ESD for EGCs with Uncommon Histology

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Introduction

Recent developments in endoscopic submucosal dissection (ESD) have enabled en bloc resection of early gastric cancer (EGC) with a negligible risk of lymph node (LN) metastasis irrespective of tumor size or the presence of submucosal fibrosis. ESD has many advantages compared with surgical treatments, such as more accurate histological diagnosis, minimally invasive procedure, high curative resection rate, and low local recurrence rate. Therefore, ESD is widely accepted as a standard treatment strategy for EGC.1-4 The indications of ESD for EGCs have been gradually expanded.1,4 ESD of absolute and expanded indications is recognized as a safe treatment modality for EGC based on recent studies of the long-term outcomes of ESD.2,4,5 However, the results of ESD in EGCs with specialized histology are somewhat different from those of ESD in EGCs with common histology. Therefore, I would like to summarize the results of ESD in EGCs with specialized histology on the basis of my experience.

Papillary adenocarcinoma

Papillary adenocarcinoma is a rare histologic variant of gastric adenocarcinoma that is characterized histologically by epithelial projections scaffolded by a central fibrovascular core.6 Its biological behavior and prognostic significance is still unclear because of its rarity. Currently, papillary adenocarcinoma is classified into differentiated-type adenocarcinoma based on the Japanese classification of gastric carcinoma7 and intestinal type based on the Lauren classification.8 However, papillary adenocarcinoma has been reported to have a higher rate of liver metastasis and LN involvement and lower overall 5-year survival rate compared with non-papillary gastric carcinoma such as tubular adenocarcinoma.6,9

Given the more aggressive features of papillary adenocarcinoma, an inevitable question is whether papillary and tubular adenocarcinomas should be treated according to the same ESD indication criteria. It is doubtful that the same ESD indication criteria can be rationally applied to gastric carcinomas with and without considerable papillary adenocarcinoma components.10-12

On the basis of the data from my hospital, 24 patients with papillary adenocarcinoma-type EGC underwent ESD as a primary treatment from January 2005 to May 2013. In the pre-treatment work-up, 10 patients had ab-
solute indication for ESD and 14 patients had expanded indication for ESD. In all cases, en bloc resection was obtained without treatment-related adverse events. In the final histopathology, 13 patients (54%) had out-of-ESD indication; 9 patients had lymphovascular invasion or deep submucosal invasion, 3 patients had intramucosal cancer > 30 mm in size with ulceration, and 1 patient had sm1 cancer > 30 mm in size. Of these patients, 9 patients underwent additional surgical operation because of non-curative resection, and the other 4 patients were followed up without operation. Recurrence was not observed during the median follow-up period of 19 months (range, 6-51 months) in the 15 patients who only underwent ESD.

Gastric carcinoma with lymphoid stroma

Gastric carcinoma with lymphoid stroma (GCLS) is a specific type of gastric cancer classified as a rare histological variants by 2010 WHO classification accounting for 1-4% of all gastric carcinomas. Typically, GCLS is characterized by poorly developed tubular structures associated with a prominent lymphoid infiltrate in a non-desmoplastic stroma. However, a standardized diagnostic criteria is lacking and histological diagnosis for GCLS is obscure. Recently, as Crohn’s disease-like lymphocytic reaction (CLR) which shows frequent tubule or gland formation revealed similar features to typical GCLS, CLR have been suggested as an expanded spectrum of GCLS.

GCLS is known to have distinct clinicopathologic characteristics and generally accepted to have favorable prognosis with lower frequency of lymph node metastasis. Increasing tumor-infiltrating lymphocytes which are reflective of host immune response to tumor cells is suggested to be significantly associated with an improved survival preventing outgrowth of metastasis.

On the basis of the data from my hospital, only two patients (3.4%) showed LN metastasis among 59 patients with EGC with GCLS underwent a surgical resection from January 2007 to December 2014. Despite of a submucosal invasion, EGC with GCLS showed lower rate of LN metastasis (4.0%), even in the patients with EGC with GCLS. Of 11 patients who underwent only ESD with out surgery, one was lost for follow-up, and 10 patients revealed no recurrence with a mean follow-up period of 37.2 months.

Conclusions

In present, the indications of ESD for EGCs are based on the tumor differentiation. EGC with papillary adenocarcinoma is classified as one of differentiated-type carcinomas and therefore, treated with ESD according to the same indication criteria as other differentiated-type carcinomas such as tubular adenocarcinoma. However, the rate of LN metastasis under the current ESD indication criteria was somewhat high. In addition, more than half of the patients who underwent ESD as a primary treatment for EGC with papillary adenocarcinoma ultimately achieved out-of-ESD indication. On the other hand, EGC with GCLS, one of undifferentiated-type EGCs is a specific type of gastric cancer having a favorable outcome related with very low rate of LN metastasis despite deep submucosal invasion. Therefore, clinicians should be aware of these disease entities, and the use of ESD should be more carefully considered for EGCs with papillary adenocarcinoma and GCLS.
References