Duodenal Adenocarcinoma – A Rare Encounter and Management in a Young Male

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Abstract

A rarely encountered tumor, Duodenal Adenocarcinoma (DA) has a poor prognosis with a 5-year survival rate at 30%. DA usually occurs in the older age group; it is diagnosed at an average age of 60 years. DA with peritoneal dissemination in a younger population has not been well reported in the literature review, so we are reporting this case. The carcinoma was diagnosed in the third segment of the duodenum (D3) with associated peritoneal carcinomatosis. The patient presented with abdominal pain, nausea, weight loss, and other symptoms with a history of cholecystectomy for his prior abdominal complaints. A large, obstructive, ulcerated mass in the third segment of the duodenum (D3) confirmed the presence of a DA. A palliative gastrojejunostomy was performed, followed by Whipple procedure with hyperthermic intraperitoneal chemotherapy (HIPEC). After surgery, the patient presented with postoperative complications including ascites and perforation of the sigmoid colon. On subsequent follow-ups, patient was well; however, one year after Whipple's procedure, there was a recurrence in the form of lung nodules.

Besides being one of the rarest malignancies, DA is significantly scarce in the younger subset. The key to a better outcome involves an aggressive approach with an early diagnosis. Lymph node assessment is an important prognostic factor. No positive correlation has been established between adjuvant chemotherapy and survival rates. Peritoneal dissemination from DA is uncommon. HIPEC, although a reasonable therapeutic strategy for disseminated peritoneal carcinomatosis, resulted in sigmoid perforation.

Keywords: *Duodenal adenocarcinoma, familial adenomatous polyposis, lymph node assessment, hyperthermic intraperitoneal chemotherapy, tumor resection.*

BACKGROUND

Clinicians need to remain aware about diagnosing duodenal adenocarcinomas at an early stage. Early diagnosis is essential for a better outcome. Patients presenting with abdominal pain, pale stools, and dark urine should undergo a preliminary DA screening. Patients suffering from Familial Adenomatous Polyposis (FAP) must be observed and closely followed, since they have an increased tendency to develop DA. Lymph node assessment has been a major prognostic factor in many studies and hence is of utmost importance. The key to a curative approach lies within complete resection of the tumor. HIPEC can be used as a therapeutic strategy in patients with advanced disseminated disease.

INTRODUCTION

Duodenal Adenocarcinoma is one of the rarest tumors encountered, accounting for half of all small bowel adenocarcinomas [1-4]. Although rarely found, it must be considered as a differential diagnosis for occult gastrointestinal bleeding [4]. The segment of the duodenum most commonly involved is the second, with the third and fourth being more uncommon in encounter; duodenal bulb (first segment) cancers are the rarest [3, 5]. Poor prognosis results because of the condition being difficult to diagnose due to the appearance of non-specific symptoms. Pancreaticoduodenectomy is a successful approach, especially in patients with resectable lesions in the first and second duodenal segments [6, 7]. An aggressive surgical approach leads to a better long-term survival rate for patients with a resectable lesion. The role and efficacy of adjuvant chemotherapy and radiotherapy are still left to be determined [5, 7, 8].

CASE REPORT

A 38-year-old male with multiple co-morbidities including essential hypertension, gastroesophageal reflux disease, dyslipidemia, urolithiasis, and renal failure presented with weight loss, abdominal pain, fatigue, poor appetite, nausea, and vomiting. There was no abdominal mass, guarding, or rigidity. There was no lymphadenopathy or edema. The patient also presented with dark urine, pale-colored stools, and pruritis. He had previously undergone cholecystectomy for post-prandial pain and other abdominal symptoms, but did not achieve any symptomatic relief. He used to be a smoker; he quit the habit 9 years before the diagnosis of DA. He consumed alcohol weekly.

