MÆDICA - a Journal of Clinical Medicine

CASE REPORT

MAEDICA – a Journal of Clinical Medicine
2023; 18(2): 368-372
https://doi.org/10.26574/maedica.2023.18.2.368

Duodenal Adenocarcinoma in a patient with Lynch Syndrome. A Case Report and Facts Related to Small Intestine Cancer

Joyce CHENG[a], Ghanshyam PATEL[a], Milan KHEALNAI[b], Hariprasad KORSAPATI[b], Shilpa REDDY[c], Advait VASAVADA[d], Shikha JAIN[e], Shrestha ADAK[f], Henok REGASSA[g]

[a]Mercyhealth Internal Medicine Residency, Javon Bea Hospital, Rockford, IL, US

[b]Mayo Clinic Health System, Mankato, MN, US

[c]Marian University, Indianapolis, IN, US

[d]MP Shah Medical College, Jamnagar, Gujarat, India

[e]MVJ Medical College & Research Hospital, Karnataka, India

[f]Medical College and Hospital, Kolkata, India

[g]St. Paul's Hospital Millennium Medical College, Gulele Sub-City, Addis Ababa, PO Box 1271, Ethiopia

ABSTRACT

Diagnosing small bowel cancer has been challenging due to its unusual presentation and inaccessibility on endoscopy. A 41-year-old male with a history of irritable bowel syndrome underwent esophagogastroduodenoscopy (EGD) for worsening fatigue and lightheadedness despite iron supplements therapy for low hemoglobin. Initial upper endoscopy showed esophagitis and non-bleeding duodenal bulb ulcer with exudate. Endoscopic ultrasound (EUS) with fine-needle aspiration was done due to persistent concern of malignancy and demonstrated moderately differentiated adenocarcinoma in the second portion of the duodenum. Endoscopic ultrasound with fine-needle aspiration may be a superior approach to diagnosing duodenal carcinoma than EGD alone. Small bowel cancer can be a part of the tumor spectrum of

Address for correspondence:
Ghanshyam Patel, MD
Mercyhealth Internal Medicine Residency, Javon Bea Hospital, Rockford, IL 8201 E Riverside Blvd, Rockford, IL 61114, US
Tel.: 516-849-9811; preferred email: grp_aaa@yahoo.com; work email: gpatel@mhemail.org

Article received on the 16th of May 2023 and accepted for publication on the 23rd of June 2023

Lynch syndrome. Duodenal adenocarcinomas present at a late stage and portend a poor prognosis. We present a case of duodenal adenocarcinoma in an otherwise healthy individual emphasizing the importance of malignancy in the differential and genetic counseling in individuals with the family risk factor.

Keywords: duodenal carcinoma, adenocarcinoma of duodenum, iron deficiency anemia, small intestine cancer, Lynch syndrome.

Abbreviations
EGD: esophagogastroduodenoscopy
EUS: endoscopic ultrasound
FNA: fine-needle aspiration
NSAID: non-steroidal anti-inflammatory drugs
GERD: gastro-esophageal reflux disease
CT: computed tomography
RDW: red cell distribution width
MCV: mean corpuscular volume
ACG: American College of Gastroenterologists

INTRODUCTION

Although the small intestine makes up more than 80% of the gastrointestinal (GI) tract, primary small intestine cancer is a rare entity. They account for less than 1% of cancers overall in the United States, and less than 5% of GI malignancies (1). Duodenum is the most common site for small bowel cancer, and adenocarcinoma of the duodenum represents 33% of small intestine malignancies (1). As of writing this article, the incidence of small intestine cancer in the year 2021 is 11390 in the United States (2). Duodenal cancer presents with non-specific and vague abdominal symptoms, which delays the diagnosis, leading to worsening of disease burden and poor prognosis. We report a case of a 41-year-old male who presented with iron deficiency anemia and was eventually diagnosed with duodenal adenocarcinoma. ❑

CASE DESCRIPTION

Initial presentation

A 41-year-old male with a past medical history of irritable bowel syndrome and anxiety presented to an outpatient clinic with a three-week history of dyspnea on exertion and craving for ice. He also experienced generalized fatigue and weakness. He denied abdominal pain, dark urine, nausea, or poor appetite. The primary laboratory measurement showed decreased hemoglobin. No previous laboratory results were available; however, he was told that his iron levels have been low in the past. He was started on iron supplements.

