Myoepithelial carcinoma of the stomach: A diagnostic pitfall

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INTRODUCTION

Myoepithelioma/myoepithelial carcinomas are not commonly found in soft tissues and are especially rare at visceral sites. This report describes a case of a rare low-grade myoepithelial carcinoma of the stomach. A 61-year-old female patient presented with postprandial abdominal discomfort. Endoscopy revealed a 1.1 cm submucosal lesion. Local excision was performed after malignancy was confirmed by biopsy. The resection margin is free of tumor and she received no adjuvant therapy. The tumor was characterized by multinodular growth with biphasic epithelioid and spindle components. Infiltrative margin and nuclear pleomorphism are seen. Tumor cells were positive for both epithelial and myoepithelial markers. Evidence of epithelial differentiation was confirmed by electron microscopy. No EWSR1 rearrangement was detected. The final diagnosis was low-grade myoepithelial gastric carcinoma. The patient is currently well, and no evidence of recurrence or metastasis was found after ten-month of follow-up. Myoepithelial carcinoma should be considered in the differential diagnosis of a biphasic gastric tumor.

Key words: Myoepithelioma; Myoepithelial carcinoma; Stomach

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placed into the same category in the recent edition of the World Health Organization classification of soft tissue tumors[6-10]. “Myoepithelial tumor” is an uncommon entity and refers to a tumor exhibiting immunohistochemical or ultrastructural evidence of myoepithelial differentiation. In addition to salivary glands, myoepithelial tumors have been reported to arise from cutaneous or soft tissues[2-5]. However, myoepithelial tumors of visceral organs are especially rare; very few case reports of such tumors have been published with most (8 of 11) describing tumors of pulmonary origin[6-10]. The present report describes a second case of a myoepithelial tumor of the stomach and the immunohistochemical, ultrastructural, and molecular findings for this tumor.

CASE REPORT

A 61-year-old female with a history of hypertension and grade A gastroesophageal reflux disease presented to our hospital with abdominal pain of one year duration. The abdominal pain was intermittent but gradually increased in intensity. The peak of her discomfort was usually observed 30-60 min after a meal. She denied nausea, vomiting, hematemesis, hematochezia, constipation, diarrhea, or weight loss. She also denied a family history of cancer or hereditary diseases. Panendoscopy revealed a 1.1 cm submucosal lesion at the posterior wall of the gastric high body (Figure 1A). Biopsy was performed, and the pathology report was positive for a malignant tumor. Computed tomography revealed a localized lesion without regional lymph node enlargement or distant metastasis (Figure 1B). Local excision was performed. Grossly, the mucosa overlying the lesion appeared ulcerated. Upon excision, the submucosal lesion appeared well-circumscribed, grayish-white, and elastic. The size of the tumor was 1.3 cm × 1.1 cm × 0.7 cm (Figure 1C and D).

Microscopically, the tumor was seen to be delineated by a fibrous capsule, and occasional lymphocytic cuffing was present (Figure 2A). Some satellite nodules were seen adjacent to the main tumor. A biphasic pattern of cells composed of epithelioid and oval to spindle cells embedded in myxoid to fibrous stroma was observed (Figure 2B). The tumor cells displayed pleomorphism, mitosis (1-2/10 HPFs), and visible nucleoli (Figure 2D). Some cell junctions were also present (Figure 2C). Ultrastructurally, the tumor cells appeared epithelioid- to spindle-shaped, with irregular nuclei and abundant cytoplasm; the latter contained abundant rough endoplasmic reticulum, intermediate filaments, and small aggregates of dense bodies. Some cell junctions were also present (Figure 3D). For detection of EWSR1 gene rearrangement, the break-apart FISH (fluorescence in situ hybridization) assay was performed on formalin-fixed, paraffin-embedded tissue sections of 4-μm thickness according to the instructions of the manufacturer. No break-apart signals were detected (Figure 3E). The final diagnosis was low-grade myoepithelial carcinoma based on the presence of mild pleomorphism, considerable mitotic activity, and the invasive nature of the borders.

No adjuvant chemotherapy was administered. The patient was alive without disease after 10 mo of follow-up.

