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SARCOMATOID CHANGE IN INTRAHEPATIC CHOLANGIOCARCINOMA

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Abstract: Sarcomatoid transformation is a rare but well documented change that may occur in intrahepatic cholangiocarcinomas. We report a tumor of this type to illustrate the difficulties in properly diagnosing cholangiocarcinoma when only the sarcomatous component is sampled by transcutaneous needle biopsy. The proper diagnosis of the tumor was suggested by finding the expression of cytokeratin 7 in the sarcomatous spindle cells. The surgically resected tumor comprised a spindle cell sarcomatous and an adenocarcinomatous component accounting for approximately 30% and 70% of the total tumor mass respectively.

Keywords*:* sarcomatoid, intrahepatic, cholangiocarcinoma, cytokeratin.

INTRODUCTION

Intrahepatic cholangiocarcinomas (ICC) are rare neoplasms accounting for approximately 5–15% of all primary malignant liver tumors (1). The incidence of ICC varies from one geographic location to another in the range from 0.8 to 84.6 per 100.000 males (2). The highest incidence of ICC has been recorded in China, Japan and countries of South East Asia, where this biliary tumor seems to be in part causally related to endemic infection with liver flukes, *Opisthorchis viverrini* and *Clonorchis sinensis* (2). The adult populations of North America and Western Europe are considered to be at low risk for ICC than those in East Asia (3).

Most ICC present microscopically as adenocarcinomas, which may have abundant connective tissue stoma and appear scirrhous like other pancreatico-biliary carcinomas (4). Several less common histological variants have been recognized, as listed in the textbook of Rosai (4) and recognized by the experts of the World Health Organization (5). One of these variants is the so-called ICC with sarcomatous transformation, which occurs in less than 5% of all tumors (6). It is especially rare in North America and Western Europe, where all ICC are generally less common than in the far East. We could find only one case reported in a Caucasian patient (6).

Sarcomatous transformation of ICC may involve large portions of the tumor or involve the entire tumor, which may be thus misinterpreted as primary liver sarcoma (7). This diagnostic fallacy should be kept in mind especially in needle biopsy specimens, which may contain only the sarcomatous portion of the tumor. Immunohistochemistry may provide a clue to proper diagnosis, since the sarcomatous ICC tends to express keratin, as shown in the present case.

CASE REPORT

A 71-year-old woman was admitted with a main complaint of weight loss of approximately 12 kg over a period of 6 months. A computerized tomography (CT) scan revealed a relatively well circumscribed mass in the right liver lobe (Figure 1a). It measured 8.7 cm in largest diameter and a subsequent proton emission tomography (PET) scan showed that the lesion had a SUV of 4.21. There was no other evidence of neoplasia. The laboratory findings included normal serum alpha fetoprotein, slight elevation of serum carcinoembryonic antigen of 5.7 I. U (upper limit for nonsmokers in our laboratory is 5.0 I.U.), elevation alkaline phosphatase of 848 I.U. (normal up to 70 I.U.), and mild elevation of asparatate aminotransferase of 51 I.U. (normal less than 35 I.U.), alanine aminotransferase of 72 I.U. (normal less than 35 I.U.). A needle biopsy of the tumor was performed. The entire cylinder measuring 4

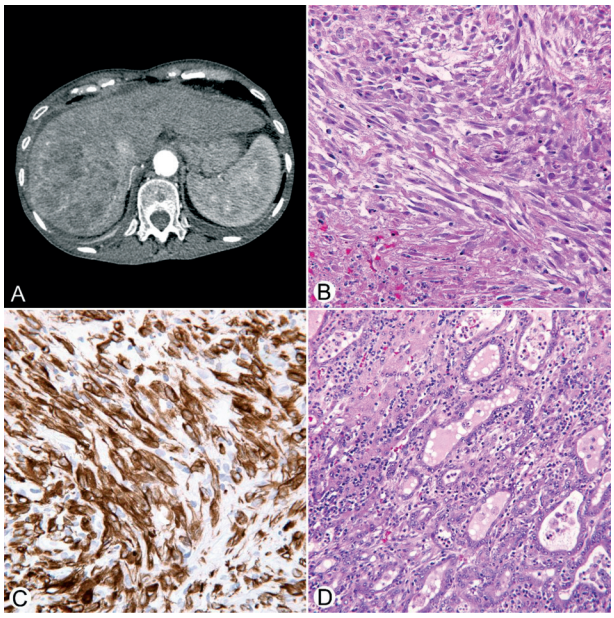

Figure 1

A. CT scan shows a large inhomogeneous mass in the right lobe of the liver, considered to be surgically resectable.
B. Needle biopsy shows that the tumor is composed of atypical spindle cells.
C. Immunohistochemistry with the antibody to keratin CK7 shows strong reactivity with essentially all spindle tumor cells.
D. Adenocarcinoma accounted for 70% of the surgically resected tumor. All microscopic section were photographed at x220 magnification, and stained with hematoxylin and eosin except for part C, which was reacted immunohistochemically with monoclonal mouse antibody to cytokeratin CK7, and secondary horseraddish peroxidase labeled antibody to mouse IgG.

