EDITORIAL

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Understanding Growth Patterns of Signet Ring Cell Carcinoma of the Stomach Is Necessary for Successful Endoscopic Resection

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See "Growth Patterns of Signet Ring Cell Carcinoma of the Stomach for Endoscopic Resection" by Hyunki Kim, et al. on page 720-726, Vol. 9. No. 6, 2015

Endoscopic resection (ER) has been widely accepted as a minimally invasive treatment for early gastric cancer (EGC) that has a negligible risk of lymph node metastasis. In the past, ER was performed mainly in differentiated-type EGCs, but recently, the indications for ER have been extended to include undifferentiated-type EGCs.[1] According to the Japanese Gastric Cancer Association, undifferentiated-type gastric carcinoma includes poorly differentiated adenocarcinoma, signet ring cell carcinoma (SRCC), and mucinous adenocarcinoma as defined by the World Health Organization classification.[2] Several recent studies have shown that patients with undifferentiated-type EGC can be candidates for endoscopic submucosal dissection under specific conditions where there is an acceptably low rate of lymph node metastasis, compatible with that of differentiated-type EGC.[3-5]

In general, ER has been performed for SRCC considered to be a type of undifferentiated adenocarcinoma. However, there are distinct differences in the clinicopathological features according to the subtype of undifferentiated adenocarcinoma. In particular, one of the important features for predicting successful ER is that poorly differentiated adenocarcinoma tends to invade vertically and SRCC tends to spread horizontally. This can lead to different patterns of ER outcomes between poorly differentiated adenocarcinoma and SRCC because histologically incomplete resections in poorly differentiated adenocarcinoma are mainly due to vertical involvement, whereas those in SRCC are mainly due to horizontal involvement of tumor cells.[6] This growth pattern indicates that the difficulty in endoscopic prediction of the tumor margins in SRCC is due to the subepithelial spreading tendency of SRCC beneath intact the surface epithelium,[7] which results in underestimation of the true histopathological margins of SRCC.

In an effort to study this phenomenon, Kim *et al*.[8] investigated the intramucosal spreading patterns of SRCC in surgical and ER specimens. In this study, the intramucosal spreading patterns were classified into two types: expanding and infiltrative types. The expanding type was defined as a tumor that had a margin that was clearly lined with nonneoplastic mucosa (an epithelial spreading pattern), and the infiltrative type was defined as a tumor that showed diffusely spreading tumor cells (a subepithelial spreading pattern). Thus, the surrounding mucosal pattern differed between the two types. The surrounding mucosa in the infiltrated type was more commonly associated with atrophy, intestinal metaplasia, lack of neutrophil infiltration, and an absence of *Helicobacter pylori*. Therefore, the authors suggested the importance of the surrounding mucosa as a mechanical barrier for tumor cell spread in SRCC. In a weak barrier state, such as in atrophy or lack of neutrophil infiltration, the tumor cells might tend to have a subepithelial growth pattern. In addition, they showed additional data in ER specimens supporting the above-mentioned assumption, namely, that the positive rate of horizontal margins in ER specimens was higher in the infiltrative type than in the expanding type.

If so, how can we exactly delineate the horizontal margins of SRCC using endoscopy? This process is very important for successful ER of SRCC. Most expert endoscopists agree that it is very difficult, sometimes impossible, to delineate the exact hori-

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zontal margins of SRCC using endoscopy alone. Accordingly, endoscopic biopsies taken outside the lesion (usually four-quadrant, apart from the endoscopically predicted horizontal margins) are strongly recommended for the accurate determination of the tumor margin before ER.[3] Several studies have shown the efficacy of acetic acid-indigo carmine chromoendoscopy and magnifying endoscopy with narrow-band imaging to identify the horizontal margins of differentiated-type carcinoma.[9-11] However, these techniques do not give additional information to delineate the horizontal margins of undifferentiated-type carcinoma, especially SRCC, because of the subepithelial spreading tendency of SRCC.[9,11]

Considering these circumstances, the findings of Kim *et al*. that the status of the surrounding mucosa can be predictive of the intramucosal spreading patterns in SRCC could give more information to an endoscopist trying to achieve successful ER for SRCC. However, this study has some limitations; the number of included cases was relatively small, and almost all cases included in this study were pure SRCC, not combined with other histologies. Therefore, further large-scale multicenter studies, including studies with a prospective design, are necessary before clinical application of this information.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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