

Signet Ring Cell Carcinoma of the Ampulla of Vater Presenting With Bone Marrow Carcinomatosis

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CASE REPORT

A 64-year-old man was hospitalized for 1 month of back pain, weight loss, jaundice, fever, fatigue, and nausea. Physical examination was unremarkable, and laboratory evaluation was notable for elevations in lipase to 435 U/L, total bilirubin to 3.3 mg/dL (direct bilirubin of 2.4 mg/dL), carbohydrate antigen (CA) 19-9 of 12,065 U/mL, and new pancytopenia (white blood cell count of 3.0 k/ μ L, hemoglobin of 7.3 g/dL, and platelet count of 39 k/ μ L). A peripheral blood smear was significant for dacrocytes, nucleated red blood cells, and immature white blood cells. Computed tomography scan showed a pancreatic head mass, and positron emission tomography demonstrated mild hypermetabolism in retroperitoneal lymph nodes and tiny nonhypermetabolic lung nodules, without other sites of suspected disease. Despite having no obvious sites of metastasis on imaging, the new pancytopenia with leukoerythroblastic findings concerning for myelophthisis prompted a bone marrow biopsy which revealed mucinous adenocarcinoma with signet ring morphology (Figure 1).

Endoscopic ultrasound showed a 17 \times 22-mm mass in the region of the ampulla (Figure 2). Endoscopic retrograde cholangiopancreatography revealed an exophytic mass involving the ampulla with biopsy consistent with the patient's bone marrow

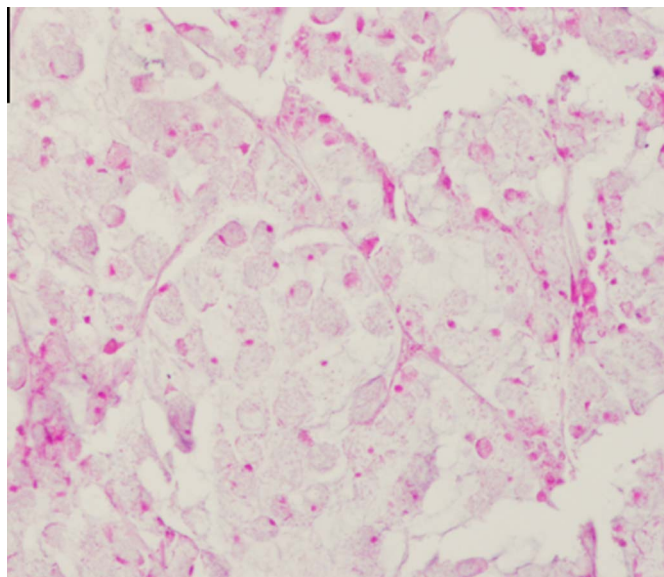


Figure 1. Bone marrow core biopsy demonstrates sheets of bland mucinous cells consistent with mucinous adenocarcinoma with signet ring morphology (hematoxylin and eosin stain, 200 \times magnification).

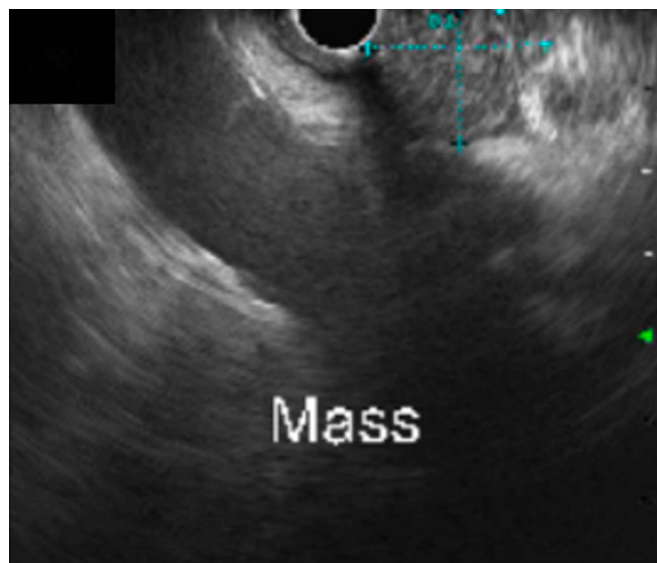


Figure 2. Endoscopic ultrasound showing hypoechoic mass measuring 17 \times 22 mm in cross-sectional diameter in the region of the ampulla.

