Primary Liposarcoma of the Stomach: a Case Report and a Review of the Literature

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Primary liposarcoma of the stomach is rare and only seven cases have been described in the English literature. Here we report the eighth case, which occurred in a 68-year-old woman who presented with repeated tarry stools and hematemesis. Endoscopic examination revealed a large ulcerated submucosal mass at the gastric angle. The patient was treated by total gastrectomy. On microscopic examination, the tumor showed the features of a well differentiated sclerosing liposarcoma. Immunohistochemically, many spindle to stellate tumor cells were diffusely positive for vimentin and CD34. Positivity for S-100 protein was found in the adipocytic component, including lipoblasts, in addition to some spindle-shaped tumor cells. On ultrastructural examination, the spindle to stellate cells had features characteristic of fibroblasts. No recurrence or metastasis was seen during 13 months. Liposarcoma of the stomach has to be considered in the differential diagnosis with other submucosal lesions, such as gastric lipoma and gastrointestinal stromal tumor.

Key words: liposarcoma – stomach – CD34 – immunohistochemistry – ultrastructure

INTRODUCTION

Liposarcoma is one of the most common soft tissue sarcomas in adults (1). It occurs most frequently in the extremities, retroperitoneum and trunk. Primary liposarcoma of the stomach is exceptionally rare and only seven cases have been reported (2–8). Here we describe an additional case of liposarcoma of the stomach, review the English literature and discuss the differential diagnosis. To our knowledge, there have been no previous immunohistochemical and ultrastructural studies of gastric liposarcomas.

CASE REPORT

A 68-year-old woman was admitted to the Shikoku Central Hospital because of hematemesis after epigastralgia lasting 1 week. She had sometimes noticed tarry stools since her first episode of hematemesis 1 year earlier. Gastric endoscopic examination revealed a large ulcerated submucosal mass at the gastric angle. Computed tomography examination revealed a well circumscribed tumor mass with soft-tissue density located in the posterior wall of the upper body and protruding into the gastric lumen (Fig. 1). The tumor did not show exophytic growth outside the stomach. The patient underwent total gastrectomy and is currently alive and well without recurrence or distant metastasis 13 months after surgery.
Figure 2. Macroscopic appearance of the present tumor, measuring 10.5 x 5.5 x 4 cm. It is a submucosal tumor with a large central ulcer.

Figure 3. Cut section of the tumor showing a well defined margin and whitish yellow, solid lesion with a transparent appearance.

Figure 4. The tumor was histologically composed of spindle to stellate-shaped cells with dense fibrils of collagen and nested mature adipocytes (H&E; original magnification x150).

PATHOLOGICAL FINDINGS

GROSS FINDINGS
A large sessile polypoid mass, measuring 10.5 x 5.5 x 4 cm, was observed in the posterior wall of the upper gastric body. It was an elastic-soft, well circumscribed submucosal tumor with a large central ulcer (Fig. 2). On the cut surface, a whitish yellow, solid lesion with a well defined margin and a transparent appearance was seen (Fig. 3). There were no areas of hemorrhage, necrosis or cyst formation.

MICROSCOPIC FINDINGS
The tumor was basically composed of relatively uniform spindle to stellate cells with dense fibrils of collagen and scattered or nested mature adipocytes (Fig. 4). The adipocytes varied in size and shape and had enlarged atypical, hyperchromatic nuclei. Uni- and multivacuolated lipoblasts were sparsely distributed throughout the lesion (Fig. 5a). In areas of relatively high cellularity, bipolar elongated spindle cells having palely eosinophilic cytoplasm were arranged in a loose fascicular pattern within a background of fine fibrillar collagen. Mitotic activity was generally very low, ranging from 0 to 1 mitosis per 10 high-power fields in these spindle-shaped tumor cells. The intercellular matrix displayed myxoid change in areas of lower cellularity. There were also a small number of pleomorphic tumor cells with abundant eosinophilic cytoplasm, large vesicular nuclei and prominent nucleoli. Blood vessels were inconspicuous and did not show a plexiform vascular pattern. Mast cells and lymphocytes were dispersed within the lesion.

