Case report

Carcinosarcoma of the pancreas: A case report with emphasis on histopathology and review of the literature

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Abstract

Introduction: Carcinosarcomas are rare tumors, usually seen in the uterus. They are histologically characterized by a carcinomatous and sarcomatous component. We report this case because of its rarity.

Case report: Our patient was a 50 year old male who presented with signs and symptoms of obstructive jaundice. Examination revealed a palpable liver and distended gallbladder. Laboratory investigations showed deranged liver function tests. Radiology work-up showed an irregular growth involving the periampullary region. Whipple procedure was done. Grossly an ill defined infiltrating growth was seen involving the periampullary region and extending into the pancreas. Histology showed malignant epithelial and stromal components. Immunohistochemical studies revealed positive cytokeratin expression by the epithelial component and vimentin expression by the sarcomatous component; hence a diagnosis of carcinosarcoma pancreas was made.

Conclusion: Though carcinosarcomas are rare in pancreas, presence of atypical spindly cells and immunohistochemical studies help in diagnosing such rare neoplasms.

Key words: Carcinosarcoma, Histology, Pancreas

Introduction

Carcinosarcomas are biphasic neoplasms with malignant epithelial and stromal elements. Though commonly encountered in the uterus, lungs, breast and GIT are other sites1,2,3. Occurrence in the pancreas is rare and till date only 18 cases have been reported1-3. Carcinosarcomas constitute a very small subset of primary pancreatic malignancies and are grouped along with sarcomatoid carcinoma and anaplastic carcinoma under undifferentiated carcinomas of pancreas 4. Since reported cases are less, an assessment of age and gender predilection for pancreatic carcinosarcomas may not be very accurate. Immunohistochemistry is very pertinent in the diagnosis of carcinosarcomas especially when it occurs in rare locations. Regarding the histogenesis of such tumors there are 4 main explanations; the collision, combination, conversion and composition tumor theories1,2,5. However the molecular workup done in certain cases favours a monoclonal origin6.

Case report

A 50 year old moderately built and nourished male presented to our surgery department for evaluation of jaundice. He gave a history of intermittent episodes
of abdominal pain for the past 1yr; itching and yellowish discolouration of urine since 3months. He was an alcoholic and a smoker; stopped 3yrs back. On examination the patient had jaundice and clubbing of fingers and toes. Abdomen was soft with a palpable liver and gall bladder. Laboratory investigations showed serum bilirubin of 9.5mg/dl, serum alkaline phosphatase 582 IU/L and SGOT/SGPT -98/110 IU/L. The clinical differentials considered were carcinoma head of pancreas and cholangiocarcinoma.

Ultrasonography revealed dilatation of intrahepatic biliary radicles, distended gall bladder, dilated CBD (20mm) with a mass lesion in the head of pancreas measuring 1.6 x1.4cm. CECT confirmed these findings, and there was no evidence of metastasis to liver, peritoneum or lymph nodes. Whipple pancreaticoduodenectomy was done and intra operatively a growth was found in the periampullary region measuring 3x 2.5cms. Patient required re-exploration on 4th postoperative day for evacuation of supracolic haematoma. After that the patient had an uneventful recovery and was discharged after 47days.

**Histopathology**

The gross examination revealed an ill defined infiltrating growth in the periampullary region, measuring 6 X 3.5 x2cms which was involving most of the pancreatic tissue [Figure 1a]. The rest of duodenum, jejunum and stomach were unremarkable. Gall bladder was enlarged. The microscopic examination revealed both carcinomatous and sarcomatous components [Figure 1b]. The carcinomatous component was an adenocarcinoma, composed of cells arranged in glandular pattern and in cords [Figure 1c]. Focal squamoid areas were present [Figure1d]. The sarcomatous component was seen as spindly cells with pleomorphic nuclei, surrounding and intermixed with the adenocarcinomatous elements. Occasional bizarre cells were also present. Perineural invasion was shown by the adenocarcinomatous component. The neoplasm was infiltrating the distal part of common bile duct in the ampullary region. The adjacent pancreas showed areas of fibrosis and acinar atrophy. Resected ends of stomach, jejunum, cut end of CBD and all resected margins of pancreas, except the lateral margin were free of neoplasm. 9/9 lymph nodes showed reactive change only. Gall bladder showed evidence of chronic cholecystitis. A pTNM stage of pT3N0M0 was assigned. Immunohistochemical studies confirmed the diagnosis of carcinosarcoma. The epithelial component was positive for cytokeratin (CK) and epithelial membrane antigen (EMA) [Fig 2a &d]. Mesenchymal component showed positive cytoplasmic staining for vimentin and smooth muscle actin (SMA) [Fig 2b&c]. However it was negative for desmin, S 100, CD34 and CD 117. Ki67 proliferation index was low.

