A Surgical Case of Inflammatory Myofibroblastic Tumor of the Liver: Potentially Characteristic Gross Features

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ABSTRACT: We herein reported a very rare surgical case of inflammatory myofibroblastic tumor (IMT) of the liver, showing potentially unique and specific gross findings on its cut surface: our IMT demonstrated a relatively well-demarcated and partly infiltrative and likely extrahepatic (ie serosal) but not intrahepatic mass, appearing firm and hemorrhagic, and yellow-whitish in color. The patient, who was a woman in her early 70s with 2-year follow-up for lung cryptococcosis and traffic accident, incidentally presented with unenhanced and low-density, heterogeneous mass on abdominal dynamic CT in the peripheral right lobe of the liver. We could conclusively diagnose the current lesion as the hepatic IMT after thorough analyses including a wide panel of immunohistochemical antibodies. Despite that, all clinicians and pathologists should be aware that the potentially characteristic, extrahepatic gross feature of IMT of the liver might also be one of the powerful supplementary tools for reaching its correct diagnosis. One of our aims in the presented case report is to emphasize that the hepatic IMT should be considered clinicopathologically in the differential diagnosis of mass lesions on the liver.

KEYWORDS: Liver, histopathology, inflammatory myofibroblastic tumor, gross findings, extrahepatic

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Introduction

In 1953, Pack and Baker first reported the features of hepatic inflammatory pseudotumor, one of the synonyms for inflammatory myofibroblastic tumor (IMT), defined as a benign, non-neoplastic, and non-metastasizing mass.[1–3] However, IMTs are now generally classified as a true neoplasm of intermediate biological potential, due to a locally aggressive behavior, such as an occasional tendency of recurrence, according to the latest World Health Organization (WHO) classification.[1,4] Indeed, the histopathological findings of IMT typically show a proliferation of myofibroblasts and/or fibroblasts, admixed with collagenized areas and infiltration of chronic inflammatory cells, including polyclonal plasma cells and macrophages.[1–4] More than 300 interesting papers focusing especially on the histopathological and immunohistochemical features of hepatic IMT cases were published;[2] by contrast, within our thorough investigation, there have been no detailed description regarding the gross findings reported in the English literature. As these tumors actually would not show any specific clinical and macroscopic features, the gross appearance might not help to consider those differential diagnoses. Despite that, it has been merely stated that the gross morphology of hepatic IMTs is mostly solitary, firm, and tan to yellow-whitish in color and usually intrahepatic;[1–4] however, we partly disagree with that description, especially "intrahepatic." We herein briefly report a very rare surgical case of extrahepatic, not intrahepatic, IMT, revealing potentially characteristic and specific gross features on its cut surface. One of our aims in the presented case report is to emphasize that the hepatic IMT should be considered clinicopathologically in the differential diagnosis of mass lesions on the liver.

Case Presentation

The patient, who was a woman in her early 70s with an unremarkable previous medical history, except for 2-year follow-up against lung cryptococcosis and traffic accident, incidentally presented with unenhanced and low-density, heterogeneous and increasing mass on abdominal dynamic computed tomography (CT) in the peripheral right lobe of the liver (Figure 1A). Besides, a right rib fracture due to the previous car accident was noted, adjacent to the hepatic mass. Ascites was not recognized. CT scans of the head, chest, and abdomen disclosed no definite evidence of metastases in the lymph nodes or other organs. The image in coregistered 2-deoxy-2-[^{18}F]fluoro-D-glucose (^{18}F-FDG PET)/CT showed a large and overtly hypermetabolic area in the peripheral right lobe of the liver (maximal standardized uptake value [SUV]: 8.17), which corresponded to a unenhanced and low-density, heterogeneous and increasing mass on abdominal CT (Figure 1C). The laboratory data, including the blood cell count, chemistry and tumor marker

