

## Case Report

# Sarcomatoid combined hepatocellular-cholangiocarcinoma: a case report and review of literature

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**Abstract:** Sarcomatoid combined hepatocellular-cholangiocarcinoma is an extremely rare primary hepatic malignancy and only a few cases have been reported. Herein, we report a case of combined hepatocellular-cholangiocarcinoma with sarcomatoid changes in a 52-year-old man, who had a history of liver cirrhosis and transarterial chemoembolization. The resected liver revealed a mass of 4.5×3.5 cm. Microscopically, the tumor was composed of adenocarcinoma intermingled with poorly differentiated hepatocellular carcinoma, which contained atypical spindle cells. We also present a short review of reported cases of sarcomatoid combined hepatocellular-cholangiocarcinoma.

**Keywords:** Sarcomatoid carcinoma, combined hepatocellular-cholangiocarcinoma, liver

### Introduction

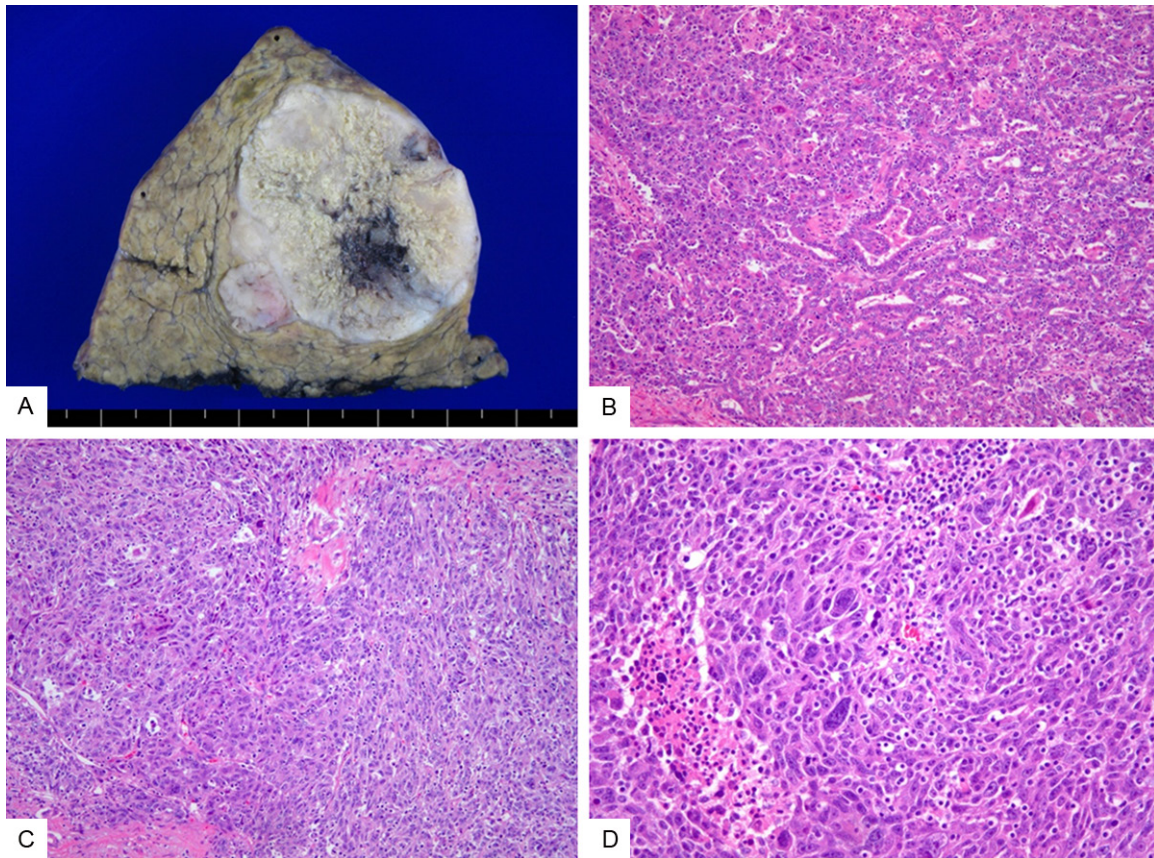
Sarcomatoid changes are rarely seen in epithelial malignancy, which is found in organs such as the breast, esophagus, lung, kidney, and urinary bladder. In the liver, most of the reported sarcomatoid changes were associated with hepatocellular carcinoma (HCC) and found in about 2% of resected HCC [1]. Combined hepatocellular carcinoma and cholangiocarcinoma (cHCC-CC) is a rare neoplasm, which comprises less than 1% of hepatic carcinoma [2]. The tumor has intimately mixed elements of both HCC and cholangiocarcinoma (CC), and sarcomatoid cHCC-CC is extremely rare. Here, we describe a case of cHCC-CC with sarcomatoid transformation.