ED presentation

After two days of initial presentation, he returned to the emergency department with worsening fatigue and lightheadedness. He described intermittent bright red blood per rectum. However, he was told it was due to hemorrhoids in the past. He denied syncopal events, chest pain, abdominal pain, melena, non-steroidal anti-inflammatory drugs (NSAID) use, or gastro esophageal reflux disease (GERD). He also denied any long-term health problems in the family. The patient was on sertraline, multivitamins, and denied taking any other medications, alternative, or herbal supplements.

The complete blood count showed decreased hemoglobin, reduced MCV and hematocrit along with slightly increased RDW. The iron studies found subsided ferritin and iron with increased reticulocyte count. The serum electrolytes and renal functions were normal. The repeat fecal occult blood test (FOBT) was positive. Due to symptomatic anemia, he was transfused with a unit of packed red blood cells (RBCs).

Esophagogastroduodenoscopy (EGD) and colonoscopy were performed to further evaluate the anemia. EGD findings showed esophagitis, erosive gastritis, and a large cratered non-bleeding duodenal bulb ulcer with an exudate at the base concerning malignancy. Biopsies of ulceration were consistent with Barrett's esophagus without dysplasia and atypical glandular proliferation. The colonoscopy demonstrated a benign rectal polyp. Abdominal and pelvic CT revealed a large mass within the pancreaticoduodenal region, measuring 6.1 cm craniocaudal by 4.6 x 4.2 cm biaxial (Figure 1). The mass appears to be centered in the wall of the duodenum with near circumferential spread without

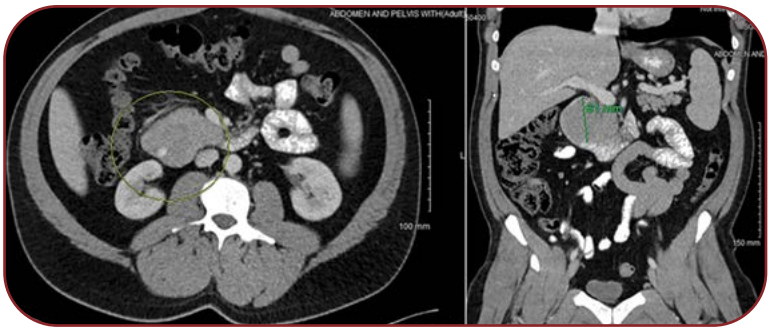

FIGURE 1. Abdominal and pelvic computed tomography with IV contrast revealing a solid soft tissue mass within the pancreaticoduodenal region, confluent with both the pancreas and duodenal C-sweep; mass measures 6.1 cm craniocaudal by 4.6 x 4.2 cm biaxial

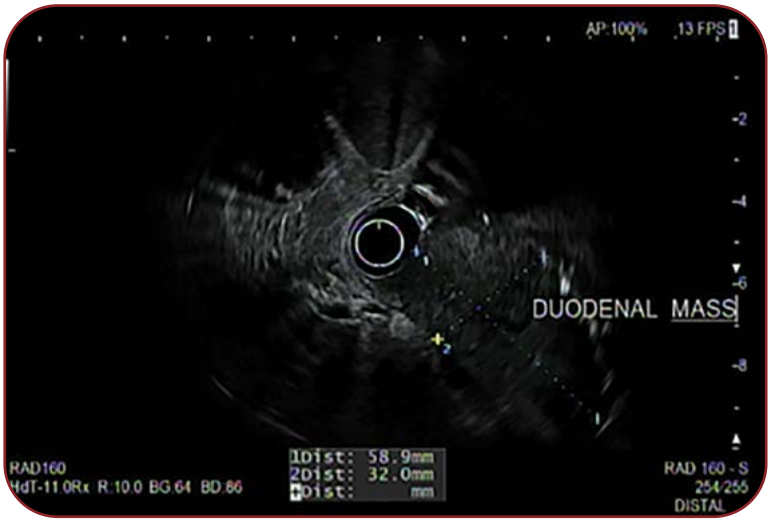

FIGURE 2. Endoscopic ultrasound showing the duodenal mass

definite evidence of regional lymph node spread or metastatic disease within the abdomen or pelvis. Repeat EGD with endoscopic ultrasound (EUS) (Figure 2) revealed a large ulcerated, friable mass that was found in the second portion of the duodenum. Biopsy was consistent with moderately differentiated adenocarcinoma.

