

Metastatic Gastric Adenocarcinoma in Cirrhosis

Dejan Micic, MD¹, Matthew B. Levine, BS², Lei Zhao, MB, PhD³, and K. Gautham Reddy, MD¹

¹Department of Internal Medicine, Division of Gastroenterology, Hepatology and Nutrition, University of Chicago, Chicago, IL

²Virginia Tech Carilion School of Medicine, Roanoke, VA

³Department of Pathology, University of Chicago, Chicago, IL

Abstract

We report the case of a woman with a new diagnosis of gastric adenocarcinoma that was found to have multifocal hepatic metastasis on routine diagnostic transjugular liver biopsy. The finding of metastatic disease in a background of cirrhosis is an unexpected finding that has negative treatment implications regarding use of cytotoxic chemotherapeutic agents.

Introduction

Liver cirrhosis has been correlated with extrahepatic malignancies including gastric cancer, which alters therapeutic options.^{1,2} However, the demonstration of metastatic disease in a cirrhotic liver is a rare finding due to it being an unfavorable site for malignant invasion.³ Extrahepatic malignancies metastatic to a cirrhotic liver are less common due to altered portal flow gradients and potential changes to the cellular microenvironment.

Case Report

A 60-year-old female with a past medical history of hypertension and insulin-requiring diabetes mellitus type II was admitted with worsening abdominal distension. She had known that she had liver disease but did not follow up after her diagnosis. She had no history of significant alcohol intake, blood product transfusion, or history of intravenous drug use. The patient was admitted 1 month prior to presentation with abdominal pain, anemia, and increasing lower extremity edema. Previous work-up included an esophagogastroduodenoscopy (EGD), which demonstrated a gastric ulceration with biopsies consistent with a poorly differentiated adenocarcinoma, and magnetic resonance imaging (MRI) without contrast that suggested a concomitant cirrhotic liver with multiple ill-defined heterogeneous lesions (Figure 1). On physical examination, the patient demonstrated abdominal distension with shifting dullness. Paracentesis demonstrating a total white cell count of 232 cells/uL, serum-ascites albumin gradient 1.2 g/dL, and protein less than 1 g/dL. Serum aspartate aminotransferase (AST) was 62 U/L and alanine aminotransferase (ALT) was 33 U/L. Alpha-fetoprotein was 289 ng/mL. Total bilirubin was 2.8 mg/dL, platelet count was 169 K/uL, and international normalized ratio (INR) was 1.4.

Given the imaging characteristics suggestive of cirrhosis, transjugular liver biopsy was performed. Within the liver biopsy specimen, there were small foci of metastatic adenocarcinoma with areas of lymphovascular invasion (Figure 2) on a background of micronodular cirrhosis and focal sinusoidal fibrosis. Review of the original gastric biopsy specimens demonstrated a poorly differentiated adenocarcinoma arising in a background of atrophic gastritis with intestinal metaplasia (Figure 3). Tumor cells from the liver biopsy specimen were positive for CDX2 and CK19 and negative for CK7, CK20, and HepPar-1, consistent with gastric adenocarcinoma.

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Correspondence: Anish K. Gautham Reddy, 5841 South Maryland Avenue, MC 7120, Chicago, IL 60637 (greddy@medicine.bsd.uchicago.edu).

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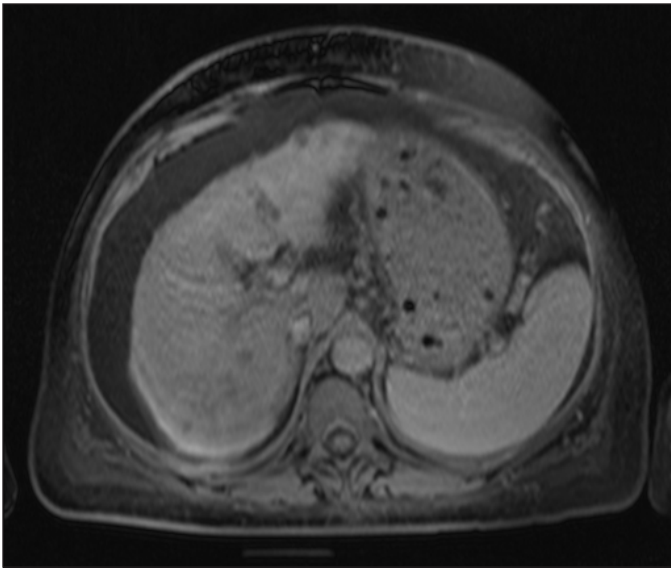


Figure 1. Cross-sectional abdominal MRI showing concomitant cirrhotic liver with multiple ill-defined heterogeneous lesions.