IMMUNOHISTOCHEMICAL FINDINGS
Almost all tumor cells, including the spindle to stellate cells and adipocytes, showed intense immunoreactivity of vimentin. Immunoreactivity of S-100 protein was detected in the nuclei and cytoplasm of mature fat cells and also signet-ring and multivacuolated lipoblasts (Fig. 5a). Some spindle-shaped tumor cells were also positive for S-100 protein and these cells were mainly distributed in the vicinity of mature fat cells (Fig. 5a). Most of the spindle to stellate tumor cells displayed diffuse membrane reactivity for CD34 (Fig. 5b). The mature fat cells and lipoblasts were negative for CD34. The S-100-positive spindle-shaped cells were morphologically indistinguishable from the spindle to stellate cells stained for CD34. Immunoreactivity of desmin and α-smooth muscle actin was absent in the tumor cells.

ULTRASTRUCTURAL FINDINGS
Electron microscopic examination showed that the spindle to stellate tumor cells were separated by an abundant intercellular
collagen matrix. The cells had large indented nuclei with condensed chromatin along the nuclear membrane (Fig. 6). The cytoplasm contained a moderate amount of rough endoplasmic reticulum, mitochondria and a few Golgi apparatus. Some tumor cells had non-membrane-bearing intracytoplasmic electron-dense lipid droplets, a few pinocytotic vesicles and dense plaques along the cell membrane, which was covered by an incomplete basal lamina, features consistent with those of lipoblasts. Fat droplets were not identified in the cytoplasm of the former fibroblastic spindled component.

DISCUSSION

Only seven cases of liposarcoma of the stomach have been reported in the English literature (2–8). Clinical data for the eight patients, including ours, are summarized in Table 1. The patients comprised six men and two women, ranging in age from 15 to 86 years, with a mean of 58.1 years (median, 62.5 years). The clinical symptoms were generally those of space-occupying lesions of the stomach or abdominal cavity. Five patients presented with abdominal pain, four with hematemesis related to ulcer, three with nausea and two with epigastric mass.

Four tumors arose in the gastric antrum, two in the body and one in the fundus. Four tumors were located in the submucosal layer and two showed exophytic growth from the gastric wall. All the tumors except one (case 1) appeared grossly as well circumscribed masses, ranging from 5 to 30 cm (mean, 13.8 cm) in the greatest diameter. The two exophytic tumors were larger than the submucosal tumors. Except for case 1, the outcome of gastric liposarcomas appeared to be favorable. All six patients for whom the clinical outcome was described underwent subtotal or total gastrectomy and did not develop recurrence or metastasis.

Figure 5. (a) Multivacuolated lipoblasts and some spindle-shaped cells showing cytoplasmic and nuclear immunoreactivity of S-100 protein (ABC method, counterstaining with Methyl Green; original magnification ×400). (b) Most of spindle to stellate-shaped tumor cells demonstrating diffuse membranous immunoreactivity for CD34 (ABC method, counterstaining with Methyl Green; original magnification ×400).

Figure 6. The spindle-shaped tumor cells showing features characteristic of fibroblasts (transmission electron micrograph; original magnification ×3000). Bar = 2 μm.
Table 1. Liposarcoma of the stomach

