performed with GIF H260Z and Q260J endoscopes with a transparent hood D-201-11804 (Olympus, Tokyo, Japan) attached to the tip. The electrosurgical generator used in the ESD was an ICC 200 device or VIO300D device (ERBE, Tübingen, Germany). The lateral margin of the recurrent SCC was marked by making spots with a needle-knife (Olympus) 3 to 4 mm outside the lesion. Then, a mixture of 30% hyaluronic acid, 70% saline solution, and a small amount of indigo carmine was injected in the submucosa to lift the lesion. This injection was repeated if necessary during ESD to keep the lesion raised. A circumferential incision was made around the lesion with an IT-knife (Olympus) just outside the marking spots. Finally, ESD was usually carried out with an IT-knife concomitantly using hemostatic instruments such as coagulation forceps (Coagrasper; Olympus) and metal clips (Olympus) to treat spurting or oozing hemorrhage. However, severe submucosal fibrosis and scarring induced by radiation during dCRT were often present, which made

ESD difficult. In such cases, careful ESD was performed with a needle-knife or a hook-knife (Olympus).

Histopathological 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 vertical and horizontal margins of the specimens resected en bloc were free of SCC, it was defined as complete resection. Although a consensus definition of curative resection for the esophageal superficial recurrence after dCRT for primary esophageal SCC has not been established, we defined curative resection according to the Japanese current consensus of the endoscopic curative resection of the primary esophageal superficial SCC.⁸ Accordingly, 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.

Follow-up after salvage ESD

After salvage ESD, follow-up endoscopy was performed 2 and 6 months after the procedure. The examinations were carried out every 6 months thereafter. The latest follow-up examination was in August 2012.

RESULTS

The characteristics of the 12 patients and the pathological analysis of the specimens resected by salvage ESD are shown in Table 1. All 12 patients were male with an average age of 66 years (range 55-79 years) at the time of detection of the primary advanced esophageal SCC. The median interval between the determination of complete remission after dCRT and the first detection of the esophagus-localized SCC recurrence was 10 months (range 4-73 months). In all 12 patients, salvage ESD of the superficial recurrent esophageal SCC was performed without any serious adverse events such as perforation and uncontrollable bleeding. The average length of the procedure was 109 minutes (range 28-235 minutes) and the average major axis length of the resected specimens was 33.3 mm (range 21-72 mm). In 11 patients (91.7%), recurrent SCC was resected en bloc. In only 1 patient, the recurrent esophageal SCC lesion was resected piecemeal in 3 blocks because the lesion in this patient was localized just on the anal side of an unusual esophageal luminal bend, which made the exact observation of the lesion during ESD difficult. However, the pathological analysis reconstituting the 3 blocks of the resected specimens revealed that both the horizontal and vertical margins of the lesion were free of SCC and the vertical margin of the SCC was limited to the lamina propria mucosa (patient 7, Table 1). Nevertheless, we did Download English Version:

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