The patient was referred to a surgical oncologist and underwent a Whipple procedure comprising exploratory laparotomy, pancreaticoduodenectomy and cholecystectomy. The omental flap of the pancreatojejunostomy along with the choledochal stent was placed. Histopathology of the pancreaticoduodenectomy demonstrated an invasive well-differentiated adenocarcinoma, 7.0 cm, arising from a tubule villous adenoma with high-grade dysplasia. The tumor invaded through the duodenal wall into the pancreas staging pT4N0Mx. All surgical resection margins were uninvolved. The Lymphovascular and perineural invasion were not identified. The biopsy of 27 lymph nodes was negative for carcinoma. The patient was referred to Oncology Genetics and found to have a harmful germline mutation in MLH1 (5'UTR_EX13del). This is consistent with a diagnosis of Lynch syndrome formerly known as hereditary non-polyposis colorectal cancer (HNPCC). ❑

DISCUSSION

The small intestine is a relatively unusual site for GI malignancy compared with the large intestine, esophagus and stomach. The common primary tumors of the small intestine include adenocarcinoma, sarcoma, carcinoid tumors, GI stromal tumor and lymphoma. The adenocarcinoma of the small bowel begins in the cells that make and release mucus and other fluids. They usually appear as sessile, stenotic, ulcerative, infiltrative, or polypoid lesions on EGD. The risk factors for small intestine adenocarcinoma have been hard to study due to its rarity. Some non-modifiable risk factors include Celiac disease, Crohn's disease, inherited conditions likewise familial adenomatous polyposis (FAP), Peutz-Jeghers syndrome (PJS), cystic fibrosis (CF) and Lynch syndrome (3). This case report depicts a rare small bowel tumor of the second portion of the duodenum as an atypical iron deficiency anemia.

As per an observational retrospective study, the most common presentation of small bowel carcinoma is abdominal pain (60%), followed by obscure GI bleeding (50%) and ileus (30%) (4). Diagnosing duodenal carcinoma in a patient presenting with iron deficiency anemia is challenging due to its paucity; therefore, it requires a high index of suspicion. Endoscopy with biopsy is the modality of choice diagnosing small intestine cancer. However, the small intestine is relatively unattainable on routine endoscopy, which delays the diagnosis. Other added diagnostic modalities include CT scan for obstruction or perforation when suspected, MRI, wireless capsule endoscopy, endoscopic ultrasound with fine-needle aspiration, and double-balloon enteroscopy.

In our case, early EGD revealed esophagitis, erosive gastritis and duodenal ulcer, which could have explained the cause of the iron deficiency

anemia. Without strong malignancy intuition, the duodenal adenocarcinoma identification may have been deferred. Endoscopic ultrasound is a relatively novel approach, which combines endoscopy and ultrasound to obtain high-quality ultrasound images of internal organs and adjacent tissues. It can be a useful tool diagnosing intestinal tumors when combined with EGD or colonoscopy (5). The ultrasound transducer is mounted on the tip of the endoscope which allows taking clear pictures through sound waves. Biopsy of the suspicious lesion can be achieved through thin needle aspiration under ultrasound guidance (6).

The study based on the Surveillance, Epidemiology, and End Results (SEER) program registry found that small bowel adenocarcinoma (SBA) had a higher predilection for males, black race, younger age, poorly differentiated histology, and a higher rate of microsatellite instability than large bowel adenocarcinoma (LBA) (7). Overman *et al* also described patients with SBA as more likely to present with stage IV disease and high-grade tumors compared to LBA. With the advancement in surgical techniques, adjuvant and systemic chemotherapy, the overall mortality has been improved over the years in both SBA and LBA; however, the reduction was smaller for SBA (7).

