Exceedingly rare synchrony of adenocarcinoma of the ampulla with an ileal gastrointestinal stromal tumor

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Introduction:

This is a unique case of a patient who was found to have two extremely primary malignancies synchronously, i.e., an ampullary adenocarcinoma arising from a high-grade dysplastic tubulovillous adenoma of the ampulla of Vater (TVAoA) with a high-grade ileal gastrointestinal stromal tumor (GIST). Based on a literature review and to the best of our knowledge, this is the first report of this synchronicity. Primary ampullary tumors are extremely rare, with an incidence of four cases per million population, which is approximately 0.0004%An adenoma of the AoA may occur sporadically or with a familial inheritance pattern, as in hereditary genetic polyposis syndrome such as familial adenomatous polyposis syndrome (FAPS).

Case Presentation:

The patient was a 77-year-old Caucasian male who presented with generalized weakness and decreased appetite associated with a weight loss of approximately 40 pounds in the prior 2 months. The patient's vital signs were stable. The physical examination was significant for scleral and palmar icterus. No lymph nodes were palpable. The rest of the physical examination findings were benign. Complete blood counts were normal. A comprehensive metabolic panel revealed a serum sodium level of 128 mmol/L, creatinine level of 1.5 mg/dL, and lipase level of 1904 U/L, which decreased to 755U/L on the day of discharge. The hepatitis panel was negative. Liver function tests are shown in Table 1, and tumor markers are shown in Table 2. Contrast-enhanced computed tomography (CT) of the abdomen and pelvis showed a polypoid, soft tissue mass at the level of the distal common bile duct (DCBD)/AoV measuring approximately 9 mm with resultant intra- and extrahepatic biliary dilatation (Figure 1A and B). The CBD measured 15 mm in diameter, and cystic lesions measuring up to 1 cm were noted in the tail of the pancreas. There was a heterogeneously enhanced lobulated mass with punctate calcifications in the posterior pelvis likely originating from the serosal surface of the pelvic small bowel (Figure 1C and D). Magnetic resonance cholangiopancreatography (MRCP) (Figure 2) showed a polypoid mass again noted at the level of the DCBD/AoV. It measured approximately 2.3 cm × 2.0 cm × 1.7 cm with a slightly prominent pancreatic duct measuring 6 mm in diameter. Given his CT and MRCP findings, medical gastroenterology and general surgery experts were consulted. He underwent endoscopic retrograde cholangiopancreatography (ERCP), which showed abnormal papillae with polypoid masses (Figure 3). Sphincterotomy and deep cannulation procedures were performed and confirmed by fluoroscopy. It showed CBD dilatation, and there was an abrupt cutoff at the distal aspect. The general surgery consultant recommended biopsy of the pelvic mass for probable metastatic disease. The patient underwent positron emission tomography (PET), which showed an endo-biliary stent in the region of the papilla, a 1.7 cm ampullary mass with intense fluorodeoxyglucose (FDG) avidity (Figure 4A) and an oval-shaped, well-defined FDG-avid lesion measuring approximately 6 cm × 3 cm (Figure 4B), with a small punctate area of calcification present within the lesion located deep in the pelvis along the posterior margin of the small bowel loops. No FDG-avid lymph nodes were identified. No lytic or blastic FDG lesions were observed. Histopathology of the ampullary mass that was biopsied on endoscopy showed a tubulovillous adenoma with high-grade dysplasia (Figure 5). This case was discussed at the hepatobiliary multidisciplinary conference, and all images and paths were discussed. It was recommended for the patient to undergo resection of both the ampullary mass and small bowel lesions. The patient was an ideal candidate for the Whipple procedure, even robotically/laparoscopically. However, the patient only consented to ampullectomy, not to the Whipple procedure. The patient underwent duodenal exploration and was found to have a broad ampullary polypoid lesion that was not amenable to endoscopic resection. However, endoscopic ultrasound and intraoperative ultrasound did not reveal any evidence of pancreatic invasion. We advanced a Fogarty catheter via the cystic duct through the ampulla down to the duodenum. The ampullary mass was excised with a negative margin as well as negative peri-pancreatic/peri-duodenal nodes per frozen section (Figure 6A and B). Subsequently, a pedunculated ileal GIST was found approximately 150 cm proximal to the ileocecal valve. This was resected en bloc with a loop of small bowel. There was no associated mesenteric adenopathy. Subsequently, side-to-side small bowel anastomoses were created (Figure 6C). With an adenocarcinoma in the specimen and a close margin on permanent section, the patient did not undergo the Whipple procedure, and the patient also wished to undergo chemotherapy and was therefore scheduled to see medical and radiation oncology experts.

