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Synchronous Primary Pancreatic Ductal Carcinoma and Colonic Adenocarcinoma Present in a Patient With History of Skin Squamous Cell Carcinoma

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Abstract. *The synchronous diagnosis of two or more primary malignancies in a patient is overall rare. This is a case report of a 70-year-old female with a history of skin squamous cell carcinoma presenting with occult hematochezia. Colonoscopy and biopsy results confirmed a microsatellite stable (MMS) adenocarcinoma in the ascending colon, and subsequent computed tomography (CT) scans identified a 3.2 cm right colonic mass and a 5.0 cm mass in the pancreatic body. Endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) confirmed the presence of pancreatic ductal adenocarcinoma (PDAC). The patient underwent neo-adjuvant FOLFIRINOX (folinic acid, fluorouracil, irinotecan and oxaliplatin) chemotherapy prior to the simultaneous distal pancreatectomy and right hemicolectomy for both pancreatic and colonic tumors. The pathology diagnoses included moderately differentiated pancreatic ductal carcinoma (PDAC) with histiocyte-like features (tumor stage: ypT3N1M0) and moderately differentiated colonic adenocarcinoma, intestinal type (tumor stage: ypT3N0M0). To the best of our knowledge, this is the first documented case of synchronous primary colonic adenocarcinoma and PDAC in the English literature.*

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Pancreatic and colorectal cancers are both among the leading causes of cancer deaths in the United States (1-2). Pancreatic ductal adenocarcinoma (PDAC), the most common pancreatic neoplasm, presents as a solid tumor arising from ductal epithelium and histologically demonstrates prominent desmoplastic stroma (1). Colon tumors are most often gland-forming adenocarcinomas arising from the mucosal epithelium (2). Synchronous cancers, defined as two or more primary neoplasms diagnosed in a single patient within six months of each other (3), rarely involve both pancreatic and colonic tumors; sparse previous reports estimate the occurrence of pancreatic cancer with either synchronous or metachronous colonic cancer as 0.06-1.7% (4-6). Herein, we report a case of a 70-year-old woman presenting with synchronous primary colonic adenocarcinoma and pancreatic ductal adenocarcinoma (PDAC) that were surgically resected simultaneously after neo-adjuvant chemotherapy. To our knowledge, this is the first documented case of such synchronous cancers. The incidence, diagnosis and treatment are discussed.

Case Report

A 70-year-old female with history of diabetes mellitus, hypothyroidism, cardiac artery disease with coronary artery bypass grafting (CABG), previously diagnosed skin squamous cell carcinoma and no family history of cancer presented to a routine visit with occult hematochezia. The patient underwent a colonoscopy revealing an ascending colon mass (3.2 cm in the greatest dimension) near the hepatic flexure that was confirmed by biopsy as invasive moderately differentiated adenocarcinoma with features (intestinal type) diagnostic of colonic primary. The colonic

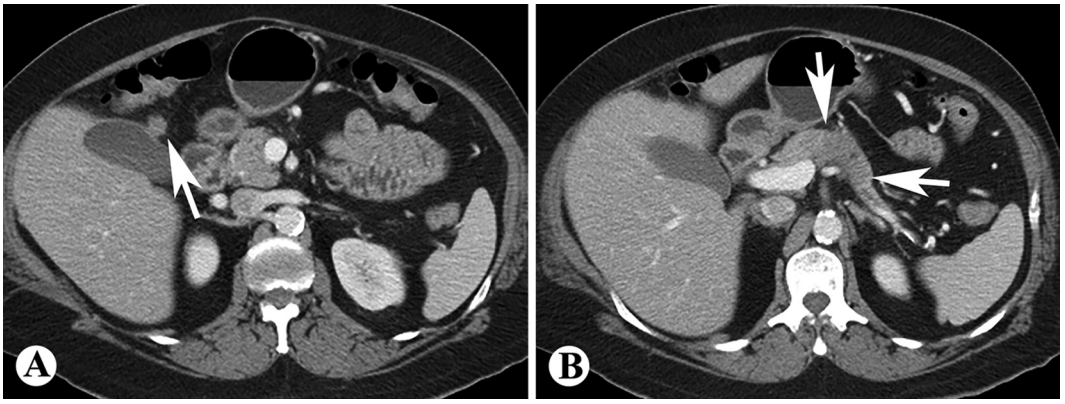

Figure 1. *Computed tomorgraphy (CT) scans (Axial) of the ascending colon mass at the hepatic flexure with adjacent nodule (A, arrow) and the pancreatic body mass (B, arrows).*

adenocarcinoma was microsatellite stable (MMS) with intact immunoreactivities for DNA mismatch repair (MMR) proteins including MLH1, MSH2, MSH6 and PMS2. Subsequent computed tomography (CT) scans did not reveal metastasis to the chest but identified a nodule measuring 1.8 cm in the greatest dimension adjacent to the colonic mass measuring 3.2 cm in the greatest dimension highly suspicious for pericolonic lymph node metastasis (Figure 1A) and a mass measuring 5 cm in the greatest dimension in the pancreatic body (Figure 1B). Samples from endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) of the pancreatic mass demonstrated morphology and immunohistochemistry consistent with primary pancreatic ductal adenocarcinoma (PDAC) with background of chronic pancreatitis, ruling out metastasis from the colon.

