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CASE REPORT

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Biliary carcinosarcoma arising in nonparasitic simple cyst of the liver

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Abstract We report a carcinosarcoma arising in a nonparasitic simple cyst of the liver. Sequential imaging findings revealed that the tumour originated in a hepatic cyst and was composed of well-differentiated tubular adenocarcinoma and high-grade spindle cell sarcoma without apparent transition between the two. At the margin of the tumour, a single layer of benign cuboidal epithelium and outer fibrous bands were present, suggesting that the tumour had arisen from a nonparasitic simple cyst of the liver. Immunohistochemically, carcinoma cells were positive for cytokeratins, epithelial membrane antigen and CA 19-9 and negative for vimentin, while sarcomatous cells were positive for vimentin and negative for cytokeratins, epithelial membrane antigen and CA 19-9. Sarcomatous cells did not show any immunophenotypic features of smooth muscle cells, striated muscle cells, histiocytes, lipocytes, nerve cells, Schwann cells or endothelial cells. Ultrastructurally, no specific differentiation was seen in the sarcomatous cells.

Key words Carcinosarcoma · Liver
Nonparasitic simple cyst of liver

Introduction

Intrahepatic cholangiocarcinoma is a malignant neoplasm arising from intrahepatic biliary epithelium, and is usually an adenocarcinoma. Although most cholangiocarcinomas arise in normal livers, a minority occur in pathological livers as in Caroli's disease (Phinney et al. 1981), hepatolithiasis (Terada and Nakanuma 1992; Terada et al. 1992) and cirrhosis (Terada et al. in press). Nonparasitic simple cysts of the liver are developmental malformations, and cholangiocarcinoma may also arise in them. There are only 13 cases of cholangiocarcinoma arising in nonparasitic simple cysts of the liver in the English literature. They are usually adenocarcinomas or, less frequently, squamous cell carcinomas, adenosquamous carcinomas, or mucoepidermoid carcinomas (Azizah and Oaradubas 1980; Bloustein 1977; Bloustein and Silverberg 1976; Greenwood and Orr 1972; Gresham and Rue 1985; Hayashi et al. 1987; Imamura et al. 1984; Landais et al. 1984; Lynch et al. 1988; Pliskin et al. 1992; Theise et al. 1993; Tomioka et al. 1987; Willis 1943).

Sarcomatous transformation of carcinoma cells occurs in many malignant tumours, including hepatocellular carcinoma (Kakizoe et al. 1987), cholangiocarcinoma (Haratake and Horie 1991; Haratake et al. 1992; Nakajima et al. 1988a; Sasaki et al. 1991), combined hepatocellular-cholangiocellular carcinoma (Haratake and Horie 1991; Nakajima et al. 1988b) and hepatobiliary cystadenocarcinoma (Pamela et al. 1987). In cholangiocarcinoma with sarcomatous transformation, the sarcomatous element has been thought to have differentiated from carcinoma cells, because there is a transition between sarcomatous and carcinomatous components and also because the carcinomatous and sarcomatous elements express some common immunophenotypes (Haratake and Horie 1991; Haratake et al. 1992; Nakajima et al. 1988a; Sasaki et al. 1991). However, there is only one report of carcinosarcoma of the liver in the English literature (Rummeny et al. 1989), and carcinosarcoma arising from nonparasitic simple cysts of the liver has not been reported. We report a case of biliary carcinosarcoma arising in a hepatic nonparasitic simple cyst.

Case report

A 75-year-old woman was admitted to Tsuruga City Hospital on 9 September 1988 because of general malaise. She had suffered