He underwent an esophagogastroduodenoscopy (EGD), which revealed a large obstructive ulcerated mass in the third segment of the duodenum (D3) that had occluded 80% of the lumen. The stomach and the proximal duodenum were also found to be dilated due to the distal obstruction. The ulcerated mass, which was diagnosed as an intramucosal duodenal adenocarcinoma, had caused a functional gastric outlet obstruction.

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The patient underwent a laparoscopic loop gastrojejunostomy along with a diagnostic laparoscopy involving a biopsy of the peritoneal metastasis. White plaque lesions, visualized on the peritoneum with a few metastatic nodules on the omentum, were biopsied; these lesions were consistent with DA. Postoperatively, a Percutaneous Transhepatic Cholangiocatheter (PTC) was introduced *via* the right lobe of the liver, and the patient was started on FOLFOX (a chemotherapy regimen of the drugs Folinic acid, Fluorouracil, and Oxaliplatin) with Avastin.

A standard Whipple procedure with distal gastrectomy, appendectomy, and cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (HIPEC) of the omental and peritoneal carcinomatosis was performed. The patient was explained the risks and benefits of the surgery and upon his consent, he was admitted for surgery. Few metastatic lesions were observed in the pelvis, cul-de-sac between the bladder and the rectum, and on the surface of the transverse colon. The hepatic flexure of the colon was mobilized; an extended kocherization of the duodenum was performed. A complete omentectomy was carried out and samples sent for pathological evaluation. The gastroepiploic vessels and the right gastric artery were ligated and divided. The common bile duct was found to be dilated and the stent visualized. The pyloric antrum was divided using a linear stapler. The jejunum and the mesentery were further divided at the duodenojejunal flexure using a linear stapler and with the LigaSure respectively. The tumor at this region was found adherent to the superior mesenteric artery and was left to be dissected in the end. The neck of the pancreas was divided with a Bovie cautery, and the main pancreatic duct was identified. The pancreas was found to be free of any pathology. Careful dissection of the head of the pancreas was done along with the uncinate process and the fourth portion of the duodenum. The peritoneum in the pelvic cul-de-sac consisting of metastatic lesions was stripped.

Next, an appendectomy was performed by dividing the mesoappendix with LigaSure. On final inspection, no other disease or lesion was identified, and successful hemostasis was achieved. Copious irrigation of the entire abdominal cavity was done with warm saline. Cannulas were placed for inflow and outflow to perform HIPEC with mitomycin-C.

Unfortunately, the HIPEC machine malfunctioned; the intervention was aborted with the intention of doing it at a later stage. The overlying abdominal fascia was closed using sutures, and the patient was successfully transported to the post-anesthesia care unit in stable condition. On the pathological evaluation of the tumor, a poorly differentiated, 5.3 cm, grade 3 duodenal adenocarcinoma staged T4N0M1 with peritoneal carcinomatosis was revealed.

The HIPEC procedure was re-executed 2 days later. The patient was explained the risks and benefits; upon his consent, he was admitted for surgery. The abdominal cavity was opened, irrigated, and suctioned with warm saline until all fluid was cleared and subsequently inflow and outflow cannulas were placed for the HIPEC procedure. The abdominal cavity was then closed using a suture, and HIPEC was given to the abdominal cavity using 30 mg of mitomycin-C at 42°C for 60 minutes. After the intervention, the cannulas were removed, and the abdominal cavity was re-irrigated. On final inspection, a satisfactory hemostasis was observed. A 19-suction drain was placed adjacent to the biliary and pancreatic anastomotic repair which was externalized on the surface of the right abdominal wall.

Postoperatively, he had persistent abdominal pain with fever. CT-scan revealed an increased amount of abdominal and pelvic ascites. Re-exploration of the abdominal cavity showed a perforation on the lateral wall of the sigmoid colon; a primary suture repair was carried out effectively.

Finally, a 19-French suction drain was placed adjacent to the sigmoid anastomotic repair which was externalized on the surface of the left abdominal wall.

