Radiology Case Reports 19 (2024) 4662–4669

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/radcr

Case Report

Duodenal adenocarcinoma at stage IV: A critical look at diagnostic pathways and treatment modalities ☆

Nathaniel Grabill, MD[a,*], *Mena Louis, DO*[a], *Mariah Cawthon, MD*[a], *Claudia Gherasim, MD*[b], *Travelyan Walker, MD*[c]

[a] *Northeast Georgia Medical Center, General Surgery Department, Gainesville, GA 30501, USA*
[b] *Northeast Georgia Medical Center, Pathology Department, Gainesville, GA 30501, USA*
[c] *Northeast Georgia Medical Center, General Surgery Department, Braselton, GA, 30517, USA*

ARTICLE INFO

Article history:
Received 25 June 2024
Revised 11 July 2024
Accepted 16 July 2024

Keywords:
Duodenal adenocarcinoma
Gastrointestinal cancer
FOLFOX
Multidisciplinary care
Palliative care

ABSTRACT

Duodenal adenocarcinoma is a rare and aggressive gastrointestinal malignancy that frequently presents with symptoms like gastric outlet obstruction and biliary obstruction, leading to delayed diagnosis and challenging prognosis. This case report explores the clinical presentation, diagnostic hurdles, and therapeutic management of late-stage duodenal adenocarcinoma in a 53-year-old woman with no significant prior medical history. The patient presented with severe epigastric pain radiating to the right upper quadrant, nausea, and decreased appetite. Elevated liver enzymes and imaging revealed multiple liver masses and a primary duodenal mass. Biopsies confirmed moderately differentiated adenocarcinoma. Tumor markers were evaluated during the staging phase, showing markedly elevated levels. The patient underwent systemic chemotherapy with FOLFOX but faced complications, including pulmonary emboli and neurological symptoms. Management required a multidisciplinary approach, integrating palliative and supportive care to address symptoms and improve quality of life. The case highlights the necessity of considering duodenal adenocarcinoma when diagnosing persistent gastrointestinal symptoms. It highlights the need for a holistic treatment approach, including tailored chemotherapy regimens and vigilant monitoring of complications. Molecular profiling was crucial in guiding treatment decisions, although MSI, HER2, and PD-1 were negative, and the tumor showed no mismatch repair protein deficiency. This article emphasizes the importance of early integration of palliative care and the value of comprehensive pathological analysis in managing advanced duodenal adenocarcinoma, providing insights into diagnostic and therapeutic strategies for this complex case.

☆ Competing Interests: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

* Corresponding author.
E-mail address: Nathaniel.grabill@nghs.com (N. Grabill).

https://doi.org/10.1016/j.radcr.2024.07.090

Introduction

Duodenal adenocarcinoma is a rare entity, accounting for only 0.5% of gastrointestinal cancers and less than half of all small bowel malignancies [1,2]. Its rarity and typically asymptomatic early course contribute to diagnostic delays and poor prognostic outcomes [1]. Despite being the shortest segment of the small intestine, the duodenum is a common site for adenocarcinoma within the small bowel, likely due to its proximity to several major bile and pancreatic ducts, exposing it to carcinogenic bile acids and pancreatic secretions [3].

The clinical presentation of duodenal adenocarcinoma often mimics more benign conditions like peptic ulcer disease or gastritis, leading to nonspecific symptoms such as abdominal pain, weight loss, nausea, and vomiting [4]. Some patients may present with more specific symptoms, including gastric outlet obstruction and biliary obstruction, which can further complicate the diagnosis [5]. The anatomical challenges posed by the location of the duodenum deep within the abdominal cavity complicate endoscopic and radiographic evaluations, often necessitating a combination of imaging modalities and invasive procedures for accurate diagnosis [1].

Management of duodenal adenocarcinoma is predominantly surgical, with resection being the only curative option [6]. However, the efficacy of surgery depends largely on the stage of the disease at diagnosis, with early-stage tumors having significantly better outcomes [7]. Adjuvant therapies, including chemotherapy and radiation, are considered based on resection margins, lymph node involvement, and the patient's overall health [8]. Despite these interventions, the prognosis remains guarded, especially in cases diagnosed at an advanced stage, where the 5-year survival rate dramatically decreases [9].

Case presentation

A 53-year-old female with no significant past medical history presented to the emergency department with complaints of severe abdominal pain that had escalated over 3 weeks. The pain was localized to the epigastric region, radiating to the right upper quadrant, and worsened postprandially, accompanied by bloating and resulting in decreased food intake. Additional symptoms included insomnia due to pain, nausea, indigestion, and fatty stools.

