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Case Report

An extremely rare case of intrahepatic sarcomatoid cholangiocarcinoma ☆,☆☆

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ABSTRACT

One uncommon histological subtype of intrahepatic cholangiocarcinoma is sarcomatoid intrahepatic cholangiocarcinoma. Histopathological and immunohistochemical tests are used to diagnose sarcomatoid intrahepatic cholangiocarcinoma, which frequently has a worse prognosis than regular intrahepatic cholangiocarcinoma. The example of a 65-year-old female with sarcomatoid intrahepatic cholangiocarcinoma, who presented with sporadic right upper abdomen discomfort, is discussed in this paper. This case study and literature analysis aims to improve physicians' comprehension of sarcomatoid intrahepatic cholangiocarcinoma and lower the frequency of missed clinical diagnoses.

Introduction

All tumors exhibiting morphological and immunological evidence of both malignant epithelial and mesenchymal differentiation are classified by the WHO as epithelial tumors with sarcomatoid alterations [1]. The upper digestive tract, lung, pancreas, skin, breast, thyroid, uterus, urinary tract, gallbladder, and liver are all known to have been affected by these uncommon neoplasms [2,3]. Sarcomatoid hepatocellular carcinomas comprise the majority of sarcomatoid carcinomas in the liver. Recent findings have shown sarcomatoid alterations in cholangiocarcinomas. The WHO classification of malignancies refers to this form of the tumor as "sarcomatoid intrahepatic cholangiocarcinoma" (s–iCCA). At present, cholangiocarcinoma sarcoma has only a few rare isolated instances worldwide. This article presents the case of a 65-year-old female patient whose condition was identified through a liver biopsy

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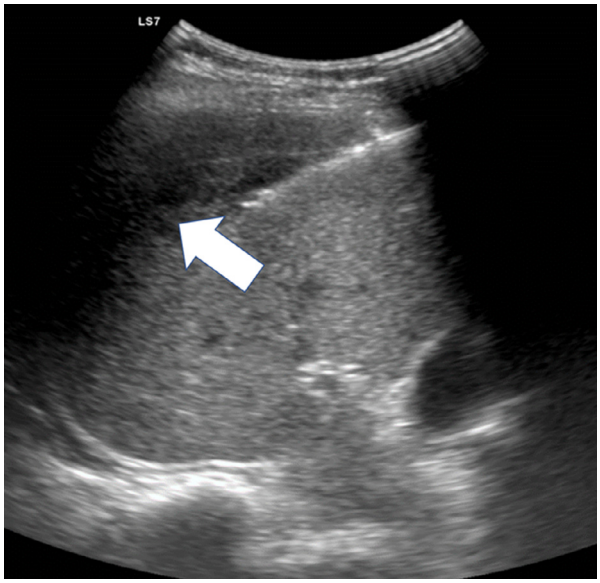

Fig. 1 – Abdominal ultrasonography revealed a 4 x 9 x 8 cm-sized heterogeneous and hypoechoic mass in the right liver lobe.

and immunohistochemistry staining. The purpose of this report is to increase understanding, diagnosis, and care for patients diagnosed with S-iCCA.

Case description

A 65-year-old Vietnamese female was found to have a liver tumor at another hospital. She was referred and admitted to our hospital due to complaints of abdominal pain in the right lower quadrant region. There was no previous history of liver or biliary disease. On physical examination, there were no abnormal findings or signs of chronic liver disease.

The laboratory data were as follows: hemoglobin 13 g/dL (normal, 13-17 g/dL), international normalized ratio 1.07, albumin 43.9 g/L (normal, 35-52 g/L), total bilirubin 8.5 umol/L (normal, <15 umol/L), glutamic oxaloacetate transaminase 85 U/L (normal, <34 U/I), glutamic pyruvic transaminase 83 U/L (normal, <49 U/L). Serum alpha-fetoprotein (AFP), alpha-fetoprotein type L3 (AFP-L3), prothrombin induced by vitamin K absence-II (PIVKA-II), carbohydrate antigen (CA) 19.9, and carcinoembryonic antigen were within normal limits. Antibodies to both the core and surface antigens of the hepatitis B virus were negative; the hepatitis C antibody was negative. Abdominal ultrasound revealed a 4 × 9 × 8 cm-sized heterogeneous and hypoechoic mass of the right liver lobe (Fig. 1). A CT scan showed that the low-density liver mass located in segment VII gradually enhanced in the arterial, venous, and delayed phases (Fig. 2). An abdominal MRI demonstrated that the mass was hyperintense on the T2-weighted and fat-suppressed T2-weighted imaging. The mass was slightly hyperintense in the diffusion-weighted imaging