Table 1 Liver function tests

Liver function tests	On admission	On discharge
ALT	299	196
AST	122	75
ALP	848	754
Total Bilirubin	5.9	2.6
Direct Bilirubin	4.2	2.0
Albumin	3.0	2.6

Table 2 Tumor markers

Tumor marker	Result	Normal range
CEA	0.99	0.01-4.00
CA-19	454	0.00-37

Figure 1

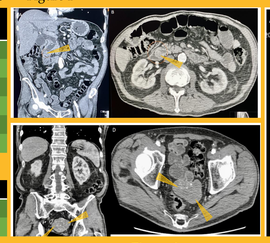


Figure 4

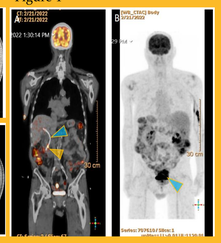


Figure 2 A,B

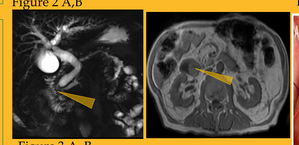


Figure 3 A, B

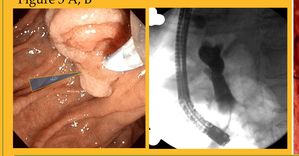
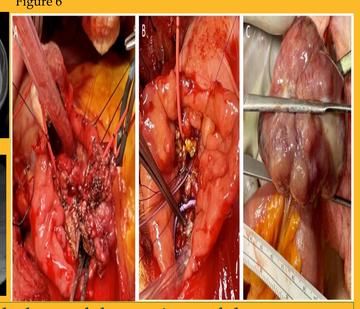


Figure 6



Surgical pathology: Histopathology of the sections of the ampullary mass (Figure 7A and B) demonstrated a 1.5 cm invasive adenocarcinoma arising from a high-grade dysplastic TVAoA. The tumor invaded the muscularis propria of the duodenum. The tumor invaded 1 mm of the pancreas but did not invade the pancreatic parenchyma. In the intact specimen, no tumor was present at the surgical margins of the resection. Given the likelihood that nonmarginal tissue may be exposed to thermal artifacts, the margins of resection were deemed to be free of tumors. Histopathology of the sections of the small bowel mass (Figure 7C and D) demonstrated a high-grade, GIST spindle cell type, with 15 mitoses per 5 square millimeters. A series of special stains (Figure 7E) with working controls was performed. The tumor cells were positive for DOG-1 and CD 117, consistent with a GIST.

Figure 5 A,B

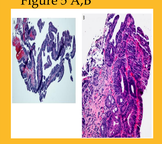
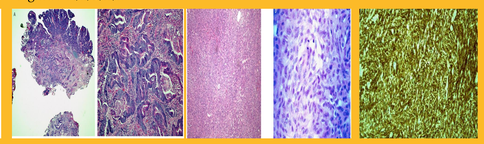


Figure 7 A,B,C,D,E



Final Diagnosis:

The final diagnosis was a T2N0M0 adenocarcinoma of the ampulla arising from a high-grade TVAoA coexisting with a T3N0M0 high-grade ileal GIST.

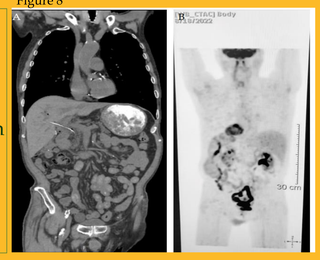
Treatment:

As mentioned above in the multidisciplinary expert consultation, the patient underwent surgical ampullectomy,ileal GIST resection with ileo-ileal side to side anastomosis. The patient was scheduled for chemoradiation as recommended by medical oncologist.

Outcome and Follow up: Surveillance CT of the chest, abdomen and pelvis w/contrast on three months after surgery showed no findings for metastatic disease (Figure 8).

After three weeks of recovery from ampullectomy, the patient underwent five and half weeks of external beam radiation therapy with concurrent chemotherapy with 5-fluorouracil. He is currently on an adjuvant therapy of imatinib (400 mg per oral daily) for the GIST. His repeat PET scan performed on August 2022 showed a complete metabolic response (16).

