Carcinosarcoma of the Pancreas: Report of a Case with a Concise Review of the Literature

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ABSTRACT

Carcinosarcomas are rare, mixed, malignant neoplasms which are composed of both carcinomatous and sarcomatous elements, showing distinct immunohistochemical and ultra structural features. While the uterus is one organ where they are encountered most often, some cases have been diagnosed in other organs, including the pancreas. We have reported a case of pancreatic carcinosarcoma which was diagnosed in our institute and have reviewed the epidemiology and the clinico-pathological characteristics of all cases of carcinosarcoma of the pancreas which have been reported worldwide.

Key Words: Carcinosarcoma, Pancreatic cancer, Pancreaticoduodenectomy, Adenosquamous carcinoma, Leiomyosarcoma, Adjuvant chemotherapy

KEY MESSAGE

- It is a rare malignancy of the exocrine pancreas.

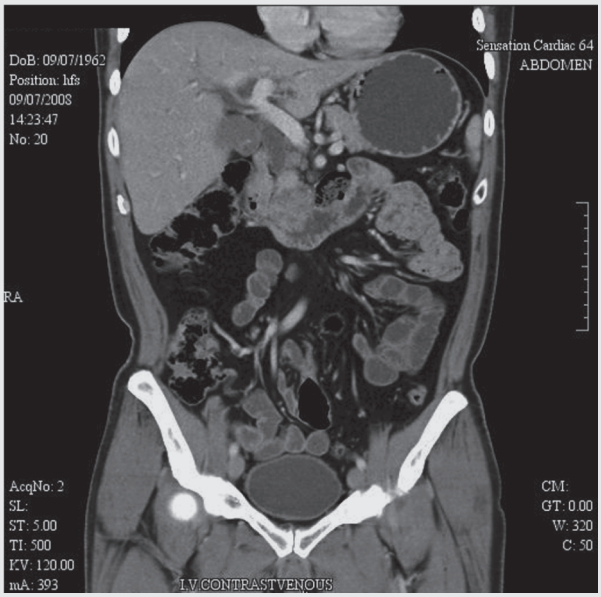
INTRODUCTION

Carcinosarcoma is a rare, mixed, biphasic, malignant neoplasm which is composed of carcinomatous and sarcomatous elements, without areas of transition between them and with distinct immunohistochemical/ultra-structural features [1], [2]. It occurs commonly in the female reproductive tract (most often in the uterus) as malignant, mixed, mullerian tumours. Although it is uncommon, it has also been occasionally described in other organs like the lung and breast and in parts of the gastrointestinal tract such as the gall bladder, the biliary tract, the liver, the pancreas, etc. [3].

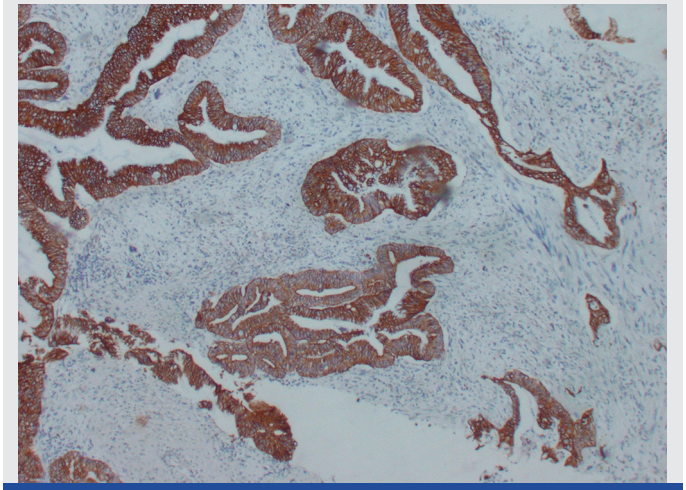
CASE SUMMARY

A 46-year-old male, a known type two diabetic and a dyslipidaemic on drugs, was referred to our center for further evaluation and management of cholestatic jaundice. Earlier he was evaluated outside for dyspeptic symptoms and jaundice of two weeks duration. At the initial visit, there were no significant clinical features, except for deep jaundice and mild itching all over the body. The routine blood tests showed a total bilirubin level of 13.6 mg/dL, transaminase levels of 87 IU/L and 233 IU/L and an alkaline phosphatase level of 319 IU/L. CA19-9 was raised (252 U/ml). Computerized tomogram [Table/Fig-1] showed a hypo dense, oval lesion of size 3.4 x 3.4 x 1.5 cm in the head and in the uncinate process of pancreas, encasing the distal common bile duct (CBD) and causing moderate intra-hepatic biliary radical dilatation in both the lobes of the liver. Both the CBD and the proximal pancreatic duct were dilated and prominent.