<table>
<thead>
<tr>
<th>No.</th>
<th>Authors (year)</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Symptom</th>
<th>Treatment</th>
<th>Site</th>
<th>Size (cm)</th>
<th>Histological subtype/course</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Abrams and Turberville (2) (1941)</td>
<td>52</td>
<td>M</td>
<td>Epigastralgia, nausea, vomiting, LOW, epigastric mass</td>
<td>Laparotomic biopsy</td>
<td>Greater curvature</td>
<td>Large infiltrative mass occupied entire length of the stomach</td>
<td>NS/ metastasis; liver and gastrocolic omentum at laparotomy, DOD at 4 months</td>
</tr>
<tr>
<td>2</td>
<td>Hohef et al. (3) (1955)</td>
<td>77</td>
<td>M</td>
<td>Epigastric mass</td>
<td>Subtotal gastrectomy, radiation</td>
<td>Anterior wall of antrum, between mucosa and submucosa</td>
<td>15 x 8 x 6 (encapsulated)</td>
<td>NS/ NED at 8 months</td>
</tr>
<tr>
<td>3</td>
<td>Hawkins and Terrell (4) (1965)</td>
<td>86</td>
<td>M</td>
<td>Bloody stool, bloody vomiting, weakness</td>
<td>Subtotal gastrectomy</td>
<td>Posterior wall of fundus, submucosa</td>
<td>12 in greatest diameter (well circumscribed)</td>
<td>Myxoid liposarcoma/ NED at 36 months</td>
</tr>
<tr>
<td>4</td>
<td>Orita et al. (5) (1968)</td>
<td>42</td>
<td>M</td>
<td>Epigastralgia, abdominal fullness, diarrhea</td>
<td>Gastroctomy</td>
<td>Posterior wall of body, submucosa</td>
<td>1.2 x 1.0 x 1.0 (spherical in shape)</td>
<td>NS/ NED at 60 months</td>
</tr>
<tr>
<td>5</td>
<td>Shokouh-Amiri et al. (6) (1986)</td>
<td>15</td>
<td>M</td>
<td>Abdominal pain, nausea, anorexia</td>
<td>Subtotal gastrectomy</td>
<td>Antrectum exophytic growth</td>
<td>30 x 20 (5 kg) (sharply demarcated)</td>
<td>Myxoid liposarcoma/ NED at 8 months</td>
</tr>
<tr>
<td>6</td>
<td>Laky and Stoica (7) (1986)</td>
<td>67</td>
<td>F</td>
<td>Dyspepsia, abdominal pain, hematemesis</td>
<td>Subtotal gastrectomy</td>
<td>Dorsal wall of antrum, submucosa</td>
<td>5 x 2 x 1.5 (relatively well delineated)</td>
<td>NS/ NED at 12 months</td>
</tr>
<tr>
<td>7</td>
<td>Ferrozzi et al. (8) (1993)</td>
<td>58</td>
<td>M</td>
<td>Abdominal fullness, discomfort</td>
<td>Resection</td>
<td>Antrectum exophytic growth</td>
<td>25 x 20 x 8 (well circumscribed)</td>
<td>Pleomorphic liposarcoma/ NS</td>
</tr>
<tr>
<td>8</td>
<td>Present case</td>
<td>68</td>
<td>F</td>
<td>Abdominal pain, hematemesis</td>
<td>Total gastrectomy</td>
<td>Posterior wall of body, submucosa</td>
<td>10.5 x 5.5 x 4 (well circumscribed)</td>
<td>Well differentiated sclerosing liposarcoma/ NED at 12 months</td>
</tr>
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LOW, loss of weight; DOD, dead of disease; NED, no evidence of disease; NS, not stated.

Liposarcoma is histologically defined as a tumor composed of lipoblasts (1). Liposarcomas are classified into five histological subtypes: well differentiated, myxoid, round cell, dedifferentiated and pleomorphic. The rates of metastasis and mortality for well differentiated and myxoid liposarcomas are much lower than those of the round cell, dedifferentiated and pleomorphic types. The present tumor was of the well differentiated sclerosing type and was made up of various-sized adipocytes admixed with lipoblasts and non-fat-storing spindle to stellate cells in a fibromyxoid background. Two of the previous tumors (cases 3 and 5) were described as myxoid liposarcoma based on the presence of lipoblasts with a rich myxoid matrix and a plexiform vascular pattern. The subtype of liposarcoma was not referred to in three tumors (cases 2, 4 and 6), which were merely described as liposarcomas with pleomorphic tumor cells having various-sized vacuoles in the cytoplasm. In case 7, no histological figures were provided, except for a computed tomography image of pleomorphic liposarcoma.

