Helicobacter pylori-negative intestinal-type gastric adenoma successfully treated by endoscopic submucosal dissection: a case report

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Background and study aims: A 49-year-old woman underwent an esophagogastroduodenoscopy as part of a health check at our hospital. Endoscopic observation revealed a flat elevated lesion 6 mm in diameter in the gastric antrum (Paris Classification type Ila). Magnifying endoscopy using narrow-band imaging showed a slightly irregular micro-surface pattern with round and oval pits, as well as a regular micro-vascular pattern without a demarcation line. Atrophy and intestinal metaplasia were not recognized in the background gastric mucosa. Furthermore, Helicobacter pylori infection was not detected by histologic, serologic, and urea breath test results.

Endoscopic resection was performed for histologic evaluation, and a pathologic diagnosis of intestinal-type gastric adenoma occurring in pyloric mucosa without atrophy or metaplasia was established.

Immunohistochemistry findings of the lesion showed the intestinal epithelium phenotype with positive staining for MUC2, CD10, and CDX2. Furthermore, irregular distribution with a higher positive proportion of Ki-67 was found in the lesion, indicating its malignant potential. We report here a rare case of gastric adenoma without surrounding intestinal metaplasia occurring in a Helicobacter pylori-negative patient.

Introduction

Gastric adenoma is a neoplastic lesion characterized by localized and polypoid proliferation of dysplastic epithelium. In affected patients, in addition to a higher probability of an adenocarcinoma found elsewhere in the stomach, the adenoma itself has potential to progress to an adenocarcinoma [1, 2]. Gastric adenomas are histologically classified as intestinal-type, gastric-type, and indeterminate type, of which intestinal-type is the most prevalent. An intestinal-type adenoma is usually found with a background of intestinal metaplasia commonly caused by infection with Helicobacter pylori (H. pylori), widely known as a carcinogenic bacterium, thus patients with a diagnosis of H. pylori-associated gastritis should be followed with endoscopic surveillance. On the other hand, H. pylori-negative patients are considered to have a lower risk of gastric neoplasms. Herein, we report a rare case of gastric adenoma in a patient without evidence of intestinal metaplasia or H. pylori infection.

Case report

A 49-year-old woman underwent an esophagogastroduodenoscopy (EGD) examination as part of a health check at our hospital, which revealed a flat elevated lesion 6 mm in diameter in the gastric antrum (Paris Classification Ila) (Fig. 1). Chromoendoscopy with 0.1% indigo carmine also clearly showed a reddened area (Fig. 1b), while magnifying endoscopy using narrow-band imaging (ME-NBI) revealed a slightly irregular micro-surface pattern with round and oval pits (Fig. 2). According to the vascular surface classification system reported by Yao et al. [3], the ME-NBI findings were categorized as a regular microvascular pattern and slightly irregular micro-surface pattern without a demarcation line. Hence, it was diagnosed as a non-cancerous lesion and biopsy specimens indicated intestinal-type gastric adenoma. Atrophy, intestinal metaplasia, spotty erythema, and edema were not recognized in the background gastric mucosa, while a regular arrangement of collecting venules (RAC), a well-known characteristic endoscopic finding in H. pylori-negative patients [4], was clearly found in the gastric corpus. These endoscopic findings strongly indicated H. pylori-nega-
ative status. Furthermore, serological examinations revealed anti-
H. pylori IgG antibodies at 4.3 U/mL (<10 U/mL), pepsinogen (PG) I at 66.3 ng/dL (>70 ng/dL), and a PGI/II ratio of 5.5 (PGI/II >3.0) in serum, while a urea breath test was 0.3‰ (<2.5‰).

An endoscopic resection was performed for a detailed histologic
evaluation and the lesion was removed en bloc without complications. We generally perform endoscopic submucosal resection (ESD), as this technique has a higher rate of successful en bloc re-
section (5) and can provide a reliable pathological diagnosis.

Although no intestinal metaplasia or H. pylori bacteria were
noted, and normal foveolar epithelium was found in the back-
ground mucosa, a histologic diagnosis of intestinal-type high-
grade gastric adenoma was established based on the WHO crite-
ria (Fig. 3a, Fig. 3b, Fig. 3c). Together, endoscopic, sero-
logic, and histologic results led us to conclude that the lesion oc-
curred in true H. pylori-negative gastric mucosa. In addition, Im-
munohistochemistry findings demonstrated an intestinal cell
phenotype with positive staining for MUC2, CD10, and CDX2,
whereas MUC5AC and MUC6 were negative (Fig. 4a, Fig. 4b,
Fig. 4c, Fig. 4d, Fig. 4e). Furthermore, the lesion showed
an irregular distribution, though with a higher positive propor-
tion of Ki-67, indicating a relatively high malignant potential
(Fig. 4f), while p53 immunohistochemistry findings revealed
scattered-type staining, which did not indicate an abnormality
(Fig. 4g). We finally diagnosed the lesion as an intestinal-type
gastric adenoma occurring in normal pyloric mucosa without
intestinal metaplasia in an H. pylori-negative patient, a rare case.

