CASE REPORT

Gastric epithelioid gastrointestinal stromal tumor with signet ring-like cell features: A case report

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ABSTRACT

A gastrointestinal stromal tumor (GIST) with signet ring cell features is a rare variant of epithelioid GIST. The current case demonstrates a 35-year-old woman with a 22.0 cm stomach mass. Tomography-guided core biopsy of the mass showed an undifferentiated tumor with abundant signet ring cells in a myxoid background. A preliminary diagnosis of adenocarcinoma was considered based on histomorphologic features; however, by immunohistochemistry studies the tumor cells were negative for cytokeratins and intensely positive for CD117/c-kit and CD34. Therefore a diagnosis of GIST with signet ring-like cells features was rendered. Making a diagnosis in a small biopsy specimen is always challenging, due to the variable histomorphological features of these tumors.

Key Words: Gastrointestinal stromal tumor, Signet ring cell features, Stomach mesenchymal tumor

1. INTRODUCTION

GISTs are mesenchymal tumors derived from interstitial Cajal cells. These tumors occur anywhere in the digestive tract, being the stomach the most frequent location (54%). They have an uncertain behavior; however, 25% of gastric GISTs are malignant. GISTs appear at any age with a peak of incidence in the sixth decade of life.[1] Microscopically, most GISTs are well-defined lesions composed of sheets or fascicles of monotonous spindle or epithelioid cells.[2]

Our case report shows a rare case of gastric GIST with epithelioid morphology and signet ring-like cell features. The differential diagnoses of a gastric mass with signet ring or clear cell features are wide. Whether a GIST is not suspected, these lesions may be easily misinterpreted with more aggressive entities such as an adenocarcinoma, melanoma, or gastric schwannoma.

2. CASE PRESENTATION

A 35-year-old female presented with approximately four weeks history of diffuse abdominal pain associated with weight loss, satiety, and one episode of hematemesis. Her past clinical and surgical history were noncontributory. On physical examination, a firm and painful mass localized in the left hemiabdomen was identified. An abdominal computerized axial tomography (CT) showed the greater curvature of the stomach opacified by a hypodense exophytic mass (22.8 cm $\times$ 19.6 cm $\times$ 18.8 cm) with areas of necrosis. The mass displaced small intestine, left kidney, and spleen. Radiologically was challenging to determine its origin. Endoscopic study showed an extrinsic compression of the gastric mucosa and biopsy was unsuccessful due to the patient's

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intolerance to the procedure. Therefore a tomography (CT) guided biopsy was performed.

The biopsy demonstrated a poorly differentiated tumor (see Figure 1), composed predominantly of cells with abundant clear cytoplasm and round central nuclei with dispersed chromatin, and inconspicuous nucleoli. Additionally, multiple tumor cells showed a "signet ring" appearance (see Figure 2), and a subset of the tumor cells also demonstrate epithelioid features (see Figure 3) arranged in sheets and ill-defined clusters on a myxoid background. The lesion showed <5 mitoses in 20 HPF (5 mm^2) without necrosis or marked cellular atypia.

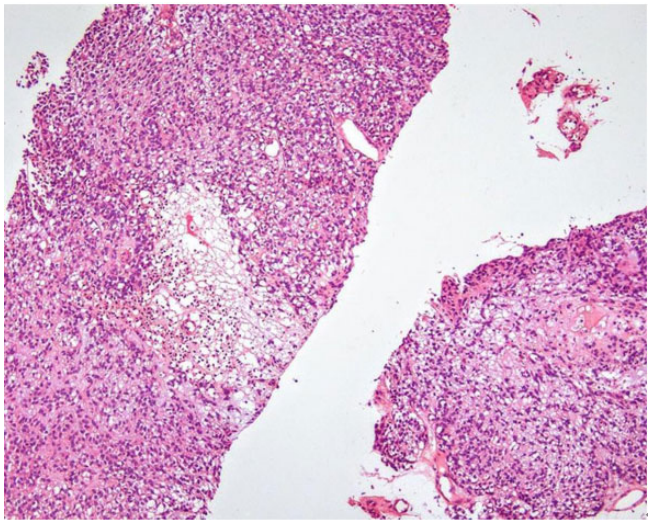

Figure 1. Histological section shows core biopsies composed by a poorly differentiated tumor. H&E 4x

