Adenocarcinoma Arising from Heterotopic Gastric Mucosa in Cervical Esophagus
- A Case Report -

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Heterotopic gastric mucosa (HGM) of the upper esophagus, referred as “cervical inlet patch (CIP)”, is a benign lesion that is present in 3.8-10% of the adult population. Adenocarcinomas arising from HGM of the upper esophagus are exceedingly rare. The authors report one additional case of histologically confirmed adenocarcinoma arising from a CIP. The patient had concomitant primary adenocarcinoma of the colon. The right hemicolectomy specimen and total esophagectomy specimen after preoperative chemoradiotherapy showed histologically different adenocarcinomas. The residual esophageal tumor was characterized by large mucin pools, fibrous septa, and floating tumor cells. HGM of both the fundic and antral types was seen on the surface and sides of the tumor. The independent origins of the two cancers were confirmed by immunohistochemical studies for cytokeratins 7 and 20. Without further treatment, the patient remained free of disease after 29 months of follow-up.

Key Words: Esophageal neoplasm; Heterotopic tissue; Adenocarcinoma

Adenocarcinomas of the esophagus predominantly arise from Barrett’s mucosa in the lower third of the esophagus, and upper esophageal adenocarcinomas are rare; they account for only 1-2% of esophageal malignancies in western countries.1 Heterotopic gastric mucosa (HGM) of the upper esophagus, referred to as “cervical inlet patch (CIP)”, is considered to be a source of these adenocarcinomas. Only 26 cases of upper esophageal adenocarcinoma associated with HGM (and 4 cases of high-gradedysplasia/intraepithelial neoplasia) have been reported in the English literature.2 Here, we report an additional case of adenocarcinoma arising from HGM in the cervical esophagus. Interestingly, the patient revealed features of mucinous adenocarcinoma after chemoradiotherapy and had another adenocarcinoma of colonic origin.

CASE REPORT

A 44-year-old male presented with a sore throat of two months duration. He was a heavy smoker (20-25 pack years) and drinker (two bottles of alcohol three times a week), but his past medical history was unremarkable. His family history showed medical problems of the stomach and colon cancers and of stroke. An endoscopic examination revealed a 2 cm-sized round protruding tumor with marked hyperemic and telangiectatic mucosa at the upper cervical sphincter area (Fig. 1). Remaining esophageal mucosa, including the gastroesophageal junction, was unremarkable. Endoscopic ultrasonography showed hypoechoic eccentric wall thickening around 18 to 20 cm from the incisors but no evidence of lymph node metastasis. During a colonoscopic examination performed for work-up, a well-defined 2.5 cm-sized polypoid tumor was incidentally found in the hepatic flexure. Biopsies taken from the esophagus and colon showed moderately differentiated adenocarcinomas. No evidence of foveolar epithelium or gastric glands was identified in the esophageal biopsy specimen. Immunohistochemical stainings for cytokeratins 7 and 20 yielded contrary results for the two tumors, i.e., the esophageal cancer was diffusely positive for CK 7 and nega-
tive for CK20 (Fig. 2A), while the colonic cancer was diffusely positive for CK20 and negative for CK7 (Fig. 2B). These immunohistochemical profiles indicated that the tumors in the esophagus and colon were of different origins with similar histologic findings.

The patient underwent right hemicolectomy for the colonic cancer. This adenocarcinoma of the colon had histological features normal for colonic adenocarcinoma with elongated nuclei and central necrosis, without a mucinous component. The tumor invaded pericolic adipose tissue with strong desmoplastic response. One nodal metastasis was found among 10 pericolic lymph nodes.

The optimal therapeutic strategy for esophageal adenocarcinoma in this case was discussed, and neoadjuvant treatment was chosen based on our experiences of esophageal squamous cell carcinomas. The patient received preoperative cisplatin and capecitabine chemoradiotherapy. A biopsy from the esophageal tumor at 4 months postoperatively showed a residual tumor in the esophagus without a recognizable treatment effect. He then underwent a McKeown operation (gastroesophageal resection and lymph node dissection).