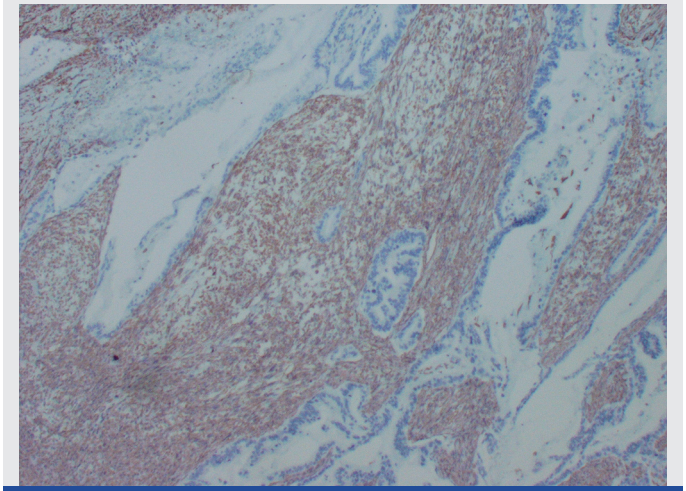
After the metastatic work-up turned out to be negative, the patient was taken up for elective laparotomy. On the table, the surgeons found a mass of size 4 x 4 cm in the lower part of the head of the pancreas, with its medial border abutting but not infiltrating the superior mesenteric vessels. The liver and the peritoneum were free of the infiltration and there was no ascites. Though the peri-pancreatic planes were clear, significant lymph nodes were found in the retro-pancreatic area and near the roots of the right gastro-epiploic artery and the superior mesenteric artery. Pancreatoduodenectomy was performed. The histopathological report of the surgical specimen was carcinosarcoma of the head of the pancreas (pT3N0M0). We treated him with Gemcitabine



[Table/Fig-1]: A coronal section of CT abdomen with contrast showing the pancreatic mass



[Table/Fig-2]: Immunohistochemistry for cytokeratin highlighting the atypical glandular patterns



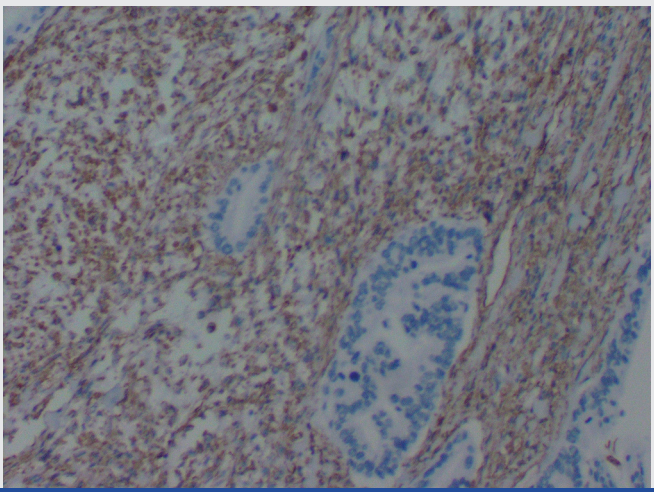
[Table/Fig-3]: Immunohistochemistry for vimentin highlighting the atypical stromal components

(1 gm/sqm on days one and eight of each three weekly cycle x six cycles) adjuvantly. He is on regular follow-up now at 28 months since diagnosis.

GROSS AND MICROSCOPIC FINDINGS

The gross pathology revealed an ill-defined mass of size 3 x 3 x 2 cm, located in the inferior aspect of the head of the pancreas. The serial cut sections of the tumour showed a bright yellow to pale green mucoid surface, with areas of necrosis. The cut section of the CBD appeared uninvolved as like those of the stomach, the duodenum and the gall bladder. Five peri-pancreatic lymph nodes and a hepatic artery node were also submitted.