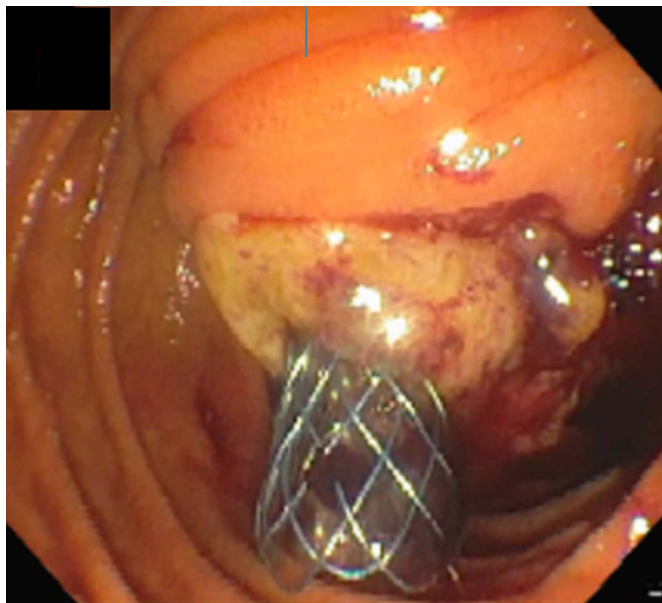


Figure 3. Endoscopic retrograde cholangiopancreatography showing an exophytic mass extending from the ampulla (with biliary stent) in the second part of the duodenum.

findings, leading to a diagnosis of ampullary signet ring cell carcinoma (SRCC) (Figures 3 and 4). No standard treatment regimen for unresectable ampullary SRCC exists. Given the patient's elevated CA 19-9 and pancreatic mass on imaging, first-line pancreatic-directed therapy of gemcitabine and nanoparticle albumin-bound paclitaxel was used.¹ This regimen was selected over FOLFIRINOX (folinic acid, fluorouracil, irinotecan, oxaliplatin) because of the patient's suboptimal performance status and baseline pancytopenia and hyperbilirubinemia.² Furthermore, incorporating a taxane is a common approach in advanced gastric SRCC, so a regimen with possible activity in both pancreatic carcinomas and SRCC, albeit extrapolating from a different primary site, was felt to be a more appropriate therapeutic choice.³ After approximately 9 months of therapy, his CA 19-9 improved to a nadir of 143 U/mL before eventually progressing and requiring second-line therapy.

SRCC is a highly malignant and invasive cancer, usually arising in the stomach.⁴ Small intestine SRCC incidence is approximately 1.1%–1.8% of all gastroenteropancreatic carcinomas.⁵ When occurring in the duodenum, SRCCs rarely localizes to the ampulla of Vater, occurring in just 2.3% of all ampullary adenocarcinomas according to recent National Cancer Institute's Surveillance, Epidemiology, and End Results data.⁴ SRCC seemingly has a greater predisposition to bone metastasis than other ampullary cancers.⁴ There are case reports of ampullary SRCC describing bone marrow involvement as a presentation of diffusely metastatic disease.⁶ Our patient with ampullary SRCC with disseminated bone marrow carcinomatosis without notable metastatic involvement elsewhere is a peculiar presentation of a rare disease without an established treatment approach. SRCC bears a poor prognosis, particularly when presenting with distant metastasis.⁵

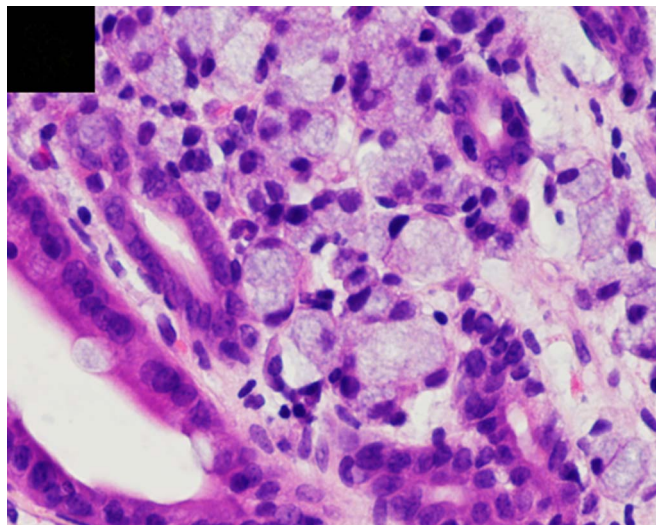


Figure 4. Duodenal mass biopsy shows large malignant cells exhibiting abundant intracytoplasmic mucin and indented nuclei, consistent with mucinous adenocarcinoma with signet ring cell morphology (hematoxylin and eosin stain, 400× magnification).

We advocate having a low threshold for performing bone marrow biopsies in patients with new primary gastroenteropancreatic malignancies, including ampullary SRCC, with unexplained cytopenias. Specifically, these biopsies should be performed in those with unexplained cytopenias even with lacking evidence of diffuse disease on cross-sectional or positron emission tomography imaging, which is typically present in cases of SRCC with bone marrow involvement based on current available literature. Furthermore, the optimal treatment approach for such patients is unknown and should be an area of future study.

DISCLOSURES

Author contributions: A. Goodwin wrote the manuscript, approved the final manuscript, and is the article guarantor. K. Pak revised the manuscript for intellectual content and approved the final manuscript. J. Sanchez, J. Laczek, and R. Matulonis edited the manuscript and approved the final manuscript.

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Informed consent was obtained for this case report.

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