Upon physical examination, the patient appeared acutely distressed and icteric. Abdominal examination revealed tenderness in the epigastric region without palpable masses or hepatosplenomegaly. Initial laboratory tests showed elevated liver enzymes (AST 86 U/L [0-48 U/L], ALT 129 U/L [13-61 U/L], alkaline phosphatase 472 U/L [45-136 U/L]), anemia (hemoglobin 9.3 g/dL [14-18 g/dL]), and total bilirubin (2.3 mg/dL [0.00-1.00 mg/dL]). Markedly elevated tumor markers (CEA 3334.7 ng/mL [0-2.5 ng/mL]), (CA 19-9 >104,000 U/mL [0-37 U/mL]) were noted. An ultrasound of the abdomen indicated numerous mass lesions occupying the liver, suggestive of metastatic disease. A subsequent CT scan confirmed these findings and revealed a retroperitoneal mass-like lesion measuring 2.7 × 3.6 cm located just below the inferior margin of the pancreas, with adjacent mildly prominent lymph nodes (Figs. 1-2). The CT of the chest identified small nodular

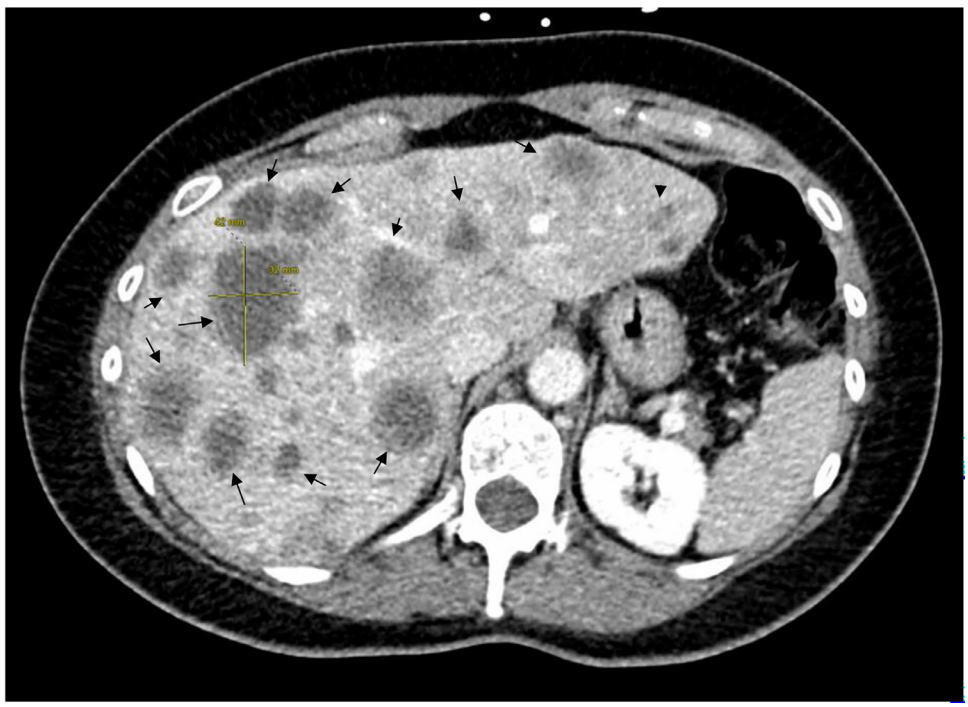

Fig. 1 – CT Abdomen and Pelvis with IV contrast, arterial phase, axial view. Multiple hypodense lesions (black arrows) are visible, ranging in size from a few millimeters to 4 cm. These lesions are dispersed throughout all liver segments, raising concerns for diffuse metastatic disease.

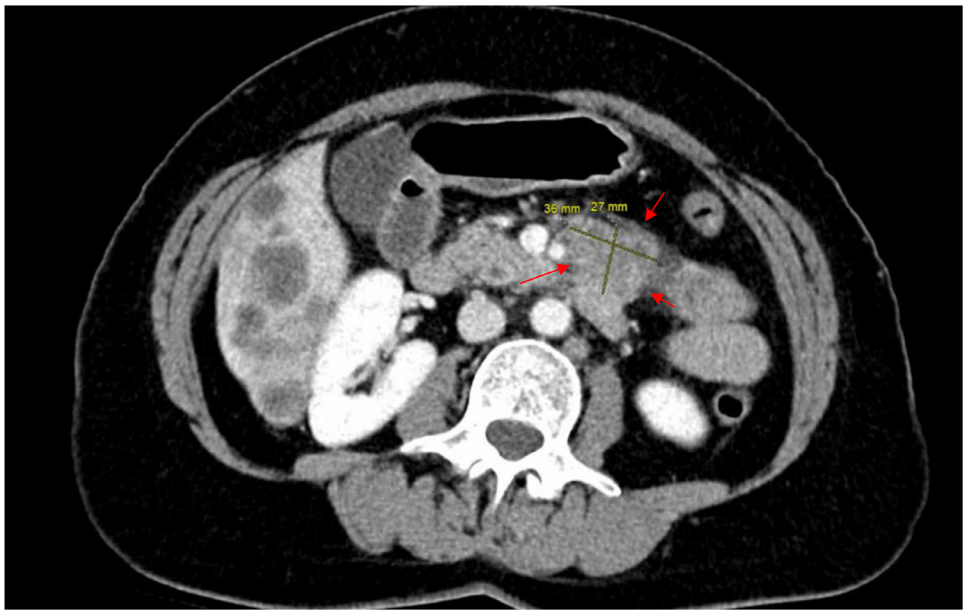

Fig. 2 – CT Abdomen and Pelvis with IV contrast, arterial phase, axial view. Red arrows indicate a soft tissue mass in the left upper quadrant within the central mesentery, inferior to the pancreas. Adjacent prominent lymph nodes are also visible, suggesting potential lymphatic involvement.