On gross examination, an ill-defined elevated lesion (2 cm in greatest dimension) was identified in the proximal esophagus around the upper sphincter area, and was found to have invaded the proper muscle layer. Its cut surface was whitish tan and myxoid. Microscopically it demonstrated large acellular mucin pools divided by fibrous septa. In some areas tumor cells floating in mucin pools formed nests or U-shaped cords. They showed small, oval to round nuclei and moderate amounts of vacuolated eosinophilic cytoplasm, which contrasted with the colonic tumor cells, which showed large, elongated nuclei with promi-
nent nucleoli and small amount of cytoplasm.

Heterotopic gastric mucosa of the antral type was identified on the surface and sides of the tumor (Fig. 3). Fundic type gastric glands with chief and parietal cells were also focally observed. Warthin-Starry staining showed numerous Helicobacter pylori organisms on the surface of the gastric mucosa but not on the esophageal mucosa (Fig. 4). Neither lymphovascular invasion nor lymph node metastasis was found. Resection margins were stated to be free of tumor cells. Without further treatment, the patient remained free of disease at his 29 month follow-up.

**DISCUSSION**

The endoscopic incidence of HGM of the upper esophagus, referred to as “CIP” in the normal adult population has been reported to be 3.8-10%, with their sizes ranging 5-30 mm.3 CIP is usually located immediately below the upper esophageal sphincter, which is not easily accessed by an endoscope because this area tends to be quickly passed to overcome sphincter resistance. Therefore, CIP can is probably best detected by gentle withdrawal of the instrument. The origin of CIP is controversial, although it is generally accepted to be a congenital condition, and it appears to result from incomplete replacement of the original columnar epithelium by squamous epithelium during the embryonic period.1

According to a previous study, the most common histologic type of CIP is oxyntic mucosa (55%), followed by cardiac mucosa (25%).5 Sixty percent of CIPs were reported to be inflamed, and 5% to 17% to be associated with H. pylori infection.6 Most CIPs are asymptomatic and are found incidentally, but they may present with various symptoms. Dysphagia is a representative complaint, though a sore throat, a tight throat, and weight loss can occur.8 Symptoms are presumably related to heterotopic HCl secretion by the HGM, which may induce chronic inflammation and ulceration. Moreover, the subsequent healing process results in the formation of esophageal strictures and webs.1,2,7,8 Ulceration may also be attributed to H. pylori colonization of the HGM.5,6,8

Malignant progression of CIP is exceedingly rare compared to the prevalence of the CIP; only 26 cases have been reported (predominantly in men aged from 37 to 79 years).2,11,12 The tumors appear as polypoid or infiltrative in the cervical esophagus, from 16 to 22 cm distant from incisors. In Korea, only one case of upper esophageal adenocarcinoma originated from a CIP has been reported.13 This second case in Korea raises several interesting points.

First, numerous H. pylori colonies were identified on the surface of the HGM together with marked lymphocytic infiltration, suggesting the involvement of H. pylori. However, since this is the first described case of H. pylori infection in CIP with adenocarcinoma, the role of H. pylori in the malignant transformation of HGM remains uncertain.

Second, the tumor was mucinous in type, which has not been specifically mentioned in previously reported adenocarcinomas of the CIP. However, this microscopic feature may have been due to a post-therapeutic effect, as the tumor according to the first endoscopic biopsy was a normal adenocarcinoma. The occurrences of esophageal or esophagogastric junction adenocarcinomas with signet-ring cell or mucinous histologies in post-treatment surgical specimens has been reported,14 and the presence of acellular mucin pools as in our case has been described in gastric ade-
The esophageal adenocarcinoma was considered to have originated from the gland portion of the CIP. Therefore, the esophageal adenocarcinoma was independent in nature.

In summary, we report a rare case of tubular adenocarcinoma arising from heterotopic gastric mucosa in the cervical esophagus with a concurrent colonic adenocarcinoma. Careful clinical and histological examinations and immunohistochemical staining are recommended for the diagnosis of adenocarcinomas arising from the CIP, to exclude the possibilities of adenocarcinoma arising in Barrett's esophagus and of metastatic adenocarcinoma.

REFERENCES