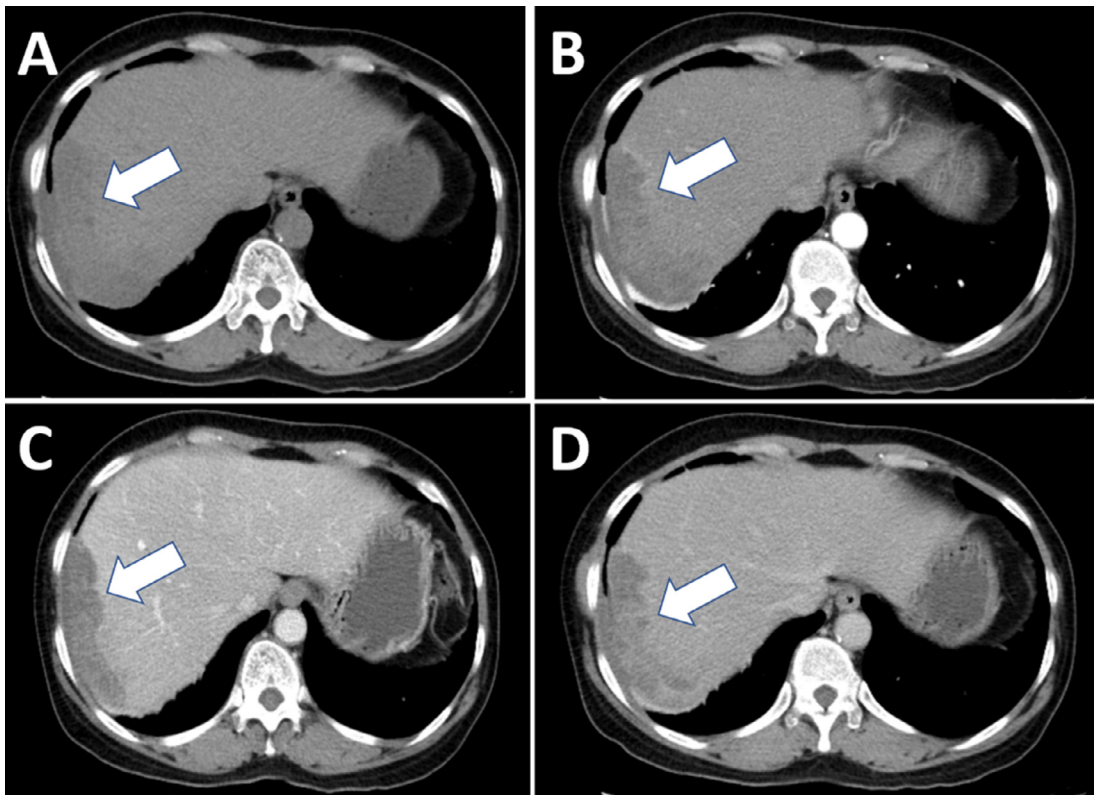

Fig. 2 – A CT scan revealed that segment VII of the low-density liver mass gradually improved the density in the arterial, venous, and delayed phases.