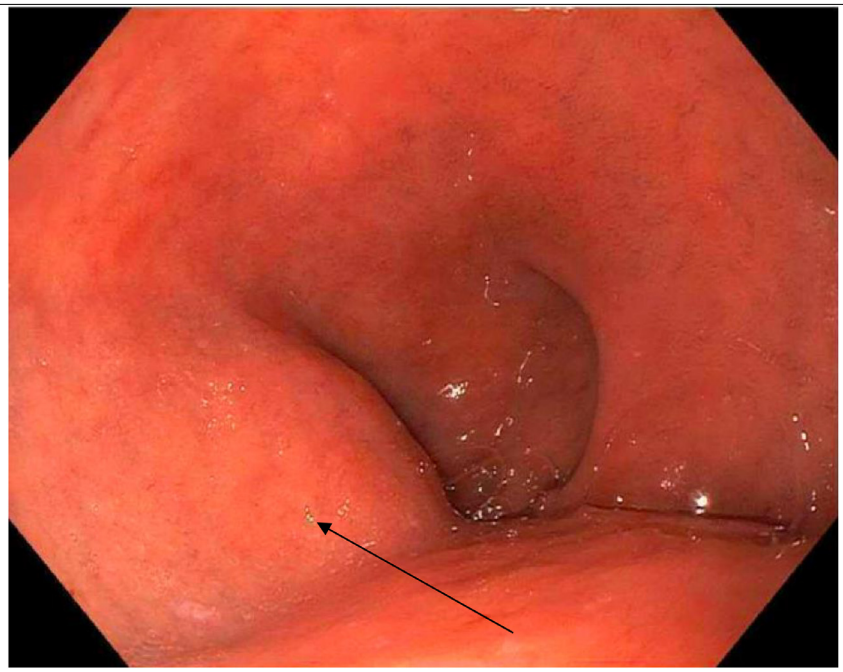

Fig. 3 – Endoscopic image of the duodenum, with the black arrow indicating the presence of a duodenal mass. The mass appears as an irregular, raised lesion within the third portion of the duodenum, consistent with the biopsy-confirmed adenocarcinoma.

densities in both lung fields, raising concerns for widespread metastatic disease.

The patient underwent an esophagogastroduodenoscopy (EGD), which noted a mass in the third portion of the duodenum (Fig. 3). Given the symptoms and imaging findings, there was a concern for gastric outlet obstruction. Endoscopic stenting was performed to relieve the obstruction and allow the patient to receive systemic therapy. Biopsies were obtained, and the pathology returned as moderately differentiated adenocarcinoma with angiolymphatic invasion (Fig. 4). The immunohistochemical (IHC) profile of the duodenal tumor and a subsequent US-guided liver biopsy (which also returned as adenocarcinoma) suggested a primary duodenal cancer with liver metastases. Staining was positive for cytokeratin 7 and