DISCUSSION

This report describes a rare case of a low-grade myoepithelial carcinoma of the stomach. Only one other comparable case, describing a “parachordoma of the gastric serosa”, has been reported in the literature (Table 1). The differential diagnosis of a myoepithelial tumor is challenging and dependent on the location of the tumor. Differential diagnoses of gastric biphasic tumors include carcinosarcoma, synovial sarcoma, gastrointestinal stromal tumor, mesothelioma, subtypes of neurogenic tumor (reticular schwannoma or epithelioid malignant peripheral nerve sheath tumor), and gastroblastoma. Rendering a diagnosis of carcinosarcoma requires identification of marked pleomorphism of both the carcinoma and the sarcoma components. Although synovial sarcomas are generally positive for cytokeratin and occasionally positive for S100 protein, the most sensitive marker for these sarcomas is TLE1[11,12]. Neither CD117 nor DOG-1 expression supports a diagnosis of gastrointestinal stromal tumor. The absence of calretinin expression by a tumor disfavors a mesothelial origin. Although lymphocytic cuffing was observed for the tumor described in the present report, the absence of Antoni structures and of cytokeratin expression disfavors a diagnosis of schwannoma. The cytological features of the tumor exclude a diagnosis of epithelioid malignant peripheral nerve sheath tumor. Gastroblastoma, a recently identified entity described in only five reports

(Dako, 1:200), epithelial membrane antigen (Leica, 1:100), synaptophysin (Leica, 1:100), DOG1 (Leica, 1:100), CD10 (spotty; Novocastra, 1:50) and melan-A (weak; Leica, 1:50) but were negative for CD117 (Genemed, 1:300), HMB-45 (Leica, 1:100), calretinin (Leica, 1:100), CD34 (Leica, 1:100), glial fibrillary acidic protein (GFAP) (Dako, 1:100), CD56 (Leica, 1:50), desmin (Dako, 1:100), or actin-M851 (Leica, 1:100) (Figure 3A-C). Ultrastructurally, the tumor cells appeared epithelioid- to spindle-shaped, with irregular nuclei and abundant cytoplasm; the latter contained abundant rough endoplasmic reticulum, intermediate filaments, and small aggregates of dense bodies. Some cell junctions were also present (Figure 3D). For detection of EWSR1 gene rearrangement, the break-apart FISH (fluorescence in situ hybridization) assay was performed on formalin-fixed, paraffin-embedded tissue sections of 4-μm thickness according to the instructions of the manufacturer. No break-apart signals were detected (Figure 3E). The final diagnosis was low-grade myoepithelial carcinoma based on the presence of mild pleomorphism, considerable mitotic activity, and the invasive nature of the borders.

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to date, is also a biphasic tumor of the stomach[13-15]. Certain features of a gastroblastoma overlap with those of a myoepithelial neoplasm, such as a variable mixture of epithelial and mesenchymal components, a bland-

Figure 1  Endoscopy reveals a polypoid mass (arrow) (A); an isolated mural lesion was seen in computed tomography scan (arrow) (B); and grossly, a polypoid submucosal tumor is noted (C, D).

Figure 2  A submucosal biphasic tumor with lymphoid cuffing noted (Magnification × 40) (A); the tumor involves mucosa (Magnification × 100) (B); some infiltrative nests penetrate through the fibrous capsule (Magnification × 40) (C); and the epithelial cells bearing low-grade pleomorphism and visible nucleoli are arranged in reticular pattern (Magnification × 400) (D).

Tseng CE et al. Low-grade gastric myoepithelial carcinoma
In the limited number of publications describing gastroblastomas, positivity for CD10 and CD56 of unknown significance was reported; in contrast, the tumor described in the present case was negative for CD56 expression and positivity for CD10 was spotty. Interestingly, the duodenoblastoma described by Poizat et al. was found to be negative for both markers. Forty-five percent of soft tissue myoepithelioma and myoepithelial carcinomas, including four pulmonary tumors, in a series were found to display EWSR1 rearrangement. Translocation of the gene with such known fusion partners as PBX1, ZNF444, and POU5F1 has been previously observed. It was therefore considered important to examine the possibility that the tumor described in the present report exhibited EWSR1 rearrangement; however, no "break-apart" signal was observed. Lack of EWSR1 rearrangement was also reported for the gastric parachordoma described by Tseng CE et al. Low-grade gastric myoepithelial carcinoma.