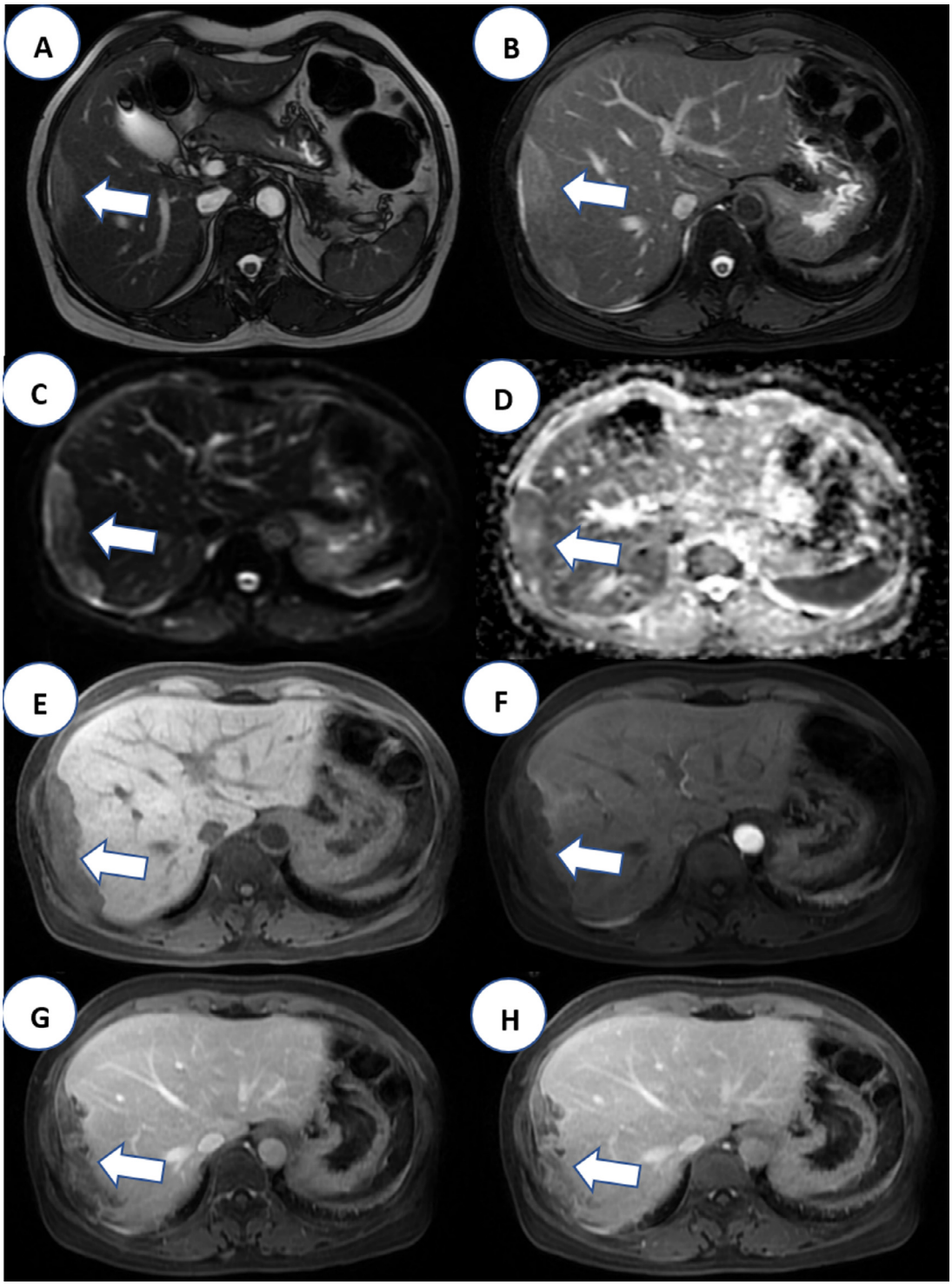

Fig. 3 – In an abdominal MRI, the mass was shown to be hyperintense on T2-weighted imaging (A) and fat-suppressed T2-weighted imaging (B). In diffusion-weighted imaging (C), the mass seemed slightly hyperintense, while in an apparent diffusion coefficient (ADC) map, it appeared slightly hypointense (D). Dynamic T1-weighted imaging using a contrast agent showed dramatic and gradual enhancement of the mass (E, F).

