ACG CASE REPORTS JOURNAL

CASE REPORT | PANCREAS

Colloid Carcinoma of the Pancreas: A Rare Initial Presentation of Lynch Syndrome

Zoon Tariq, MD[1], Joanna Riess, MD[1], Lynt B. Johnson, MD[1], and Mamoun Younes, MD[1]

[1]*George Washington University School of Medicine and Health Sciences, Washington DC*

ABSTRACT

Patients with Lynch syndrome, most commonly associated with colorectal cancer, have an increased risk of developing other tumors including pancreatic ductal adenocarcinoma and precursor lesions, such as intraductal papillary mucinous neoplasms. Here, we present a case of a man in his early 20s who presented with a retroperitoneal mass involving the head of the pancreas. Following a pancreaticoduodenectomy combined with para-aortic lymphadenectomy, a pathologic diagnosis of colloid carcinoma, also known as mucinous noncystic carcinoma, of the pancreas was reported. Further testing established the diagnosis of Lynch syndrome. This case is unique because colloid carcinoma of the pancreas is rare and has never been reported as an initial presentation of Lynch syndrome.

KEYWORDS: lynch syndrome; colloid carcinoma; pancreatic cancer; mismatch repair; genetic testing

INTRODUCTION

Lynch syndrome is the most common cause of hereditary colorectal cancer.[1–6] Patients with this syndrome also have an increased risk of developing malignant tumors of other organs including uterus, stomach, liver, kidney, and skin usually before the age of 50 years. Testing of tumor samples for defects in DNA mismatch repair (MMR) genes *MLH1, MSH2, MSH6, PMS2,* and *EPCAM* by

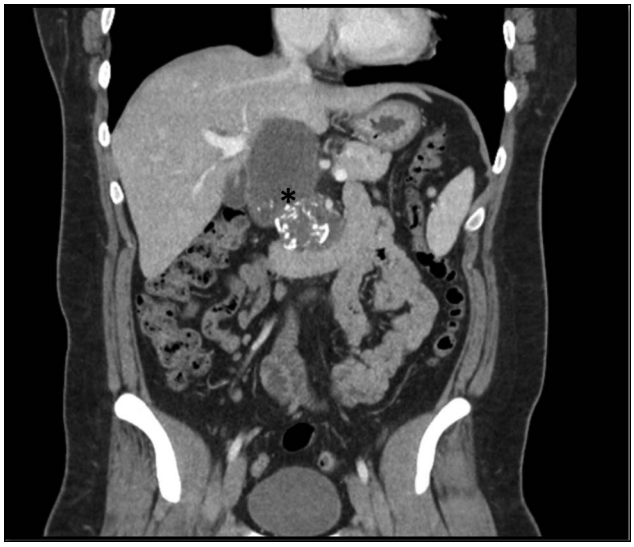

Figure 1. Computed tomography scan of the abdomen pelvis. Note large complex cystic retroperitoneal mass (*; 10.1 × 5.2 cm) with internal calcifications involving the head of the pancreas, extending superiorly to the caudate lobe of the liver.

ACG Case Rep J 2024;11:e01415. doi:10.14309/crj.0000000000001415. Published online: July 12, 2024

Correspondence: Mamoun Younes, MD (myounes@mfa.gwu.edu).

