Case Report



Unusual Presentation of Metastatic Diffuse Gastric Carcinoma - Report of An Interesting Case with Literature Review

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Abstract:

Diffuse gastric adenocarcinoma or "linitis plastica" is characterized by a thickened and rigid stomach wall due to the diffuse infiltration of signet ring cells into the lower parts of the mucosa and submucosa of the stomach. This type of cancer is known to commonly metastasize to the liver, lungs, and ovaries, and metastasis to the gallbladder is extremely rare. We now report a case of a 79-year-old Caucasian female with diffuse gastric adenocarcinoma that metastasized to the gallbladder. The patient presented with symptoms mimicking acute cholecystitis. Histological analysis of the cholecystectomy specimen showed signet ring cells in the submucosa of the gallbladder wall. Further workup, which included esophagogastroduodenoscopy, revealed linitis plastica. This is the first case of gallbladder metastasis from diffuse gastric carcinoma reported in the United States.

Keywords: diffuse gastric adenocarcinoma, metastasis, gallbladder, acute cholecystitis

Introduction

Diffuse gastric adenocarcinoma, sometimes referred to as "linitis plastica", is cancer of the stomach that is not associated with Helicobacter pylori. Its name, linitis plastica or "leather-bottle stomach", refers to the thickened and rigid stomach wall, which is due to the diffuse infiltration of signet ring cells into the lower parts of the mucosa and the upper layers of the submucosa of the stomach. Because of the thickening of the stomach, which interferes with its peristalsis, patients may present with symptoms ranging in intensity from a vague sense of postprandial fullness to a severe, steady pain, diarrhea, weight loss, cachexia, and vomiting [1]. It usually presents in an advanced stage and carries a poor prognosis [2]. Diffuse gastric adenocarcinoma most commonly metastasizes to the liver, lungs or ovaries. Only a few studies in Asia report metastasis to the gallbladder, and it has not been previously reported in the United States.

Case report

Clinical History and Presentation

A 79-year-old Caucasian female presented to the Emergency Department complaining of an acute onset of right upper quadrant pain. The pain was characterized as sharp, radiating to her back, and was associated with nausea. The patient had an episode of the same symptoms one month prior to presentation, which resolved on its own. Because her presentation was typical for acute cholecystitis, the patient underwent a right upper quadrant ultrasound as part of the initial workup for her pain. The ultrasound revealed a thickened gallbladder wall but no stones. The patient was taken to the operating room with a presumed diagnosis of acute cholecystitis, but intraoperatively, we discovered a hard mass in the gallbladder infundibulum with multiple enlarged lymph nodes. We performed biopsies of the perigastric lymph nodes and gallbladder, and intraoperative frozen sections revealed underlying malignancy.

A CT scan was done post-operatively after we suspected underlying malignancy, and it revealed a thickened stomach wall with air in the midline, and multiple enlarged nodules between the liver and stomach, suspicious for gastric malignancy with metastasis (Figure 1). In order to determine whether the adenocarcinoma was of gastric origin, an esophagogastroduodenoscopy with biopsy was performed.

Pathologic Findings

Gross

The gallbladder showed no external masses or focal mucosal lesions, but the wall was thickened over an area of 4.3 cm in greatest dimension. The tissues submitted as perigastric lymph nodes were two portions of adipose tissue with areas of induration.

The gastric mucosal biopsies were from an area that was described as diffusely irregular and firm.



Figure 1. Non contrast-enhanced computed tomography (CT) of abdomen of patient showing a thickened stomach and gallbladder wall and multiple enlarged nodules.

Histopathology

The gallbladder showed a poorly differentiated adenocarcinoma, including tumor cells with a signet ring morphology, involving the external aspect of the gallbladder, including the subserosal connective tissue and muscle wall (Figure 2). The mucosa was uninvolved by carcinoma or dysplasia. This distribution of tumor strongly suggested a metastasis. Immunohistochemical stains were performed to further characterize the carcinoma. The positive results for the polyclonal and monoclonal carcinoembryonic antigen stains confirmed the presence of an adenocarcinoma. Thyroid transcription factor-1, a marker for thyroid and lung carcinomas, was negative. Markers for breast, including gross cystic disease fluid pro-