Small intestine cancer treatment depends on whether the tumor can be resected. Duodenal carcinoma is usually resected with the Whipple procedure. Depending on the tumor spread through the lymph node, it may require neoadjuvant chemotherapy, adjuvant chemotherapy or radiation therapy. The new area of research for the treatment of small bowel adenocarcinoma includes intraperitoneal chemotherapy, targeted therapy and checkpoint inhibitors such as immunotherapy (1). Based on SEER 18 (2011-2017), the overall and localized small intestine cancer five-year relative survival is 68.3% and 84.9%, respectively (3).

Small bowel cancer is part of the tumor spectrum of Lynch syndrome, which is caused by an alteration in DNA mismatch repair genes including MLH1. Patients with the mutation have an estimated 4% lifetime risk of developing small bowel cancer (8). Lynch syndrome is also associated with an increased risk of developing stomach, pancreatic and bladder cancers, including uterine/ovarian cancer in women. Lynch syndrome patients generally present with small bowel cancer 10-20 years earlier than the general population, and it can be the initial clinical manifestation (8). The American College of Gastroenterologists (ACG) clinical guideline on genetic testing and management of Lynch syndrome suggests colonoscopy every 1 to 2 years, starting at age 20–25 or 10 years younger than the earliest diagnosis in the family, and baseline upper endoscopy at age 40 (9). ❑

CONCLUSION

Adenocarcinoma of the duodenum is a relatively rare entity. The diagnosis is usually delayed due to its imprecise presentation and unreachable site on regular endoscopy. Endoscopic ultrasound is advantageous in identifying small intestine cancer. This case highlights the importance of small bowel malignancy in the differential when assessing iron deficiency anemia and importance of genetic counselling at risk patients. ❑

Ethics statement: Ethical approval is not required for this study in accordance with local or national guidelines.

Written informed consent was obtained from the patient for publication of the medical case details and any accompanying images.

Conflicts of interest: none declared.

Financial support: none declared.

Article Guarantor: J. Cheng

Notice of prior presentation: Poster presented at American College of Physician (ACP) Illinois Northern chapter meeting, November 17th, 2021, Virtual.

Data availability: All data generated or analyzed during this study are included in the present article. Further enquiries can be directed to the corresponding author.

CARE Checklist: 'The CARE Checklist has been completed by the authors for this case report, attached as supplementary material.' (Supplementary file).

References

1. About Small Intestine Cancer. Accessed November 17, 2021. https://www.cancer.org/content/dam/CRC/PDF/Public/8833.00.pdf.
2. Small Intestine Cancer — Cancer Stat Facts. Accessed November 17, 2021. https://seer.cancer.gov/statfacts/html/smint.html.
3. Small Intestine Cancer Causes, Risk Factors, and Prevention. Accessed November 17, 2021. https://www.cancer.org/content/dam/CRC/PDF/Public/8834.00.pdf.
4. **Yamagami H, Oshitani N, Hosomi S, et al.** Usefulness of Double-Balloon Endoscopy in the Diagnosis of Malignant Small-Bowel Tumors. *Clin Gastroenterol Hepatol* 2008;6:1202-1205. doi:10.1016/J.CGH.2008.05.014.
5. **Cheng J, Patel G, Dawood A, Aqeel A.** Gastric and Duodenal Neuroendocrine Tumor Incidentally Found on Endoscopy During the Evaluation of Iron-Deficiency Anemia. *Cureus* 2022;14:e22208. doi:10.7759/CUREUS.22208
6. Endoscopic Ultrasound (EUS) – American Gastroenterological Association. Accessed November 17, 2021. https://gastro.org/practice-guidance/gi-patient-center/topic/endoscopic-ultrasound-eus/.
7. **Overman MJ, Hu CY, Kopetz S, et al.** A population-based comparison of adenocarcinoma of the large and small intestine: Insights into a rare disease. *Ann Surg Oncol* 2012;19:1439-1445. doi: 10.1245/S10434-011-2173-6.
8. **Koornstra JJ, Kleibeuker JH, Vasen HF.** Small-bowel cancer in Lynch syndrome: is it time for surveillance? *Lancet Oncol* 2008;9:901-905. doi:10.1016/S1470-2045(08)70232-8
9. **Syngal S, Brand RE, Church JM, et al.** ACG Clinical Guideline: Genetic Testing and Management of Hereditary Gastrointestinal Cancer Syndromes. *Am J Gastroenterol* 2015;110:223. doi: 10.1038/AJG.2014.435.