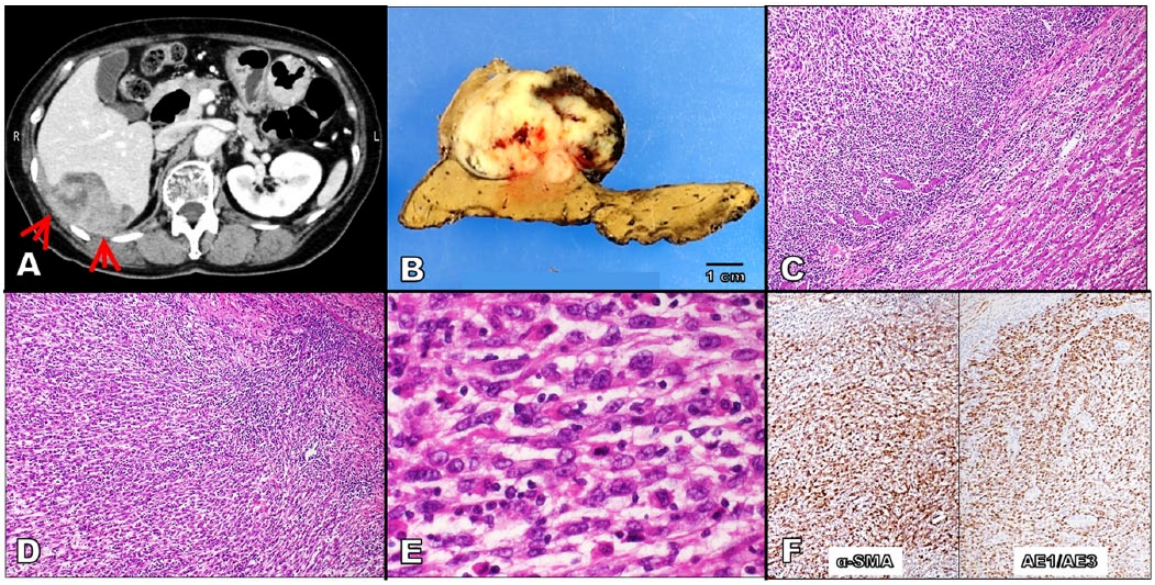

Figure 1. The imaging, gross, microscopic, and immunohistochemical examinations of the hepatic IMT. (A) Abdominal dynamic CT shows an unenhanced and low-density, heterogeneous and increasing mass (arrows) in the peripheral right lobe of the liver. (B) The cut surface of the hepatic IMT case characteristically demonstrates a relatively well-demarcated and partly infiltrative and likely extrahepatic (ie serosal) but not intrahepatic mass, measuring 51 × 32 mm in diameter, which appears firm and hemorrhagic and yellow-whitish in color. The background of this liver reveals no remarkable change (bar = 1 cm). (C) A microscopic examination of the hepatic IMT case (H&E staining) also shows an unencapsulated, partly ill-defined and expansive or infiltrative mass, potentially growing from the extrahepatic, serosal side. (D) On a low-power view (H&E staining), this mass reveals a solid proliferation of myofibroblast- or fibroblast-like spindled to oval cells, arranged in fascicles in a small amount of collagenous stroma, admixed with many inflammatory cells including lymphocytes, plasma cells, histiocytes, neutrophils, and eosinophils. (E) On a high-power view, these tumor cells are mildly atypical, having enlarged hyperchromatic nuclei, prominent nucleoli, and rare mitotic figures. (F) Immunohistochemistry demonstrates that those mildly atypical tumor cells are specifically positive for α-SMA (left) and cytokeratins including AE1/AE3 (right).

levels, were within the normal limits, with the exception of mildly elevated C-reactive protein (CRP; 1.64 mg/dL). Neither infection of hepatitis B virus (HBV) nor hepatitis C virus (HCV) was noted. Based on the clinical findings, the initial diagnosis by the clinicians was most likely hepatocellular carcinoma, and it was not completely excluded out. Therefore, right partial hepatectomy was performed. On gross examination, the cut surface of right hepatic mass (Figure 1B) demonstrated a relatively well-demarcated and partly infiltrative and likely extrahepatic (ie serosal) but not intrahepatic mass, measuring 51 × 32 mm in diameter, which appeared firm and hemorrhagic and yellow-whitish in color. The background of this liver revealed no remarkable change (Figure 1B). A microscopic examination of the tumor showed an unencapsulated, partly ill-defined and expansive or infiltrative mass (Figure 1C), potentially growing from the extrahepatic, serosal side. On a low-power view, this cancerous mass revealed a solid proliferation of myofibroblast- or fibroblast-like spindled to oval cells, arranged in fascicles in a small amount of collagenous stroma, admixed with many inflammatory cells including lymphocytes, plasma cells, histiocytes, neutrophils, and eosinophils (Figure 1D). On a high-power view, these tumor cells were mildly atypical, having enlarged hyperchromatic nuclei, prominent nucleoli, and rare mitotic figures (Figure 1E). In immunohistochemistry, the above-mentioned atypical tumor cells were specifically positive for α-SMA (Dako Cytomation Co., Glostrup, Denmark; diluted 1:500; Figure 1F), cytokeratins including AE1/AE3 (Dako; diluted 1:1; Figure 1F), CK7 (Dako; diluted 1:150), and CK18 (Dako; diluted 1:100), whereas negative for hepatocyte (Dako; diluted 1:50), CK19 (Dako; diluted 1:100), c-kit (Dako; diluted 1:300), CD56 (Leica Biosystems, Tokyo, Japan; diluted 1:50), desmin (Dako; diluted 1:1), CA125 (Dako; diluted 1:100), calretinin (Nichirei Biosciences Inc., Tokyo, Japan; diluted 1:50), CD68 (KP-1; Dako; diluted 1:200), IgG4 (The Binding Site, Birmingham, UK; diluted 1:1000), CD23 (Dako; diluted 1:10), CD35 (Dako; diluted 1:25), MDM2 (Invitrogen, Carlsbad, CA, USA; diluted 1:200), CDK4 (Santa Cruz Biotechnology, Dallas, TX, USA; diluted 1:50), and ALK (Dako; diluted 1:25). All of the immunohistochemical stainings were conducted using the Dako Envision kit (Dako Cytomation Co., Glostrup, Denmark) in accordance with the manufacturer's instructions. Based on all of these features, the final diagnosis was primary hepatic IMT. To date, this patient has been followed for 7 months since surgery, and she remains well without any sign of recurrence.

