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Case Report

Carcinosarcoma of the Pancreas: A Rare Type of Pancreatic Neoplasia

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Abstract

Carcinosarcoma of the pancreas is a rare type of pancreatic neoplasm, and only a few cases have been described in the literature. This tumor is characterized by distinct biphasic histopathology consisting of carcinomatous and sarcomatous component. We present a case of pancreatic carcinosarcoma in a patient who underwent successful resection but was found to have metastatic disease on follow up. Based on the very limited number of reported cases, the prognosis of carcinosarcoma of the pancreas appears poor.

Keywords: *Carcinosarcoma of the Pancreas; Pancreatic Cancer; Carcinosarcoma*

Introduction

Carcinosarcoma is a rare neoplasm composed of mixed malignant epithelial and mesenchymal elements with distinct immunohistochemical features [1,2]. The most common site of presentation is the uterus although some cases have been described in the breast, lungs and occasionally, the gastrointestinal tract [3]. Pancreatic carcinosarcoma represents a very rare variety of exocrine malignancy of the pancreas, and few cases have been reported thus far in the literature. According to the World Health Organization (WHO) classification of tumors of the digestive system, the carcinosarcoma of the pancreas is classified together with sarcomatoid carcinoma and anaplastic giant cell carcinomas as undifferentiated carcinoma of the pancreas [4]. The histo-pathogenesis of the tumor is not clear. Although a few theories have been proposed but due to the extreme rarity of the tumor, these remain to be elucidated [5,6].

Case Presentation

An 85-year-old Caucasian male presented with complaints of abdominal pain, dark colored urine and pale stool. His past medical history was significant for coronary artery disease, peripheral vascular disease, hypertension, and hyperlipidemia. Physical exam revealed jaundice, scleral icterus, generalized muscle wasting and abdominal tenderness in the right upper quadrant without guarding or rigidity. Initial labs were significant for elevated total bilirubin (12.1 mg/dL), alkaline phosphatase (443 IU/L), SGOT (149 IU/L) and SGPT (298 IU/L). Ultrasound of the right upper quadrant revealed a 6.0 cm mass in the pancreatic head with moderate dilatation of the intrahepatic bile ducts and common bile duct. Endoscopic Retrograde Cholagiopancratography (ERCP) was unsuccessful as deep guidewire access could not be obtained. The patient underwent interventional radiology (IR) assisted Percutaneous Transhepatic Cholangiography (PTC) with catheter placement for biliary drainage and subsequent decrease in total bilirubin to 4mg/dL. IR guided brushings were non-diagnostic. The patient was discharged with a plan for an outpatient Endoscopic Ultrasound (EUS).

Four days later, he developed severe fatigue, fever, and chills. He returned to the hospital with worsening jaundice and increased WBC count. Blood cultures grew gram-negative rods. CT scan of the abdomen and pelvis showed an unchanged pancreatic head mass with duodenal compression and bile duct dilatation. Labs showed an elevation in total bilirubin (10.4 mg/dL), alkaline phosphatase (505 IU/L), SGOT (133 IU/L), SGPT (122 IU/L), WBC (14,000/mcL) and CEA (3286 U/ml). Broad spectrum antibiotics were started, and a revision of his PTC drain was performed with effective biliary drainage. EUS followed, with fine needle aspiration (FNA) of the tumor. On EUS, the pancreatic head mass appeared with well-defined borders and sonographic evidence of invasion into the portal vein (Figure 1). A large amount of bilious fluid was also found in the stomach demonstrating outlet obstruction secondary to tumor mass effect.