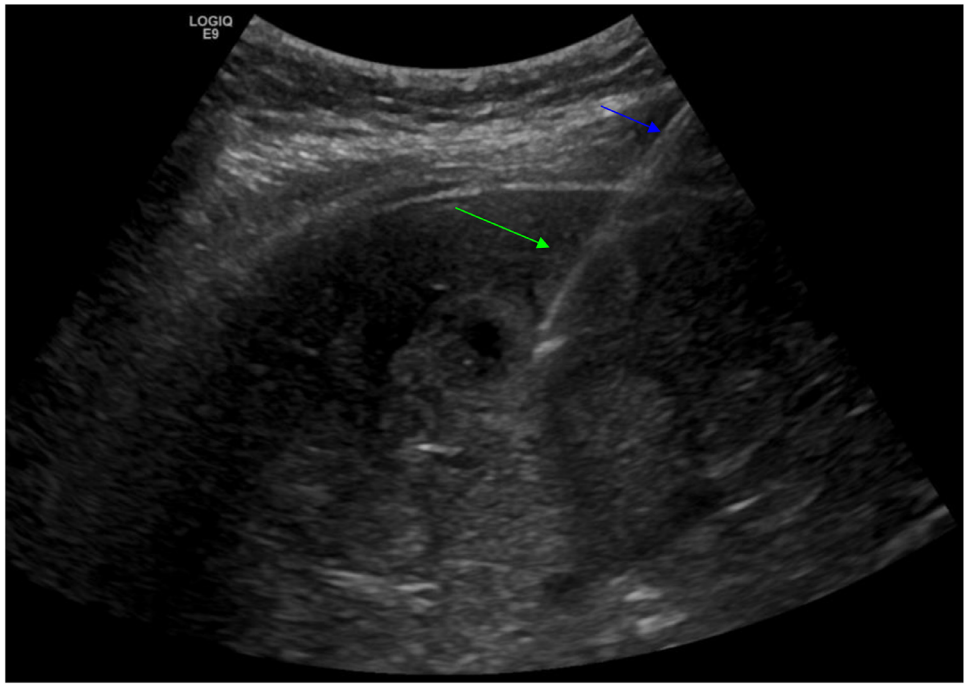

Fig. 4 – Ultrasound-guided core needle biopsy, with the blue arrow indicating the biopsy needle and the green arrow pointing to the liver mass. The procedure was performed to obtain tissue samples for histopathological analysis, confirming metastatic adenocarcinoma.

20, and CA 19-9, and negative for markers indicating other primary sites, supporting the diagnosis. Additionally, the tumor was tested for microsatellite instability (MSI), HER2, and PD-1 status, which were all negative.

Given the advanced nature of her disease, the patient was referred to hematology-oncology, where FOLFOX systemic chemotherapy was initiated with plans to hold Bevacizumab (Avastin) until after reassessment of the primary tumor. The patient endured chemotherapy with significant challenges, including a presentation to the emergency department with left chest pain that CT angiography confirmed to be multiple pulmonary emboli. This was managed with a heparin drip followed by the transition to oral anticoagulation. Unfortunately, the patient experienced neurological symptoms, including transient difficulty speaking and hand spasms, during her second cycle of chemotherapy, which were managed as chemotherapy-related neurotoxicity without definitive evidence of a stroke.

Throughout her treatment course, the patient's condition was discussed in a multidisciplinary tumor board. Chemotherapy was combined with palliative care to manage symptoms, improve quality of life, and provide psychosocial support. The management of duodenal adenocarcinoma, in this case, required addressing both the malignancy and its complications, such as gastric outlet obstruction and thromboembolic events.

Pathological examination confirmed the diagnosis of duodenal adenocarcinoma. Biopsy samples obtained during esophagogastroduodenoscopy (EGD) revealed moderately differentiated adenocarcinoma in the third portion of the duodenum (Figs. 5-8). The presence of angiolymphatic invasion within the biopsy specimens indicated an aggressive disease course and potential for widespread metastasis, as further corroborated by metastatic lesions identified in the liver. IHC staining was crucial in pinpointing the tumor origin and ruling out other potential primary sites. The tumor cells were positive for cytokeratin 7 and 20 and CA 19-9, while negative for SATB2, PAX-8, GATA-3, and TTF-1, supporting a gastrointestinal tract origin. This IHC profile, combined with the endoscopic imaging findings and morphological features of the cells, solidified the diagnosis of duodenal adenocarcinoma. Furthermore, the absence of mismatch repair protein deficiency, indicated by positive staining for MLH1, PMS2, MSH2, and MSH6, suggested that the tumor was not likely to respond to immunotherapy targeting mismatch repair deficiencies. These detailed pathology findings supported the clinical diagnosis and informed the therapeutic strategy, highlighting the integral role of comprehensive pathological analysis in managing complex cancer cases.

Discussion

This case illustrates the complex nature of diagnosing and managing advanced duodenal adenocarcinoma, a rare yet aggressive gastrointestinal malignancy [10]. The patient presented with nonspecific symptoms such as abdominal pain and indigestion, commonly associated with benign conditions. This highlights the diagnostic challenge and often leads to delays in identifying such malignancies. The lack of specific symptoms early in the disease course complicates timely diagnosis, emphasizing the need for high clinical suspicion and