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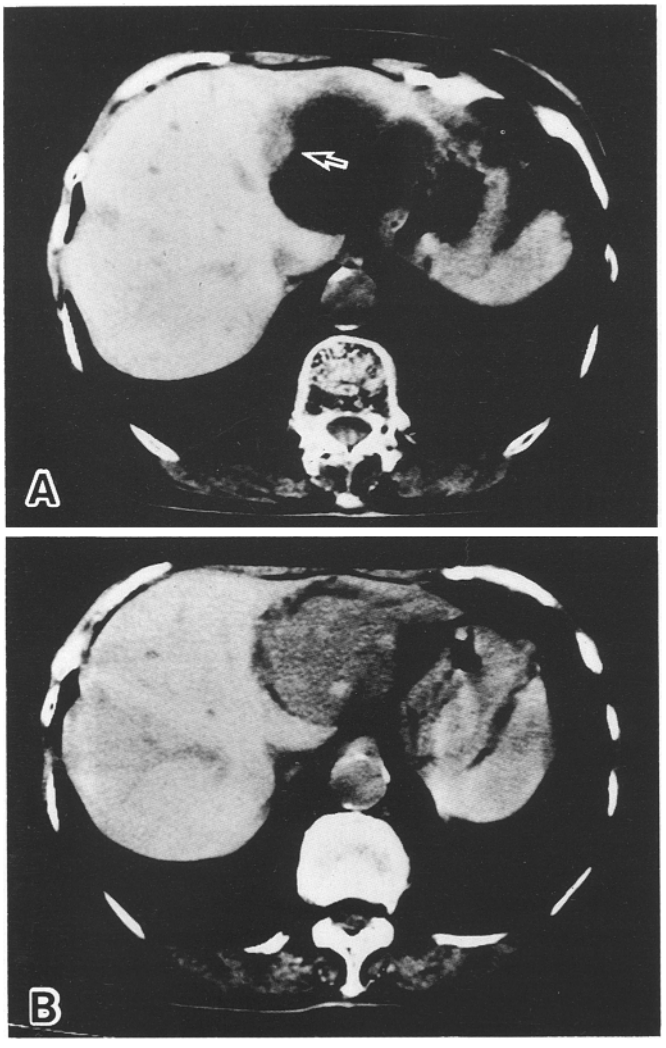

Fig. 1A, B Computed tomography of the liver. **A** A tumorous mass (*arrow*) is seen to protrude into the large hepatic cyst (20 February 1992). **B** The tumour mass completely occupies the hepatic cyst (13 October 1992)

from chronic persistent hepatitis since 1978. Laboratory data showed mild liver dysfunction and antibodies against hepatitis C virus. A liver biopsy revealed chronic persistent hepatitis. Computed tomography (CT) revealed a liver cyst in the left hepatic lobe. On 20 February 1992 she was found to have elevated serum CA 19-9 (212.4 U/ml; normal <37 U/ml). CT revealed a tumour mass protruding into the hepatic cyst (Fig. 1A). On 13 October 1992 CT disclosed that the liver cyst was engorged by the tumour tissue (Fig. 1B). She underwent surgical resection of the left hepatic lobe on 6 November 1992. Serum CA 19-9 returned to normal levels 2 months after the operation.

Pathological findings

Grossly, the resected hepatic left lobe contained a solid tumour ($5 \times 5 \times 6$ cm) with yellowish white colour, focal haemorrhage, and a soft fragile consistency (Fig. 2). It was well demarcated from the surrounding liver parenchyma by a thin fibrous capsule, although it invaded

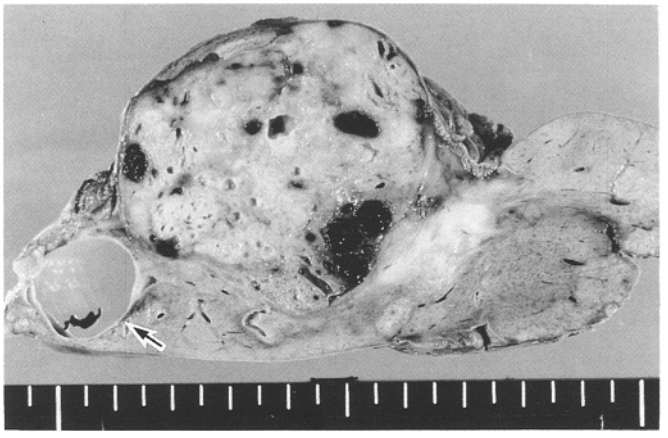

Fig. 2 Gross features of the resected left lobe of the liver. A solid tumour ($5 \times 5 \times 6$ cm) was present. The tumour is well demarcated from the surrounding liver parenchyma by a thin fibrous capsule. In some areas, the tumour is invading the surrounding liver parenchyma. A cyst measuring $1.3 \times 1.2 \times 1.2$ cm (*arrow*) is located in the vicinity of the tumour

the surrounding liver parenchyma in some places (Fig. 2). A cyst measuring $1.3 \times 1.2 \times 1.2$ cm was located in the vicinity of the tumour (Fig. 2).