cm in length was composed of anaplastic spindle cells and the tumor was considered to be a sarcoma (Figure 1b). The differential diagnosis included spindle cell (sarcomatoid hepatocellular carcinoma), sarcomatoid cholangiocarcinoma, and spindle cell lymphoma. Immunohistochemical stains were performed and the results excluded the possibility of leiomyosarcoma, malignant peripheral nerve sheath tumor, gastrointestinal stromal tumor, hepatocellular carcinoma, and angiosarcoma. The only two immunohistochemical stains that were positive included those performed with antibodies to cytokeratin 7 and polyvalent cytokeratin AE1/AE3 (Figure 1c).

The patient underwent right hepatectomy and the resection margins were negative for malignancy. Several sections were taken for histological examination from different parts of the tumor. Some parts of the tumor appeared sarcomatous and were composed of pleomorphic spindle cells with numerous mitoses, whereas other parts were composed of adenocarcinoma cells (Figure 1d). In some parts of the tumor these two components were intermixed one with another. Adenocarcinoma accounted for approximately 70% of the tumor mass, whereas the sarcomatous part accounted for 30% of it.

The patient recovered from surgery and is free of neoplasia two months after diagnosis. Unfortunately the patient later died of noncancerous related cause but the family gave consent for publication.

DISCUSSION AND CONCLUSION

Spindle cell malignant tumors of the liver may pose diagnostic problems, as illustrated in this case report. The differential diagnosis includes primary hepatic or metastatic sarcomas, sarcomatoid hepatocellular carcinoma, or sarcomatoid cholangiocarcinoma. In our case, the positive reaction with the antibody to CK7, a cytokeratin normally expressed in bile ductular cells, prompted us to consider strongly the possibility of ICC with sarcomatoid transformation. The final resection of the tumor proved that we were right suggesting that the needle biopsy specimen must have been taken from the sarcomatous part of the tumor.

Sarcomatous transformation of cholangiocarcinoma is found in less than 5% of all ICC (6). Only a few of documented tumors of this type have been reported, all of which, except for one (8) were from East Asian countries (7, 8, 9, 10, 11, 12). The cholangiocarcinomatous nature of the tumor can be finally recognized histologically by finding typical adenocarcinoma elements, although in at least two cases described by Tsou et al. (7) the entire tumor was composed exclusively of spindle cells. In all cases reported so far, including the two cases composed entirely of spindle cells, the tumor cells expressed CK7, which proved to be diagnostically the most important finding.

With this case presentation we would like to reemphasizes the value of the immunohistochemical stain for cytokeratin CK7 in spindle cell lesions of the liver. Keratins are generally not expressed in sarcomas, but they are found in epithelial liver tumors and hepatic metastases from other organs. The differential diagnosis of primary hepatic spindle cell tumor must include the spindle cell variant of hepatocellular carcinoma, which may react with the antibody to wide spectrum keratins, but it is usually unreactive with antibodies to CK7. Since CK7 is expressed in bile ductular cells and in adenocarcinoma originating from these cells, it is not surprising that even the cells that have undergone sarcomatous transformation have retained CK7 from their ancestral cells.

Abbreviations:

ICC = Intrahepatic CholangioCarcinoma
CK7 = Cytokeratin 7

Sažetak

SARKOMATOIDNA TRANFORMACIJA KOD INTRAHEPATIČNIH HOLANGIOKARCINOMA

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Sarkomatoidna transformacija je retka, ali dobro dokumentovana promena koja se može javiti kod intrahepatičnih holangiokarcinoma. Cilj ovog rada je da prikaže ovaj tip tumora kako bi ilustrovao teškoće u tačnom dijagnostikovanju holangiokarcinoma kada je jedino sarkomatoidna komponenta tumora dobijena transkutanom biopsijom. Za tačnu dijagnozu se predlaže ispitivanje ekspresije Citokreatina 7 u sarkomatoidnim vretenastim ćelijama. Nakon hirurške resekcije potvrđeno je da je tumor građen od vretenastih ćelija sarkomatoidne i adenokarcinomatozne komponente tumora koje su činile 30% i 70% od ukupne mase tumora.

Ključne reči: sarkomatoid, intrahepatični, holangiokarcinoma, citokeratin.

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