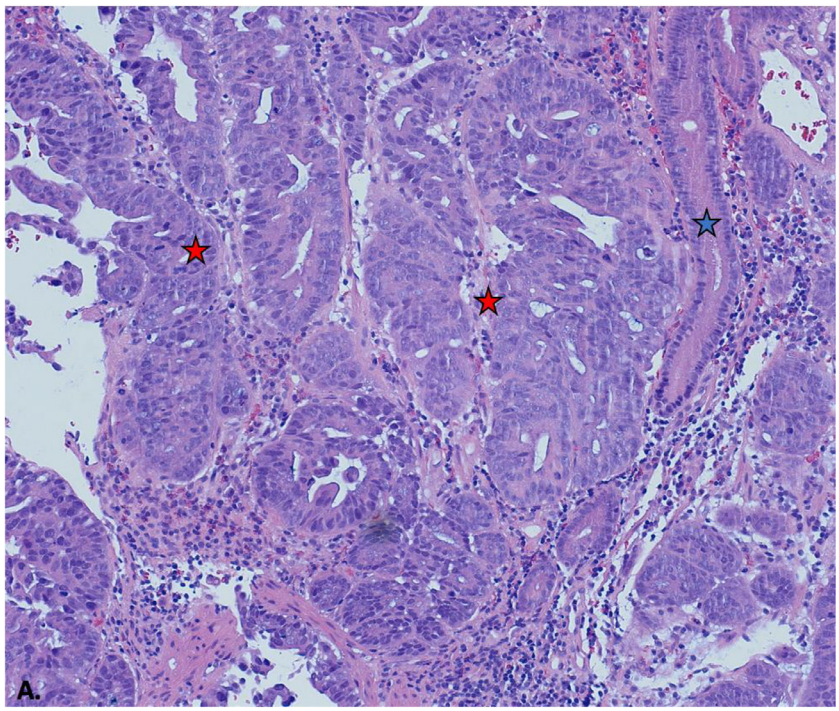

Fig. 5 – Hematoxylin and eosin (H&E) stain of the duodenal tumor at 20X magnification. Red stars indicate regions of adenocarcinoma, characterized by abnormal glandular structures. The blue star highlights the crypts of Lieberkühn, which are normal anatomical features of the small bowel.

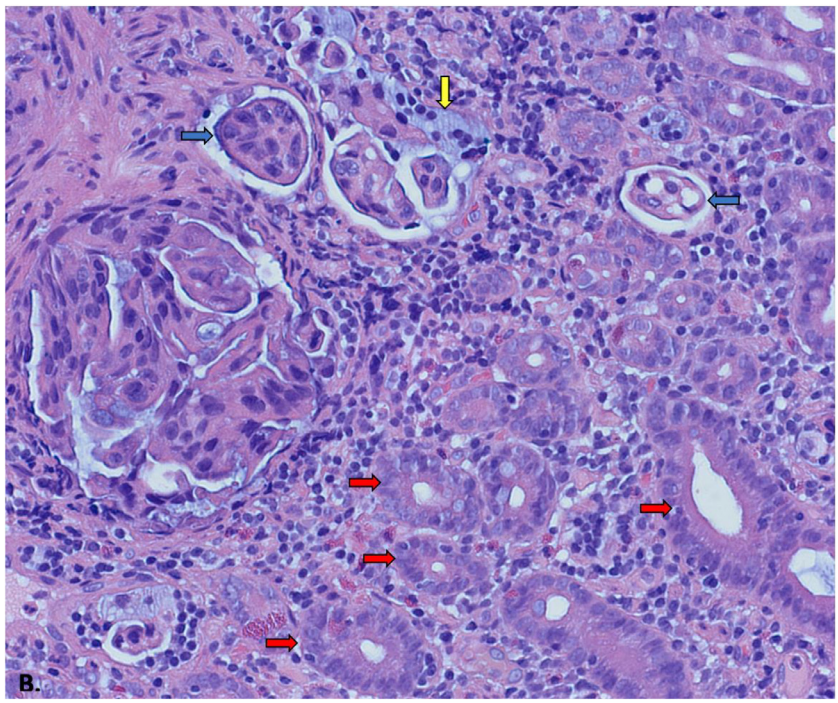

Fig. 6 – Hematoxylin and eosin (H&E) stain of the duodenal tumor at 20X magnification. Blue arrows highlight areas of lymphovascular invasion, indicating the spread of cancer cells through the lymphatic and vascular systems. The yellow arrow points to the presence of mucin, a common feature in adenocarcinomas. Red arrows indicate benign crypts of the small bowel (duodenum), demonstrating the contrast between malignant and normal tissue.