Discussion

It is very likely that the present case report of a surgical hepatic IMT patient is clinicopathologically remarkable for 2 reasons at least. First, the possible etiologies in our case might include not only right rib fracture due to the previous car traffic accident but also lung cryptococcosis. In fact, it has been proposed

that a large number of hepatic IMTs could be closely related to various infectious organisms, ranging from certain bacteria to virus, and inflammatory processes, such as trauma, radiotherapy, and malignancies.[2,3,5] However, as the true pathogenesis for IMT of the liver remains to be elucidated, our above arguments cannot be proven.

Second, very intriguingly, in case of the present gross findings for relatively well-demarcated but infiltrative and unencapsulated mass, very uniquely looking extrahepatic (ie serosal) but not intrahepatic and appearing firm and hemorrhagic and yellow-whitish in color, we pathologists should consider the very rare possibility of hepatic IMT. Despite that, to reach to the correct diagnosis, a wide panel of immunohistochemical analyses should be critically performed, as shown here. In our opinion, it is possible that the macroscopic features of extrahepatic, serosal tumor might be very specific for IMTs of the liver. Indeed, hepatic IMTs occur predominantly in the peripheral right lobe, as in the current case, and sometimes in the peripheral Spiegel lobe and extrahepatic hilar lesion,[2,3] which can support our suggestion. Nevertheless, the hepatic IMT should be considered clinicopathologically in the differential diagnosis of mass lesions on the liver.

The critical differential diagnoses in the present case included sarcomatoid carcinoma, myoepithelial carcinoma, follicular dendritic cell sarcoma, and dedifferentiated liposarcoma, despite the fact that it should be relatively easy to rule out these possibilities through various clinicopathologic examinations (ie anatomical locations and/or histological cellular atypia) or immunohistochemistry. Nevertheless, as hepatic IMTs are known to potentially show post-operative recurrence or metastasis with various aggressive/infiltrative behaviors,[1–4] it should be raised to alert the surgeons to the careful follow-up and additional treatment, at the very least. This short case report, taken together with the potentially specific findings of cut surface for the hepatic IMT, might promote interest within the scientific community.

Conclusions

In conclusion, we herein reported a very rare surgical case of hepatic IMT, showing potentially characteristic and specific gross findings on their cut surface: it showed a relatively well-demarcated and partly infiltrative and most likely extrahepatic (i.e. serosal) but not intrahepatic mass. We were finally able to accurately diagnose the current lesions after thorough analyses including an appropriate and wide panel of immunohistochemical antibodies. Despite that, all pathologists should be aware that the potentially characteristic gross features of hepatic IMT might also be one of the powerful supplementary tools for reaching its correct, conclusive diagnosis. Furthermore, the hepatic IMT should be considered clinicopathologically in the differential diagnosis of mass lesions on the liver.

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Author Contributions

SY and JW participated in conception of the idea and writing of the manuscript. SY, JW, YS, XG, NK, KK, MI, and HI performed the clinical investigation and pathological/immunohistochemical interpretation of this hepatic IMT case. KK, MI, and HI performed the surgery. All authors have read and approved the final manuscript.

Availability of Data and Materials

The dataset supporting the findings and conclusions of this case report is included within the article.

Consent for Publication

Written informed consent was obtained from the patient and her family on admission for the publication of this case report and any accompanying images.

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