On subsequent follow-ups, the patient appeared to be doing fine. One year after the Whipple procedure, nodules, less than 5 mm, were noted on CT scan of the chest. Further in time, the lesions progressed in the lung, with the largest measuring 9mm. The patient was started on chemotherapy.

DISCUSSION

Small Bowel Adenocarcinoma accounts for only 1% of all gastrointestinal malignancies. Duodenal adenocarcinomas (DA) accounts for about half of all small bowel adenocarcinomas [2, 4, 9]. For a better perspective of the cancers located in the duodenal segments, the duodenum has been classified into four segments mainly D1 (proximal horizontal 5 cm beginning with the 3-cm duodenal bulb), D2 (descending), D3 (distal horizontal), and D4 (ascending). Primary adenocarcinoma of the duodenum accounts for 0.3–0.5% of all gastrointestinal malignancies, with a study suggesting that the segment most commonly involved is the D2 (the second part of the duodenum) [2, 3, 10-12]. The adenocarcinomas of the third and fourth segments of the duodenum are more uncommon; about 45% of the carcinomas occur in this region [4, 13]. Because duodenal adenocarcinomas are rare in the vast variety of GI-related cancers, it causes a delay in the confirmation of its diagnosis by presenting with nonspecific symptoms and eventually leading to a poor prognosis with a 30% 5-year survival for patients with resectable tumors [10, 13-15]. Literature review suggests that the mean age at diagnosis of carcinoma is typically about 60 +/- 10 years [16, 17].

Since DA is encountered rarely, its etiology is still not completely known. Certain factors have been identified to have a role in its carcinogenesis. Patients with Gardner syndrome, duodenal polyps, duodenal adenomas, and villous tumors have been shown to have an increased predisposition towards developing DA [5, 6]. Literature review suggests that 25-50% of duodenal adenocarcinomas occur in patients with villous adenomas [6, 20]. Patients with Familial Adenomatous Polyposis (FAP) are also at an increased risk of developing DA. 2-4.5% of all patients with Familial Adenomatous Polyposis (FAP) develop DA in their lifetime, making their prognosis poor [5, 6, 18]. This has been demonstrated by a 10-year prospective study conducted on patients of DA with concurrent FAP; the study suggested that DA is the leading cause of death in patients with FAP [19]. Studies also suggest that DA is the most frequent extracolonic malignancy in patients with FAP [20].

The symptomatology of DA is non-specific. Symptoms present when the tumor has grown to a sufficient size. The non-specific symptoms include abdominal pain with cramps, nausea, vomiting (biliary), fatigue, weakness, and weight loss. Anemia due to chronic gastrointestinal bleeding, gastrointestinal obstruction, and jaundice are associated with the advanced stage of the disease. These non-specific symptoms make it difficult to diagnose the condition. The most common presenting symptom is abdominal pain, which has been observed in 56% of patients in some studies [3, 5, 6, 8, 15].

Usually, the initial investigation for DA is the esophagogastroduodenoscopy (EGD), which has been successful in screening this rare tumor [5, 21]. The preferred diagnostic intervention, which provides a simultaneous visualization and biopsy, is the endoscopy [5]. A study conducted on 89 patients with primary adenocarcinoma of the duodenum highlights the use of duodenography and endoscopy as the most effective diagnostic tests [14]. The literature review suggests that diagnosis and staging can be performed in 80-100% of cases if EGD and endoscopy remain the principal tests being carried out, integrated with other examinations [15]. Keeping these diagnostic modalities in consideration, studies note the challenging task of visualizing the third and fourth segments of the duodenum. In such cases, the use of extra-long fiber optic scopes has been beneficial [3, 5, 7, 8, 15].