Following input from a multidisciplinary tumor board, the patient began neo-adjuvant FOLFIRINOX (folinic acid, fluorouracil, irinotecan and oxaliplatin) chemotherapy. After eight treatment cycles, CT scans demonstrated the overall stability of the disease. The patient underwent subtotal distal pancreatectomy, splenectomy with celiac axis resection and a reconstruction of common hepatic artery and portal vein patch graft with saphenous vein graft (Appleby procedure with hepatic artery reconstruction). The patient also had a simultaneous right hemicolectomy, and cholecystectomy. Multiple specimens were sent for pathological evaluation.

Pathological assessment indicated, grossly, within the ascending colon, a 2.8×2.0×0.7 cm, firm, white lesion was found to be grossly invading the muscularis propria (Figure 2A). Subjacent serosa was retracted. The closest distal resection margin was 6 cm from the tumor. Multiple pink-tan to black-stained lymph nodes were identified and their greatest dimension ranged between 0.1 and 0.9 cm. In histology, Hematoxylin and eosin (H&E) staining of the main lesion revealed a moderately-differentiated adenocarcinoma (Figure 2B) arising in a tubular adenoma with high grade dysplasia. Examination of seventeen pericolonic lymph nodes revealed no evidence of metastasis. The tumor stage was ypT3N0M0.

Gross examination of the distal pancreatectomy specimen measured 9.5×6.2×3.1 cm was resected in continuity with the spleen. A firm, spiculated white lesion measuring 4.1×3.0×2.4 cm occupied most of the parenchyma and completely obliterated the main pancreatic duct (Figure 3A). The lesion abutted the anterior pancreatic surface and was 0.1 cm from the posterior pancreatic surface, 0.6 cm from the pancreatic parenchymal margin and 0.4 cm from the portal vein margin. Within the peripancreatic soft tissue were several firm tan-to-white lymph nodes measuring up to 1.1 cm in the greatest dimension. In histology, H&E staining revealed a moderately-differentiated PDAC with foamy histiocyte-like features in the desmoplastic background (Figure 3B). The background pancreas revealed chronic pancreatitis and low-grade pancreatic intraepithelial neoplasia (PanIN I). The tumor was found to have invaded the perivascular tissue of the celiac artery, hepatic artery, splenic artery, and hepatic portal vein. Two of seventeen associated lymph nodes were positive for adenocarcinoma. The tumor stage was ypT3N1M0.

The patient experienced ileus and hematochezia post-operatively that resulted in additional hospitalization but was successfully treated with few complications. She restarted FOLFIRINOX chemotherapy eight weeks after surgery and tolerated treatment well. At the 4 months follow up after completion of chemotherapy, the patient was doing well with no carcinoma identified.

Discussion

Overall, synchronous primary tumors of the pancreas and colon are rare. Of the few reports investigating the

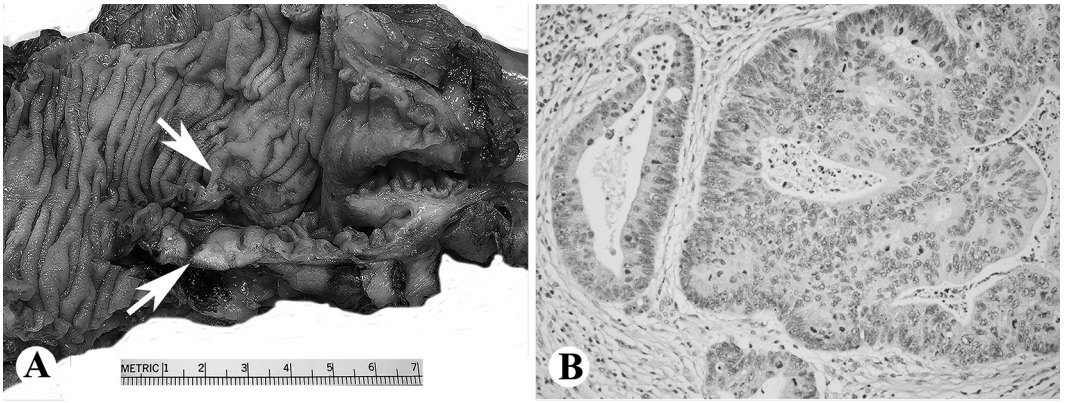

Figure 2. *Right hemicolectomy showing a 2.8 cm mass in the ascending colon (arrows) (A) and histology of the tumor showing typical features diagnostic of colonic adenocarcinoma (B, H&E stain, 200×).*