### Case report

A 52-year-old man presented with a new mass, which was detected in segment 6 of the liver following a computed tomography (CT) scan. The patient had a history of liver cirrhosis due to chronic hepatitis B virus infection. He had undergone transarterial chemoembolization 8 years previously to treat a 1.8-cm HCC in the

right lobe of the liver. Physical examination was unremarkable. Laboratory findings showed the following levels: total bilirubin 1.44 mg/dL, aspartate aminotransferase 33 IU/L, alanine transaminase 7 IU/L, alkaline phosphatase 112 IU/L, gamma-glutamyl transferase 31 IU/L, and alpha-fetoprotein 2.0 ng/mL. A CT scan revealed a 3.6-cm mass with subtle arterial enhancement. Magnetic resonance imaging revealed that the mass had low signal intensity on T1-weighted images and high signal intensity on T2-weighted images. Segmentectomy was performed, and the resected liver showed a relatively well-defined mass with extensive necrosis, measuring 4.5×3.5 cm (**Figure 1A**). The background liver is cirrhotic. On microscopic examination, the tumor showed a heterogeneous pattern. An adenocarcinoma component, which had an irregular lumen was intermingled with poorly differentiated HCC (**Figure 1B**), which had cell-to-cell heterogeneity, pleomorphic nuclei, and sarcomatoid transformation (**Figure 1C**). The sarcomatoid component was composed of atypical, sometimes bizarre spindle-shaped cells with vesicular nuclei and prominent nucleoli (**Figure 1D**). Atypical mitoses were frequently found, and necrosis was

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**Figure 1.** A. The resected liver shows a well defined mass with central necrosis. The background parenchyma is cirrhotic; B. Microscopically, the tumor consists of poorly differentiated HCC (left) and adenocarcinoma (right) component which are tightly intermingled (H-E stain,  $\times 100$ ); C. The poorly differentiated HCC component transformed into atypical spindle-shaped cells, showing sarcomatoid change (H-E stain,  $\times 100$ ); D. The sarcomatoid component is composed of pleomorphic spindle-shaped cells and necrosis (H-E stain,  $\times 200$ ).

