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Spindle Cell Carcinoma of the Common Bile Duct: Case Report with Immunohistochemical Analysis

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Key Words

Spindle cell carcinoma · Common bile duct · Immunohistochemistry

Abstract

The author reports a very rare case of spindle cell carcinoma of the common bile duct with an emphasis on immunohistochemical features. A 65-year-old man was admitted to our hospital because of jaundice. Imaging modalities revealed a tumor of the common bile duct, and bile cytology demonstrated malignant cells. A pancreatico-duodenectomy was performed. Grossly, an elevated tumor (15 × 10 × 3 mm) was present in the middle portion of the common bile duct. Microscopically, the tumor consisted of well-differentiated adenocarcinoma (20% in area) and spindle cell carcinoma (80% in area). There were gradual transitions between the two. The tumor cells invaded into the serosa. Immunohistochemically, the spindle cell carcinoma element was positive for four types of pancytokeratins, cytokeratin 7 (CK7), CK8, CK18, CK19, CK20, epithelial membrane antigen, vimentin, p53 protein, Ki-67 (labeling = 52%), and CEA. It was negative for high-molecular-weight CK, CK5/6, CK14, p63, neuron-specific enolase chromogranin, synaptophysin, CD56, CA19-9, CD34, desmin, S100 protein, myoglobin, α-smooth muscle antigen, CD34, CD68 and KIT. The adenocarcinoma element showed similar immunoreactivity except for negative vimentin, and positive CA19-9. The present case is the first report of spindle cell carcinoma of the common bile duct demonstrating an extensive immunohistochemistry. The spindle cell carcinoma in the present case may be derived from sarcomatous transformation of the adenocarcinoma element. CK20 newly emerges in the development of spindle cell carcinoma of the common bile duct.

Introduction

Sarcomatoid carcinoma of the extra- and intrahepatic bile ducts is very rare; only a few case reports and case studies of small series have been reported [1–9]. In particular,

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sarcomatoid carcinoma of the common bile duct is extremely rare [6–9]. Spindle cell carcinoma, a variant of sarcomatoid carcinoma, is also extremely rare in the common bile duct; only two case reports have been published in the English language literature [8, 9]. There have been no reports examining extensive immunohistochemical features in sarcomatoid carcinoma of the biliary tree. The author herein presents a case of spindle cell carcinoma of the common bile duct with an emphasis on immunohistochemical features.

Case Report

A 65-year-old man was admitted to our hospital because of jaundice. Imaging modalities including ERCP, CT, and MRI revealed a tumor of the common bile duct, and bile cytology identified malignant cells. A pancreatico-duodenectomy was performed. Grossly, an elevated tumor (15 × 10 × 3 mm) was present in the middle portion of the common bile duct (fig. 1). Microscopically, the tumor consisted of well-differentiated adenocarcinoma (20% in area) and spindle cell carcinoma (80% in area) (fig. 2). There were gradual transitions between the two. The tumor cells invaded into the serosa.

An immunohistochemical study was performed, using the Dako Envision method (Dako Corp., Glostrup, Denmark), as previously described [10–14]. The antigens examined and their results are shown in table 1. Immunohistochemically, the spindle cell carcinoma element was positive for four types of pancytokeratins, cytokeratin 7 (CK7) (fig. 3a), CK8, CK18 (fig. 3b), CK19, CK20, epithelial membrane antigen, vimentin (fig. 3c), p53 protein (fig. 3d), Ki-67 (labeling = 52%), and CEA (fig. 3e). It was negative for high-molecular-weight CK, CK5/6, CK14, p63, neuron-specific enolase chromogranin, synaptophysin, CD56, CA19-9, CD34, desmin, S100 protein, myoglobin, α -smooth muscle antigen, CD34, CD68 and KIT. The adenocarcinoma element showed similar immunoreactivity, except for negative vimentin and positive CA19-9 (table 1).