Microscopically, the tumour consisted of a mixture of two components, a well-differentiated adenocarcinoma and a spindle cell sarcoma (Fig. 3A). There was no transition between the carcinomatous and sarcomatous areas (Fig. 3A). A few giant cells and mitoses, including abnormal mitoses, were scattered in the sarcomatous component. No characteristic arrangements such as a storiform pattern were recognized in the sarcomatous component and no differentiation toward other mesenchymal elements was seen (Fig. 3A). In some places at the margin of the tumour, a single layer of benign cuboidal cells lining fibrous walls was recognized, and a transition of benign epithelium to malignant was seen (Fig. 3B). Both the carcinomatous and sarcomatous components invaded the surrounding liver parenchyma. The cyst adjacent to the tumour was a nonparasitic simple cyst and the non-tumour liver showed features of chronic persistent hepatitis.

Immunohistochemically, cells of the carcinoma were positive for cytokeratins, epithelial membrane antigen (Fig. 4A) and CA 19-9 and negative for vimentin (Fig. 4B), while cells of the sarcoma were negative for cytokeratin, epithelial membrane antigen (Fig. 4A) and CA 19-9 and positive for vimentin (Fig. 4B). Cells of the sarcomatous component were negative for other antigens (Table 1).

Ultrastructurally, cells of the carcinomatous component showed many junctional complexes and microvilli. The sarcomatous cells were elongated or fusiform cells, containing intermediate filaments and well-developed rough endoplasmic reticulum. Junctional complexes, basal lamina, dense bodies and Z bands were absent from the sarcomatous cells. Lysosomes were not abundant, and there was no phagocytosis.