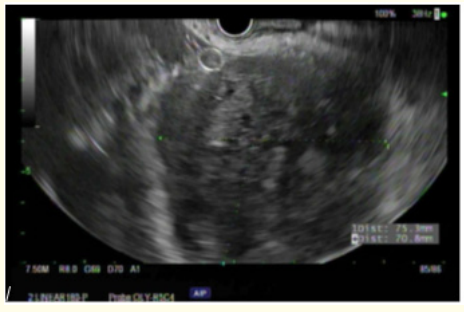

Figure 1: *EUS appearance of the head of the pancreas mass.*

Preliminary cytology results were positive for spindle cells. Final cytopathology showed the presence of atypical hyperchromatic spindle cells set in a myxoid stroma with moderate cellularity. A panel of immune-histochemical stains was performed which revealed negative staining for cytokeratin AE1/3 and GIST markers CD117 and DOG-1. The tumor cells were also negative for HHF-35 (muscle marker) and S-100 (neural marker). The differential diagnosis at that time included a de-differentiated liposarcoma or a myxofibrosarcoma.

The patient continued to have signs and symptoms of gastric outlet obstruction due to the mass effect of the tumor compressing the duodenum. A decision was made for surgical resection, and the patient underwent pancreaticoduodenectomy with partial omentectomy in an attempt to completely resect the tumor. Gastro-jejunal tube was also placed for feeding. Postoperatively, his performance and nutritional status were poor, so adjuvant chemotherapy was postponed until acceptable post-operative recovery was achieved. Two months later, a follow-up PET-CT scan showed new hypermetabolic hepatic lesions, lung nodules and increased activity along T9 vertebra compatible with metastasis. No significant Fludeoxyglucose (FDG) activity was noted in the surgical bed to suggest recurrence. He remained asymptomatic and chose hospice care as he was not a candidate for chemotherapy due to distant metastasis and poor functional status.

Histopathology

The gross specimen from Whipple's pancreaticoduodenectomy consisted of a stomach measuring 6.0 cm in length, a duodenum measuring 23.0 cm in length, pancreatic head measuring 11.0 x 9.0 x 5.0 cm (Figure 2). In the duodenum, there was a slightly firm, reddish-black mass protruding from the ampulla, measuring 7.0 x 7.0 x 5.0 cm (Figure 3). Serial sections of the mass had a heterogeneous appearance consisting of dark reddish-brown, hemorrhagic tissue and slightly firm to soft, yellow-white, lipomatous tissue. The pancreas was sectioned to reveal a 10.0 x 9.0 x 4.0 cm soft, white to yellow, diffusely infiltrating tumor mass involving a near majority of the pancreas and obliterating the main pancreatic duct and common bile duct. The tumor was present at the ampulla of Vater and protruded through it into the duodenum, continuous with the previously mentioned 7.0 cm heterogeneous mass. The total dimensions of the mass were 12.0 x 12.0 x 8.0 cm. On cut section, the tumor appeared fairly homogenous with soft, yellow parenchyma. The mass grossly involved the duodenal muscularis and mucosa. The only grossly unremarkable pancreatic tissue consisted of a firm, nodular parenchyma present near the pancreatic neck margin. The gastric mucosa was unremarkable.

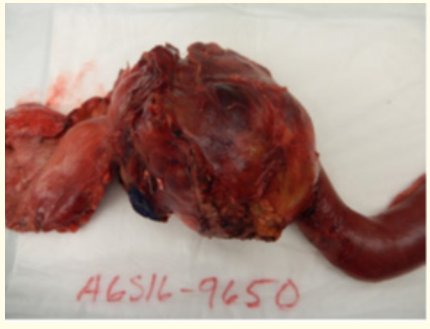

Figure 2: *The gross specimen from the pancreaticoduodenectomy, consisting of a stomach, duodenum and a pancreatic head measuring 11 x 9 x 5 cm which is frankly enlarged.*

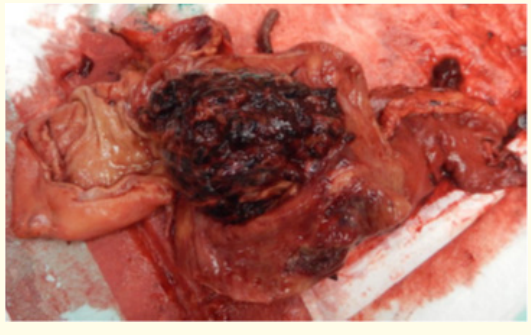

Figure 3: *Open section of the duodenum which shows a slightly firm, reddish-black mass protruding from the ampulla.*

