Case Report

Carcinosarcoma of the bile duct: a case report and review of literature

Ser Yee Lee[1,2], Jinru Shia[3], T. Peter Kingham[1], William R. Jarnagin[1]

[1]Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, NY 10065, USA; [2]Department of Hepatopancreatobiliary and Transplant Surgery, Singapore General Hospital, Singapore; [3]Department of Pathology, Memorial Sloan Kettering Cancer Center, New York, NY 10065, USA

Correspondence to: T. Peter Kingham, MD. Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, NY 10065, USA. Email: kinghamt@mskcc.org.

Abstract: Carcinosarcomas of the bile ducts are very rare tumors consisting of both epithelial and mesenchymal elements. We report a case of bile duct carcinosarcoma and its clinical, radiological and pathological features and a brief review on this rare condition.

Keywords: Carcinosarcoma; sarcomatoid carcinoma; bile duct

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Introduction

Carcinosarcomas, also known as sarcomatoid carcinomas, are very rare tumors consisting of both epithelial and mesenchymal elements. These tumors have been reported in many different organs, including the pancreas, lung, uterus, ovary, esophagus, stomach and kidney (1-5). However, carcinosarcoma of the biliary tree is rare, with only a handful of cases reported in the bile ducts (6-11). We report an interesting case of a bile duct carcinosarcoma and a brief literature review.

Case presentation

A 91-year-old female patient was referred to the hepato-pancreato-biliary (HPB) service for further management of an intrabiliary mass near the biliary confluence detected on her CT scan (*Figure 1*). She had elevated liver enzymes [aspartate aminotransferase (AST): 133 U/L; alanine aminotransferase (ALT): 141 U/L and alkaline phosphate (ALP): 728 U/L], but bilirubin was within the normal range. Tumor markers were abnormal; alpha-fetoprotein (αFP), carbohydrate antigen 19-9 (CA 19-9) and carcinoembryonic antigen (CEA) were all elevated at 6.7 ng/mL, 5.8 ng/mL and 147 U/mL, respectively.

The consensus at a multi-disciplinary HPB tumor conference was an intraluminal soft tissue mass at the confluence of the left and right main bile ducts resulting in marked bilobar intrahepatic biliary dilatation, suspicious for a papillary hilar cholangiocarcinoma. A decision was made for limited surgical resection of the hilar cholangiocarcinoma, peri-hilar lymphadenectomy and a hepatojejunostomy without a liver resection due to patient's age and personal preference to avoid a major hepatectomy. Additionally, given the difficulties of palliating jaundice in the setting of a large intraductal tumor, even a limited resection was considered preferable to non-operative decompression.

Intraoperatively, after exclusion of peritoneal metastases, a large papillary intrabiliary duct tumor arising from the biliary confluence was found and a complete gross resection was achieved by removing the biliary confluence and the tumor in-situ, and hepatojejunostomy was fashioned to the right, left and caudate ducts separately. The patient recovered uneventfully but the disease recurred after 2 months and she passed away soon after.

Histological features

On gross examination, the tumor was primarily exophytic with masses seen within both the right and left hepatic ducts. An area of mural invasion was noted involving the