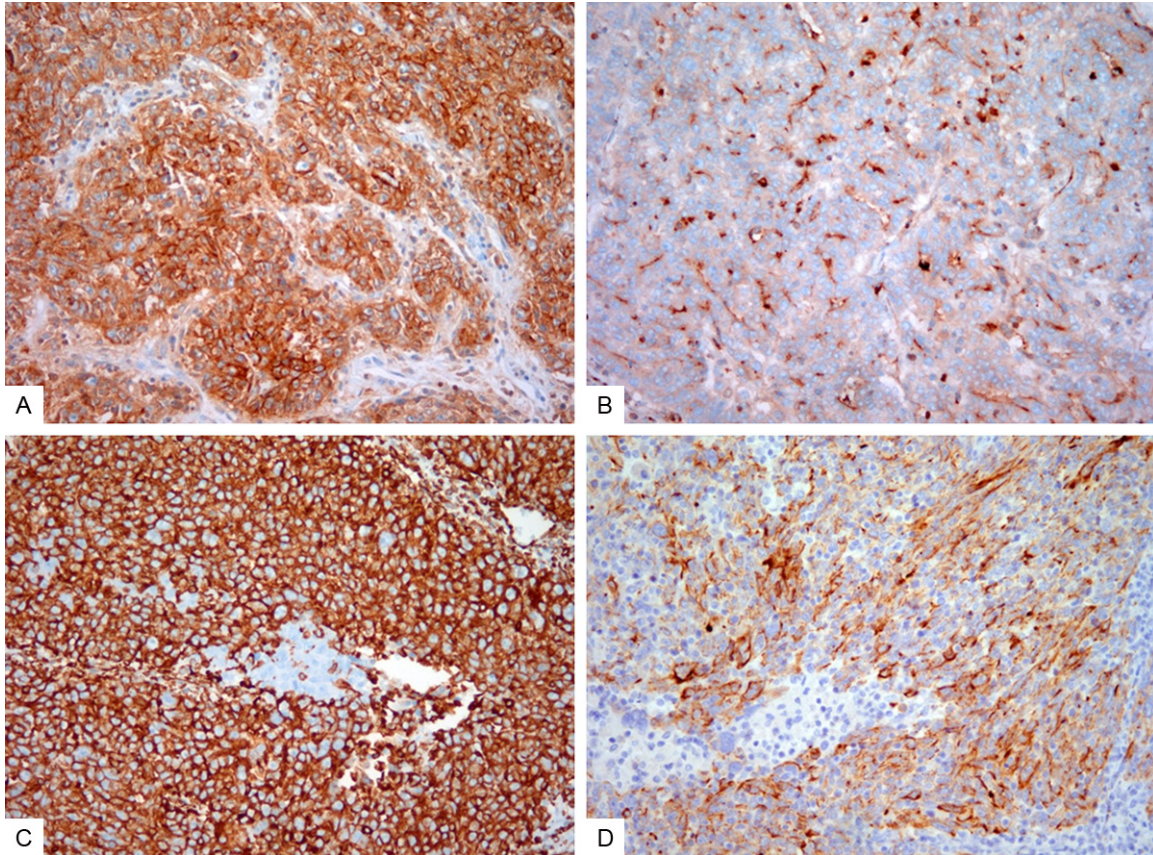
extensive. Immunohistochemical investigation showed that the poorly differentiated HCC component was focal positive for glypican-3 and negative for hepatocyte antigen, alpha-fetoprotein, cytokeratin (CK) 7, and CK19. The adenocarcinoma component was focally stained with CK7 and CK19, but not with glypican-3, hepatocyte antigen, and alpha-fetoprotein. Carcinoembryonic antigen (CEA) staining revealed a different pattern in both components. The adenocarcinoma component showed cytoplasmic staining, while the HCC component showed a canalicular staining pattern (**Figure 2A, 2B**). The sarcomatoid component was strongly stained with vimentin (**Figure 2C**) and also focally expressed cytokeratin (**Figure 2D**), revealing its diverse differentiation. KIT and CD56 were not expressed in the carcinoma and sarcomatoid components. The patient had received adjuvant chemotherapy with cisplatin and 5-fluorouracil and showed no evidence of recurrence or metastasis during the 6 months of follow-up.

### Discussion

CHCC-CC is an uncommon primary hepatic malignancy. It is defined as the presence of unequivocal, intimately mixed elements of both HCC and CC. The histogenesis of cHCC-CC has been in doubt for many years, but recent studies revealed that it might originate from hepatic progenitor cells, which can differentiate into either hepatocytes or cholangiocytes [3]. Current World Health Organization classification divides cHCC-CC into the classical type and cHCC-CC with stem cell features [4]. Tumors containing typical HCC and CC are categorized as classical-type cHCC-CC, and tumors showing phenotypical or immunophenotypical features of stem/progenitor cells are classified as cHCC-CC with stem-cell features. The latter type is subdivided into three subtypes: typical subtype, intermediate-cell subtype, and cholangiocellular subtype. Classical-type cHCC-CC is the most common form of cHCC-CC, wherein



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**Figure 2.** A. The adenocarcinoma component shows a cytoplasmic staining, pattern for CEA (CEA,  $\times 200$ ); B. The HCC component reveals a canalicular staining pattern for CEA (CEA,  $\times 200$ ); C. The sarcomatoid component is diffuse and strongly stained with vimentin (Vimentin,  $\times 200$ ); D. Cytokeratin is also focally expressed in sarcomatoid component (Cytokeratin,  $\times 200$ ).