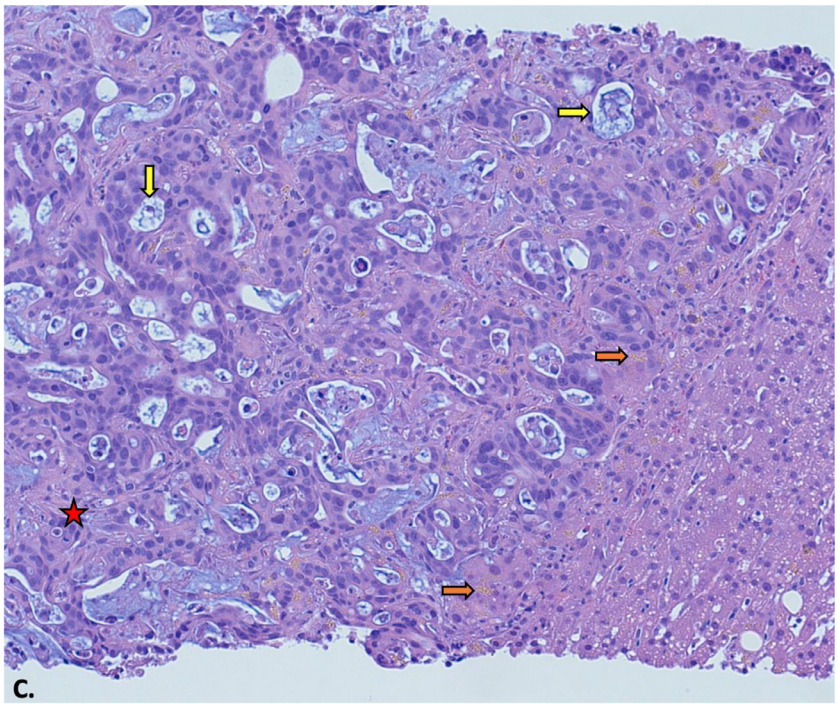

Fig. 7 – Hematoxylin and eosin (H&E) stain of the liver tumor at 40X magnification. Orange arrows indicate the bilious background, which is typical in liver tissue. Yellow arrows point to areas containing mucin, a substance commonly associated with adenocarcinomas. The red star marks a region of adenocarcinoma within the liver, showcasing malignant glandular formations. This slide provides a detailed view of the liver metastasis and its pathological features.

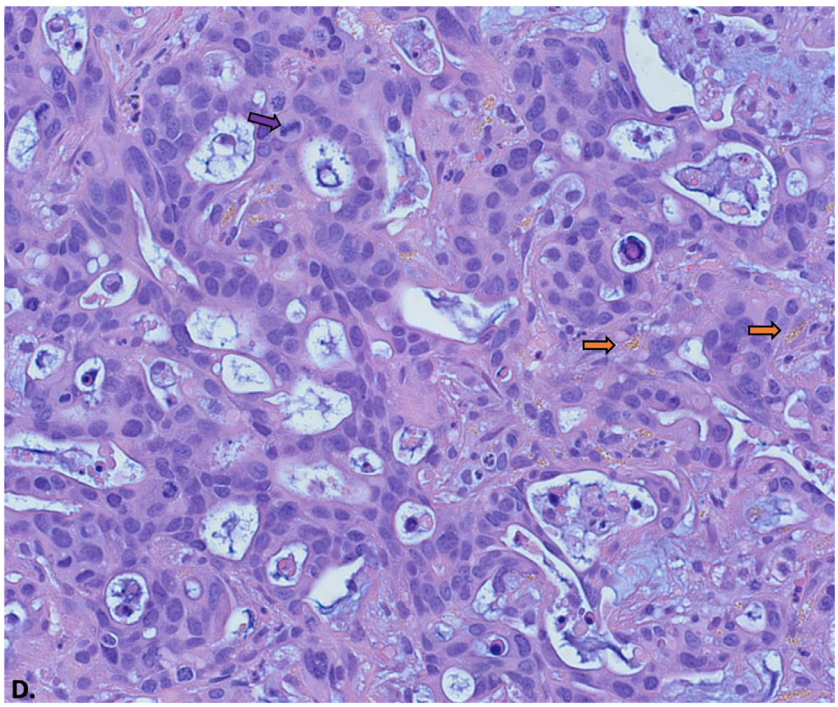

Fig. 8 – Hematoxylin and eosin (H&E) stain of the liver tumor at 40X magnification. The purple arrow indicates cells undergoing mitosis, highlighting active cellular proliferation within the tumor. Orange arrows point to the bilious background characteristic of liver tissue.

comprehensive diagnostic evaluations in patients presenting with similar symptoms [1].

In this case, the diagnostic process was guided by a combination of imaging studies and biochemical markers. The markedly elevated tumor markers, mainly CA 19-9, were pivotal in raising suspicion of a malignant process, given their association with gastrointestinal cancers. However, the specificity of CA 19-9 is limited, necessitating further imaging and histopathological confirmation [11,12]. The identification of a primary duodenal mass and liver metastases through CT and subsequent confirmation via EGD and biopsy exemplifies the multimodal approach necessary for accurate diagnosis.

A significant aspect of managing advanced duodenal adenocarcinoma involves addressing complications such as gastric outlet obstruction and biliary obstruction to prepare the patient for systemic therapy [13]. In this case, endoscopic stenting was effectively used to relieve the obstruction, allowing the initiation of chemotherapy.

The choice of FOLFOX as a first-line chemotherapy regimen is grounded in its efficacy in gastrointestinal cancers, leveraging the synergistic effects of fluorouracil, leucovorin, and oxaliplatin [14]. Fluorouracil acts as a pyrimidine analog that inhibits DNA synthesis, leucovorin enhances the binding of fluorouracil to thymidylate synthase, increasing its effectiveness, and oxaliplatin, a platinum compound, forms DNA adducts that prevent DNA replication and transcription [15]. However, the benefits of FOLFOX come with significant side effects, such as neuropathy, myelosuppression, and increased risk of thromboembolic events, all of which necessitate meticulous management [16].

