Case report

Gastric carcinoma resembling submucosal tumor

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Abstract:

A case of stomach carcinoma showing features of submucosal tumor is reported. The patient was a 50-year-old man presenting with hematemesis. Endoscopic examination was performed and revealed a submucosal tumor-like lesion with central ulceration in the fornix of the stomach. The biopsy specimen from this lesion showed poorly differentiated adenocarcinoma, and surgery was performed. The tumor, measuring 3.5×2.7 cm in size, invaded to the muscularis propria with proliferation of the interstitial connective tissue and lymphoid follicles consisting mainly of B lymphocytes in the submucosal layer. In situ hybridization of tumor tissue for Epstein-Barr virus (EBV)-encoded small RNA1 as target revealed negative results. In stomach carcinoma simulating submucosal tumor, as in this patient, preoperative diagnosis is important to plan treatment strategies.

Key words: gastric carcinoma resembling submucosal tumor, lymphocyte infiltration, Epstein-Barr virus

Introduction

Epithelial tumors in the stomach sometimes exhibit a macroscopic appearance similar to submucosal tumors [1–4], for which there may be various causes. We report a case of gastric cancer which appeared to be a submucosal tumor due to submucosal proliferation of lymphoid follicles and interstitial connective tissue.

Case report

A 50-year-old man with hematemesis was admitted to our hospital as an emergency patient on February 2, 1996. Endoscopic examination showed a protuberant

lesion covered with normal-appearing mucosa in the gastric fundus. The lesion was characterized by bridging folds and a central ulceration (Fig. 1). A biopsy of the ulcerated site confirmed the diagnosis of poorly differentiated adenocarcinoma. Radiological examination of the upper digestive tract showed a filling defect with a comparatively blunt edge. A depressed change was noted around the center of the defect. Endoscopic ultrasonography revealed a low echoic tumor with a comparatively clear margin in the third and fourth layers of the stomach. The first and second layers were disrupted in the area of the central ulceration (Fig. 2). Based on the above findings, total gastrectomy associated with pancreatosplenectomy and lymph node dissection was performed, on March 11, with the preoperative diagnosis of advanced gastric cancer of submucosal appearance in the fundus. A protuberant lesion, 3.5×2.7 cm in size, was found on the greater curvature side of the anterior aspect of the fundic wall of the resected specimen (Fig. 3A). When seen through a magnifying glass, the cancer tissue was predominantly located in the submucosal and proper muscular layers with proliferation and enlargement of lymphoid follicles. An approximately 7-mm-long section of the tumor was exposed on the mucosal surface (Fig. 3B). Histological examination showed that small nests of cancer cells or separate cancer cells had diffusely infiltrated the interstitial connective tissue (Fig. 4A). Proliferation of lymphoid follicles was also confirmed. Immunohistochemical staining with L26 showed that lymphoid follicles and infiltrating lymphocytes in cancer tissue consisted mainly of B lymphocytes (Fig. 4B). The definite pathological diagnosis was poorly differentiated adenocarcinoma with infiltration of the proper muscle layer.

The serum Epstein-Barr virus (EBV) antibody titer (anti-VCA-IgG, anti-EBNA-1) determined after the operation was 1:160 (normal value, $<1:10$). However, in situ hybridization of tumor tissue for EBV-encoded small RNA1 as target revealed negative results.

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Fig. 1. Endoscopic finding shows an elevated lesion in the fornix. Its surface is covered with normal gastric mucosa, except for central ulceration

Fig. 2. Endoscopic ultrasonography shows a hypoechoic lesion which exists in the third and fourth layers

The patient is now under observation as an outpatient with no evidence of recurrence.

Discussion

Gastric cancer of submucosal appearance is generally a protuberant lesion covered with normal mucosa. The cancer exposed on the mucosal surface is limited to less than 20%–30% of the whole tumor [5,6]. Based on the above criteria, the prevalence of this type of tumor has been estimated to be as low as 0.2%–0.62% of all gastric

Fig. 3. **A** Macroscopic picture of the resected specimen. The tumor is located on the posterior wall of the fornix and its size is 3.5×2.7 cm (arrow). **B** Loupe view of the tumor. Tumor cells are located mainly in the submucosal and muscularis propria with lymphoid follicles

cancers [1,5]. Kodoi et al. [3] and Chonan et al. [6] reported that this type of gastric cancer had the following clinicopathological characteristics: the tumor tended to arise in the upper and middle third of the stomach, it was accompanied by a central depression, and the depth of the infiltration was limited to the proper muscular layer in most patients. A size less than 20 mm was reported in 86% of patients. From the histological point of view, 40%–60% of gastric cancers of submucosal appearance were classified as differentiated types and the remaining 40%–60% as undifferentiated types [3,6]. In the present patient, the lesion was a 3-cm undifferentiated gastric cancer with a central depression and infiltration limited to the proper muscular layer, arising in the upper third of the stomach.

In a pathological study, Hayabe et al. [1] speculated that the submucosal appearance of gastric cancer, an epithelial neoplasm, was attributable to either (1) submucosal infiltration of cancer cells, (2) proliferation of lymphoreticular tissue, or (3) cancer originating in a submucosal ectopic gastric gland. Other reports [2,5]

Fig. 4. **A** High power view of Fig. 3B. Poorly differentiated adenocarcinoma is seen in the interstitial connective tissue. **B** L26 Immunohistochemical staining of the tumor infiltrating lymphocytes. The majority of them are positive for L26 (B-cell)

suggested the possibility of submucosal proliferation of interstitial connective tissue (scirrhous type gastric cancer) as the etiology of this type of cancer. In the present patient, lymphoid follicular formation, lymphocyte infiltration, and interstitial connective tissue proliferation were predominant in the submucosal layer. These changes were considered to have led to the mucosal surface being elevated, with an appearance similar to that of a submucosal tumor. Such biological reactions of lymphocytes and connective tissue are the first reported etiology of this rare condition in the literature.

In gastric cancer, cancer accompanied by marked lymphocyte infiltration (lymphocyte infiltrating medullary cancer) has long been known to have a good prognosis. In recent years, attention has also been directed to the association between this cancer and EBV, in terms of pathogenesis [7]. However, some investigators have refuted this association [8]. Indeed, in our patient,

the serum EBV antibody titer was high, but EBV infection in the cancer tissue could not be demonstrated, which excluded the involvement of EBV infection.

The most important issue in the treatment of gastric cancer with a submucosal appearance is to establish an accurate diagnosis of the tumor. The choice of treatment depends on histological differences between benign or malignant submucosal tumors and gastric cancer. In a report by Kodoi et al. [3] the preoperative diagnostic rate of gastric cancer of submucosal appearance was cited to be 78%, with 60% in patients in whom the lesion was accompanied by a central ulceration and 30% in patients without ulceration. Fortunately, 20% of the tumor was exposed on the mucosal surface in the present patient. The first biopsy confirmed the diagnosis of cancer, and radical surgery was performed. In consideration of gastric cancer of submucosal appearance, cytological methods such as repeated biopsies under an endoscope, artificial ulceration, endoscopic mucosal resection [4], and auxiliary diagnostic methods such as endoscopic ultrasonography should be performed to establish the correct diagnosis of submucosal tumors. In addition, it is necessary to frequently examine, by repeated endoscopy, any lesions of submucosal appearance for changes in size and surface characteristics.

Because of its rarity, the prognosis of gastric cancer of submucosal appearance is not well known.

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