**Table 1.** Previously reported cases of sarcomatoid combined hepatocellular-cholangiocarcinoma

Age	Sex	Viral Marker	Anti-cancer therapy	Size	Metastasis	Outcome	Ref.
74	Male	-	Hepatic artery chemoinfusion	21 cm	Intrahepatic Lung, stomach Multiple LNs	Died (Autopsy)	[7]
78	Male	-	TAE	N/A	N/A	Died (Autopsy)	[8]
59	Male	-	-	20 cm	Intrahepatic	Died, 4 months	[9]
68	Female	HCV	-	3 cm	Hilar LN	Died, 24 months	[10]
59	Male	HBV	TACE	2 cm	-	Alive, 25 months	[11]
28	Male	HBV	-	12 cm	N/A	Lost to follow-up	[12]
71	Male	-	-	10 cm	Lung, pleura Multiple LNs	Died, 6 weeks	[13]

HCV: hepatitis C virus, HBV: hepatitis B virus, N/A: not available, LN: lymph node, TAE: transarterial embolization, TACE: transarterial chemoembolization.

the CC component is usually a typical adenocarcinoma, while the HCC component may be well-to-poorly differentiated. Our case also corresponded to this type and had a moderate-to-poorly differentiated CC component intermixed with a poorly differentiated Edmondson-Steiner grade IV HCC-containing sarcomatoid transformation.

Sarcomatoid HCC is rare. It is present in about 2% of resected HCC and 3.9-9.4% of autopsy

cases [1, 5, 6]. Sarcomatoid changes in cHCC-CC are even rarer, and to the best of our knowledge, only seven cases have been reported in the English literature thus far. The clinical findings of the reported cases of sarcomatoid cHCC-CC are summarized in **Table 1** [7-13]. The mean age of the patients was 62 years (range 28-78), and the tumors were predominantly found in men. Viral markers were positive in only three cases [10-12]. Aggressive anticancer procedures such as transarterial emboliza-

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tion or radiofrequency ablation are also believed to be responsible for sarcomatoid change in HCC [6, 14]. Our patient had a history of transarterial chemoembolization. However, in four of the seven reported cases of sarcomatoid cHCC-CC, anticancer therapy was not administered before diagnosis [9, 10, 12, 13].

Most reported cases of sarcomatoid cHCC-CC showed an infiltrative growth pattern and extensive necrosis [7, 9, 12, 13]. Histologically, the epithelial components of all seven tumors were cHCC-CC. However, their differentiation varied. The sarcomatoid components were composed of atypical spindle-shaped or epithelioid cells, while osteoid cells were found in one case [7]. Sarcomatoid transformation was found mainly in the CC component in four cases, in both HCC and CC in two cases, and in HCC in only one case. The prognosis of sarcomatoid cHCC-CC is known to be unfavorable. Four of the seven reported cases had nodal, intrahepatic, or extrahepatic metastasis, and five patients died of the disease [7-10, 13].

In conclusion, sarcomatoid cHCC-CC is an extremely rare primary hepatic malignancy, of which only a few cases have been reported. We have described an additional case of sarcomatoid cHCC-CC that had intimately mixed elements of both HCC and CC accompanied by a pleomorphic, spindle-shaped sarcomatoid component. The tumor typically shows an unfavorable prognosis with frequent nodal or distant metastasis. While sarcomatoid change in HCC is known to be strongly associated with anticancer therapy such as transarterial embolization, sarcomatoid cHCC-CC has been reported in patients without previous anticancer therapy. Further investigations are needed to clarify the pathogenesis of sarcomatoid transformation.

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### Disclosure of conflict of interest

None.

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