VIDEO CASE REPORT

Detection of multiple intramucosal signet-ring cell carcinomas by white-light endoscopy and magnifying endoscopy with narrow-band imaging in a hereditary diffuse gastric cancer patient with a *CDH1* germline mutation

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Hereditary diffuse gastric cancer (HDGC) is an autosomal-dominant syndrome, accounting for approximately 1% of gastric cancers. The germline pathogenic variant of *CDH1*, encoding for the tumor-suppressor protein E-cadherin, is implicated in the genetic pathogenesis of HDGC.[1,2] Patients with a pathogenic variant of *CDH1* are recommended to undergo a prophylactic gastrectomy owing to a high cumulative risk of diffuse-type gastric cancer over the age of 80 years: 70% for men and 56% for women.[3,4] Thus, it is important to identify this hereditary cancer syndrome to provide an appropriate treatment.

For some patients with the pathogenic variant of that gene who decline to undergo prophylactic gastrectomy, histologic assessment of the presence of microscopic foci of intramucosal signet-ring cell carcinoma (SRCC) and its precursor lesions (which are characteristic of early HDGC)[5,6] could be a helpful factor during the decision-making process. Owing to the difficulty of detecting the tiny SRCC foci endoscopically, collecting at least 30 random endoscopic biopsy specimens is recommended in the Cambridge protocol.[7] In contrast, some studies have reported that targeted biopsies or a combination of targeted and random biopsies might increase diagnostic accuracy.[8,9] However, the usefulness of that approach is controversial.[10] To improve the diagnostic performance for early HDGC

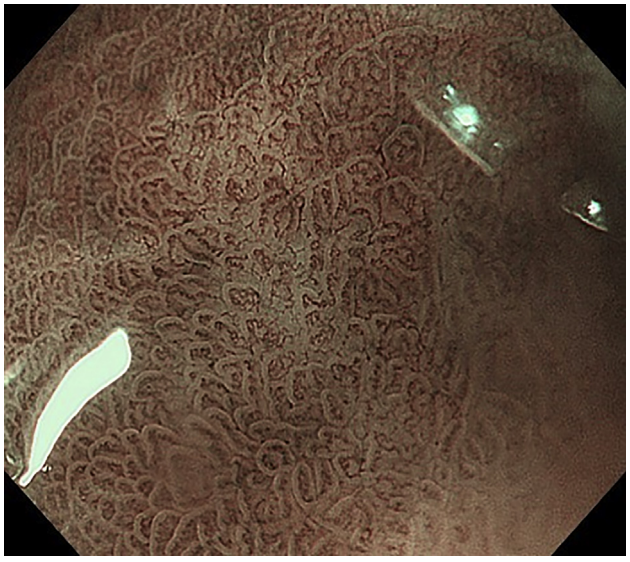

Figure 2. Magnifying endoscopy with narrow-band imaging revealed unclear surface structures and irregular microvessels.

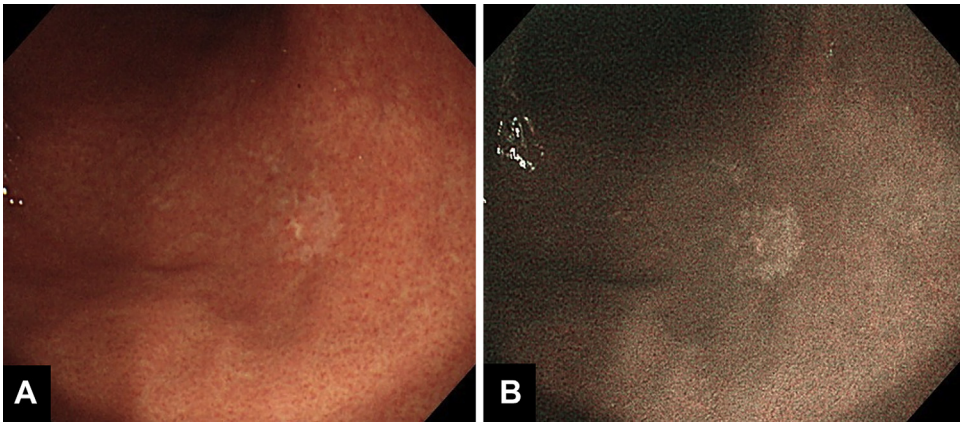

Figure 1. A, White-light imaging revealed a pale lesion at the greater curvature of the gastric antrum. This lesion had been diagnosed as signet-ring cell carcinoma in another hospital. The lesion was flat, and a postbiopsy scar left after the previous procedure was detected in its center. **B,** Narrow-band imaging revealed the lesion to be a whitish one.