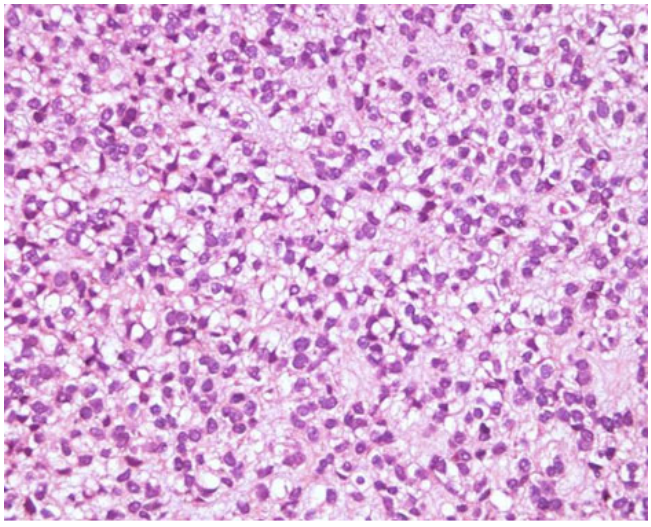

Figure 2. The tumor shows signet ring-like cells features in a myxoid background. H&E 20x

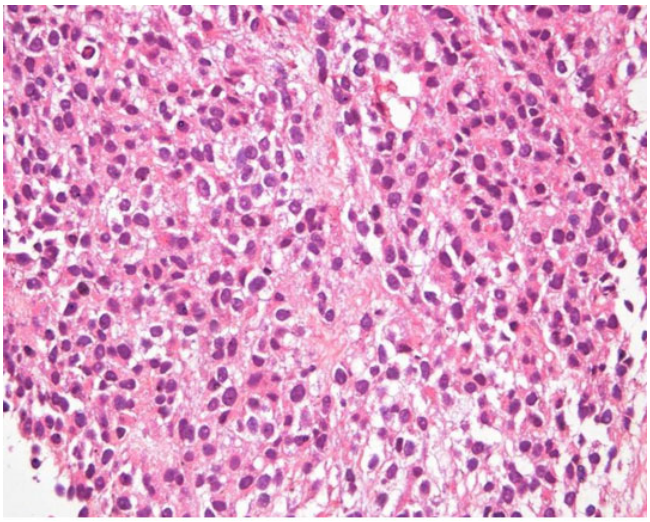

Figure 3. The tumor focally shows epithelioid cells. H&E 20x

Additional immunohistochemical studies were performed. The tumor cells were negative for cytokeratin 7, cytokeratin 20, CD45, Melan-A, Chromogranin A and CD20; while they were positive for CD117/c-kit (see Figure 4A), CD34 (see Figure 4B), and vimentin. Ki-67 highlights a proliferation index of less than 20%.

Based on the immunostaining profile and the clinical and histopathological features, the diagnosis of a low-grade (G1) gastrointestinal stromal tumor, epithelioid type with signet ring-like cells features was rendered. Unfortunately, since the patient was transferred to an outside institution to receive treatment, we could not retrieve the cell block to perform molecular studies. According the guidelines for risk assessment of primary gastrointestinal stromal tumor, our case with a gastric mass measuring 22.8 cm with <5 mitoses in 20 HPF (5 mm^2) shows a moderate risk of progressive disease (10%).

3. Discussion

GIST has two well-known histologic variants; the spindle and the epithelioid cell types. Most of these tumors are spindle cell type. The epithelioid cell type comprises 20% to 30% of all cases.[3] Mixed, pleomorphic and other rare variants have also been reported, such as GIST with signet ring-like cells, a feature which has been described in spindle and epithelioid cell variants.[5,6] As these variant features do not affect the prognosis they should be considered as a histologic nuance of these types of GISTs and potential diagnostic pitfall, but not as a separate entity.

