**Linitis Plastica-type Gastric Adenocarcinoma Diagnosed by Endoscopic Ultrasound-guided Fine Needle Aspiration**

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**Abstract:** The diagnosis of linitis plastica-type adenocarcinomas of the stomach has traditionally been made by brush cytology and mucosal biopsy. These techniques may yield false-negative results due to the often submucosal location of these lesions. We present a case of a 46-year-old female that presented with epigastric abdominal pain and loss of appetite. Computed tomography imaging of her abdomen revealed diffuse thickening of a portion of the gastric wall. Subsequent endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) of the stomach yielded abundant single, discohesive malignant cells suspicious for lymphoma versus poorly differentiated adenocarcinoma. Special stains and immunohistochemical stains confirmed the diagnosis of poorly differentiated adenocarcinoma of signet ring-cell type. With its ability to sample deep submucosal lesions, EUS-FNA is an appropriate technique for establishing this diagnosis and guiding patient treatment.

**Introduction:** Linitis plastica refers to the diffuse thickening of a portion of the wall of the gastrointestinal tract as demonstrated by imaging studies or gross examination of resection specimens. While the term may be used in the general context of thickening due to any etiology, many restrict the term to the infiltration of a poorly differentiated adenocarcinoma, frequently with signet ring cell features. Linitis plastica lesions involving the stomach, jejunum, rectum, and entire gastrointestinal tract have been documented in the medical literature. The relatively recent utilization of sampling techniques such as endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) has proven effective in diagnosing lesions which may otherwise evade superficial mucosal sampling.

**Case Report:** A 46-year-old female presented to her primary care physician complaining of early satiety and epigastric pain. She stated that the epigastric pain had begun approximately six months earlier while on a trip to Mexico and that the pain had progressed and now radiated to her back. Since the onset of her symptoms, she had suffered an unintentional weight loss of 10 pounds. The patient had noted no change in bowel habits, nor had she noticed blood in her stool. A computed tomography scan of her abdomen showed gastric wall thickening. She was also noted at that time to be *Helicobacter pylori*-positive, and antimicrobial therapy was initiated to eradicate the bacterium. She was subsequently referred to a gastroenterologist for endoscopy. At the time of endoscopy, she was noted to have diffuse thickening of a portion of the gastric wall on the greater curvature. The endoscopic impression was that of a linitis plastica-type carcinoma versus lymphoma. EUS-FNA of the lesion was performed and a mucosal biopsy was also performed.

**Cytoplogic Findings:** Examination of the aspiration specimen showed abundant small, single, discohesive cells with high nuclear/cytoplasmic ratios and unevenly distributed, clumped chromatin (Figures 1 and 2). Rare cells exhibited nucleioli. Multinucleation and micrometastases were seen. Occasional cells contained eccentric nuclei with vacuolated cytoplasm, and they were rarely, nuclei eccentrically displaced by a single prominent cytoplasmic vacuole were seen (Figure 3). The findings were felt to be diagnostic for malignancy with the differential diagnosis including a lymphoproliferative disorder versus poorly differentiated adenocarcinoma.

**Histologic Findings:** Hematoxylin and eosin-stained histologic sections of the gastric biopsy performed at the time of endoscopy showed gastric mucosa with an infiltrate of chronic inflammatory cells in the lamina propria, indicating chronic gastritis. No evidence of an epithelial neoplasm was identified despite an extensive search of the tissue for infiltrates of single malignant cells like those seen in the aspiration specimen. No active gastritis or intestinal metaplasia were identified.

**Special Stains and Immunohistochemical Stains:** Given the initial differential diagnosis of the aspiration sample as lymphoma versus poorly differentiated adenocarcinoma, immunohistochemical stains including low molecular-weight cytokeratin and CD45 were performed. The neoplastic cells showed strong cytoplasmic staining with low molecular-weight cytokeratin (Figure 4), but they were uniformly negative for CD45, indicating epithelial rather than hematopoietic differentiation. Based upon the bubbly cytoplasm and the well-formed cytoplasmic vacuoles in rare neoplastic cells, a mucoxyenic stain was performed. Mucin production by the tumor cells was conclusively demonstrated (Figure 5), establishing the diagnosis of poorly differentiated adenocarcinoma of the stomach with signet ring-cell features. A Leung stain demonstrated no *H. pylori*-like microorganisms in the biopsy specimen.

**Discussion:** Linitis plastica of the stomach and rectum secondary to poorly differentiated adenocarcinoma has been well-defined historically in the medical literature, but appropriate diagnostic sampling may be problematic. Mucosal biopsy and brushings alone have been reported to have a false-negative rate approaching 38% for linitis plastica-type lesions of the stomach. In addition to conventional brush cytology of superficial lesions, other cytoplogic sampling techniques have been used to sample deeper gastrointestinal lesions including percutaneous aspiration/biopsy using computed tomography or ultrasound guidance and, as in the current case, EUS-FNA. The efficacy of EUS-FNA for diagnosing gastric lesions was investigated by Vander Noot et al in a series of 68 cases over a 30-month period. The authors found that EUS-FNA had a sensitivity of 88% in the diagnosis of gastrointestinal lesions. Additionally, in a smaller series of 10 cases, Arantes et al found that EUS-FNA had a sensitivity of 80% for submucosal tumors of the gastrointestinal tract.

In cytoplogic samples, the cells of poorly differentiated gastric adenocarcinoma are discohesive, generally have high nuclear/cytoplasmic ratios, and may manifest only rare classic signet ring forms, widening the morphologic differential diagnosis to include lymphoma. The differential diagnosis of poorly differentiated, diffusely infiltrating adenocarcinomas involving the stomach must include metastasis to the stomach from a primary adenocarcinoma at a separate site. Reports in the medical literature have documented metastatic lobular carcinoma of the breast and metastatic signet ring cell adenocarcinomas of the colon and rectum as causing a linitis plastica-like picture in the stomach. Infectious causes of a linitis plastica-like gastric wall thickening on imaging studies have also been reported in association with tuberculosis and cytomegalovirus infection.