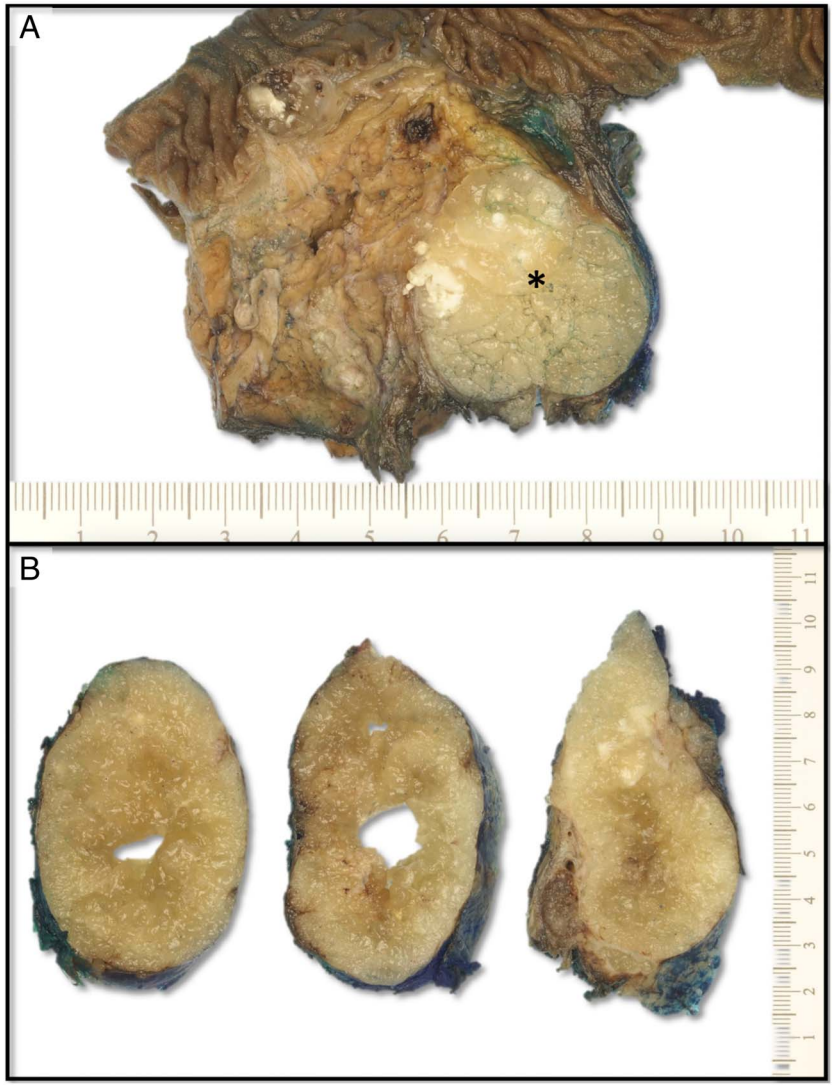

Figure 2. A) Macroscopic (gross) appearance of the pancreatic mass showing a well-demarcated tan-yellow firm mass (*) attached to the adjacent duodenum. B) Further cross-sections reveal a tan-white mucinous cut surface with focal areas of necrosis.

immunohistochemical staining, followed by molecular testing, aids in diagnosis of Lynch syndrome, so patients and their relatives can be screened and counseled, appropriately.

CASE REPORT

The patient was a man in his early 20s, without any previous known medical history, who initially presented with intermittent episodes of abdominal pain. Computed tomography of the abdomen at that time demonstrated a 10.1 × 5.2 cm large complex cystic retroperitoneal mass involving the head of the pancreas, extending up to the level of the caudate lobe of the liver (Figure 1), with mass effect on the main and left portal vein, inferior vena cava, and left renal vein. Findings were also notable for diffuse para-aortic and left iliac chain lymphadenopathy. Subsequent magnetic resonance cholangiopancreatography suggested the bulk of the mass to be extrapancreatic but in continuity with the duodenal loop and extending up to the porta hepatis with some mass effect on the portal vein and common bile duct. An endoscopic ultrasound-guided fine needle aspiration showed acellular mucin and small fragments of acinar tissue and gastrointestinal epithelium.

One month later, a computed tomography-guided biopsy of a retroperitoneal lymph node showed scant atypical glandular epithelium in a background of abundant thick mucin. Of note, carcinoembryonic antigen was 2.1 (0–2.5 μg/L) and CA19-9 was 22.7 (<37 U/mL). At that time, the patient was mainly asymptomatic except for early satiety and an intentional 60 lb weight loss over the course of the previous 1–2 years. He was a current cigarette smoker and recreational marijuana user, without any reported alcohol use or relevant family history. Given the possibility of malignant degeneration of this complex mucinous mass, surgical resection was recommended.