Discussion

Gastric adenomas (low-grade intraepithelial neoplasia, low-
grade dysplasia), a type of benign noninvasive intraepithelial
neoplasia, are considered to be premalignant lesions [1,2]. Most
occur in the background of atrophic gastritis or intestinal meta-

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**Fig. 1** Endoscopic images of the lesion. a Conven-
tional white-light imaging showed a reddish colored
slightly elevated lesion 6 mm in diameter located
in the gastric antrum. b Chromoendoscopy using
0.1% indigo carmine dye showed a clearly defined
flat elevated lesion with a slightly irregular surface
pattern.

**Fig. 2** Magnifying
endoscopy with nar-
row-band imaging. We
observed a slightly ir-
regular micro-surface
pattern and regular mi-
cro-vessel pattern with
an unclear demarcation
line.

**Fig. 3** Histologic appearance of lesion (HE stain-
ing). a On low-power view (× 20), the lesion was
slightly elevated and showed a tubular structure
with slight structural atypia, suggesting an intes-
tinal-type gastric adenoma. No metaplasia was seen
in the background mucosa. b,c On high-power
views (b × 100, c × 200), the lesion had histologic
characteristics of intestinal epithelium with goblet
cells (arrows) and round hyperchromatic nuclei.
H. pylori organisms were not seen in the Giemsa-
stained specimen (not shown).
plasia, and are commonly found in patients with *H. pylori* infection. Because of their involvement in the pathological process of adenocarcinoma development [1,2], endoscopic resection is usually chosen for treatment [6]. Recently, ME-NBI was introduced as a useful tool for management of gastric adenomas [7]. In addition, histologic examination of expressed mucin in such lesions is becoming popular as a new diagnostic method to evaluate their biological behavior. Gastric neoplasms are classified into gastric-phenotype, intestinal-phenotype, and indeterminate, based on expression of the human gastric mucin markers MUC2, MUC5AC, MUC6, and CD10 [8]. At our institution, we use MUC5AC as an immunohistochemical marker for foveolar cells, MUC6 for mucous neck or pyloric gland cells, MUC2 for goblet cells, CD10 for the intestinal brush border, and CDX2 for intestinal differentiation. In general, the gastric-phenotype is classified based on expression of MUC5AC and MUC6, while the intestinal-phenotype is defined by positive expression of MUC2, CD10, and CDX2. On the other hand, proliferative activity and malignant potential are assessed by expression of Ki-67 and p53.

The current lesion was positive for MUC2, CD10, and CDX2, whereas it was negative for MUC5AC and MUC6, indicating intestinal-type. In addition, its malignant potential was considered to be relatively high because of the irregular distribution and higher positive proportion of Ki-67. There was no evidence of *H. pylori* infection in the background mucosa shown in histological and serological examination findings, and endoscopy revealed no atrophic changes. As described above, this case met all criteria proposed by Matsuo T, et al. for *H. pylori*-negative gastric cancer [9]. Finally, we diagnosed the current gastric neoplasm as occurring in true *H. pylori*-negative gastric mucosa.

Previous investigators have reported gastric-type adenomas and gastric adenocarcinomas with chief-cell differentiation in *H. pylori*-negative patients. To the best of our knowledge, this is the
first report of an intestinal-type gastric adenoma occurring in an
\textit{H. pylori}-negative patient. Some reports of \textit{H. pylori}-negative
gastric cancer (HpNGC) have been presented, although the prev-
ulence differs, because diagnostic criteria for HpNGC have yet to
be definitively established. According to a report that used the
strict criteria of Matsuo \textit{et al.} [9], the prevalence of HpNGC was
0.66\% of all gastric cancer patients, while 66.7\% of the HpNGC
cases were undifferentiated type in histological findings. There-
fore, the current case of \textit{H. pylori}-negative intestinal-type differ-
entiated adenocarcinoma is rare, though Ozaki \textit{et al.} [10] recent-
ly reported an affected patient.

In the current case, our histologic examination revealed neither
\textit{H. pylori} infection nor intestinal metaplasia in the background
gastric mucosa, thus we suspected that the lesion underwent \textit{de
novo} progression instead of the common pathway associated
with \textit{H. pylori} infection. Its high malignant potential, as indicated
by Ki-67 staining, in spite of lower histologic atypism may have
been due to this uncommon pathogenesis. Although we diag-
nosed the lesion as high-grade dysplasia/adenoma based on the
\textit{WHO} criteria, other pathologists in Asian countries may make a
diagnosis of well-differentiated adenocarcinoma. Diagnostic dis-
crepancies between Asian and Western pathologists for gastric
intraepithelial neoplasia are considered to be problematic, be-
cause of different terminology, diagnostic criteria, and grading
systems. The Vienna classification was developed for use as com-
mon terminology throughout the world, although it has yet to
be fully implemented.

**Conclusions**

In summary, we report a rare case of intestinal-type gastric ade-
nomas in an \textit{H. pylori}-negative patient without intestinal metapla-
sia. It is important for gastroenterologists to keep in mind that
intestinal-type gastric adenomas can be found in patients nega-
tive for \textit{H. pylori} infection. Further investigations of biological dif-
ferences between adenomas in mucosa with and without intesti-
tinal metaplasia, as well as \textit{H. pylori} infection are warranted.

**Competing interests:** None

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