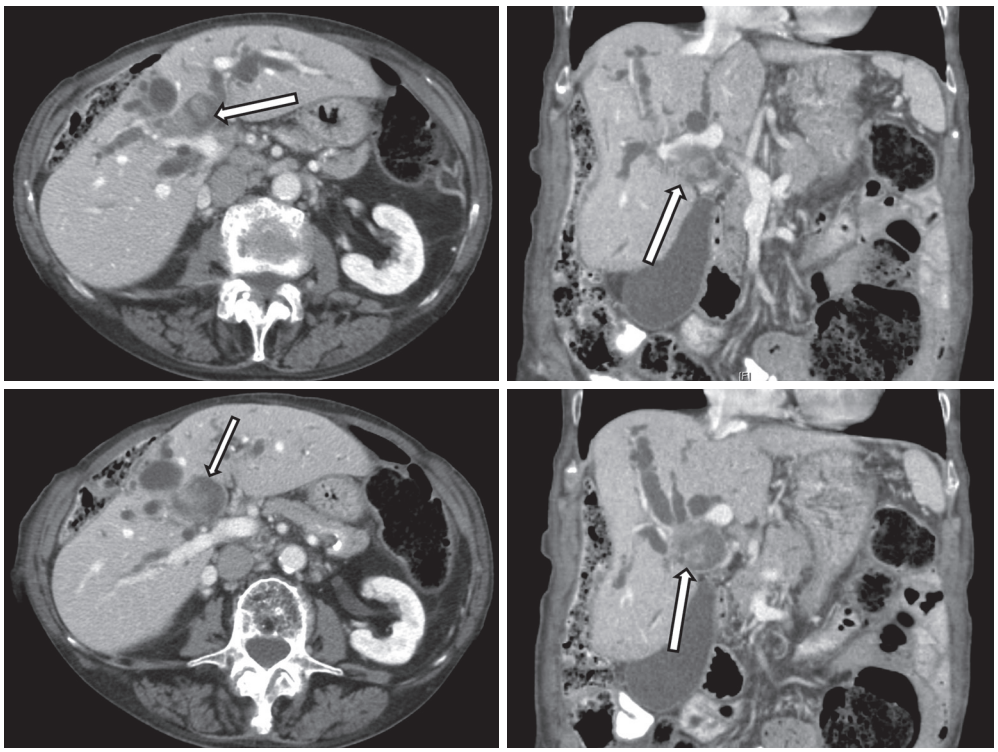

Figure 1 Computed tomography cross-sectional and coronal images. White arrows illustrate the hilar location and the intraductal papillary—like features of the bile duct carcinosarcoma distending the biliary confluence and causing proximal intrahepatic biliary dilatation.

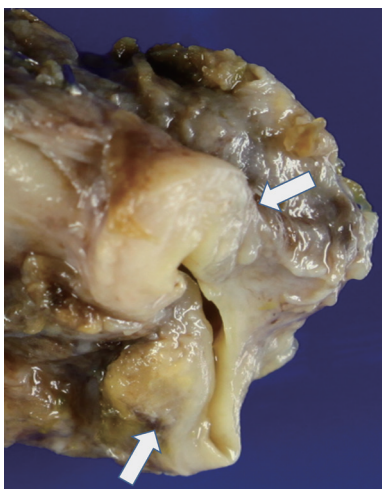

Figure 2 Gross specimen. Arrows illustrate the areas of mural invasion involving the right hepatic duct wall near the resection margins when the tumor specimen was bivalved.

right hepatic duct wall (*Figure 2*). Histologically, both the exophytic and murally invasive components were composed primarily of sarcomatoid elements, mostly in the form of spindle and pleomorphic tumor cells with prominent mitotic activity (*Figure 3A*). A minor component of the tumor showed osteogenic differentiation with formation of malignant osteoid (*Figure 3B*). The carcinoma component was minor, constituting about 10% of the entire tumor with morphological features of biliary adenocarcinoma and the overall architectural pattern being papillary (*Figure 3C*). Notably, the underlying bile duct epithelium showed foci of low and high grade dysplasia (*Figure 3D*).

Discussion

Carcinosarcomas are pathologically characterized by the presence of both epithelial and mesenchymal components within the same tumor. The most common site for carcinosarcoma of the biliary tract is the gallbladder with fewer than 100 cases reported in the literature; comparatively, there are only 7 cases of carcinosarcoma of the bile ducts reported in the English literature to date (*Table 1*) (6-13).

The pathogenesis of these rare tumors is uncertain but several hypotheses exist. It has been theorized that