As Stout (9) has commented, the first report of gastric liposarcoma (case 1) was doubtful because the clinicopathological features were completely different from the other seven cases. The primary tumor was a large infiltrative mass occupying the entire length of the greater curvature of the stomach and metastatic tumors were found in the omentum and liver. Biopsy specimens taken from the lymph nodes revealed metastasis of signet ring-like cells with centrally placed large nuclei, suggesting gastric carcinoma. However, the authors concluded that these cells were fat cells on the basis of staining with Sudan III in the vacuolated cells.

Our ultrastructural examination revealed that the present tumor was composed of a mixture of two cell types: non-fat-storing mesenchymal cells and lipoblasts, in keeping with the results of the previous electron microscopic study (10). These non-fat-storing spindle to stellate tumor cells showed diffuse membrane immunoreactivity of CD34, whereas the mature fat cells and lipoblasts were negative for this antigen. CD34 is a 115 kDa transmembrane glycoprotein, that was initially identified on the surface of hematopoietic progenitor cells among myeloid stem cells (11,12). Immunoreactivity of this antigen has been demonstrated in normal and neoplastic vascular endothelium (13,14), dendritic cells of the dennis and around adnexal structures (15), endoneurial cells (16) and in a variety of unusual mesenchymal tumors of unknown etiology, such as Kaposi's sarcoma (17,18), dermatofibrosarcoma protuberans (19,20), epithelioid sarcoma (21,22), gastrointestinal stromal tumor (23,24) and solitary fibrous tumor (25,26). Suster and Fisher (27) reported that a significant population of CD34-positive dendritic spindle cells admixed with lipomatous elements were present in both benign lipomatous tumors and well differentiated liposarcomas. The CD34 positivity observed in the atypical spindle to stellate cells of this tumor seems to suggest that such cells are more closely related to interstitial fibroblastic cells, similar to those described previously in solitary fibrous tumors (25,26), giant cell fibroblastomas (28) and giant cell angiofibromas of the orbit (29), than to lipoblasts.

Some clinical symptoms and radiological features of this tumor may overlap with those of other neoplasms which occur as submucosal tumors. Lipoma, a benign counterpart of liposarco-
ma, is a relatively rare gastric tumor. Three-quarters of all gastric lipomas occur in the antrum; most of them are located in the submucosa, the remainder being usually subserosal (30). Although gastric lipomas tend to be relatively small, a large lesion measuring 10 cm in the greatest diameter has recently been described as a well circumscribed sessile polyp arising in the submucosa of the antrum (31). Gastric lipomas usually appear soft and yellowish on the cut surface and consist of mature fat tissue divided into lobules. The absence of cellular atypia and lipoblasts can help to distinguish them from liposarcomas.

Gastrointestinal stromal tumors are the most common primary non-epithelial neoplasms of the stomach, except for lymphomas. About 60% of stromal tumors occur in the submucosa and grow toward the lumen (32). The clinical symptoms and tumor site in the stomach are similar to those of gastric liposarcomas. Grossly, gastrointestinal stromal tumors are different from the present tumor, the former being well circumscribed and having a smooth, lobulated or whorled-silk appearance with focal hemorrhage and cystic degeneration (32,33). Recently, CD34 immunoreactivity has been found to be expressed in the cells of many gastrointestinal stromal tumors (23,24). CD34 positivity is also present in undifferentiated or poorly differentiated gastrointestinal stromal tumors, i.e. those which do not show smooth muscle or neural differentiation, as demonstrated immunohistochemically. Common CD34 reactivity might imply some histogenetic connection of the constituent cells between gastric liposarcoma and gastrointestinal stromal tumor. However, gastrointestinal stromal tumor, being more cellular than gastric liposarcoma, is characterized by proliferation of spindle cells with elongated nuclei and eosinophilic cytoplasm, most often arranged in interlacing broad fascicles and never containing mature adipose tissue or lipoblasts.

References