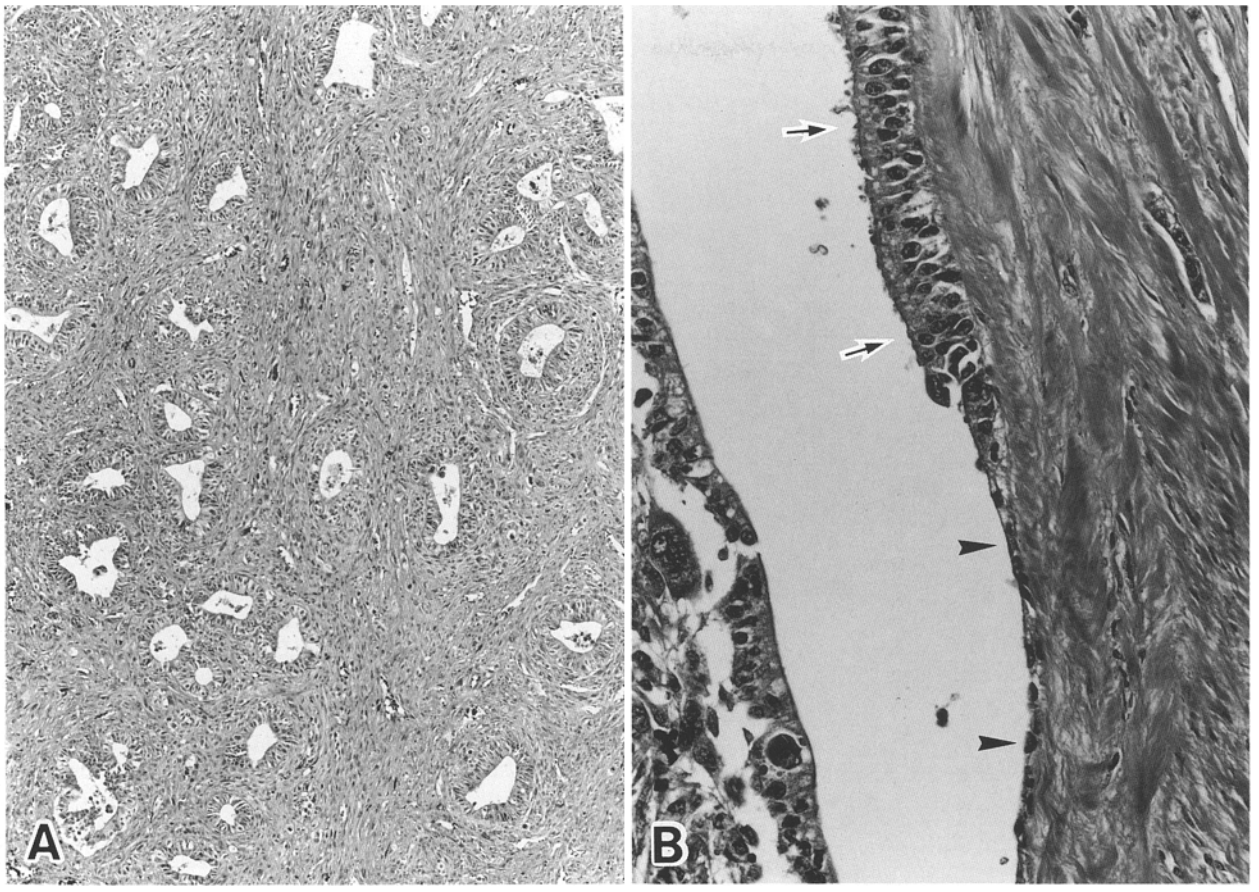

Fig. 3 **A** The tumour is composed of a well-differentiated tubular adenocarcinoma component and a spindle cell sarcomatous component. There is no transition between the two components. Haematoxylin and eosin, ×160. **B** At the margin of the tumour, benign cuboidal epithelial cells (*arrowheads*) coexist with malignant epithelial cells (*arrows*), suggesting that the cuboidal epithelium of the nonparasitic simple cyst has undergone malignant transformation. Haematoxylin and eosin, ×250

Table 1 Antibodies used for immunohistochemistry and the results of immunostainings (*M* monoclonal antibody, *P* polyclonal antibody)

Antibody	M/P	Source	Carcinoma component	Sarcoma component
Anti-cytokeratin AE1	M	ICM Biomedicals	+	−
Anti-cytokeratin CAM5.2	M	Becton Dickinson	+	−
Anti-cytokeratin KL1	M	Immunotech	+	−
Anti-keratin	P	Dakopatts	+	−
Anti-carcinoembryonic antigen	M	Dakopatts	−	−
Anti-carbohydrate antigen 19-9	M	CIS Biointernational	+	−
DU-PAN-2	M	Kyowa Medex	+	−
Anti-α fetoprotein	P	Dakopatts	−	−
Anti-epithelial membrane antigen	M	Dakopatts	+	−
Anti-vimentin	M	Dakopatts	−	+
Anti-desmin	M	Dakopatts	−	−
Anti-actin	M	Amersham	−	−
Anti-α smooth muscle actin	M	Dakopatts	−	−
Anti-myoglopin	P	Dakopatts	−	−
Anti-lysozyme	P	Dakopatts	−	−
Anti-α 1-antitrypsin	P	Dakopatts	−	−
Anti-α 1-antichymotrypsin	P	Dakopatts	−	−
Anti-S100 protein	P	Dakopatts	−	−
Anti-neuron specific enolase	P	Dakopatts	−	−
Anti-factor-VIII-related antigen	P	Dakopatts	−	−
Anti-tenascin	M	Chemicon	−	+[a]
Anti-p53	M	Dakopatts	−	−