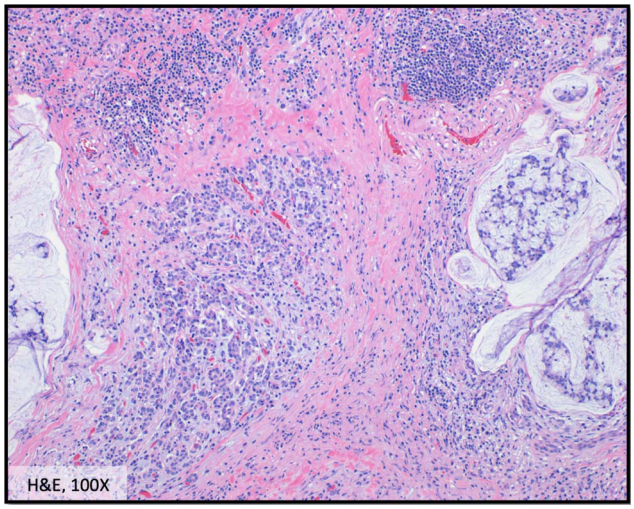

Figure 3. Section of the mass showing small groups of neoplastic cells in mucin lakes in fibrotic stroma surrounding atrophic pancreatic parenchyma. Hematoxylin and eosin, 100X.

Two months after the initial presentation, a pancreaticoduodenectomy and para-aortic lymphadenectomy was performed. The pathology of this specimen was reported as well-differentiated colloid carcinoma (mucinous noncystic carcinoma) of the pancreatic head (Figures 2, 3, 4 and 5), 9.6 cm in greatest dimension, stage (American Joint Committee on Cancer 8th edition): pT3 N2 Mn/a. The tumor invaded the duodenal wall up to the submucosa and the peripancreatic soft tissue; the duodenal mucosa was normal. No background intraductal papillary mucinous neoplasm was identified. All resection margins were negative for dysplasia or malignancy. Nine (5 peripancreatic and 4 para-aortic) of 11 lymph nodes were positive for metastatic colloid carcinoma. The patient was discharged on the sixth postoperative day without complications.

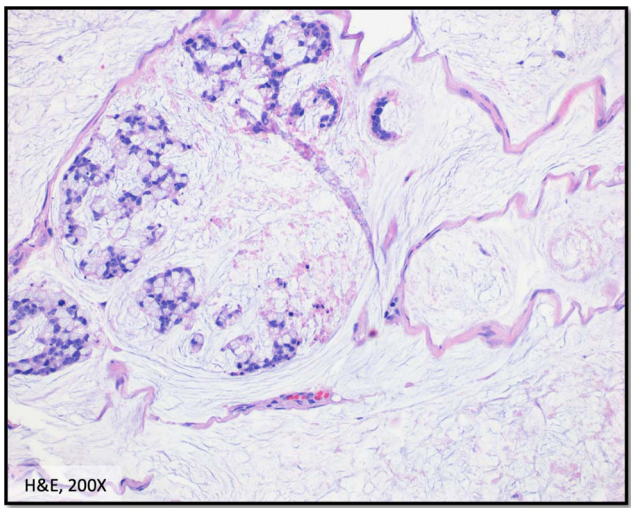

Figure 4. High-power view showing aggregates and small nests of neoplastic cells (some with signet ring morphology) in large extracellular mucin pools. Hematoxylin and eosin, 200X.