Histopathology reports revealed sections of the tumor with a high-grade sarcomatoid component with myxoid features and some floret-like cells (Figure 4). There were many mitotic figures and areas of geographic necrosis. Focal cartilaginous differentiation was noted (Figure 5). Extensive angiolymphatic and perineural invasion was seen (Figure 6). In addition to the sarcomatoid component, there was a glandular component suggestive of invasive ductal adenocarcinoma. Overall findings were consistent with undifferentiated carcinosarcoma. Immunostains for CAM 5.2, CK7, CK5/6, p63, desmin and myogenin were used in the evaluation which confirmed the diagnosis as well. CAM 5.2 and CK7 were diffusely positive in the glandular component (Figure 7). Desmin and myogenin were negative in the entire tumor.

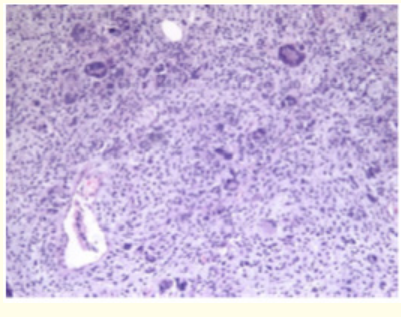

Figure 4: *Bizarre cells in the myxoid background: sections of the tumor show a high-grade sarcomatoid component with myxoid features and some floret-like cells.*

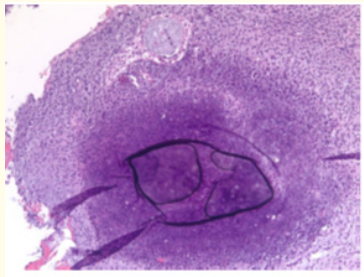

Figure 5: *Cartilaginous differentiation: focal cartilaginous differentiation with an area recapitulating chondroid matrix present in the tumor.*

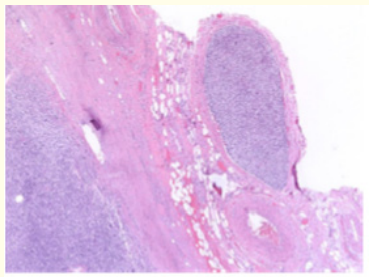

Figure 6: *Lymphovascular invasion: extensive lymphovascular invasion seen in the tumor.*

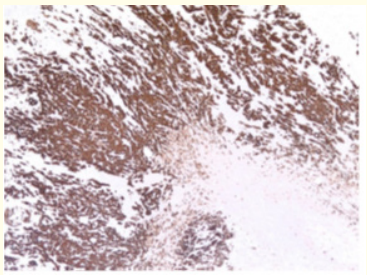

Figure 7: *CAM 5.2 stain: the carcinomatous component was strongly and diffusely positive for CAM 5.2.*

Discussion

Carcinosarcoma is an uncommon malignant neoplasm that is usually found in the uterus and is currently referred to as malignant mixed mullerian tumor (MMMT). It is often further typed as having homologous or heterologous elements by examining the sarcomatous component. The homologous type is usually non-specific high-grade sarcoma. Diffuse positivity for vimentin and focal positivity for smooth muscle actin (SMA) is typically seen. Heterologous elements include rhabdomyosarcoma, chondrosarcoma, osteosarcoma or liposarcoma. Presence of these elements is demonstrated by immunoreactivity for markers of muscle, cartilaginous, bone, or adipose differentiation, respectively. In the pancreas, these tumors fall under the heterogeneous group of malignancies referred to as undifferentiated carcinoma. The four subtypes are as follows: 1) Sarcomatoid (Spindle cell) carcinoma, consisting primarily of malignant spindle cells; 2) osteoclastic giant cell tumors, demonstrating an admixture of malignant spindle and epithelioid appearing cells with osteoclast-like giant cells; 3)