Discussion

Only two cases of spindle cell carcinoma of the common bile duct have been reported in the English language literature, to the best of the author's knowledge [8, 9]. Oikawa et al. [8] reported a case of sarcomatous carcinoma of the common bile duct composed of spindle cells, giant cells, and adenocarcinoma cells. Their case was immunohistochemically positive for pancytokeratins, epithelial membrane antigen and vimentin. The diagnosis was spindle cell and giant cell undifferentiated carcinoma [8]. Nakanishi et al. [9] reported spindle cell carcinoma of the common bile duct at the hepatic hilus. Their case was composed of spindle cells and adenocarcinoma cells, and immunohistochemically positive for two kinds of pancytokeratin [9].

The present tumor was composed of a spindle cell carcinoma element (80% in area) and a well-differentiated adenocarcinoma element (20% in area). Immunohistochemically, the tumor cells were positive for a wide range of CK, CEA and vimentin. They were also positive for p53 protein and Ki-67 antigen with high labeling indices. In contrast, they were negative for other mesenchymal markers and neuroendocrine markers. Therefore, the present tumor of the common bile duct is not a sarcoma but a carcinoma. Thus, spindle cell carcinoma was the correct diagnosis in the present study.

Sarcomatous transformation of carcinoma can occur in any carcinoma, though the frequency is very rare. In the present case also, the carcinoma was composed of spindle cell carcinoma and adenocarcinoma. There were gradual transitions between the two.

These findings strongly suggest that the spindle cell carcinoma element is derived from sarcomatous transformation of the adenocarcinoma element. The immunohistochemical data support this hypothesis in the present case.

There have been few studies of immunohistochemistry in spindle cell carcinoma of the common bile duct [8, 9], and extensive immunohistochemical studies of sarcomatoid carcinoma of the biliary tree have been performed. CK profiling has not been performed in sarcomatoid carcinoma of the bile ducts. It is well known that bile duct epithelium shows CK7, CK8, CK18 and CK19. In the present study, these CKs and CK20 were positive, indicating that CK20 emerged during the carcinogenesis of the present tumor. Positive expression of vimentin indicates a sarcomatous nature of the present carcinoma. Positive expression of CEA suggests an adenocarcinomatous nature of the present spindle cell carcinoma.

Mesenchymal markers including S100 protein, α -smooth muscle actin, CD34, myoglobin and desmin were absent in the present tumor, indicating that it was not a sarcoma but a carcinoma and that these antigens did not emerge during the spindle cell transformation of the adenocarcinoma of the present case. The present case was negative for neuroendocrine markers, suggesting that these antigens were absent from spindle cell carcinoma of the biliary tree. The present study also showed p53 protein and Ki-67 antigen. High Ki-67 labeling predict poor prognosis. In the present case, Ki-67 labeling of both elements was very high, suggesting a poor prognosis. The present tumor was free of neuroendocrine markers (chromogranin, synaptophysin, neuron-specific enolase, and CD56). The present findings indicate that the present tumor was not a neuroendocrine tumor. The present case was negative for CD34, CD68 and KIT, suggesting that the present tumor was not a KIT-positive tumors such as extragastrointestinal stromal tumor or other carcinomas and sarcomas.

In summary, the present case is the first report of spindle cell carcinoma of the common bile duct demonstrating an extensive immunohistochemistry. The spindle cell carcinoma in the present case may be derived from sarcomatous transformation of an adenocarcinoma element.