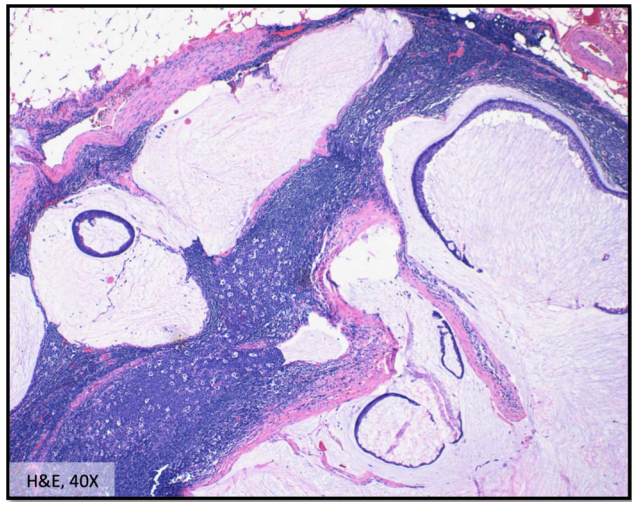

Figure 5. Lymph node with metastatic carcinoma with similar morphology as above. Large extracellular mucin pools are visible with scant sheets of neoplastic cells. Hematoxylin and eosin, 40X.

MMR protein testing on the surgical resection specimen by immunohistochemistry showed loss of nuclear expression of *MSH2* and probable loss of nuclear expression of *MSH6* (Figure 6), with a high probability of diagnosis of Lynch syndrome. Further microsatellite instability (MSI) testing reported as MSI-High (with 4 altered markers: *BAT-25/26; NR-21/24*). The tumor was positive for PD-L1 by immunohistochemical staining.

The patient had no reported family history of cancer and had never had a colonoscopy. In the next month, his pancreatic stent was removed, and he was started on chemotherapy. He is doing well on his regimen and is currently being managed as an outpatient by a multidisciplinary team, with a plan to screen for other cancers and genetic counseling for first-degree relatives.

DISCUSSION

Although classically Lynch syndrome initially presents with colorectal polyps/cancers and increases the risk of associated commonly presenting neoplasms (endometrial and ovarian), there is also an increased risk of rarer tumors, such as colloid carcinoma of the pancreas. This report emphasizes that presentation of Lynch syndrome is not confined to colorectal sites, and healthcare professionals must remain vigilant regarding the initial presentation with rarer extracolonic cancers.

Pancreatic cancer has a high mortality, and although pancreatic cancer is not one of the top cancer types associated with Lynch syndrome, these patients are often young and amenable to curative surgical management.

Although screening recommendations for colorectal and endometrial cancers in patients with Lynch syndrome have been formulated, surveillance for pancreatic cancer is limited. Current guidelines recommend that for patients with Lynch syndrome, only those with an affected first-degree relative should