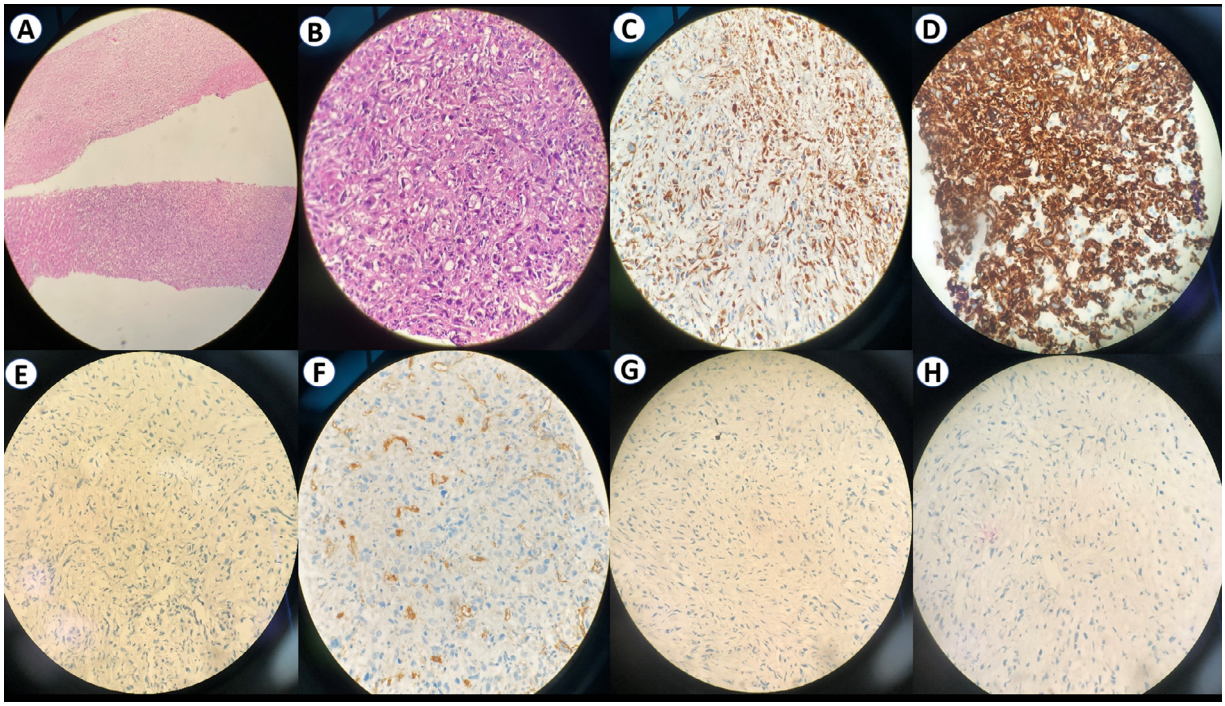

Fig. 4 – Histologic findings of the liver biopsy in the described patient with sarcomatoid intrahepatic cholangiocarcinoma. Images A and B illustrate hematoxylin and eosin staining, ×10 and ×40, respectively. The tumor consists of epithelioid cells with pleomorphic, hyperchromatic nuclei and prominent nucleoli (carcinomatous component: black arrows) and spindle cells with hyperchromatic, enlarged nuclei (sarcomatoid component: red arrows) (C). Immunohistochemistry for positive CK (D), positive CK19 (E), positive vimentin (F), negative HepPar1 (G), negative CD 31 (H), negative arginase (I), and negative calretinin (J).

and slightly hypointense in the apparent diffusion coefficient (ADC) map (Fig. 3). The ADC map was 1.280×10^{-3} mm^2/s. The mass was vividly and progressively enhanced on the dynamic T1-weighted imaging when using a contrast agent.

A percutaneous needle biopsy of the tumor was performed. Histological examination showed a malignant tumor with a carcinomatous and sarcomatoid component without cirrhosis. The latter was composed of pleomorphic spindle cells with prominent nucleoli. The tumor cells reacted positively with CK, CK19, and vimentin but negatively with HepPar1. It was then classified as sarcomatoid cholangiocarcinoma based on histological and immunohistochemical findings (Fig. 4).

The patient was offered surgery, but she did not accept it. Due to the COVID-19 pandemic, we lost contact with the patient after this.

Discussion

Rare cancers, known as epithelial tumors with sarcoma phenotype, have been observed in a variety of locations, including the liver. Both hepatocellular cancer and cholangiocarcinoma have the sarcoma phenotype. Hepatocellular carcinoma (which accounts for 75%-85% of cases) and intrahepatic cholangiocarcinoma (10%-15%) are 2 common types of primary liver cancer, according to GLOBOCAN 2020 [1]. Therefore, it is uncommon to have intrahepatic cholangiocarcinoma with a sarcoma phenotype. Although its incidence is unclear, 4.5% of cholangiocarcinoma instances are said to be caused by it [2].