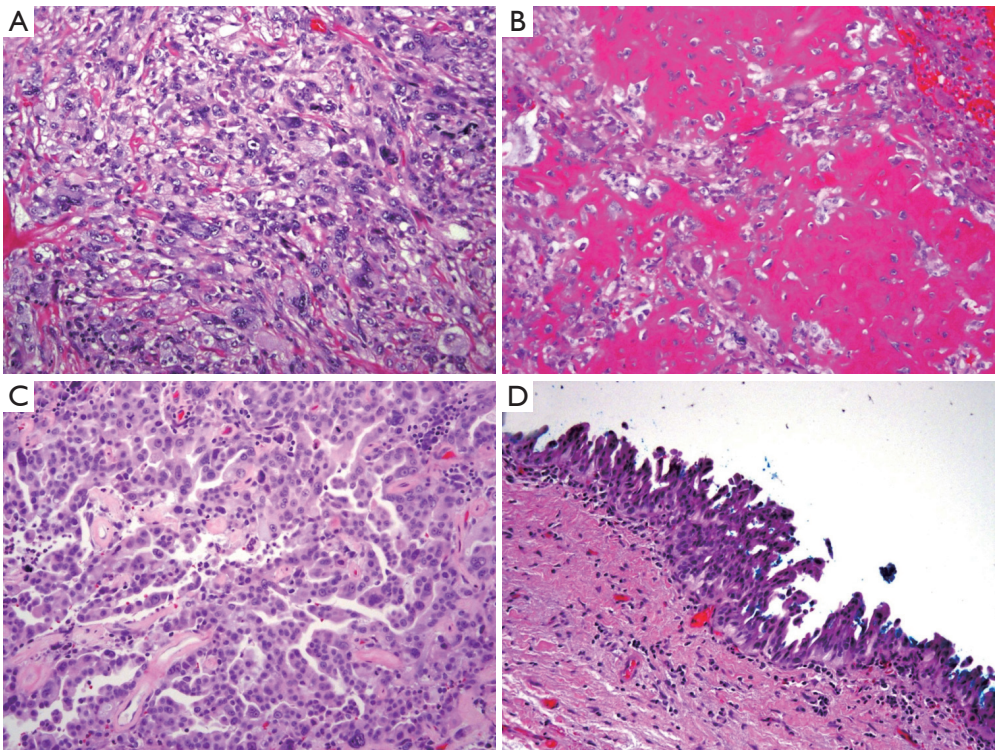

Figure 3 Histological features illustrating the mixed components of the tumor. (A) Both the exophytic and morally invasive components contained prominent sarcomatoid elements, in the form of spindle and pleomorphic tumor cells with prominent mitotic activity; (B) minor component of the tumor showed osteogenic differentiation with formation of malignant osteoid; (C) the carcinoma component, constituting about 10% of the entire tumor, had morphological features characteristic of biliary adenocarcinoma with tumor cells being cuboidal and the overall architectural pattern being papillary; (D) the underlying bile duct epithelium showed foci of low and high grade dysplasia. Hematoxylin and Eosin stain. Magnification: (A-C) is 100× and (D) is 40×.

carcinosarcoma arises from totipotent stromal stem cells that are capable of divergent differentiation. Another postulation is the collision tumor theory that suggests the distinct and concurrent malignant proliferation of both the epithelial and mesenchymal components within the same tissue. It has also been suggested that a carcinoma can transform into a sarcoma by metaplastic transformation (14-16). A distinguishing feature of a true carcinosarcoma is the biphasic nature of the tumor with a lack of transition between the two epithelial and sarcomatous components as opposed to a poorly differentiated carcinoma with spindle cell pattern (6,14). The sarcomatous element commonly consists of undifferentiated spindle cells and a variety of heterogeneous components such as, chondro-, osteo-, leiomyo-, rhabdomyosarcoma cells (*Table 1*). The epithelial element usually consists of adenocarcinoma and occasionally, components such as squamous-, small cell- and undifferentiated carcinomas (17-20). Genetic analysis has been utilized to evaluate the pathogenesis of these tumors (21). They have also been sub-classified into two sub-groups: one with predominant sarcomatous differentiation or predominantly carcinomatous differentiation.