Figure 8



DISCUSSION

This is a unique case of a patient who was found to have two extremely primary malignancies synchronously, i.e., an ampullary adenocarcinoma arising from a high-grade dysplastic TVAoA with a high-grade ileal GIST. Based on a literature review and to the best of our knowledge, this is the first report of this synchronicity. Primary ampullary tumors are extremely rare, with an incidence of four cases per million population, which is approximately 0.0004%. Adenomas are the most common ampullary tumors. AoAs can occur as sporadic in a familial inheritance pattern, such as in the setting of FAPS. Two essential points prompted us to write this case report. First, when an AoA is found on upper endoscopy, patients should be sent for screening and periodic surveillance colonoscopy for FAPS. Second, AoAs or premalignant lesions can progress to an ampullary adenocarcinoma, which should be identified early for appropriate management and improved outcome. An AoA in the setting of FAPS has a high risk for progression to an ampullary adenocarcinoma. Compared with non-FAPS patients, these patients have an approximately 124-fold increased risk of progression[3]. The diagnosis of an AoA is usually incidental. However, some patients present with obstructive symptoms, such as painless jaundice associated with weight loss, which occurred in our patient due to CBD obstruction[3 Endoscopic forceps biopsy is only diagnostic in 64% of cases. Diagnostic accuracy is greater when histopathological studies are performed on surgical specimens. Therefore, a final diagnosis should only be made when surgical pathology is available[3,4].

Ampullary carcinoma is the 2nd most common periampullary regional cancer and metastasizes locally in the abdomen and to the liver. Distant metastasis is less common, but there are case reports describing skeletal and brain metastases[1]. Carcinoma of the ampulla of Vater is a rare tumor accounting for approximately 0.2% of all gastrointestinal malignancies, with an estimated incidence of < 6 cases per million people per year[1]. AoAs and adenocarcinomas of the AoV originate from the glandular epithelium of the AoV[5]. The cell of origin of these cancers is the epithelial covering of the distal parts of the CBD, pancreatic duct, and periampullary duodenum. Histological subtypes that are common are mucinous, signet ring cell, neuroendocrine, and undifferentiated carcinomas.

Management of an ampullary adenocarcinoma and GIST:

The patient had a broad-based adenoma in the ampulla, and ampullectomy could have been performed robotically, but it would have been performed for a longer time, and we were concerned about negative margins. On the other hand, a robotic Whipple procedure is possible, but the patient did not agree to that procedure.

In regards to the ileal GIST, minimally invasive surgical resection and robotic resection are available options, although rupture of the tumor may be a potential complication. We have done many of these procedures and have never had a rupture at our facility; in fact, robotic articulation does help to maneuver the tumor without traumatizing it. Therefore, we can perform both ampullectomy, duodenal polyp excision and GIST with minimally invasive surgery either robotically or laparoscopically; some at our facility prefer robotic procedures because of the ease of anastomosis and articulation of the robot. With the Whipple procedure, we can obtain clear margins, but duodenal/ampullary lesions are more challenging because of the risk of positive margins.

GISTs are rare tumors comprising 3% of gastrointestinal tumors but are the most common mesenchymal tumors of the GI tract[4]. The most common sites are the stomach (60%) and small bowel (30%)[2,3]. These are sporadic tumors, unlike ampullary adenomas. Some studies report that the incidence significantly varies from 0.4 to 2.0 cases per 100000 per year, with a slight male preponderance and a median age of 60-65 years[7-9].

GISTs are malignant mesenchymal tumors whose cell of origin is the myenteric interstitial cells of Cajal; they are also known as pacemaker cells of the GI tract and are found in the proximal muscles surrounding the intermuscular plexus of the GI tract. They are soft tissue sarcomas of the GI tract, but they differ in genetics, pathogenesis, clinical presentation, and management[4].

CONCLUSION

This case is distinctive because the patient was diagnosed with two synchronous and extremely rare high-grade primary malignancies, i.e., an ampullary adenocarcinoma arising from a high-grade dysplastic TVAoA with a high-grade ileal GIST. An AoA can occur sporadically and in a familial inheritance pattern in the setting of FAPS. We emphasize screening and surveillance colonoscopy when one encounters an AoA in upper endoscopy to check for FAPS. An AoA is a premalignant lesion, particularly in the setting of FAPS that carries a high risk of metamorphism to an ampullary adenocarcinoma. Final diagnosis should be based on a histopathologic study of the surgically resected ampullary specimen and not on endoscopic forceps biopsy. The diagnosis of AoA is usually incidental on upper endoscopy. However, patients can present with constitutional symptoms such as significant weight loss and obstructive symptoms such as painless jaundice, both of which occurred in our patient. Patient underwent ampullectomy with clear margins and ileal GIST resection. Patient is currently on imatinib adjuvant therapy and showed complete metabolic response on follow up PET scan.