Table 1. Reported cases of metastasis of gastric carcinoma to gallbladder

Reference	Country of study	Type of gastric cancer	Presentation	Diagnosis
Yoon et al. [8]	South Korea	Adenocarcinoma, signet ring cell carcinoma	Cholecystitis, abdominal pain, jaundice, weight loss	Carcinoma confirmed by pathology
Masamune et al. [10]	Japan	Moderately differentiated adenocarcinoma	Right upper quadrant pain, fever, jaundice	Right upper quadrant ultrasound showed thickening of gallbladder, dilation of intrahepatic ducts and common bile ducts, smooth focal elevation of gallbladder Carcinoma confirmed by pathology
Kanno et al. [11]	Japan	Poorly differentiated adenocarcinoma	Epigastric discomfort, abdominal full feeling	Right upper quadrant ultrasound showed multiple echogenic lesions of the gallbladder Carcinoma confirmed by pathology

55

tein-15, estrogen receptor and progesterone receptor, were all negative. The positive cytokeratin 7 and negative cytokeratin 20 results suggested stomach, pancreas, and biliary tract as the most likely primary sites. The tissue submitted as a perigastric lymph node showed mesentery extensively involved by poorly differentiated adenocarcinoma.

The gastric body mucosal biopsy showed poorly differentiated adenocarcinoma, including rare tumor cells with signet ring morphology (Figure 3), and it resembled the carcinoma in the gallbladder.



Figure 2. Signet ring cell carcinoma in the gallbladder subserosa (H&E x 400).



Figure 3. Poorly differentiated adenocarcinoma in gastric mucosa (H&E x 100).

Discussion

Signet ring cell carcinoma is an extremely uncommon primary carcinoma in the gallbladder with five published

case reports [3-6]. Given the rarity of primary signet ring cell carcinoma of the gallbladder, it is important to determine whether a signet ring cell carcinoma is primary or metastatic. In our case, adenocarcinoma involved the external aspect of the gallbladder, and the absence of mucosal involvement by carcinoma or dysplasia strongly suggested metastasis. Metastasis to the gallbladder is rare in clinical practice and is usually encountered incidentally at surgery or during autopsies [7]. One study found that it accounts for 4.8% of all pathologically diagnosed gallbladder malignancies, and the most common primary malignancy was from the stomach [8].

Signet ring cell adenocarcinoma of the stomach is a subtype of diffuse gastric adenocarcinoma. It is characterized by round tumor cells that contain abundant intracytoplasmic mucin and nuclei flattened against the periphery of the cells. Signet ring cell adenocarcinoma is thought to be on the rise in the US, even though there is an overall decline in gastric cancer rates [9].

The majority of reported cases of metastatic adenocarcinoma to the gallbladder are those from gastric primaries in Asia (Table 1) [8,10-11], and only one patient was noted to have signet ring cell pathology [8]. There are no known reports of patients in the United States with signet ring cell adenocarcinoma of the stomach metastasizing to the gallbladder.

In this case, the clinical presentation was unique in that it mimicked a benign condition of acute cholecystitis. While both the clinical and radiological studies pointed to a benign condition, the histological study showing signet ring cell pathology encroaching the outer layers of the gallbladder wall uncovered an underlying malignant etiology. Metastasis to the gallbladder is an extremely rare clinical finding, since diffuse gastric cancer most commonly metastasizes to the liver, lungs or ovaries.

The clinical presentation of a secondary tumor can often mimic acute or chronic inflammation of the gallbladder [12]. Therefore, a patient with a metastatic gallbladder tumor can present with cholecystitis, as seen in our case. Our patient had no evidence of cholelithiasis, and ultrasound studies of gallbladder wall thickening without evidence of cholelithiasis may suggest a metastatic gallbladder tumor, since primary gallbladder carcinoma appears to be associated with gallstones in approximately 80% of primary gallbladder malignancies [7,13].

This case of metastatic diffuse signet ring carcinoma to the gallbladder is a unique one in that the patient was an elderly Caucasian female who presented with symptoms mimicking acute cholecystitis. To our knowledge, this is the first reported case in the United States, and it provides additional clinicopathological insight into the sites of metastasis of diffuse gastric adenocarcinoma.

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Conflict of interest statement

The authors do not declare any conflict of interest or financial support in this study.

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