The demographics of biliary carcinosarcoma are similar to that of gallbladder adenocarcinoma, with the majority occurring in elderly women and strongly associated with cholelithiasis (22). The prognosis is dismal, largely extrapolated from the experience of gallbladder carcinosarcomas. The reported median survival time of patients with carcinosarcomas of the gallbladder after surgical resection was only 7 months with a 1-, 2-, and 3-year survival rates of 37.2%, 31.0%, and 31.0% respectively (23). The median time to recurrence for patients who died was less than 2 months (23). The TNM staging system is a valuable prognostic tool in gallbladder carcinoma but has little role in gallbladder carcinosarcoma; a recent review

Table 1 Summary of patients' characteristics in current series and in literature

Author/ year	Gender/ age	Presentation	Investigation/ tumor markers	Location	Gross/size (mm)*	Surgery	Pathology	IHC makers (carcinomatous component)	IHC makers (sarcomatous component)	Prognosis
Loud *et al.* 1997 (8)	F/35	Obstructive jaundice	ERCP, CT, PTC	Hilar	Polypoidal/ Size-NR	BD resection	Biphasic pattern of carcinomatous and sarcomatoid components	NR	NR	NR
Yoon *et al.* 2003 (9)	M/78	Abdominal pain and obstructive jaundice	CT, PTC/ tumor markers not done	Mid CBD	Infiltrative/40	PD	Biphasic pattern of carcinomatous and sarcomatoid components merging into another, 2/22 LN + ve for sarcomatoid component	Cytokeratin++; CEA+; P53+; PCNA+	Cytokeratin++; Vimentin++; α-SMA+; NSE focal +; P53++; PCNA++	Died on 5POD due to cardiac complications
Kadono *et al.* 2005 (7)	F/75	Acute obstructive suppurative cholangitis	ERCP with cytology(-), PTC, CT/ CEA ↑, CA19-9 ↑	Mid CBD	Infiltrative/ Size-NR	PD	Biphasic pattern of carcinomatous and sarcomatoid components with chondroid tissue, osteoid formation with focal ossification and a squamous differentiation	EMA+; Mucin-1 antigen+; Keratin+	Vimentin+; EMA+; thrombomodulin+; α1-antichymotrypsin+; S100+	2 years; died from local recurrence
Jang *et al.* 2005 (10)	F/68	Abdominal pain, anorexia and weight loss	CT, EUS/ AFP-ve, CEA-ve, CA19-9 ↑	Distal CBD	Polypoidal/35	PD	Biphasic pattern of predominantly sarcomatous and focally carcinomatous components, no heterologous sarcomatous components	Cytokeratin ++; CEA++	Cytokeratin+; vimentin+ (diffuse)	1 year disease free
Sodergren *et al.* 2005 (6)	F/64	Ill health and anorexia	US, ERCP, CT/tumor markers not done	Hilar	Polypoidal/20	BD resection	Biphasic pattern with epithelial and mesenchymal elements with foci that resemble smooth muscle and other foci with a chondroid appearance	Cytokeratin +; EMA+; CEA +	Vimentin+; SMA+; desmin+; myoglobin+; S100+ (focal)	5-year disease free

Table 1 (*continued*)

Table 1 (*continued*)

Author/ year	Gender/ age	Presentation	Investigation/ tumor markers	Location	Gross/size (mm)*	Surgery	Pathology	IHC makers (carcinomatous component)	IHC makers (sarcomatous component)	Prognosis
Aurello *et al.* 2008 (11)	F/73	Obstructive jaundice	US, ERCP with cytology(+), PTC, CT/ CEA ↑, CA19-9 ↑	Distal CBD	Polypoidal/26	PD	Biphasic pattern with heterologous differentiation ki-67 YMIB-1 (80%, uniformly distributed)	Cytokeratin AE1/AE3+; EMA+; CAM 5.2+	Cytokeratin AE1/ AE3+ (focal); EMA+ (focal); CAM 5.2+ (focal); vimentin+ (diffuse)	Alive, 7 months; disease-free
Tanaka *et al.* 2012 (12)	M/71	Recurrent cholangitis	CT, ERCP	Distal CBD	Polypoidal/75	PD	Biphasic pattern with predominant sarcomatous and a few carcinomatous components in the ductal wall and invasive front; ki-67 index (40%)	NR	Negative for epithelial and non-epithelial markers (not specified)	3 months; disease-free, died at 10 months
Lee *et al.* (present case)	F/91	Fatigue and abnormal LFT	CT/AFP ↑, CEA ↑, CA19-9 ↑	Hilar	Polypoidal/20	BD resection	Biphasic pattern of papillary adenocarcinoma, poorly; differentiated carcinoma, spindle cell and pleomorphic sarcoma, with a heterologous element of osteoid sarcoma	NR	NR	Died at 2 months