Figure 1a.gross appearance of carcinosarcoma pancreas, an ill-defined growth involving most of the pancreas; 1b.(H&E x 200) showing malignant epithelial and mesenchymal elements; 1c.(H&E x 40) showing adenocarcinomatous component 1d.(H&E x 100) shows focal squamoid areas-Inset shows bizarre stromal cells(H&E x 400)
Figure 1a. Gross appearance of carcinosarcoma pancreas, an ill-defined growth involving most of the pancreas; 1b. (H&E x 200) showing malignant epithelial and mesenchymal elements; 1c. (H&E x 40) showing adenocarcinomatous component; 1d. (H&E x 100) shows focal squamous areas-Inset shows bizarre stromal cells (H&E x 400)

Figure 2a&d. Glandular elements showing immunopositivity for CK (a. x 400) and EMA (d. x 200);
2b&c. Mesenchymal elements showing immunopositivity for vimentin (b. x 400) and SMA (c. x 200)
Discussion

Carcinosarcomas are biphasic tumors with both malignant epithelial and mesenchymal elements without areas of transition between them. They have distinct immunohistochemical and ultrastructural features\(^3\). Uterus is the common location, where they are also called malignant mixed mullerian tumors. Pancreas is an unusual site for carcinosarcoma. Since first reported by Millis et al in 1994, review of literature yielded only a handful of cases\(^3\). Most malignant tumors of pancreas are adenocarcinomas (85%) and show a male predilection. However carcinosarcomas showed a greater incidence in females (10:9) (Table1). They are usually seen in elderly patients with mean age of 65yrs (46 to 90). The usual presenting symptoms were upper abdominal pain and jaundice \(^3\). Carcinosarcomas are different from sarcomatoid carcinomas which are true carcinomas as shown by positivity for CK but have spindle cell morphology. On the other hand in carcinosarcomas, the carcinomatous component shows positivity for epithelial markers (CK and EMA), while the sarcomatous component shows positivity for mesenchymal markers (vimentin). Certain cases showed positivity for SMA, Muscle specific actin, S100, CD10 and p53 by stromal component \(^10, 11\). In our case the carcinomatous component was positive for CK and EMA, while the sarcomatous component was positive for vimentin and SMA (diffuse cytoplasmic staining). However S100, desmin, CD 34, and CD117 were negative.
<table>
<thead>
<tr>
<th>Cases</th>
<th>Age &amp; sex</th>
<th>SITE</th>
<th>GROSS</th>
<th>Histology</th>
<th>Epithelial component</th>
<th>Mesenchymal component</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Millis et al 1994</td>
<td>50/F</td>
<td>HOP**</td>
<td>NIA*</td>
<td>Adenocarcinoma</td>
<td></td>
<td>Leiomyosarcoma focal chondroid differentiation</td>
</tr>
<tr>
<td>2. Weing et al 1997</td>
<td>48/F</td>
<td>Tail</td>
<td>Multicystic</td>
<td>Mucinous cystadenocarcinoma</td>
<td></td>
<td>Undifferentiated Spindle cell sarcoma</td>
</tr>
<tr>
<td>3. Weing et al 1997</td>
<td>66/F</td>
<td>Tail</td>
<td>Multicystic</td>
<td>Mucinous cystadenocarcinoma</td>
<td></td>
<td>Undifferentiated Spindle cell sarcoma</td>
</tr>
<tr>
<td>4. Weing et al 1997</td>
<td>67/M</td>
<td>Tail</td>
<td>Multicystic</td>
<td>Mucinous cystadenocarcinoma</td>
<td></td>
<td>Undifferentiated Spindle cell sarcoma</td>
</tr>
<tr>
<td>5. Yoshiharu et al 1997</td>
<td>75/M</td>
<td>HOP*</td>
<td>Solid &amp; cystic</td>
<td>Anaplastic carcinoma</td>
<td></td>
<td>Sarcoma</td>
</tr>
<tr>
<td>6. Darvishan et al 2002</td>
<td>74/M</td>
<td>HOP**</td>
<td>Solid, yellowish white, firm</td>
<td>Adenocarcinoma</td>
<td></td>
<td>Malignant fibrous histiocytoma</td>
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<tr>
<td>7. Yamazaki et al 2003</td>
<td>90/M</td>
<td>NIA</td>
<td>Solid</td>
<td>Adenocarcinoma</td>
<td></td>
<td>Undifferentiated spindle cell sarcoma</td>
</tr>
<tr>
<td>8. Bharathulla et al 2005</td>
<td>67/F</td>
<td>NIA</td>
<td>NIA</td>
<td>Adenocarcinoma</td>
<td></td>
<td>Spindle cell sarcoma. (triphasic, OTGC*)</td>
</tr>
<tr>
<td>9. Bloomston et al 2006</td>
<td>67/F</td>
<td>HOP**</td>
<td>Solid and cystic</td>
<td>Mucinous cystadenoma</td>
<td></td>
<td>Spindle cell sarcoma</td>
</tr>
<tr>
<td>10. Gelos et al 2008</td>
<td>61/F</td>
<td>HOP**</td>
<td>Solid exophytic localized to duodenum</td>
<td>MD Adenocarcinoma</td>
<td></td>
<td>Poorly differentiated sarcoma</td>
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<td>11. Nakano et al 2008</td>
<td>82/f</td>
<td>HOP”</td>
<td>NIA</td>
<td>Adenocarcinoma</td>
<td></td>
<td>Spindle cell sarcoma</td>
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<td>12. Okamura et al 2010</td>
<td>64/F</td>
<td>Tail</td>
<td>Solid polypoidal</td>
<td>Adenocarcinoma(IDPM*)</td>
<td></td>
<td>Osteosarcoma</td>
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<tr>
<td>13. Shen et al 2010</td>
<td>72/f</td>
<td>HOP**</td>
<td>Solid, yellow white</td>
<td>Adenocarcinoma</td>
<td></td>
<td>Pleomorphic spindle cell sarcoma</td>
</tr>
</tbody>
</table>
Table 1: Epithelial and mesenchymal components detected in reported cases of Carcinosarcoma Pancreas

