We report a case of primary gastric carcinoma with a macroscopic appearance indistinguishable from that of a submucosal tumor. A 48-year-old man visited our hospital with a chief complaint of epigastric discomfort. Endoscopic examination revealed a protruding lesion with a well defined margin on the anterior wall of the gastric antrum. Most of the tumor surface was covered with apparently normal gastric mucosa and a shallow recess with mild erosion was observed on the top. Abdominal ultrasonography showed a hypoechoic lesion with an irregular margin under the gastric mucosa. Laboratory examination revealed an elevated CA19–9 level of 106.9 U/ml. In spite of repeated bouling biopsies, no histological diagnosis could be obtained before surgery. However, gastrectomy with regional lymph node dissection was performed because of the high likelihood of gastric cancer, in view of the markedly elevated CA19–9 level and irregular tumor margin demonstrated by abdominal ultrasonography. The tumor was diagnosed histologically as papillo-tubular adenocarcinoma invasive to the serosa with marked vessel infiltration. No metastasis was found in the regional lymph nodes. Gastric cancer resembling submucosal tumor is rare and often difficult to diagnose. Careful estimation of the possibility of gastric cancer and the informed consent of the patient are critically important, in cases of suspected primary gastric cancer resembling submucosal tumor, in order to decide the form of treatment.

Key words: gastric cancer – submucosal tumor – diagnosis

INTRODUCTION

Gastric cancers show various macroscopic appearances ranging from well defined protuberant to diffuse infiltrating tumors but histological diagnosis is usually easy using endoscopic biopsy. In contrast, gastric submucosal tumor is often difficult to diagnose histologically, the tumor surface being covered with normal mucosa. Macroscopically diagnosed gastric submucosal tumors encompass various different types with distinct biological characteristics.

Here we report a rare case of advanced gastric cancer which was difficult to distinguish from submucosal tumor of the stomach. To our knowledge, previous reports of primary gastric cancer resembling submucosal tumor have been published only in Japanese. The clinical management and pathogenesis of this type of tumor are discussed and the literature is reviewed.

CASE REPORT

A 48-year-old man visited our hospital in December 1994 with a chief complaint of epigastric discomfort. On physical examination, the abdomen was soft and flat with neither palpable mass nor tenderness. No peripheral lymphadenopathy was observed. Endoscopic examination revealed a protruding lesion 1.5 cm in diameter with a well defined margin on the anterior wall of the gastric antrum. A biopsy sample taken from the lesion was not diagnosed histologically as malignant. Follow-up endoscopic examination after 7 months demonstrated that the tumor had increased in size to 2.0 cm in diameter. Most of the tumor surface was covered with apparently normal gastric mucosa and a shallow recess with mild erosion was observed on the top (Fig. 1). Normal gastric mucosa, but not tumor tissue, was obtained by repeated bouling biopsy. Double-contrast radiography showed a tumor mass 2.0 cm in diameter with a well defined margin on the greater curvature of the gastric antrum (Fig. 2). CT demonstrated a tumor mass with a distinct border on the anterior wall of the stomach (Fig. 3). Abdominal ultrasonography (US) showed a hypoechoic tumor measuring 3.0 × 2.0 cm with an irregular margin under the gastric mucosa (Fig. 4). CT and US showed no findings suggestive of lymph node or liver metastasis. Laboratory examination revealed an elevated CA19–9 level of 106.9 U/ml;
the level of carcinoembryonic antigen (CEA) was within normal limits.

Although a histological diagnosis was not achieved before surgery, subtotal gastrectomy with regional lymph node dissection was performed after obtaining informed consent from the patient, since gastric cancer was highly suspected in view of the markedly elevated level of CA19–9 and the irregular tumor margin demonstrated by US.

The resected specimen is shown in Fig. 5. A protuberant tumor 2.0 cm in diameter was observed on the anterior wall of the gastric antrum. The tumor surface was covered with apparently normal mucosa which was reddish in comparison with the surrounding mucosa. The recess found on endoscopic examination was unremarkable. The tumor was exposed on the serosa of the stomach. Macroscopic stagings according to the TNM classification (1) and the guidelines of the Japanese Research Society for Gastric Cancer (2) were T3N0M0 (stage II) and T3P0H0N0M0 (stage II) respectively.