*, largest dimension; +/++, positive staining/strongly positive staining. PD, pancreaticoduodenectomy; CT, computed tomography; US, ultrasound; ERCP, endoscopic retrograde cholangiopancreatogram; PTC, percutaneous transhepatic cholangiogram; EUS, endoscopic ultrasound; LFT, liver function tests; CA 19-9, carbohydrate antigen 19-9; CEA, carcinoembryonic antigen; αFP, alpha-fetoprotein; BD, bile duct; CBD, common bile duct; NR, not reported; IHC, immunohistochemistry; α-SMA, α-smooth muscle actin; NSE, neuron specific enolase; PCNA, proliferating cell nuclear antigen; EMA, epithelial membrane antigen.

demonstrated that the survival time is in matter of months regardless of their tumor stage (24-29).

In general, carcinosarcomas are locally aggressive tumors with a propensity to metastasize systemically even in early stages (7,30). It been suggested that the aggressiveness of the tumor depends on the sarcomatoid component, as they metastasize to the lymph nodes and distant organs more readily. Interestingly, it is also the sarcomatoid component that forms the bulk of polypoidal element that leads to an earlier presentation as it obstructs the bile ducts, in contrast to gallbladder carcinosarcomas, where the carcinomatoid element forms the infiltrative component of the tumor (6,7,9,11,17). Kubota *et al.* (31) studied ki-67 in a case of gallbladder carcinosarcoma and compared it to a cohort (n=11) of patients with ordinary gallbladder adenocarcinoma: the ki-67 index in the spindle-cell component was higher than that in the epithelial component, which may account for the more aggressive biological behavior of the carcinosarcoma. This observation is consistent with other studies reporting that Ki-67 has prognostic value in various types of carcinosarcoma and other malignant tumors as well (31,32). Due to the rarity of bile duct carcinosarcoma, its true prognosis and clinicopathological features are not well established. Based on the reported cases, the survival time can vary widely, from 2 months to 5 years of disease-free survival (*Table 1*).

Management of all biliary malignancy, including carcinosarcoma, remains challenging, and this is particularly true for those arising from the proximal biliary tree. The strategy has largely been extrapolated from the experience in treating cholangiocarcinoma, with resection as the mainstay of treatment. As is also true for the more common biliary adenocarcinoma, there is no clear evidence that chemotherapy or radiotherapy confers any survival benefit, either as adjuvant treatment or in the palliative setting (20,25). However, judging from the poor results, it is clear that surgery alone is inadequate. Adjuvant chemotherapy has been used in carcinosarcomas of the female genital tract but with disappointing results and the role of radiation is currently unclear as well (6,7,20,30). Lumsden *et al.* reported improved survival with the use of intracavitary radiotherapy via a T-Tube for a case of a gallbladder carcinosarcoma (28).

This case report includes interesting radiologic and histologic features of carcinosarcoma of the bile duct. Carcinosarcomas often demonstrate unusual gross and radiographic features. Polypoid growth, which was also observed in this patient, was reported to be the characteristic gross feature of carcinosarcomas (5,7,8,33). The features of intraductal expansion, distension of the biliary confluence by the polypoidal tumor and subsequent proximal biliary tree obstruction were noted in our patient and are illustrated in *Figure 1*. This growth pattern is also seen in papillary cholangiocarcinoma, which is often a more indolent disease. As the present cases illustrates, the radiographic features of carcinosarcoma and papillary cholangiocarcinoma may be indistinguishable.

Conclusions

We report a case of carcinosarcoma of the bile duct with biphasic areas of papillary adenocarcinoma, poorly differentiated carcinoma intermingled with spindle cell and pleomorphic sarcoma and a heterologous element of osteoid sarcoma. To the best of our knowledge, this is the eighth case of biliary carcinosarcoma, it's pathological and immunohistochemical characteristics define and distinguish it from a hilar cholangiocarcinoma. Complete resection is the optimal mode of treatment when possible, but the prognosis for most patients is poor; roles for chemotherapy and/or radiation therapy are undefined.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Informed Consent: Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the editor-in-chief of this journal.

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