<table>
<thead>
<tr>
<th>Case</th>
<th>Gender</th>
<th>Age</th>
<th>Location</th>
<th>Epithelial Component</th>
<th>Mesenchymal Component</th>
</tr>
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<tr>
<td>14. Kim et al 2011</td>
<td>48/M</td>
<td>Tail</td>
<td>Solid &amp; Cystic with mural nodule</td>
<td>Mucinous adenocarcinoma &amp; anaplastic carcinoma</td>
<td>Pleomorphic spindle cell sarcoma</td>
</tr>
<tr>
<td>15. Palani et al 2011</td>
<td>46/M</td>
<td>HOP”</td>
<td>Solid with mucoid areas</td>
<td>Adenosquamous carcinoma</td>
<td>Leiomyosarcoma</td>
</tr>
<tr>
<td>16. Wen Yang et al 2012</td>
<td>53/F</td>
<td>HOP”</td>
<td>Solid yellowish white</td>
<td>Adenocarcinoma</td>
<td>Pleomorphic spindle cell sarcoma (SMAϒ +ve)</td>
</tr>
<tr>
<td>17. Wayne et al 2013</td>
<td>46/m</td>
<td>Neck, body &amp; tail</td>
<td>Multiple cysts</td>
<td>Mucinous cystic neoplasm</td>
<td>Sarcomatous stroma</td>
</tr>
<tr>
<td>18. E. Oymaci et al 2013</td>
<td>66/m</td>
<td>HOP”</td>
<td>Cyst with mural nodule</td>
<td>Adenocarcinoma</td>
<td>Malignant fibrous histiocytoma (focal SMAϒ +ve)</td>
</tr>
<tr>
<td>19. Ours 2012</td>
<td>50/M</td>
<td>HOP”</td>
<td>Solid yellowish white</td>
<td>Adenocarcinoma with focal squamous areas</td>
<td>Pleomorphic spindle cell sarcoma (SMAϒ +ve)</td>
</tr>
</tbody>
</table>

*NIA – No information available. ** HOP – Head of Pancreas. ¹IDPM – Intraductal papillary mucinous. ²OTGC – Osteoclastic tumor giant cell. ϒSMA- Smooth muscle actin.

Of the total 19 cases compiled, the epithelial component in 11 were adenocarcinoma, 1 adenosquamous, 4 mucinous cystadenocarcinoma, 2 mucinous cystadenoma, 1 showed 2 epithelial components (anaplastic carcinoma and mucinous cystadenocarcinoma), and 1 case showed anaplastic carcinoma. The sarcomatous components in descending order were pleomorphic spindle cell sarcoma (9), undifferentiated spindle cell sarcoma (5), leiomyosarcoma (2), malignant fibrous histiocytoma (2) and osteosarcoma (1).

There are different theories and controversies regarding the origin of carcinosarcomas, but molecular studies favour a monoclonal origin. Some have proposed an initial carcinomatous origin with acquisition of subsequent genetic alterations causing sarcomatous differentiation. Even in tumors with benign epithelial elements presence of sarcomatous foci confers an aggressive nature. Molecular workup was not done in our case. Prognosis is dismal and the overall survival is 6 months. Treatment options are surgical excision and chemoradiation. The longest reported survival was 28 months with combined surgery and chemotherapy. Some authors have suggested chemotherapy with Gemcitabine and surgery in similar cases.

Conclusion
In a rapidly growing pancreatic tumor, with the gross specimen showing solid, firm areas the possibility of...
a sarcomatous component should be kept in mind. Adequate sampling and detailed immunohistochemical studies are necessary to exclude different sarcomatous elements in suspicious cases, since desmoplastic stroma is seen in pancreatic carcinomas. This becomes important as it influences the behavior and hence the prognosis of the neoplasm. Inspite of its rarity, recognition of carcinosarcomas are important for planning further management.

References
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