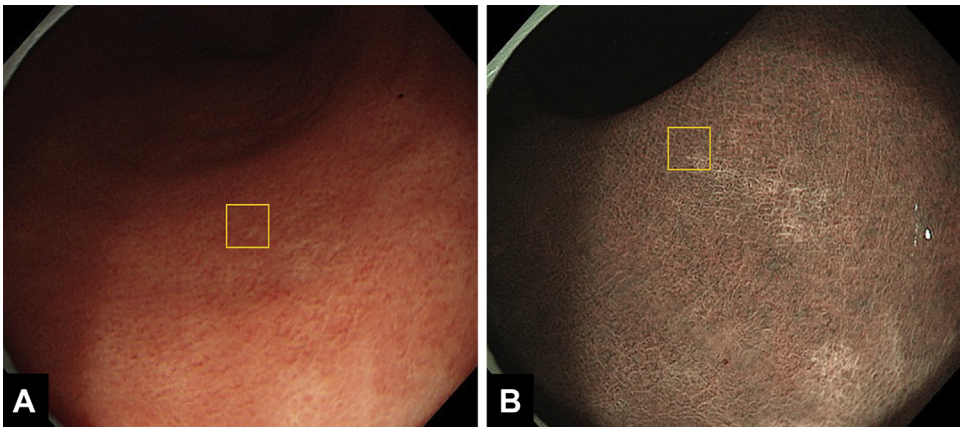

Figure 3. A, White-light imaging revealed a flat and slightly pale lesion at the greater curvature of the gastric antrum, located distal side of the main lesion (Fig. 1). **B,** The pale mucosa was visualized more clearly as a whitish lesion under narrow-band imaging.

lesions, it is essential to describe the characteristic endoscopic features of those tumors.

In this video report, we detected multiple SRCC foci in preoperative EGD for endoscopic submucosal dissection, which led to the successful diagnosis of HDGC with a *CDH1* mutation. We introduce a video (Video 1, available online at www.giejournal.org) showing multiple lesions of early HDGC in white-light imaging, narrow-band imaging (NBI), and magnifying endoscopy with NBI.

ETHICS

This study was conducted according to the Helsinki Declaration of the World Medical Association and was approved by the Institutional Review Board of the Cancer Institute Hospital of the Japanese Foundation for Cancer Research (approval number 2020–1158).

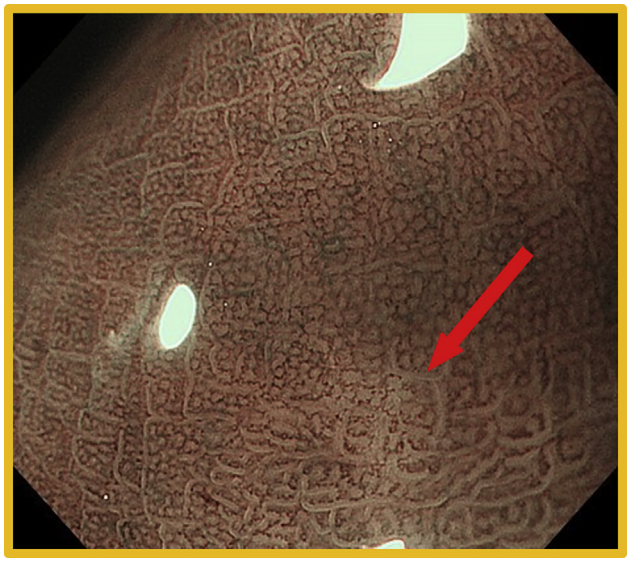

Figure 4. Magnifying endoscopy with narrow-band imaging of the area in the *yellow square frame* in Figure 3A and B (marginal area of distal side of the lesion) revealed unclear surface structures and irregular microvessels (*arrow*).

CASE REPORT

A 34-year-old man with a family history of gastric cancer underwent EGD in another hospital to assess the cause of discomfort in his throat. There, he was histologically diagnosed with an early diffuse-type gastric cancer (DGC). He was referred to our institution for further investigation by EGD. He was intended to undergo endoscopic submucosal dissection for DGC, which was suspected to be a sporadic cancer. He had no history of *Helicobacter pylori* infection or eradication therapy.

EGD in our institution revealed 6 more pale lesions under white-light imaging with slightly irregular microvessels and/or microsurface structures under magnifying endoscopy with NBI, suggesting cancerous lesions (Figs. 1 to 4; Video 1, available online at www.VideoGIE.org). We conducted a targeted biopsy for 4 highly suspicious lesions, and SRCC foci were detected histologically in 2 of 4 lesions (Figs. 3 to 5). Considering the clinical and endoscopic findings, genetic counseling and germline *CDH1* genetic testing were performed for this patient, which revealed the presence of the *CDH1* pathogenic variant (c.603del, p.Val202Leufs*13).