In terms of the etiology, researchers have hypothesized that anticancer therapies may cause the emergence of sarcomatoid alterations or hasten the conversion of cells generated from the epithelium into sarcoma cells [3]. However, there are no reports on the interaction between S-iCCA and anticancer treatment. Although a few hypotheses have been advanced, the pathophysiology of S-iCCA is still unclear. First, it was proposed that it was caused by primary epithelial cancer cells that had undergone sarcomatoid transdifferentiation or dedifferentiation, also known as metaplastic transformation or epithelial-mesenchymal transition. Additionally, depending on how each tumor type develops, pluripotent stem cells may be biphasically differentiated into sarcoma or carcinoma in distinct ways, resulting in a mixture of both cell types. Last, carcinoma cells may develop into cancer cells with multipotent differentiation potential that later go through sarcomatoid redifferentiation [4].

The most prevalent clinical symptom of S-iCCA, which has only been documented in case reports or series in the English literature, is abdominal discomfort. For the diagnosis of S-iCCA, serum CA19-9 and carcinoembryonic antigen may not be sensitive enough. Notably, S-iCCA shares common traits with regular iCCA, such as a low-echogenic liver mass on ultrasound that exhibits hypo-attenuation and peripheral region enhancement after a contrast injection on a computed

tomography scan [5]. Hypoechoic features were observed in 3 (27.3%) patients, hyperechoic features in 3 (27.3%) patients, and mixed echoic features in 5 (45.5%) patients. An MRI was performed in three patients with heterogeneous hyperintensity (n = 3) based on the T2-weighted image, gradual centripetal (n = 2) or rim (n = 1) enhancement on the dynamic enhancement scan, and diffusion restriction (n = 3) based on the diffusion-weighted image [4]. In a few previously reported cases, the tumor showed hypointensity relative to liver parenchyma on T1-weighted images and hyperintensity relative to liver parenchyma on T2-weighted images. In some reports, the mixed signal intensity of the mass was present on both T1- and T2-weighted images [6].

As a result, it could be challenging to differentiate between S-iCCA and regular iCCA using radiological imaging. By conducting a biopsy, S-iCCA can be diagnosed with certainty. Histopathological and immunohistochemical examinations are used to determine the tumor's diagnosis [7,8]. Histopathological analyses of S-iCCA show the coexistence of adenocarcinoma cells with differentiated and sarcomatoid cells, which are spindle-shaped and arranged in bundles or weaves. Immunohistochemistry reveals that S-iCCA tumors are positive for both epithelial cholangiogenic tumor markers (CK7, CK8) and the mesenchymal tumor marker vimentin, negative for HepPar-1. As a marker of hepatocytes, HepPar-1 provides useful diagnostic information for distinguishing HCC from cholangiocarcinoma and metastatic carcinoma in the liver. In addition, our patient was positive for CK, CK-19, and vimentin but negative for HepPar-1, which is consistent with our diagnosis.

Watanabe et al. [9] demonstrated that the prognoses for patients with sarcomatoid ICC, with or without surgery, were considerably worse than those for the matching conventional ICC, notwithstanding analytical limitations in the specifics of tumor expansion caused by a literature study. Further demonstrating the dismal prognosis of sarcomatoid ICC, the MST of sarcomatoid ICC after surgery (11 months) was equivalent to that of conventional ICC without surgery (8 months). However, compared to individuals with conventional ICC, who underwent surgery but did not live more than a year, the prognosis for patients with sarcomatoid ICC was more encouraging.

This information would help to demonstrate the relevance of choosing surgery as the initial course of treatment. Radical liver resection is now the sole option for treating S-iCCA patients because there are no reliable standards for predicting their prognosis and survival. This example highlights the need for tighter follow-up in patients with these malignancies and the necessity of early discovery, drastic surgery, and thorough follow-up to help improve the prognosis of patients with S-iCCA. It's also necessary to investigate more extensive therapy choices.

Conclusion

S-iCCA is an uncommon type of cancer. Due to the lack of disease specificity in clinicomorphological findings and serologic and radiologic investigations, diagnosis can only be made through pathology and immunohistochemistry studies. S-iCCA has a poor prognosis due to its high degree of invasiveness, making careful and thorough follow-up essential.

Author's contributions

Dau QL and Tran NA contributed equally to this article as first authorship. Dau QL and Tran NA: Case file retrieval and case summary preparation. Dau QL and Nguyen MD: preparation of manuscript and editing. All authors read and approved the final manuscript.

Availability of data and materials

Data and materials used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

Our institution does not require ethical approval for reporting individual cases or case series.

Consent for publication

Not applicable.

Patient consent

Informed consent for patient information to be published in this article was obtained.

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