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CASE REPORT | PANCREAS

Treatment of Rare and Aggressive Pancreatic Carcinosarcoma

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ABSTRACT

A 42-year-old African American woman presented with 4 days of worsening midepigastric pain that radiated to her back. Computed tomography confirmed a diagnosis of acute pancreatitis and revealed a mass within the distal body and tail of the pancreas. After an endoscopic ultrasound with fine-needle aspiration yielding atypical cells suspicious for adenocarcinoma, the patient underwent an en bloc resection of the intra-abdominal mass with subtotal pancreatectomy, splenectomy, left colectomy, and left partial adrenalectomy. Histopathologic examination findings, in addition to immunohistochemical staining, revealed a diagnosis of pancreatic carcinosarcoma. Postoperatively, the patient has undergone 20 cycles of chemotherapy and has been transitioned to comfort measures at 16 months postoperatively because of progressive disease.

INTRODUCTION

Carcinosarcomas are rare biphasic neoplasms composed of malignant epithelial and mesenchymal differentiation. They are most commonly located within the uterus; however, other locations have been described, including the pancreas.[1] Lesions of the pancreas are very rare, with less than 40 cases documented in the literature. Prognosis is generally poor for those with carcinosarcoma. For uterine disease, it has been found that carcinosarcoma accounts for 15% of all deaths caused by uterine malignancy, while only comprising approximately 5% of all uterine cancers.[2] A similarly dismal prognosis exists for those with pancreatic tumors, with most patients surviving less than 12 months postoperatively.[3]

CASE REPORT

A 42-year-old African American woman with no significant medical history presented with 4 days of worsening midepigastric pain that radiated to her back. The pain was accompanied by nausea, bloating, anorexia, and several episodes of nonbloody, watery diarrhea. The patient denied alcohol use or any history of similar symptoms. Computed tomography (CT) confirmed a diagnosis of acute pancreatitis and also revealed a heterogenous complex mass measuring 11.9 by 8.4 cm in the distal body and tail of the pancreas.

After admission, the patient underwent endoscopic ultrasound. During the procedure, an electronic radial echoendoscope was advanced to the duodenum. The endoscopic ultrasound revealed a 9-cm hypoechoic mass with cystic components in the body of the pancreas (Figure 1). There was no evidence of invasion of the celiac artery or portal vein. The pancreatic duct, bile duct, and gallbladder all appeared normal. A linear echoendoscope was then advanced to the stomach. Two passes of transgastric fine-needle aspiration were then performed using a 22-gauge standard needle. Harvested specimens showed atypical cells suspicious for adenocarcinoma.

A repeat CT was then performed looking for signs of metastasis. The pancreatic mass was observed again-a complex cystic, multiloculated mass inseparable from the anterior aspect of the pancreatic body and tail measuring 11.3 × 7.3 × 10.6 cm (Figure 2). In addition, there was a cystic lesion of unknown etiology found in the porta hepatis, abutting the medial margin of the liver,

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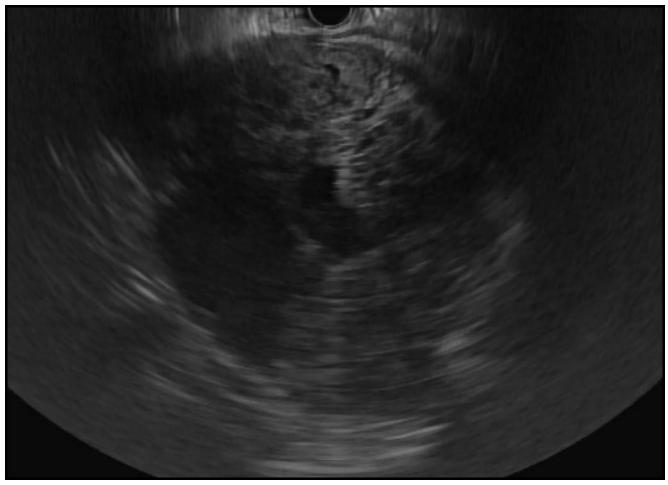

Figure 1. Endoscopic ultrasound demonstrating a 9-cm hypoechoic pancreatic mass.

measuring 7.0 × 4.0 × 7.8 cm, suggestive of lymphadenopathy. No other evidence of metastatic disease was found. Despite the large size of the mass, a multidisciplinary tumor board decided that the patient would first undergo surgical resection because of the mass' unclear features, inconclusive biopsy, and the absence of definitive metastatic disease.