The patient underwent total gastrectomy with lymph node dissection. Histopathologic analysis of the entire resected specimen, which had been cut into 400 blocks,

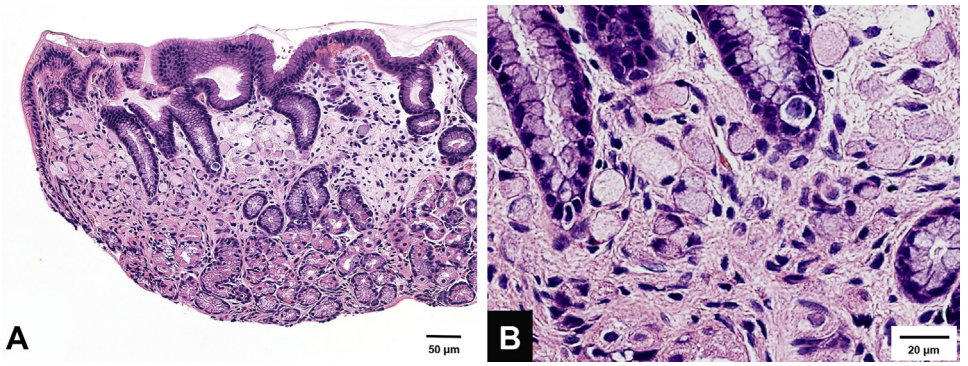

Figure 5. A, Biopsy specimen from the lesion in Figures 3 and 4 histologically revealed signet-ring cell carcinoma distributed from the middle to the superficial layer of the mucosa (hematoxylin and eosin staining, low-power magnification, scale bar = 50 μm). **B,** Signet-ring cell carcinoma in Figure 5A composed of mucin-rich cytoplasm and crescent-shaped hyperchromatic nuclei (hematoxylin and eosin staining, high-power magnification, scale bar = 20 μm).

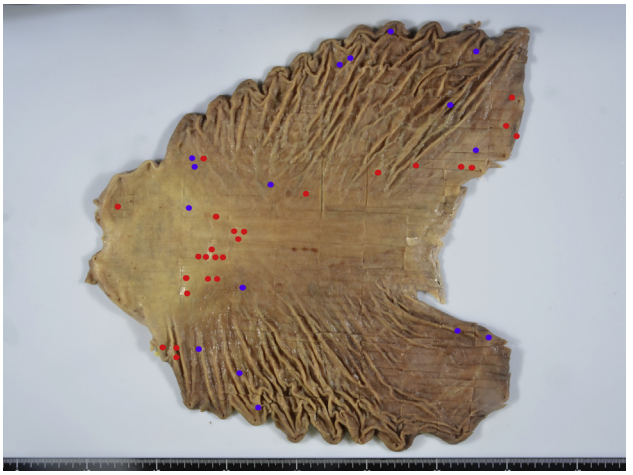

Figure 6. The topographic scheme of signet-ring cell carcinoma foci distribution in the gastrectomy specimen obtained from the patient. The whole resected stomach was cut into 400 blocks and examined histologically. In total, 42 carcinoma foci were detected. Of these, 26 foci of an intramucosal invasive signet-ring cell carcinoma (pT1a) and 16 foci of a noninvasive signet-ring cell carcinoma (pTis) are indicated by *red and blue dots*, respectively.

revealed the presence of 42 intramucosal SRCCs without any component of poorly differentiated adenocarcinoma, including 26 intramucosal invasive carcinomas (pT1a) and 16 noninvasive carcinomas (SRCC in situ, pTis) (Fig. 6). No lymph node metastasis was found. The final pathologic staging of the tumor was pT1aN0M0.

Abbreviations: DGC, diffuse-type gastric cancer; HDGC, hereditary diffuse gastric cancer; NBI, narrow-band imaging; SRCC, signet-ring cell carcinoma.

ACKNOWLEDGMENTS

The authors thank Dr Shoichi Yoshimizu (Department of Gastroenterology, Cancer Institute Hospital, Japanese Foundation for Cancer Japanese Foundation for Cancer Research) and Soya Nunobe (Department of Gastroenterological Surgery, Cancer Institute Hospital, Japanese Foundation for Cancer Japanese Foundation for Cancer Research) for advice on this article.

DISCLOSURE

All authors disclosed no financial relationships.

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https://doi.org/10.1016/j.vgie.2020.11.020