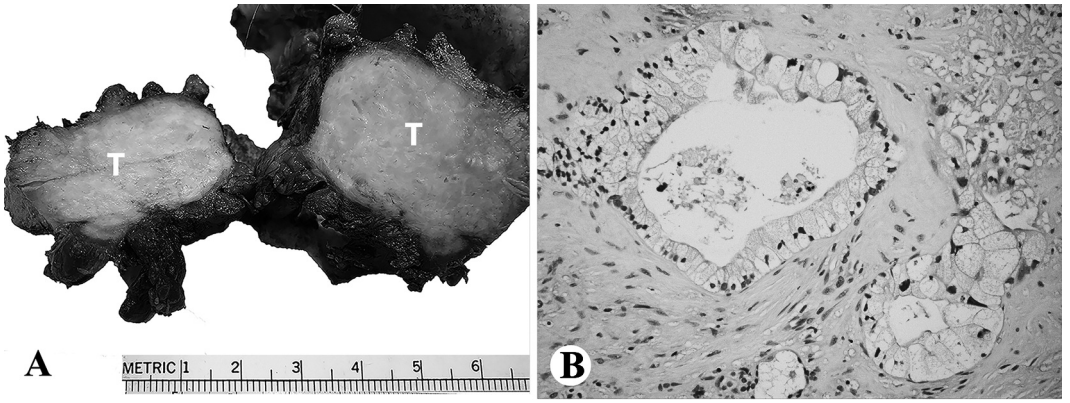

Figure 3. *Partial pancreatectomy showing a 4.1 cm flesh pancreatic mass (T) (A) and histology of the tumor showing a foamy histiocyte-like pancreatic adenocarcinoma (C, H&E stain, 200×).*

prevalence of a second primary neoplasm in patients diagnosed with PDAC, the co-occurrence of PDAC and colonic carcinoma is estimated between 0.06-1.7% (4-6). On its own, PDAC is a highly fatal cancer. The primary treatment for PDAC is surgical resection which may be combined with chemotherapy, but because up to 85% of patients are diagnosed with late-stage, unresectable tumors, the overall five-year survival rate is only 7% (1). Colorectal cancers have a more favorable prognoses, with an overall five-year relative survival rate of 64%, though over half of patients are diagnosed at advanced stages associated with poorer outcomes (7). Like pancreatic cancers, the main treatment is surgical, making early diagnosis critical.

Unfortunately, both pancreatic and colorectal cancers generally produce few signs and symptoms in early stages (7). Screening has contributed to the large decline in mortality from colorectal cancer but currently does not exist for pancreatic cancer. Recently, EUS-FNA has emerged as a useful method to confirm diagnoses of PDAC in patients with small pancreatic tumors (<3 cm) or with painless obstructive jaundice and questionable tumor presence in imaging (1). In this reported case, EUS-FNA was used to confirm a primary PDAC diagnosis based on incidental CT scan findings after a confirmed colonic adenocarcinoma diagnosis.

The diagnosis of synchronous cancers in this case was important to decision-making on chemotherapy. Neo-adjuvant FOLFIRINOX therapy has become standard for patients with potentially unresectable PDAC and was used in the reported case. While the main target was the pancreatic cancer, the therapy panel also appeared effective on the patient's metastatic MSS colon cancer. Early CT scans of the colon cancer noted a nodule that was likely a lymph

node metastasis from the colon (Figure 1A). Post-chemotherapy, this nodule became smaller, and 17 pericolonic resected lymph nodes revealed no metastases. Thus, the outcomes of this case support indicate that FOLFIRINOX chemotherapy is effective in both advanced PDAC and MMS colon cancer.

In summary, this report documents a rare case of synchronous PDAC and MMS colonic adenocarcinoma in a 70-year-old female with previous history of skin squamous cell carcinoma. The PDAC was identified incidentally after the colon carcinoma diagnosis, leading to the use of neo-adjuvant FOLFIRINOX chemotherapy prior to simultaneous resection of both tumors. Evidence of therapeutic efficacy on both cancers was noted, which may have aided surgical success. Overall, this case demonstrates the importance of prompt identification of additional primary malignancies despite the relatively low incidence of such cases, as it could majorly impact the therapeutic approach and ultimately patient outcomes.

Conflicts of Interest

The Authors declare that they have no conflicts of interest in regard to this case report.

Author's Contributions

CC wrote the article; PP performed the surgery; KM performed the biopsy; AA ordered the chemotherapy; AA performed the biopsy; and JL made the diagnoses, collected and analyzed the data and finalized the manuscript. All Authors reviewed and approved the final article.

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