The histological diagnosis was papillo-tubular adenocarcinoma infiltrating the serosa. The tumor was located mainly under the mucosa and only a small part of it was exposed (Fig. 6).
Figure 5. The resected specimen shows a protruding lesion 2.0 cm in diameter in the anterior wall of the gastric antrum. The mucosal surface is slightly red in comparison with the surrounding gastric mucosa and no ulcer is evident.

Figure 6. Low-power histological examination reveals that the growth of the papillo-tubular adenocarcinoma is located mainly under the mucosa. Most of the cancer cells are covered with noncancerous epithelium.

Papillo-tubular adenocarcinoma with a reticulated gland structure was found in the lamina propria mucosae (Fig. 7), while less differentiated adenocarcinoma with abundant edematous fibrosis was observed in the submucosal layer (Fig. 8). Lymphatic and vascular vessel infiltration was remarkable but no metastasis was evident histologically in the regional lymph nodes.

The patient was discharged in the second postoperative week without complication. No recurrence has been observed during a follow-up period of 1 year and 6 months after the operation.

DISCUSSION

Gastric cancers resembling submucosal tumor are characterized by a predominance of submucosal or sometimes deeper invasion in the gastric wall, suggesting that they are likely to be more advanced with an increased risk of metastasis, compared with ordinary gastric cancers of similar size. Therefore, a gastric cancer resembling a submucosal tumor, even if small, should be treated in the same way as an advanced gastric cancer. In contrast, for smooth muscle tumor, the most frequent type of submucosal tumor in the stomach, the principle of surgical treatment is local excision (3). Regional lymphadenectomy is not of proven value because local lymph node involvement is rarely observed in malignant smooth muscle tumor (3).

Histological diagnosis of gastric submucosal tumor by endoscopic biopsy is often difficult and even detailed image analysis can hardly provide definite evidence for distinguishing benign from malignant tumors. It is reported that gastric submucosal tumors >3 cm in diameter have a higher risk of malignancy than those measuring <3 cm. Surgical resection is recommended for submucosal tumors exceeding 3 cm in diameter or those which grow rapidly, irrespective of the findings of image analysis and
endoscopic biopsy (3). This is partly because smooth muscle tumors may occasionally appear benign microscopically yet behave in a malignant manner clinically (3).

In spite of repeated bouling biopsies, no pathological diagnosis was obtained before surgery in this case. However, gastrectomy with regional lymph node dissection was performed since elevation of the CA19–9 level and an irregular tumor margin demonstrated by US are highly suggestive of gastric cancer. Histological examination of the resected specimen revealed that the tumor was indeed gastric cancer located mainly under the mucosa with infiltration to the serosa.

The incidence of primary gastric cancer resembling submucosal tumor has been reported to be 0.1% (4) to 0.62% (5) of all resected gastric cancers. Our review of the literature revealed that about 30% of such cancers were not diagnosed by endoscopic biopsy prior to surgical resection. Gastric cancer resembling submucosal tumor frequently has an ulcer or a recess on the top of the tumor (5). However, it should be noted that in some tumors the cancer cells are almost entirely covered with normal mucosa (6,7).

Improved preoperative diagnostic accuracy can be obtained using endoscopic biopsy combined with high-power laser cautery and ethanol injection. An ultrasound endoscope, although unavailable for our present case, is useful for obtaining further information on malignant potential, depth of invasion and tumor localization in the gastric wall. Ultrasound-guided biopsy has recently been developed and allows reliable histological diagnosis of gastric submucosal tumors (8).

A number of pathogenetic mechanisms for gastric cancer resembling submucosal tumor have been described, including marked lymphocyte infiltration in medullary adenocarcinoma (5), large amounts of mucin produced by mucinous adenocarcinoma (5), reduced thickness of the muscularis mucosa at the site of carcinogenesis (9) and adenocarcinoma arising from an ectopic pancreas in the gastric wall (10,11). In the present case, a substantial amount of fibrosis in the submucosal layer appeared to be the main cause of submucosal elevation. These factors may facilitate the predominance of submucosal growth and penetration of the muscularis mucosa in the early stage of carcinogenesis, contributing to the macroscopic appearance which is indistinguishable from submucosal tumor.

In view of the difficulty in diagnosis of gastric submucosal tumor, careful estimation of the possibility of gastric cancer, as well as the informed consent of the patient, is critically important for suspected cases of primary gastric cancer resembling submucosal tumor in order to decide the mode of treatment.

References