The routine H and E staining of the sections of the pancreatic mass exhibited cells that were arrangedin glandular, focal papillary and cord patterns. The cells were pleomorphic with scanty to moderate cytoplasm, pleomorphic nuclei, prominent nucleoli and frequent mitoses. Focal mucin production and squamoid differentiation were seen. In addition, perineural invasion and lymphovascular emboli were noted. The stroma showed focal chrondroid areas as well as spindle shaped cells with pleomorphism and giant cell transformation. Some occasional bizarre cells with increased mitotic rate were also observed. The tumour had infiltrated the adjacent duodenal wall up to its sub-mucosal layer, while the resected margins were negative on all the sides. All the five peri-pancreatic lymph nodes and the hepatic artery node showed sinus histiocytosis. On running a battery of immunohistochemical markers [Table/Fig-2, 3, 4 and 5], the areas with the glandular, focal papillary and cord patterns showed positivity for cytokeratin and negativity for all other antibodies. The stromal areas tested positively for vimentin and SMA, negatively for cytokeratin, S-100 and desmin, and non-specifically for CD68 and alpha-1-antitrypsin. Both the areas had a high Ki67 index.



[Table/Fig-4]: Immunohistochemistry for smooth muscle actin showing positivity in areas of smooth muscle differentiation

IHC markers	Mesenchymal component (Leiomyosarcoma)	Epithelial component (Adenosquamous carcinoma)
Cytokeratin	Negative	Positive
Vimentin	Positive	Negative
Alpha-1-Antitrypsin	Non-specific	Negative
S - 100	Negative	Negative
Smooth Muscle Antigen	Positive	Negative
CD68	Non-specific	Negative
Desmin	Negative	Negative
Ki67 index	High	High

[Table/Fig-5]: Immunohistochemical expressions of the two components in our case

DISCUSSION

EPIDEMIOLOGY

A thorough search of the PubMed literature showed only thirteen cases (including ours) of pancreatic carcinosarcoma to date, from various parts of the world [Table/Fig-6]. Though it is premature to say as yet, with scanty number of cases in hand, it was seen that carcinosarcoma of the pancreas had a gender predilection towards females (69% females against 31% males). The mean age of the patients was 65 years and the median age was 67 years, with a range of ages from 46 to 90 years. The disease has been diagnosed most often in patients in their seventh decade of life.

CLINICAL FEATURES

The clinical features of carcinosarcoma of the pancreas are similar to that of the conventional one. From [Table/Fig-2], it is obvious that pain in the epigastrium and/or in the right upper quadrant is the most common presenting complaint. The duodenum was the most commonly infiltrated local organ. Peri-pancreatic nodal infiltration, gastric infiltration, invasion of the large vessels and involvement of

the CBD and the peri-pancreatic adipose tissue, are some other extents of the loco-regional spread.

PATHOLOGICAL FEATURES

The carcinomatous component varies widely, depending upon the morphology, the character and the arrangement of its atypical cells. The most common histopathological type is adenocarcinoma. Mucinous cystadenocarcinoma [5] is another variant where the atypical epithelial cells form gland-like structures, the lumen of which contains the secreted mucinous material. In one case [2], though the epithelial component was largely a mucinous cystic neoplasm with its lining epithelium showing a range of dysplasia from adenomatous to carcinoma-in-situ, it was classified as carcinosarcoma due to the presence of focal invasive areas of infiltrating carcinoma (of the poorly differentiated and the squamous types). On the other hand, there was a similar kind of diversity in its sarcomatous counterpart also. Around 60% of the cases showed sarcoma of the spindle cell type. Recently, osteosarcoma was demonstrated by Japanese authors in a case of carcinosarcoma that was shown to arise from intraductal papillary-mucinous carcinoma [6-11].