The patient's treatment was complicated by neurological symptoms and pulmonary emboli, indicating the hypercoagulable state often seen in cancer patients [17]. These complications required immediate and coordinated adjustments in treatment, including initiating intravenous heparin infusion followed by long-term anticoagulation with enoxaparin and careful monitoring of hematological parameters. Adherence to the National Comprehensive Cancer Network (NCCN) guidelines for thromboprophylaxis in cancer patients at high risk of thromboembolic events was crucial in managing these complications and ensuring patient safety [17,18].

The poor prognosis associated with stage IV duodenal adenocarcinoma is well-documented, with survival rates significantly lower than those for localized disease [9]. This case further emphasizes the prognostic importance of molecular profiling, which can guide targeted therapies [19]. Although no actionable genetic variants were identified in this patient, the comprehensive molecular profiling provided essential information on the tumor's characteristics and potential therapeutic targets. Furthermore, the molecular characterization of the tumor also included analysis of mismatch repair protein expression. The presence of MLH1, PMS2, MSH2, and MSH6 indicated proficient mismatch repair, suggesting that the tumor was less likely to respond to pembrolizumab, a treatment option typically reserved for mismatch repair-deficient cancers, which are more common in colorectal and endometrial cancers. This aspect of molecular profiling highlights its pivotal role in selecting appropriate chemotherapy agents and potentially avoiding ineffective treatments and the associated toxicities [19].

As the field of oncology continues to evolve, integrating detailed molecular diagnostics into treatment planning is crucial for enhancing personalized medicine approaches [20]. These approaches aim to tailor treatments based on individual genetic profiles of tumors, potentially improving outcomes and efficiency in managing complex cases like this one.

The management strategy was not limited to addressing the malignancy and its direct complications [21]. It also involved preemptive and responsive care measures to maintain quality of life and manage adverse side effects. Palliative care was integrated early in the treatment process, providing symptom relief and psychosocial support while helping the patient navigate her treatment journey with dignity [5]. The role of palliative care is particularly crucial in advanced cancer stages, where the focus shifts to enhancing the quality of life and managing symptoms rather than curative treatment [22]. The chemotherapy plan was tailored to the patient's evolving clinical status, considering dose adjustments based on tolerance and side effect management [5,7]. Regular multidisciplinary team meetings were pivotal in adapting the treatment plan to respond to the patient's complex needs, highlighting the necessity for dynamic treatment strategies in managing advanced duodenal adenocarcinoma [8].

In summary, this case of a 53-year-old woman with advanced duodenal adenocarcinoma highlights the intricate challenges involved in diagnosing and managing this rare and aggressive malignancy. The patient's initial presentation with nonspecific gastrointestinal symptoms necessitated a thorough diagnostic workup, including advanced imaging, tumor marker evaluation, and histopathological confirmation. The identification of extensive metastatic disease highlights the critical importance of a comprehensive and multifaceted diagnostic approach in accurately identifying such malignancies. Integrating molecular profiling, early palliative care and a multidisciplinary approach is essential in optimizing outcomes and managing the complex needs of patients with advanced duodenal adenocarcinoma.

Conclusion

This case of advanced duodenal adenocarcinoma highlights several critical aspects in the diagnosis and management of rare gastrointestinal malignancies. Malignancy must be recognized in patients with persistent gastrointestinal symptoms, even when nonspecific and often associated with benign conditions. Comprehensive diagnostic tools, including advanced imaging and histopathological evaluation, are vital for accurate diagnosis and staging.

Properly addressing complications such as gastric outlet and biliary obstructions is crucial for facilitating systemic therapies. This case illustrates the importance of a multidisciplinary approach in managing complex cancer cases, ensuring all aspects of patient care are addressed collaboratively.

Molecular profiling has become a critical component in guiding therapeutic decisions. Although no actionable genetic variants were identified in this instance, molecular diagnostics provided valuable insights into the tumor's characteris-

tics, informing treatment strategies and demonstrating the potential for personalized medicine.

Early integration of palliative care is another essential aspect, focusing on symptom relief and quality of life. Combining aggressive oncologic management with comprehensive supportive care is necessary to optimize patient outcomes. The insights gained from this case contribute to a better understanding of the multifaceted approach required in treating rare and advanced gastrointestinal cancers like duodenal adenocarcinoma.

Patient consent

We confirm that we have obtained written, informed consent from the patient for the publication of this case report. The patient has been thoroughly informed about the details that will be published and understands the implications of the publication. The written consent is stored securely and is available for review by the editorial team upon request.

REFERENCES

[1] Goldner B, Stabile BE. Duodenal adenocarcinoma: why the extreme rarity of duodenal bulb primary tumors? Am Surg 2014;80(10):956–9.

[2] Ushiku T, Arnason T, Fukayama M, Lauwers GY. Extra-ampullary duodenal adenocarcinoma. Am J Surg Pathol 2014;38(11):1484–93. doi:10.1097/pas.0000000000000278.

[3] Yabuuchi Y, Yoshida M, Kakushima N, Kato M, Iguchi M, Yamamoto Y, et al. Risk factors for non-ampullary duodenal adenocarcinoma: a systematic review. Dig Dis 2022;40(2):147–55. doi:10.1159/000516561.