Given the unexpected finding of metastatic multifocal gastric adenocarcinoma in the setting of cirrhosis, further malignancy staging was not performed because therapeutic options were limited. The patient was referred to oncology, which recommended palliative therapies including fluorouracil (5-FU) and trastuzumab.

Discussion

Gastric carcinoma remains a significant global healthcare burden accounting for 934,000 new diagnoses annually (8.6% of new cancer diagnoses), with 21,130 new cases in the United States and 10,620 associated deaths in 2009.⁴ The most common presenting symptoms include weight loss, abdominal pain, and nausea, and the most common clinical sign is anemia.⁵ Primary dissemination of disease can occur via lymphatic and hematogenous spread, and the

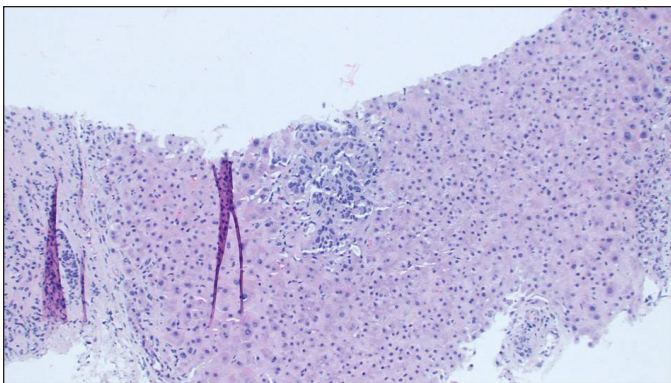


Figure 2. Liver biopsy specimen showing small foci of metastatic adenocarcinoma with areas of lymphovascular invasion on a background of micronodular cirrhosis and focal sinusoidal fibrosis.

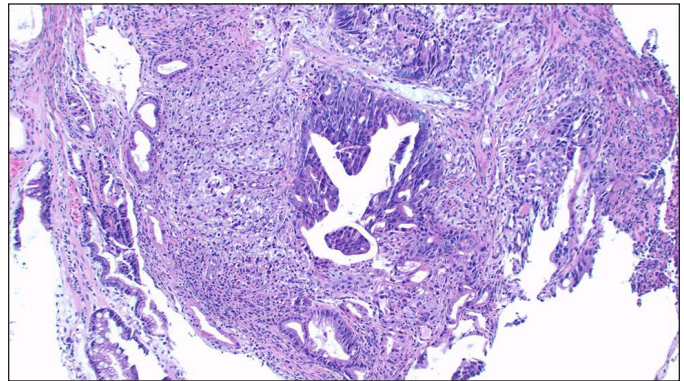


Figure 3. Pathologic review of gastric biopsy specimen showing poorly differentiated adenocarcinoma arising in a background of atrophic fundic gastritis with intestinal metaplasia.

liver is the most commonly affected organ via the hematogenous route.⁵

Various studies have documented an increased risk of extrahepatic (non-hepatocellular carcinoma) cancer in patients with cirrhosis.^{1,6} A nationwide cohort study from Denmark demonstrated standardized incidence ratio (SIR) of 1.9 for the diagnosis of gastric cancer among patients with cirrhosis.¹ An Italian retrospective cohort of patients with cirrhosis undergoing screening for portal hypertension demonstrated a 2.6-fold increased risk of gastric cancer when compared to an estimated risk from the general population.⁶

Although cirrhosis has been correlated with an increased risk of extrahepatic malignancies, the demonstration of metastatic disease to a cirrhotic liver remains a rare finding. A systematic review of 11 post-mortem studies demonstrated that the crude rate of metastatic spread of an extrahepatic malignancy to a cirrhotic liver was decreased when compared to the frequency of metastatic spread to a non-cirrhotic liver.³ Hypotheses to explain this decrease include the disruption of portal blood flow leading to the development of porto-systemic shunting, the loss of endothelial fenestrations in cirrhosis creating a physical barrier to tumor cell invasion, and changes in the expression of adhesion molecules and the cytokine microenvironment.³

Our case demonstrates the rare finding of metastatic gastric adenocarcinoma presenting in a cirrhotic liver. The etiology of the cirrhosis was most likely nonalcoholic fatty liver disease, given the patient's long history of diabetes mellitus II and exclusion of etiologies to include alcohol, viral, autoimmune, metabolic, and biliary tract disease. Findings from the ascitic fluid attributed the ascites to portal hypertension. The observation of metastatic gastric adenocarcinoma to a cirrhotic liver is a rare finding, and, in this case, limited therapeutic options to palliative management.

Disclosures

Author contributions: D. Micic designed and drafted the manuscript, and is the article guarantor. MB Levine and KG Reddy designed and drafted the manuscript. L. Zhao drafted the manuscript and prepared the figures.

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