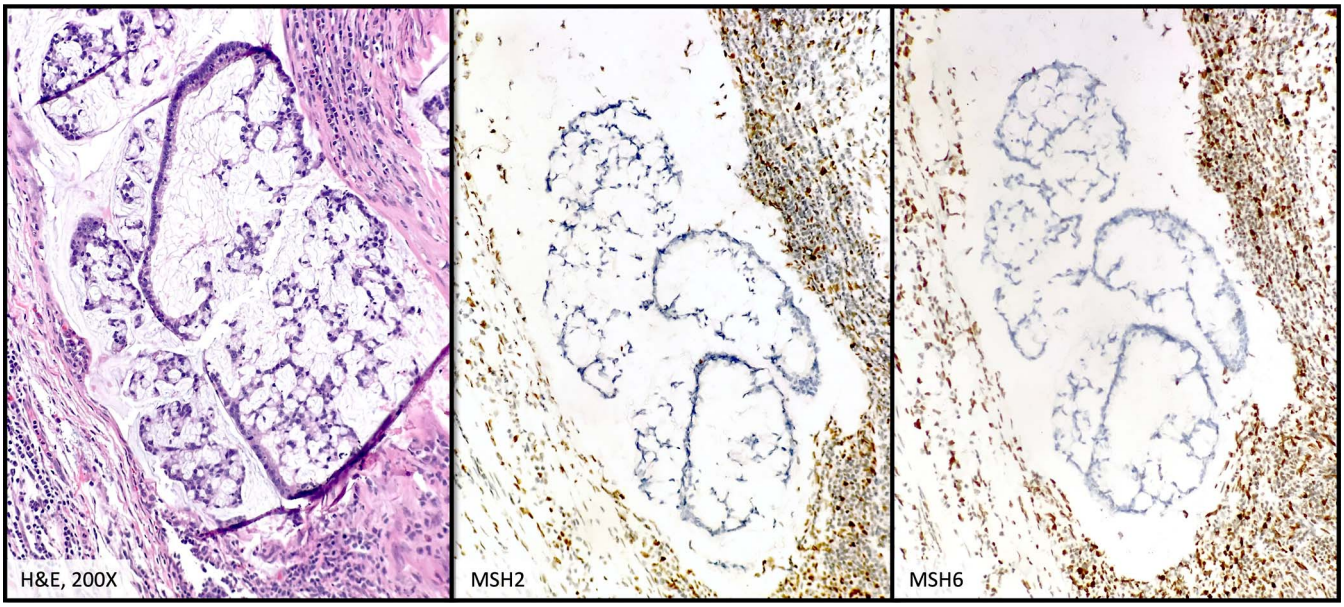

Figure 6. Immunohistochemistry testing for mismatch repair proteins. Nuclear expression of MSH2 and MSH6 is lost in tumor cells. Background non-neoplastic tissue serves as internal control with intact nuclear expression. Hematoxylin and eosin, 200X.

be screened for pancreatic cancer.[7] Advances in imaging and biomarkers may help in earlier diagnosis and management for better outcomes.

Colloid carcinoma of the pancreas can be associated with mutations in DNA MMR genes amidst other oncogenes. Patients with this tumor should be tested for Lynch syndrome.

In addition to establishing a diagnosis of Lynch syndrome, MMR/MSI testing is also important to determine eligibility for immune checkpoint inhibitor therapy in patients with PD-L1-positive tumors, such as the patient reported in this study.

DISCLOSURES

Author contributions: Manuscript conceived by Z. Tariq and M. Younes; all authors contributed to the drafting of the manuscript; M. Younes, LB Johnson and J. Riess reviewed and edited the manuscript. M. Younes is the article guarantor.

Financial disclosure: None to report.

Informed consent was obtained for this case report.

Received February 9, 2024; Accepted May 31, 2024

REFERENCES

1. Lee SH, Kim WY, Hwang DY, Han HS. Intraductal papillary mucinous neoplasm of the ileal heterotopic pancreas in a patient with hereditary non-polyposis colorectal cancer: A case report. *World J Gastroenterol.* 2015; 21(25):7916–20.
2. Lubezky N, Ben-Haim M, Lahat G, et al. Intraductal papillary mucinous neoplasm of the pancreas: Associated cancers, family history, genetic predisposition? *Surgery.* 2012;151(1):70–5.
3. Flanagan MR, Jayaraj A, Xiong W, Yeh MM, Raskind WH, Pillarisetty VG. Pancreatic intraductal papillary mucinous neoplasm in a patient with Lynch syndrome. *World J Gastroenterol.* 2015;21(9): 2820–5.
4. Sparr JA, Bandipalliam P, Redston MS, Syngal S. Intraductal papillary mucinous neoplasm of the pancreas with loss of mismatch repair in a patient with Lynch syndrome. *Am J Surg Pathol.* 2009;33(2): 309–12.
5. Lynch Syndrome. CDC, 2023 Accessed May 17, 2024 (https://www.cdc.gov/genomics/disease/colorectal_cancer/lynch.htm).
6. Bujanda L, Herreros-Villanueva M. Pancreatic cancer in Lynch syndrome patients. *J Cancer.* 2017;8(18):3667–74.
7. Syngal S, Brand RE, Church JM, Giardiello FM, Hampel HL, Burt RW. ACG clinical guideline: Genetic testing and management of hereditary gastrointestinal cancer syndromes. *Am J Gastroenterol.* 2015;110(2): 223–63.