Table 1. Immunohistochemical reagents and results

Antigens	Antibodies (clone)	Sources	Results	
			spindle cell carcinoma	adeno- carcinoma
Pancytokeratin	AE1/3	Dako Corp., Glostrup, Denmark	+++	+++
Pancytokeratin	polyclonal wide	Dako	++	+++
Pancytokeratin	KL-1	Immunotech, Marseille, France	+++	+++
Pancytokeratin	CAM5.2	Becton Dickinson Co., CA, USA	++	+++
HMWCK	34βE12	Dako	–	–
CK5/6	D5/16	Dako	–	–
CK7	N1626	Dako	+++	+++
CK8	35βH11	Dako	++	++
CK14	LL002	Novocastra, Newcastle upon Tyne, UK	–	–
CK18	DC10	Dako	+++	+++
CK19	RCK 108	Progen, Heidelberg, Germany	++	++
CK20	K20.8	Dako	+	++
EMA	E29	Dako	+	+
Vimentin	Vim 3B4	Dako	++	–
CEA	polyclonal	Dako	+	++
Desmin	D33	Dako	–	–
S100 protein	polyclonal	Dako	–	–
Myoglobin	polyclonal	Dako	–	–
ASMA	1A4	Dako	–	–
CD34	NU-4A1	Nichirei, Tokyo, Japan	–	–
p53 protein	DO-7	Dako	+++	+++
p63	polyclonal	Dako	–	–
Ki-67	MIB-I	Dako	52%	46%
CA19-9	NA19-9	TFB Lab, Tokyo, Japan	–	+
Chromogranin	DAK-A3	Dako	–	–
Synaptophysin	polyclonal	Dako	–	–
NSE	BBS/NC/VI-H14	Dako	–	–
CD56	UJ13A	Dako	–	–
CD68	KP-1	Dako	–	–
KIT	polyclonal	Dako	–	–

+++ = 67–100% positive; ++ = 33–67% positive; + = 1–33% positive; – = negative.

HMWCK = High-molecular-weight cytokeratin; CK = cytokeratin; EMA = epithelial membrane antigen; CA19-9 = carcinoma antigen 19-9; CEA = carcinoembryonic antigen; ASMA = α-smooth muscle antigen; NSE = neuron-specific enolase.



Fig. 1. Gross features of the common bile duct tumor. An elevated tumor is seen (central part).

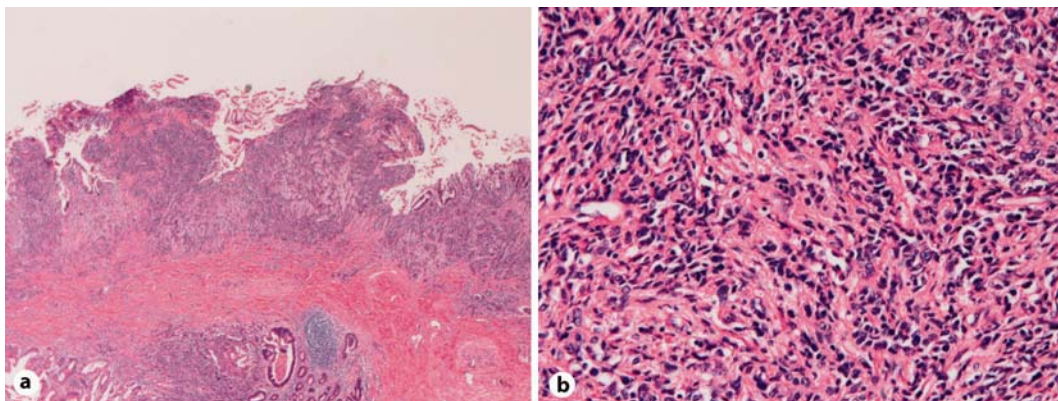


Fig. 2. a Microscopic features. The spindle cell carcinoma element (upper) and the adenocarcinoma element (lower) are seen. There is a gradual transition between the two. HE, $\times 20$. **b** High power view of the spindle cell carcinoma element. Malignant features are apparent. There are many mitotic figures. HE, $\times 100$.