Literature review also recommends the use of second and third-level examinations when encountering adenocarcinoma in the third and fourth segments of the duodenum. Second-level examinations include Computed Tomography (CT), Magnetic Resonance Imaging (MRI), and Ultrasonography (U/S). Third-level examinations include echoendoscopy, celiac axis arteriography, endoscopic retrograde cholangiopancreaticography (ERCP), and laparoscopy. These radiological techniques allow preoperative staging of the tumor and planning of an effective therapeutic strategy [15]. A recent study also reports the advantage of capsule endoscopy as part of an additional workup in patients with DA. The capsule is swallowed, and the duodenum is visualized. This can be of great value in determining precancerous or cancerous pathologies of the duodenum [22].

To further aid in the staging and diagnosis of the tumor, endoscopic U/S may be performed to determine the local extension and regional lymph nodes involved [5, 6]. The abdominal U/S can be of great value in the diagnosis and assessment of the vascular structures involved, showing lesions as irregularly marginated hypoechoic masses. Characteristic malignant lesions exhibit an exophytic or intramural mass, central necrosis, and ulceration. If the location of the tumor lies intraluminal, a benign tumor is justified. These classic features are sensitive but non-specific [5, 8].

The definitive diagnosis of DA is confirmed by a histopathological analysis of tissue specimens with an assessment of the degree of dysplasia [3, 5, 7, 23]. Differentials should include adenocarcinoma of the stomach, pancreatic carcinoma, distal cholangiocarcinoma, and ampullary adenocarcinoma. Four phenotypic variations are considered when analyzing the histopathology of DA, namely the intestinal, gastric, pancreaticobiliary, and the indeterminate, with a favorable prognosis of the intestinal phenotype [5].

Staging of DA by the TNM staging system is maintained by the American Joint Committee on Cancer (AJCC). Once the T, N, and M categories have been determined, this information is combined to assign an overall stage of 0, I, II, III, or IV sometimes followed by a letter [5]. DA can be diagnosed most reliably by performing endoscopy and a biopsy, whereas endoscopic ultrasonography and CT scan techniques are best in assessing tumor extension [6]. A study conducted on 89 patients with primary DA concluded that early diagnosis was the main factor in improving outcome [14].

Treatment of DA involves surgical intervention. No strict definite path has been adopted to approach such cases. The key to a better prognosis involves an early diagnosis combined with an aggressive surgical approach [7, 8, 10, 13-15, 21]. Literature review suggests radical surgical excision as the treatment of choice for primary malignant duodenal tumors probably due to a higher resectability rate of 60-70% [5, 8, 15, 23]. Various surgical methods have been mentioned in the literature review: endoscopic excision, local excision, segmental resection, pancreaticoduodenectomy (PD – Whipple procedure), and pylorus-preserving pancreaticoduodenectomy [6]. According to a recently published article, PD is required for tumors arising in the second part of the duodenum, having proximity to the head of the pancreas, distal bile duct, and the hepatopancreatic ampulla of Vater. Tumors arising in the first, third, or

fourth segments of the duodenum may be managed by either PD or segmental resection [5].

Another study also highlights pancreaticoduodenectomy and its variant pylorus-preserving pancreaticoduodenectomy as the most frequently performed curative surgical intervention [15]. Two other literature reviews suggest that PD offers the best chance of long-term survival in patients who have a resectable lesion [7, 10]. The resectability of the tumor has a profound effect on the survival rate. One study mentions that the five-year survival rate for patients with non-resected tumors is around 15-30%; for patients who have had resections, it is about 40-60% [4].

Lymph node assessment is a major prognostic factor. Studies show a survival period of 6 months with lymph node invasion in contrast to 56.5 months in patients without lymph node invasion [5, 23]. Literature review suggests that the lymph node metastasis has a significant relationship with the occurrence of distant metastasis [6, 15]. The American Joint Committee on Cancer has recommended pathological evaluation of a minimum of 6 lymph nodes.

Regarding palliative surgery, the purpose is to relieve gastric outlet obstruction, biliary obstruction, and pain. The surgical approach for gastroduodenal obstruction may include a gastrojejunostomy or duodenojejunostomy. Duodenal and biliary stents can also be placed in patients not undergoing surgery [5, 24].