[a] Positive in the extracellular matrix

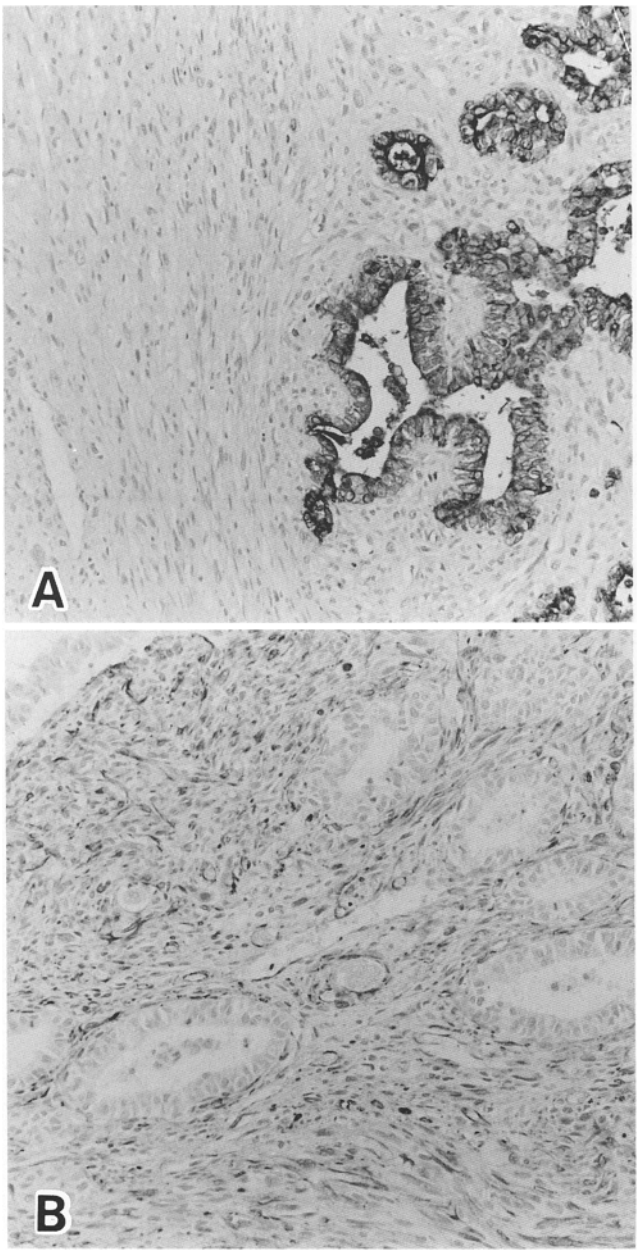

Fig. 4A, B Immunohistochemical findings of the tumour. **A** Cells of the carcinomatous component express epithelial membrane antigen, but cells of the sarcomatous component do not express it. Immunostain (ABC method) for epithelial membrane antigen, ×120. **B** Cells of the sarcomatous component express vimentin, but cells of the carcinomatous component do not express it. Immunostain (ABC method) for vimentin, ×120

Discussion

The sequential imaging findings of the present case suggest that the tumour arose in a hepatic cyst. The presence of benign cuboidal epithelium and outer fibrous bands in the margin of the tumour also suggests that it arose in a nonparasitic simple cyst of the liver. The presence of a transitional area of benign and malignant epithelium at the tumour margin suggests that epithelium of the nonparasitic simple cyst underwent malignant transformation.

Hepatobiliary cystadenoma is also known to undergo malignant transformation into hepatobiliary cystadenocarcinoma occasionally (Wheeler and Edmondson 1985). However, our tumour did not resemble cystadenocarcinoma grossly, and there was no papillary proliferation of the epithelial lining of the cyst walls. In addition, we did not find the mesenchymal stroma which is characteristic of hepatobiliary cystadenoma and cystadenocarcinoma (Wheeler and Edmondson 1985). It seems unlikely that our tumour arose from hepatobiliary cystadenoma.

The lesion is unique as a biliary carcinosarcoma. In cholangiocarcinoma with sarcomatous transformation, it is reported that both carcinomatous and sarcomatous components express common immunophenotypes (see Introduction). For example, Sasaki et al. (1991) and Haratake and Horie (1991) reported that cytokeratins and epithelial membrane antigen were expressed in both carcinomatous and sarcomatous areas in cholangiocarcinomas with sarcomatous features. Similar observations have recently been reported in seven cases of cholangiocarcinoma (Nakajima et al. 1993). In contrast, in our tumour the cells of the carcinomatous component expressed cytokeratins and epithelial membrane antigen and did not express vimentin, while cells of the sarcomatous component expressed vimentin and did not express cytokeratins and epithelial membrane antigen. In addition, there was no transition between carcinomatous and sarcomatous components. Therefore, this lesion is not a cholangiocarcinoma with sarcomatous transformation but a carcinosarcoma of the liver. Although the histogenesis is unclear, it seems likely that both the epithelial cells of the nonparasitic simple cyst and the stroma underwent malignant transformation, giving rise to the carcinosarcoma.

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