Figure 3 The tumor cells are diffusely positive for S-100 protein (Magnification × 40) (A); Vimentin is expressed by both components (Magnification × 40) (B); the tumor cells express AE1/AE3 (Magnification × 200) (C); and presence of cell junctions (arrow) indicates the epithelial differentiation (D); No break-apart signals observed by FISH (E).
hybridization is performed to detect CK+2, EMA+, S100+, VIM+, BU-, CD117-, CD10-.

Immunohistochemical findings

Table 1  Findings for currently described gastric myoepithelial tumors

| Patient | Age (yr) | Gender | Tumor size (cm) | Diagnosis | Follow-up finding (mo) | Immunohistochemical findings |
|---------|----------|--------|-----------------|-----------|------------------------|-------------------------------|
| Spivach et al[9], 2007 | 65 | Female | 5.5 | Parachordoma | NED, 36 | CK+, EMA+, S100+, VIM+, BLU, CD117, CD10, GFAP, calponin, calretinin, GFAP, AE1/AE3+, CK+, EMA+, S100+, VIM+, synaptophysin+, DOG1, desmin, actin M851, HMB-45, melan-A(weak), CD117, CD10(splotty), GFAP, calretinin, CD56 |
| The present case | 61 | Female | 1.3 | Low grade myoepithelial carcinoma | NED, 10 | CK+2, EMA+, S100+, VIM+, BLU, CD117, CD10, GFAP, calponin, calretinin, P63 AE1/AE3+, CK+, EMA+, S100+, VIM+, synaptophysin+, DOG1, desmin, actin M851, HMB-45, melan-A(weak), CD117, CD10(splotty), GFAP, calretinin, CD56 |

*: Positive finding; -: Negative finding. NED: No evidence of disease; CK: Cytokeratin; EMA: Epithelial membrane antigen; VIM: Vimentin; GFAP: Glial fibrillary acidic protein.

Spivach et al[9]. The recurrent cytogenetic changes present in gastric myoepithelial tumors remain to be characterized.

Discrimination between benign myoepithelioma and malignant myoepithelial carcinoma is essential. As compared with necrosis, mitotic index, and infiltrative pattern, the most reliable parameter for discrimination is cytological atypia[3]. The presence of non-negligible cytological pleomorphism and an infiltrative growth pattern, despite the small tumor size, prompted the diagnosis of low-grade myoepithelial carcinoma rather than myoepithelioma. Age of onset appears to influence prognosis for patients with myoepithelial carcinoma in that this cancer is more prevalent and aggressive in children[10]. Genetic events are proposed to account for the observation that EWSR1 rearrangement, which is more common in children and young adults with these tumors, portends more aggressive tumor behavior[10]. These findings support the detection of EWSR1 rearrangement in the diagnosis of these tumors and as an assessment of prognosis for patients with these tumors.

In conclusion, a case of a rare low-grade myoepithelial carcinoma is reported and the morphological, immunohistochemical, ultrastructural, and molecular features of this tumor are described. The rarity, diverse morphologies, and variable immunoprofiles of visceral myoepithelial tumors are potential causes for diagnostic pitfalls. Multidisciplinary approaches are therefore required for precise diagnosis of these tumors. Myoepithelial tumor should be considered in the differential diagnosis of gastric biphasic tumors.

**Diagnosis**

Pathological diagnosis

A biphasic tumor composed of epithelioid and spindle cells is noted. Both CK and S100 protein are positive. No EWSR1 rearrangement is seen. The diagnosis is a low-grade myoepithelial carcinoma.

Treatment

The patient received local excision without adjuvant therapy.

Related reports

A case of gastric parachordoma, which is classified in the spectrum of myoepithelial tumor, has been reported.

**Term explanation**

Dual-color fluoresence in situ hybridization is performed to detect EWSR1 rearrangement. Positive cases were defined as those having split red and green signals separated by a distance at least twice the signal diameter in at least 20 of 100 counted tumor cells.

**Experiences and lessons**

As for gastric tumors, myoepithelial tumor is not listed in the differential diagnoses due to lack of reports in the literature. The authors exclude other possible mimickers cautiously and render the diagnosis of low grade myoepithelial carcinoma.

**Peer-review**

This case report illustrates a rare low-grade myoepithelial carcinoma of stomach and its morphological, immunohistochemical and molecular characteristics.

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