Chemotherapeutic strategy must be adopted in all patients with an unresectable tumor or a metastatic outcome. Patients with a high-risk factor such as nodal metastasis are treated with oxaliplatin-based chemotherapy. Some studies report no significant benefit of adjuvant chemotherapy on survival rates as well as prognosis [3, 8]. According to a recent study, no correlation between adjuvant radiotherapy and DA has been established [5].

Our DA case presented with peritoneal carcinomatosis. Literature review suggests that the majority of peritoneal carcinomatosis arises from either the jejunum or the ileum, and rarely as a consequence of DA. The study demarcated the duodenum predominantly as a retroperitoneal structure; peritoneal dissemination from DA is a difficult process due to a natural peritoneal barrier.

The literature review markedly supports the use of HIPEC. According to a study, 17 patients underwent HIPEC with mitomycin for peritoneal carcinomatosis arising from small bowel adenocarcinoma (PCSBA). These patients achieved a mean overall postoperative survival of 18.4 months. The study concluded that systemic chemotherapy along with HIPEC remains uncertain and requires further evaluation with larger prospective clinical data [25]. Two further studies identified cytoreductive surgery and HIPEC as attractive options for small bowel cancer peritoneal carcinomatosis with encouraging survival results [26, 27].

Literature review also suggests HIPEC as a reasonable surgical option for patients diagnosed at an advanced stage [25]. Although HIPEC has the advantage of increasing survival, it cannot guarantee the non-progression of the disease. In a study, 6 patients who underwent cytoreductive surgery and HIPEC with Mitomycin C were retrospectively analyzed. These patients were diagnosed with PCSBA. Three patients successfully thrived; three died of disease progression [27]. A similar encounter of disease progression was found in our case, and the patient was started on chemotherapy. Sun Y. *et al.* in their study Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for peritoneal carcinomatosis from small bowel adenocarcinoma also state early treatment with HIPEC may prolong survival in patients with PCSBA. However, whether a repeat HIPEC would improve survival in patients with primary SBA remains unclear [25].

Complications arising from HIPEC have also been a major concern. Table **1** summarizes complications more commonly encountered in the literature review. Complications and toxicity of 102 patients were analyzed in a study to determine the side effects of HIPEC. Toxicity was graded according to National Cancer Institute Common Toxicity Criteria (NCI CTC) classification. The study concluded toxicity of cytoreduction followed by HIPEC was around 65% (Grade 3-5 NCI CTC) with fistulae most frequently encountered. This highlighted HIPEC as a treatment with high morbidity [28]. On the contrary, our case had a unique sigmoid perforation which has not been reported in the literature review. Nesher E. *et al.* describe HIPEC as a safe treatment modality with an acceptable complication rate in their study, Cytoreductive surgery and intraperitoneal hyperthermic chemotherapy in peritoneal carcinomatosis [29]. The literature review also suggests that the toxicity is mainly related to surgery; this may explain the cause of sigmoid perforation in our case [30].

Table 1: Complications of HIPEC.

Complications of HIPEC
Bleeding
Infection
Development of enterocutaneous fistula
Anastomotic leak
Formation of blood clots
Reduced caloric intake
Bone marrow suppression
Nephrotoxicity
Neutropenic infection
Pulmonary toxicity
Small bowel perforation

Source: [30, 31]

CONCLUSION

The key to a successful outcome involves an aggressive approach with an early diagnosis. There is a lack of recent literature on the diagnosis of DA in the younger subset. Screening EGD alongside lymph node assessment could be considered a cardinal tool in aiding the preliminary diagnosis of DA, specifically in patients with a positive family history of FAP, bowel ailments, or SBA. Peritoneal dissemination from DA occurs rarely; if encountered, HIPEC should be considered as part of the efficacious therapeutic strategy by analyzing the risks and benefits effectively.

CONSENT FOR PUBLICATION

Verbal consent was taken from the patient. Patient specific demographic data/personal information was not utilized in the preparation of this case report.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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