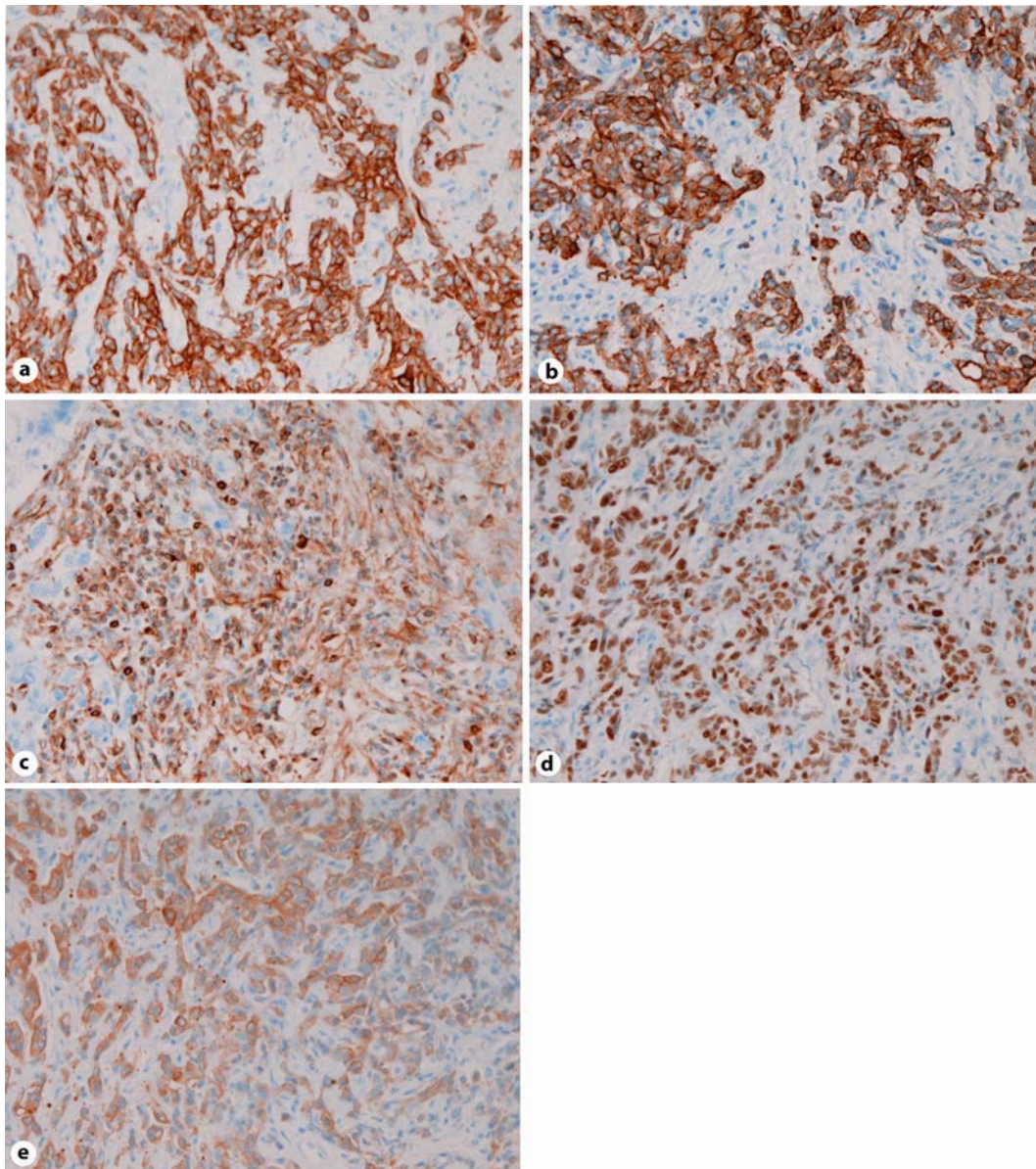


Fig. 3. **a** Positive reaction of CK7 in the spindle cell carcinoma element. Immunostaining, $\times 100$. **b** Positive reaction of CK18 in the spindle cell carcinoma element. Immunostaining, $\times 100$. **c** Positive reaction of vimentin in the spindle cell carcinoma element. Immunostaining, $\times 100$. **d** Positive reaction of p53 in the spindle cell carcinoma element. Immunostaining, $\times 100$. **e** Positive reaction of CEA in the spindle cell carcinoma element. Immunostaining, $\times 100$.

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