pleomorphic giant cell carcinoma, exhibiting highly pleomorphic mononuclear and multinucleated giant cells; and 4) round cell anaplastic carcinoma. Pancreatic carcinosarcoma and sarcomatoid (spindle cell) carcinoma are interchangeable diagnostic terms. Gastrointestinal primary sites are extremely rare. To the best of our knowledge, only 20 such cases have been reported in the literature including ours. The tumor has distinct biphasic histopathology characterized by a carcinomatous and a sarcomatous component. Both the carcinomatous and sarcomatous components typically demonstrate high-grade dysplastic morphology (Figure 8). Diagnosis is established by the reactivity of the carcinomatous and sarcomatous elements to cytokeratin and vimentin, respectively. The carcinomatous component is also positive for epithelial membrane antigen (EMA) and the sarcomatous component can be focally positive for smooth muscle actin (SMA). In our case cytokeratins CAM5.2 and CK7 were diffusely positive in the glandular component, consistent with carcinomatous elements. Desmin and myogenin, which are markers of muscle differentiation, were negative in the entire tumor and thus excluded pleomorphic rhabdomyosarcoma. Vimentin was not performed. A more important finding present in this lesion was that the cytokeratins were only positive in the glandular component. If these were also positive in the sarcomatous component, then the diagnosis would be sarcomatoid carcinoma, a true carcinoma, rather than a carcinosarcoma. In the initial cytopathology sample, the tumor cells were negative cytokeratin AE1/3, CD117, DOG-1, HHF-35, and S-100. This immunohistochemical pattern ruled out pleomorphic liposarcoma, extragastrointestinal stromal tumor (GIST), and rhabdomyosarcoma.

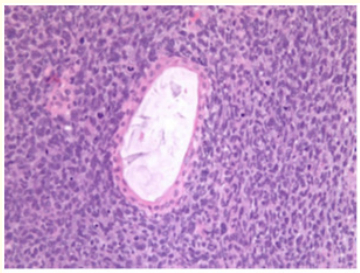

Figure 8: *Malignant gland in malignant stroma: high power demonstrates that both the carcinomatous and sarcomatous components display high-grade morphology.*

The origin and histogenesis of carcinosarcomas have not been clearly delineated. Based on limited experience and molecular testing done in other reported cases different theories have been proposed. Huszar., *et al.* postulated that these neoplasms represent cellular elements derived from two different histologic origins proliferating in one tumor [7]. On the contrary, van den Berg., *et al.* suggest a monoclonal origin with subsequent divergence of the neoplastic epithelial and sarcomatous portions [8]. Other proposed mechanisms include the collision and composition tumor theories [5,6,9]. Further studies with molecular and genetic testing are needed to clearly define the exact mechanism of histogenesis in these tumors. Clinical presentation is seen in the age group of 46 - 90. Gender predilection is hard to establish given the limited number of cases reported. Prognosis is poor, and the overall survival is 6 months [1,2,9]. Treatment options are surgical excision and chemo-radiation. The most extended reported survival was 28 months with combined surgery and chemotherapy [10].

It is essential to correctly identify carcinosarcoma and differentiate it from adenocarcinoma as the tumor is highly aggressive and carries a worse prognosis and less response to current treatment. EUS has been shown to be highly accurate for evaluation of solid pancreatic masses especially adenocarcinomas [11]. But diagnosis may be challenging for carcinosarcoma, as seen in our case, wherein the EUS FNA sample was inadequate to establish the diagnosis. Our patient developed new metastatic disease even after complete tumor margin-free pancreaticoduodenectomy and thus could not undergo adjuvant chemotherapy. More case reports and molecular testing would be necessary for a better understanding of the origin, progression, clinical behavior and treatment response of this tumor to adjuvant chemo-radiation therapy.

Conclusion

Carcinosarcoma of the pancreas is a rare type of pancreatic neoplasm characterized by distinct biphasic histopathology consisting of carcinomatous and sarcomatous component. It is essential to correctly identify carcinosarcoma since this tumor is highly aggressive and carries a poor prognosis and response to current treatment.

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