Age / Sex	Clinical symptoms / signs	Local extent / recurrence / distant metastasis	Carcinomatous component	Sarcomatous component	Treatment	Survival period	Author, year of publication, country
50/F	–	Duodenal wall infiltration by primary.	Adenocarcinoma	Leiomyosarcoma	Surgical resection	–	Millis JM, 1994, USA4
48/F	Epigastric pain / palpable abdominal mass	Wide spread abdominal disease as recurrence/mets.	Mucinous cystadenocarcinoma	Undifferentiated malignant spindle cell sarcoma	Surgical resection	Dead - 12 months *	Wenig BM, 1997, USA5
66/F	Epigastric pain / palpable abdominal mass	Wide spread abdominal disease as recurrence/mets.	Mucinous cystadenocarcinoma	Undifferentiated malignant spindle cell sarcoma	Surgical resection	Dead - 9 months *	Wenig BM, 1997, USA5
67/M	Epigastric pain / palpable abdominal mass	–	Mucinous cystadenocarcinoma	Undifferentiated malignant spindle cell sarcoma	Surgical resection	Alive - 16 months	Wenig BM, 1997, USA5
74/M	Unexplained DVT of lower extremity.	Peripancreatic adipose tissue and duodenal wall infiltration by primary.	Adenocarcinoma	Malignant fibrous histiocytoma	Radical pancreaticoduod enectomy	Alive - 4 months	Darvishian F, 2002, USA1
90/M	–	–	Adenocarcinoma	Undifferentiated spindle cell sarcoma	Nil	Post-mortem diagnosis	Yamazaki K, 2003, Japan6
67/F	Abdominal pain	Peripancreatic nodal infiltration by primary followed by liver mets.	Adenocarcinoma	Spindle cell sarcoma †	Pancreaticoduod enectomy	Dead - 8 months *	Barkatullah SA, 2005, USA7
67/F	Nausea, vomiting, and jaundice	Duodenal invasion by primary followed by liver and peritoneal mets.	Mucinous cystadenoma ‡	Pleomorphic spindle cell sarcoma	Pancreaticoduod enectomy.	Dead – 4 months *	Bloomston M, 2006, USA2
61/F	Anemia	Stomach, duodenal, peripancreatic nodal infiltration by primary followed by peritoneal carcinomatosis.	Adenocarcinoma	Poorly differentiated sarcoma	Radical pancreaticoduod enectomy §	Dead - 11 months *	Marcos Gelos, 2008, Germany8
82/F	–	–	Adenocarcinoma	Spindle cell sarcoma	Pancreaticoduoden ectomy	Dead - 13 days ‖	Nakano T, 2008, Japan9
72/F	Right upper quadrant pain, nausea and vomiting.	Liver mets, CBD and duodenal infiltration by primary followed by multiple liver mets and tail of pancreas recurrence.	Adenocarcinoma	Spindle cell sarcoma	Radical pancreaticoduod enectomy **	Dead - 2 months *	Shen ZL, 2009, China10
64/F	–	Polypoidal mass within the main pancreatic duct of tail region.	Adenocarcinoma	Osteosarcoma	–	–	Okamura J, 2010, Japan11
46/M	Dyspeptic symptoms and jaundice.	Duodenal wall infiltration by primary.	Adenosquamous carcinoma	Leiomyosarcoma	Pancreaticoduod enectomy with lymph nodes dissection.	Alive – 28 months.	Our patient, 2010, India

[Table/Fig-6]: List of published cases.

* Due to disease
† Along with osteoclastic giant cell-rich spindle cell proliferation
‡ With foci of invasive poorly differentiated carcinoma and squamous cell carcinoma
§ Followed by 6 cycles of gemcitabine.
‖ Due to postoperative sepsis.
** With left hepatic lobe resection and gastric mass resection.

PATHOGENESIS

The pathogenesis of carcinosarcoma of the pancreas is not clearly understood, as of now. Some researchers have offered explanations like composition, combination and conversion theories [2]. One group of authors put across the theory of organ-induced tumour differentiation, where they showed that the two components were monoclonal in nature and that only the other anatomical organs which were present in their vicinity, like the duodenum, had influenced their lines of further differentiation [4].

Another theory suggested that the tumour originates as a single cell (monoclonal origin), which would then undergo subsequent diversion and differentiation into carcinomatous and sarcomatous portions. Van den Berg and his colleagues [12] who studied genetic alterations in three cases of pancreatic carcinosarcoma, supported this theory. In another case which was reported recently [6], it is concluded that the well-differentiated adenocarcinoma had gradually enlarged in size, with some of its areas accumulating genetic alterations and subsequently transforming into rapidly growing segments of undifferentiated sarcomatous cells.

MANAGEMENT, PROGNOSIS AND SURVIVAL

Almost all the cases have been primarily treated by surgical therapy, the standard of which is pancreaticoduodenectomy. Scanty information is available about chemotherapy and radiotherapy in the management of this rare tumour. Gelos M and his colleagues treated their patient with six cycles of Gemcitabine following radical pancreaticoduodenectomy and achieved a survival period of 11 months [8]. Gemcitabine delays disease progression when given adjuvantly to a patient with pancreatic cancer, who has undergone curative-intent surgery [13]. From [Table/Fig-2], it is obvious that the prognosis of carcinosarcoma of the pancreas is very poor, irrespective of any kind of treatment, with most of the patients having died within one year of diagnosis. Only three patients (including ours) are alive at the time of reporting of this case, with a mean survival period of 16 months among them.

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