Epithelioid GISTs are composed of round cells with clear or eosinophilic cytoplasm, with round nuclei and fine chromatin; they can also present prominent intracytoplasmic vac-

uoles that give the appearance of signet ring cells, although it is a rare and focal feature.[2] Myxoid stroma is also a finding in epithelioid GISTs.[3] These intracytoplasmic, perinuclear vacuoles have been studied with electron microscopy; some authors characterize them as true lumens or lipid-like structures,[4] and others have observed that these vacuoles are empty and uncoated, perhaps due to artifacts from the paraffin block preparation.[2] The epithelioid type is not more aggressive than other types of GIST. The malignant potential of these tumors depends on the mitotic activity, their location and size.[3]

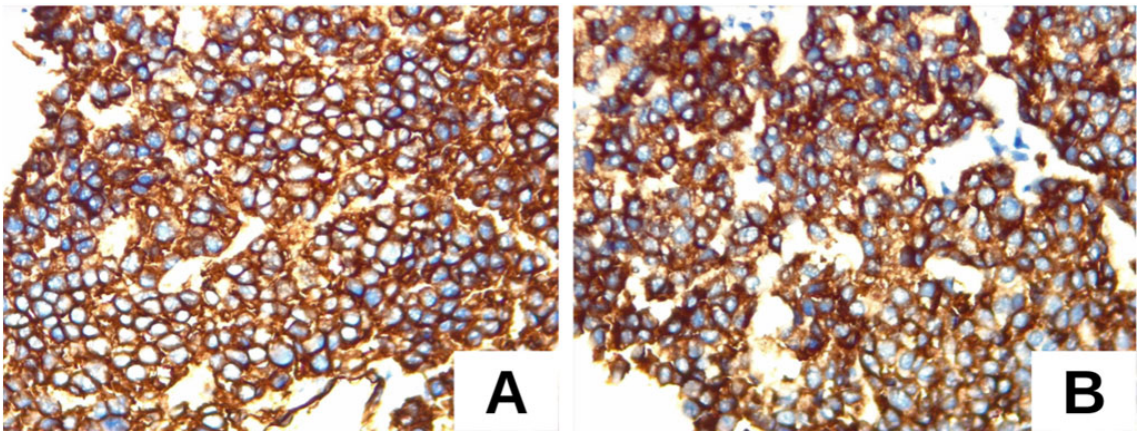

Figure 4. Immunohistochemical staining shows tumor cells strong and diffusely positive for CD117 (C-kit) (A) and CD34 (B)

The immunohistochemical profile of these tumors shows intense positivity for vimentin, CD117 and DOG1, while variable staining pattern for CD34, S100 and actin (.[6] Unfortunately, since the patient was transfered to an outside institution we could not retrieve the cell block to perform molecular studies in our laboratory.

The differential diagnoses of gastric epithelioid GISTs with signet ring-like cell features includes gastric adenocarcinoma with signet ring cells, melanoma, metastatic adenocarcinoma, gastric schwannoma with signet ring cells, and basically any tumor with clear cell features or mucin production.[5]

Adenocarcinoma with signet ring cells is a good differential diagnosis in our case. Morphologically it is almost impossible to differentiate them, especially given the small size of our biopsy. In this scenario what may help to distinguish them is that in adenocarcinoma the mitotic rate is high and shows more nuclear pleomorphism.[7] However, stains for cytokeratins and mucicarmine or alcian blue are essential.

It is well known that melanomas have very variable cytomorphologic features; cases of melanomas with signet ring cell appearance located in the stomach have been described. Signet ring cell melanomas represent 0.5% of melanomas. By definition, this type of melanoma shows a signet ring cell component that exceeds 50% of the tumor.[8] In these cases, the presence of melanin pigment in association with the positivity for melanocytic markers and the lack of mucin staining help reach the correct diagnosis.[7]

Schwannomas in the gastrointestinal tract are rare benign tumors, with the remote potential for malignant degeneration. Histologically, gastric schwannoma is similar to its soft tissue counterpart; however, there are reported cases where these tumors acquire signet ring cell morphology.[9] The presence of a lymphoid cuff surrounding the tumor would hint towards the correct diagnosis, but the only way to confirm this is with immunostains showing positivity for S100 and negativity for CD117 and cytokeratins.

Cases of adenocarcinoma-GIST collision tumors in the stomach have also been described,[10] causing even more diagnostic problems.

All mentioned differential diagnoses need to be considered when evaluating a gastric biopsy with signet ring cell morphology in order to request the diagnostic markers appropriately since the prognosis and treatment vary among them.

4. Summary

We report a rarely documented case of a gastric epithelioid gastrointestinal stromal tumor with signet ring-like cell features. This histologic type is a diagnostic pitfall when evaluating gastric biopsies because of the full spectrum of tumors that can arise in the gastrointestinal tract with signet ring cell morphology.

Conflicts of Interest Disclosure

We declare that we have no conflict interests.

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