Three days after the biopsy, the patient underwent en bloc resection of the intra-abdominal mass with subtotal pancreatectomy, splenectomy, and left partial adrenalectomy. Owing to the invasion of the tumor into the left colon, the patient also underwent a left hemicolectomy. The mass at the porta hepatis was identified as significant lymphadenopathy intraoperatively, with resultant portal lymphadenectomy performed. The pancreas contained a multilobular mass of 10 cm at the greatest dimension. The mass was well-circumscribed, with multicystic areas filled with hemorrhagic materials and walls appearing to invade the interface connection with the spleen and colon. Histopathologic examination revealed tumor heterogeneity with irregular glandular structures invading into a hypercellular stroma (Figure 3). Higher magnification revealed pseudostratified epithelial lining of the glands with the surrounding stroma containing numerous atypical spindle cells containing pleomorphic nuclei (Figure 4). These findings are characteristic of a carcinosarcoma composed of mixed mucinous adenocarcinoma and heterologous anaplastic sarcomatous components. Immunohistochemical staining was positive for CD31 (mesenchymal) and smooth muscle actin (epithelial). Examination of the periportal lymph nodes did not find evidence of nodal metastasis, only the presence of fibroinflammatory tissue with active scarring. Despite the absence of nodal metastasis, the patient was still scheduled to undergo systemic therapy.

Postoperatively, the patient was started on a combination chemotherapy of gemcitabine and paclitaxel. Two months postsurgery, hypodense lesions were identified in the liver on routine imaging, suggestive of metastases. The patient continued with the same chemotherapy regimen with further imaging suggesting that the lesions remained stable. The patient completed 9 cycles of gemcitabine and paclitaxel; however, the patient's carbohydrate antigen 19-9 remained elevated despite a lack of disease progression seen on CT scans. A decision was made to start the patient on folinic acid, fluorouracil, and oxaliplatin (FOLFOX). At postoperative month 15, after 11 cycles of FOLFOX, the patient began to experience increased fatigue, constipation, nausea, vomiting, and abdominal distension with accompanying lower abdominal pain.

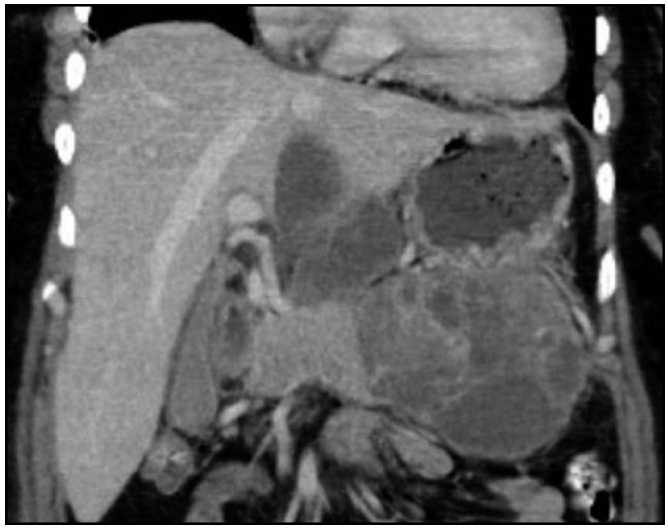

Figure 2. Coronal view of computed tomography demonstrating a complex mass in the pancreatic body and tail.

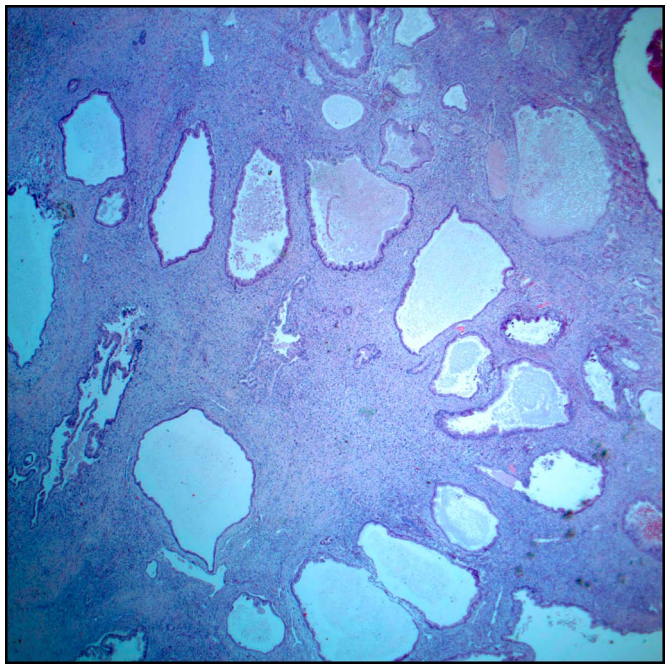

Figure 3. Histopathology showing irregular glandular structures invading into a hypercellular stroma (hematoxylin and eosin stain, 40× magnification).

