Locally advanced carcinosarcoma of the pancreas

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ABSTRACT

Carcinosarcoma is a rare subtype of pancreatic neoplasm including both carcinomatous and sarcomatous components. Fewer than 30 cases have been reported to the Surveillance, Epidemiology, and End Results Program database. Given such rarity, definitive treatment guidelines are not well defined. We report a case of pancreatic carcinosarcoma diagnosed in our institution, review tumor clinicopathological characteristics, and describe our medical and surgical management strategy.

KEYWORDS Carcinosarcoma; chemotherapy; pancreas

CASE DESCRIPTION

A 59-year-old woman with gastroesophageal reflux disease, hypertension, asthma, congestive heart failure, and a prior laparoscopic cholecystectomy presented to an outside hospital with abdominal pain, nausea, and emesis. Workup was consistent with acute pancreatitis. Computed tomography of the abdomen showed evidence of common bile duct dilation, and a magnetic resonance cholangiopancreatography demonstrated narrowing of both the common bile duct and pancreatic duct with prominence of the pancreatic head (*Figure 1*). The patient was transferred to Baylor University Medical Center at Dallas.

At admission, cancer antigen 19-9 and carcinoembryonic antigen were within normal limits. The patient underwent endoscopic retrograde cholangiopancreatography with endoscopic ultrasound. A small infiltrative, hypoechoic mass was noted just above the major papilla measuring 29 × 17 mm. Fine-needle aspiration was performed and cytology was diagnostic for adenocarcinoma. Staging workup was negative for metastasis. The patient was discharged and enrolled in a neoadjuvant trial, receiving six cycles of modified FOLFIRINOX (oxaliplatin, irinotecan, fluorouracil, and leucovorin) over a 3-month period followed by a definitive pancreaticoduodenectomy. Surveillance imaging after the first postoperative cycle of adjuvant chemotherapy (with gemcitabine and paclitaxel) demonstrated widely metastatic disease. Computed tomography-guided biopsy of a liver nodule confirmed

metastatic sarcoma. The patient died 13 months after diagnosis.

Pathologic studies were completed on the resected specimen, which consisted of the duodenum, distal common bile duct, main pancreatic duct, and pancreas head. A 2.5-cm mass was noted in the head of the pancreas with focal extension into the duodenum, main pancreatic duct, and intrapancreatic bile duct. Margins were negative. Two out of 28 nodes were positive for malignancy. Final staging was pT3N1M0. There was no lymphovascular invasion. Microscopic examination demonstrated a carcinosarcoma consisting of roughly 60% sarcoma and 40% adenocarcinoma (*Figure 2*). The adenocarcinoma component was predominantly moderately differentiated. The sarcomatous component was classified as high-grade spindle cell that contained focal chondrosarcoma and myogenic differentiation. (Immunohistochemical [IHC] studies showed nonspecific staining for myoglobin and were negative for myogenin and myo-D1.) Treatment response was moderate and primarily affected the carcinomatous component. IHC studies showed patchy positivity for cytokeratin and desmin throughout the tumor, consistent with carcinosarcoma.

DISCUSSION

Carcinosarcoma is a rare neoplasm composed of carcinomatous and sarcomatous cellular components. Although carcinosarcoma is predominantly found in the uterus, it has

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Figure 1. Magnetic resonance imaging demonstrating a pancreatic head mass (arrow B) with common bile duct dilation (arrow A).

been identified in salivary glands, skin, breast, liver, prostate, kidney, and pancreas. Pancreatic carcinosarcoma tends to occur more often in women and presents in the seventh decade of life.¹ Only 19 cases of pancreatic carcinosarcoma have been reported worldwide.

Carcinosarcoma is best characterized by IHC staining. The origin of these mixed tumors has been controversial. Three histogenic theories have been proposed to explain the mechanism behind their development: collision, combination, and conversion.² In the collision theory, carcinomatous and sarcomatous elements arise independently, whereas the combination theory suggests that both cellular components develop from a single progenitor cell. In the conversion theory, the mesenchymal (sarcomatous) component evolves from its epithelial (carcinomatous) counterparts. Current literature supports the conversion theory as the developmental basis of carcinosarcoma tumors, because most cases appear to represent cancers of monoclonal epithelial origin.²

The IHC diagnosis of carcinosarcoma is established by visualizing positive reactivity of the carcinomatous elements to cytokeratin and of sarcomatous elements to vimentin or desmin. Additional IHC investigation typically is done to verifiably rule out other types of tumors. In the current study, the tumor tested positive for desmin and cytokeratin. Histologically, the tumor demonstrated moderately differentiated adenocarcinoma and high-grade spindle cell sarcoma. The majority of carcinosarcoma cases in the literature are composed of similar cellular components.^{3,4}

The prognosis is generally poor for those diagnosed with pancreatic carcinosarcoma. In a review of pancreatic carcinosarcoma case reports from 1994 to 2010, Palaniappan and Bindhu demonstrated that postoperative survival was often <12 months.¹ In their review, the majority of tumors were locally advanced at presentation. Two patients were alive at 16 and 28 months, the latter treated with 6 cycles of gemcitabine. Similar to previous published reports, our patient survived 13 months after diagnosis.

Not previously reported in the literature, our patient was treated with neoadjuvant chemotherapy (modified FOLFIRINOX). A partial response was noted histologically, as indicated by cellular necrosis among the majority of the tumor's carcinomatous elements. Postoperatively, while undergoing adjuvant therapy with gemcitabine and paclitaxel, the patient developed biopsy-proven sarcomatous-type metastatic disease. These findings suggest that chemotherapy, preoperative and/or postoperative, may alter the balance of tumor elements and may ultimately lead to progression of a single cell lineage.

The pattern of carcinosarcoma metastasis has been explored in the otolaryngologic and gynecologic-oncologic literature. Studies report that the majority of metastases from carcinosarcoma tumors are carcinomatous.^{5,6} Our patient's development of postoperative metastatic sarcomatous disease could suggest that the carcinoma had been fully treated by adjuvant chemotherapy. On the other hand, the dominance of the sarcomatous elements could simply reflect its more aggressive nature. To date, there has been no report of this rare tumor treated with neoadjuvant chemotherapy. Evidence of cellular necrosis on the resected pathologic

Figure 2. (a) Adenocarcinoma intermixed with spindle cells within the pancreatic tumor. (b) Lymph node positive for metastatic adenocarcinoma. (c) Liver core needle biopsy demonstrating metastatic sarcoma.

specimen suggests that neoadjuvant treatment may be beneficial, although it did not appear to improve outcomes.

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1. Palaniappan JW, Bindhu S. Carcinosarcoma of the pancreas: report of a case with a concise review of the literature. *J Clin Diagn Res.* 2011;5:621–624.
 2. Somarelli JA, Boss MK, Epstein JI, et al. Carcinosarcomas: tumors in transition? *Histol Histopathol.* 2015;30:673–687.
 3. Gelos M, Behringer D, Philippou S, et al. Pancreatic carcinosarcoma. Case report of multimodal therapy and review of the literature. *JOP.* 2008;9:50–55.
 4. Oymaci E, Argon A, Coskun A, et al. Pancreatic carcinosarcoma: case report of a rare type of pancreatic neoplasia. *JOP.* 2013;14:212–215.
 5. Loh TL, Tomlinson J, Chin R, et al. Cutaneous carcinosarcoma with metastasis to the parotid gland. *Case Rep Otolaryngol.* 2014;2014:173235. doi:10.1155/2014/173235.
 6. Singh R. Review literature on uterine carcinosarcoma. *J Cancer Res Ther.* 2014;10:461–468.