[4] de Sousa Miranda I, Ávila L, Castro L, Rocha S, Monteiro M, Domingos R. Synchronous neoplasms of the small bowel: a diagnostic challenge. Eur J Case Rep Intern Med 2022;9(3):003231. doi:10.12890/2022_003231.

[5] Cloyd JM, George E, Visser BC. Duodenal adenocarcinoma: advances in diagnosis and surgical management. World J Gastrointest Surg 2016;8(3):212–21. doi:10.4240/wjgs.v8.i3.212.

[6] Tesarikova J, Skalicky P, Kurfurstova D, Svebisova H, Urban O, Flat P, et al. Surgical treatment of duodenal adenocarcinoma: ampullary vs. non-ampullary, short- and long-term outcomes. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub 2022;166(3):290–6. doi:10.5507/bp.2021.028.

[7] López-Domínguez J, Busquets J, Secanella L, Peláez N, Serrano T, Fabregat J. Duodenal adenocarcinoma: surgical results of 27 patients treated at a single center. Cir Esp (EnglEd) 2019;97(9):523–30. doi:10.1016/j.ciresp.2019.06.014.

[8] Ye X, Zhang G, Chen H, Li Y. Meta-analysis of postoperative adjuvant therapy for small bowel adenocarcinoma. PLoS One 2018;13(8):e0200204. doi:10.1371/journal.pone.0200204.

[9] Hirashita T, Ohta M, Tada K, Saga K, Takayama FH, Endo Y, et al. Prognostic factors of non-ampullary duodenal adenocarcinoma. Jpn J Clin Oncol 2018;48(8):743–7. doi:10.1093/jjco/hyy086.

[10] Tuan HX, Lieu DQ, Anh TN, et al. A rare case of duodenal adenocarcinoma. Radiol Case Rep 2023;18(12):4400–3. doi:10.1016/j.radcr.2023.09.037.

[11] Pavai S, Yap SF. The clinical significance of elevated levels of serum CA 19-9. Med J Malaysia 2003;58(5):667–72.

[12] Scarà S, Bottoni P, Scatena R. CA 19-9: biochemical and clinical aspects. Adv Exp Med Biol 2015;867:247–60. doi:10.1007/978-94-017-7215-0_15.

[13] Suh CH, Tirumani SH, Shinagare AB, Kim KW, Rosenthal MH, Ramaiya NH, et al. Diagnosis and management of duodenal adenocarcinomas: a comprehensive review for the radiologist. Abdom Imaging 2015;40(5):1110–20. doi:10.1007/s00261-014-0309-4.

[14] Yasui T, Mukubo H, Nakanuma S, Sato N, Kita I. [A case of recurrent duodenal carcinoma successfully controlled with FOLFOX treatment]. Gan To Kagaku Ryoho 2013;40(12):1726–8.

[15] Mishima H, Ikenaga M, Tsujinaka T, Yasui M, Kashiwazaki M, Miyazaki M, et al. [FOLFOX]. Gan To Kagaku. Ryoho 2006;33(7):911–14.

[16] Salehifar E, Avan R, Janbabaei G, Mousavi SK, Faramarzi F. Comparison the incidence and severity of side effects profile of FOLFOX and DCF regimens in gastric cancer patients. Iran J Pharm Res Spring 2019;18(2):1032–9. doi:10.22037/ijpr.2019.1100663.

[17] Dardiotis E, Aloizou AM, Markoula S, Siokas V, Tsarouhas K, Tzanakakis G, et al. Cancer-associated stroke: pathophysiology, detection and management (Review). Int J Oncol 2019;54(3):779–96. doi:10.3892/ijo.2019.4669.

[18] Ikezoe T. Cancer-associated thrombosis and bleeding. Int J Hematol 2024;119(5):493–4. doi:10.1007/s12185-024-03716-0.

[19] Irmisch A, Bonilla X, Chevrier S, Lehmann K, Singer F, Toussaint NC, et al. The tumor Profiler Study: integrated, multi-omic, functional tumor profiling for clinical decision support. Cancer Cell 2021;39(3):288–93. doi:10.1016/j.ccell.2021.01.004.

[20] Choi RS, Lai WYX, Lee LTC, Wong WLC, Pei XM, Tsang HF, et al. Current and future molecular diagnostics of gastric cancer. Expert Rev Mol Diagn 2019;19(10):863–74. doi:10.1080/14737159.2019.1660645.

[21] Kaklamanos IG, Bathe OF, Franceschi D, Camarda C, Levi J, Livingstone AS. Extent of resection in the management of duodenal adenocarcinoma. Am J Surg 2000;179(1):37–41. doi:10.1016/s0002-9610(99)00269-x.

[22] Temel JS, Petrillo LA, Greer JA. Patient-centered palliative care for patients with advanced lung cancer. J Clin Oncol 2022;40(6):626–34. doi:10.1200/jco.21.01710.