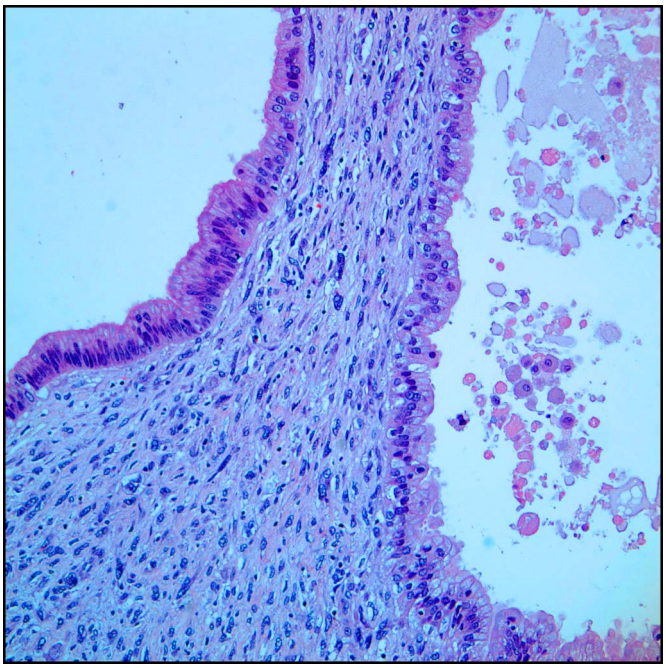

Figure 4. Histopathology showing pseudostratified epithelial lining of the glands with the surrounding stroma containing numerous atypical spindle cells containing pleomorphic nuclei (hematoxylin and eosin stain, 200× magnification).

A CT scan revealed progressive disease with new liver lesions, loculated-appearing ascites in the abdomen and pelvis, and trace peritoneal stranding likely representing carcinomatosis. Owing to the significant worsening of the disease and clinical status, chemotherapy was stopped at postoperative month 16, with a transition to comfort measures.

DISCUSSION

Owing to its rarity and biphasic nature, pancreatic carcinosarcoma is seldom diagnosed preoperatively. Pancreatic carcinosarcoma typically resembles pancreatic ductal adenocarcinoma (PDAC) in presentation, with many patients presenting with symptoms due to mass effect: abdominal pain, jaundice, nausea, and emesis. In addition, a portion of the tumors identified in the published literature was identified incidentally.[4] Although biopsy can aid in the diagnosis, there is the potential to sample only one phase of the tumor, as seen in our case. In our patient, biopsy alone revealed the carcinomatous portion of the tumor and it was not until after her histopathological review that the proper diagnosis was made.

Given the rarity of pancreatic carcinosarcomas, there are currently no treatment guidelines. Most cases within the published literature note a treatment plan of resection with subsequent adjuvant chemotherapy with gemcitabine. Owing to the current support of pancreatic carcinosarcomas originating as PDAC with subsequent metaplasia, following the treatment guidelines for PDAC has been recommended.[4] Despite a change in diagnosis postoperatively, the management for our patient remained the same.

Current recommendations for PDAC treatment include resection with either adjuvant, neoadjuvant, or combination medical therapy. The use of gemcitabine for PDAC originates from the landmark randomized CONKO-001 study, which revealed a 5-year survival of 20.7% vs 10.4%—when comparing surgery with adjuvant gemcitabine to resection alone.[5] Combination therapies include gemcitabine in addition to selected target therapies (eg, Kirsten rat sarcoma viral oncogene and growth factor receptor), immunotherapies, taxanes, and multidrug combinations such as FOLFIRINOX (ie, irinotecan, oxaliplatin, fluorouracil, and leucovorin). FOLFIRINOX is most commonly used as an adjuvant therapy for metastatic treatment regimens.[5]

For our patient, the initial treatment strategy included resection followed by a combination chemotherapy of paclitaxel and gemcitabine, which has shown promise in the recent clinical trials for locally advanced pancreatic cancer.[6] Because the patient's CA 19-9 remained elevated after 9 cycles of treatment, she was switched to a multidrug combination of FOLFOX. This decision was based on the results from the CONKO-003 trial, which demonstrated FOLFOX to be an efficacious second-line treatment in patients' refractory to gemcitabine therapy.[7] Other potential second-line treatments include capecitabine (CAP) or fluorouracil (5-FU), oxaliplatin with CAP or 5-FU, or gemcitabine with erlotinib. When comparing the overall survival, the use of second-line therapies shows a statistically significant increase compared with best supportive care.[8]

In summary, this case details the successful management of pancreatic carcinosarcoma with current treatment recommendations for PDAC. With the patient surviving the past 1 year, she has surpassed survival estimates from the published literature.[3] Our goal in presenting this case is to bolster the literature regarding this rare neoplasm. Without treatment guidelines available, we encourage reporting of long-term survival in these patients.

DISCLOSURES

Author contributions: All authors contributed equally to this manuscript. RJ Chokshi is the article guarantor.

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Previous presentation: This case was presented at the Americas Hepato-Pancreato-Biliary Association; March 20–24, 2019; Miami Beach, Florida.

Informed consent was obtained for this case report.

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