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Clinical report

A benign liver tumor mimics hepatic metastasis from colon cancer

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Background: Liver is the most common distant metastasized organ in advanced colon cancer. Surgical resection of metastatic lesions would offer the best chance of a long-term survival. An accurate diagnosis and evaluation of extent of disease is crucial in the management of liver metastasis.

Objective: Report a benign hepatic condition mimicking liver metastasis in a colon cancer patient.

Case presentation: A 53-year-old male with an early stage sigmoid colon cancer was treated with sigmoidectomy followed by adjuvant chemotherapy consisting of 5-FU, leucovorin, and oxaliplatin for six months. Annual computerized tomography of abdomen at two years after the surgery revealed three hypervascular nodules in the liver. Investigations including MRI of the liver and whole body FDG-F18 PET/CT demonstrated evidence consistent with non-metastatic liver nodules. Liver biopsy of one of the lesions led to the diagnosis of "focal nodular hyperplasia".

Conclusion: The possible etiology, diagnosis, and further management of this benign liver tumor, the focal nodular hyperplasia became clear.

Keywords: Colonic carcinoma, focal nodular hyperplasia, liver metastasis, oxaliplatin

Hepatic metastasis frequently occurs in patients with advanced colon cancer. An accurate diagnosis and determination of the extent of disease is crucial in the management of liver metastasis. Patients have a survival benefit from treatments including chemotherapy and partial hepatic resection. However, the diagnosis of the condition may not be straightforward. Here, we report a challenging case of colon cancer with a benign hepatic condition mimicking liver metastasis.

Case presentation

Written consent was obtained from the patient for publication of their details.

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A 53 year-old male presented with vague abdominal discomfort and was found to have colon carcinoma in September 2005. He denied any significant past medical history other than hyperlipidemia, which had been well controlled with atorvastatin for eight years prior to the cancer diagnosis. Staging investigation with an abdominal CT scan showed a lesion at sigmoid colon and no distant metastasis. His preoperative serum CEA level was within normal range. Sigmoidectomy was performed and revealed a 3.5 cm grade II mucin-producing adenocarcinoma invading into the pericolonic fat. All four lymph nodes removed showed no evidence of metastasis. Vascular invasion was identified. He received adjuvant chemotherapy with 5-FU, leucovorin, and oxaliplatin for six-months. Mild elevations of aspartate aminotranferase 61 U/L (normal 0-38 U/L) and alanine aminotransferase 77 U/L (normal 0-38 U/L) were observed during the chemotherapy treatment.

Following completion of the adjuvant chemotherapy, he did well except for mild elevations of the liver enzymes. He denied a history of active hepatitis. His hepatitis serology showed the presence of anti-HBc IgG and undetectable levels of both anti-HBsAg and HBsAg. He continued taking atorvastatin without additional medications. He was on no complementary medications or androgens. He previously drank a few glasses of wine weekly, but discontinued after the diagnosis of colon cancer.

The follow-up CT scan in July 2007, which was approximately two years after surgery, revealed three small hypervascular nodules in the right hepatic lobe measuring of 2.0, 0.5, and 0.6 cm (**Fig. 1A**). There was no elevation of the CEA. MRI of the liver was performed and confirmed the three small hypervascular nodules. All nodules were hypointense on T1 weighted image, mildly hyperintense on T2 weighted image, and enhanced during arterial phase to three minute-delayed phase (**Fig. 1B**). In light of the hypervascular nature of the lesions from both CT and MRI, we further performed a PET/CT evaluation that showed no significant uptake of isotope in any of the liver lesions. Additional investigation with a fine needle aspiration and biopsy of one of the nodules revealed no malignant cells. The patient agreed to observation with no immediate treatment. Serial imaging every 3 months showed a gradual increase in the size of all monitored lesions. In July 2008, the MRI with a hepatocyte specific contrast, Gd-EOB-DTPA, injection was performed. This showed increased size and number of the hypervascular nodules in the right hepatic lobe (**Fig. 1C** and **1D**). All nodules were hyperintense during the hepatobiliary phase (**Fig. 1E** and **1F**). There was a small hemangioma that showed differential density and enhancement compared to the lesions (arrow head in **Fig. 1D** and **1E**). Taken together, all imaging characteristics were consistent with a benign tumor containing functioning hepatocytes such as focal nodular hyperplasia or nodular regenerative hyperplasia. We repeated additional core needle biopsies to one of the liver lesions.

The pathology showed a fibrous scar containing blood vessels and a few bile duct-like structures with a nodular appearance of surrounding liver parenchyma (**Fig. 2A**). Trichome staining displayed portions of fibrous tissue in blue (**Fig. 2B**) and the reticulin stain revealed a reticulin framework pattern in liver parenchyma (**Fig. 2C**). These findings are consistent with "focal nodular hyperplasia".

Conclusion

Focal nodular hyperplasia (FNH) is a common benign condition of the liver, which occurs spontaneously in young women [1]. Occasionally, FNH may present as multifocal hepatic lesions which are confused with liver metastases. The pathogenesis of FNH remains enigmatic. However, one possible explanation is an acquired anomaly of the arterial blood supply leading to a focal hyperperfusion of injured hepatic parenchyma. This causes a focal hyperplastic change. [2]. A few reports have demonstrated the association between FNH in pediatric cancer patients treated with chemotherapeutic agents such as high dose alkylating agents including melphalan and busulfan. These agents are known to induce hepatic vascular disruption [3]. To our knowledge, this is the first possible case of FNH associated with oxaliplatin treatment. Our patient showed evidence of prior HBV infection, which may be a contributing factor to the formation of FNH. We did not find a typical hepatitis pattern or cirrhosis in the liver. Additionally, his HBV serology profile was not consistent with active hepatitis at the time of diagnosis of FNH. The patient was on no other medications associated with FNH.

The FDA approval of oxaliplatin for colon cancer has led to an increase in its use especially in adjuvant therapy [4, 5]. Though FNH may be an uncommon chemotherapy associated condition, it could cause confusion with a true liver metastasis. Fortunately, there were a few hints in this case, including a long disease free interval in an early stage patient who had received aggressive adjuvant treatment. This led us to investigate throughly the abnormal liver findings. It is interesting to note that our patient developed FNH two years after the first exposure to oxaliplatin. However, the average interval between the diagnosis of malignancy and the diagnosis of FNH may be variable depending on the degree of hepatic damage [6]. Careful imaging evaluation and confirmed tissue diagnosis could avoid unnecessary surgery for a benign liver tumor.Radiographic features of typical gadolinium enhancement during arterial phase but isointensity or slightly hyperintensity during portal venous and delayed phases may help distinguishing FNH from the liver metastasis. When using hepatocyte specific contrast, FNH often displays hyperintensity in the hepatobiliary phase. In contrast, liver metastasis from colon cancer usually has hypovascularity and hypointensity during the hepatobiliary phase using hepatocyte specific contrast agent [7]. Additionally, the PET scan is very

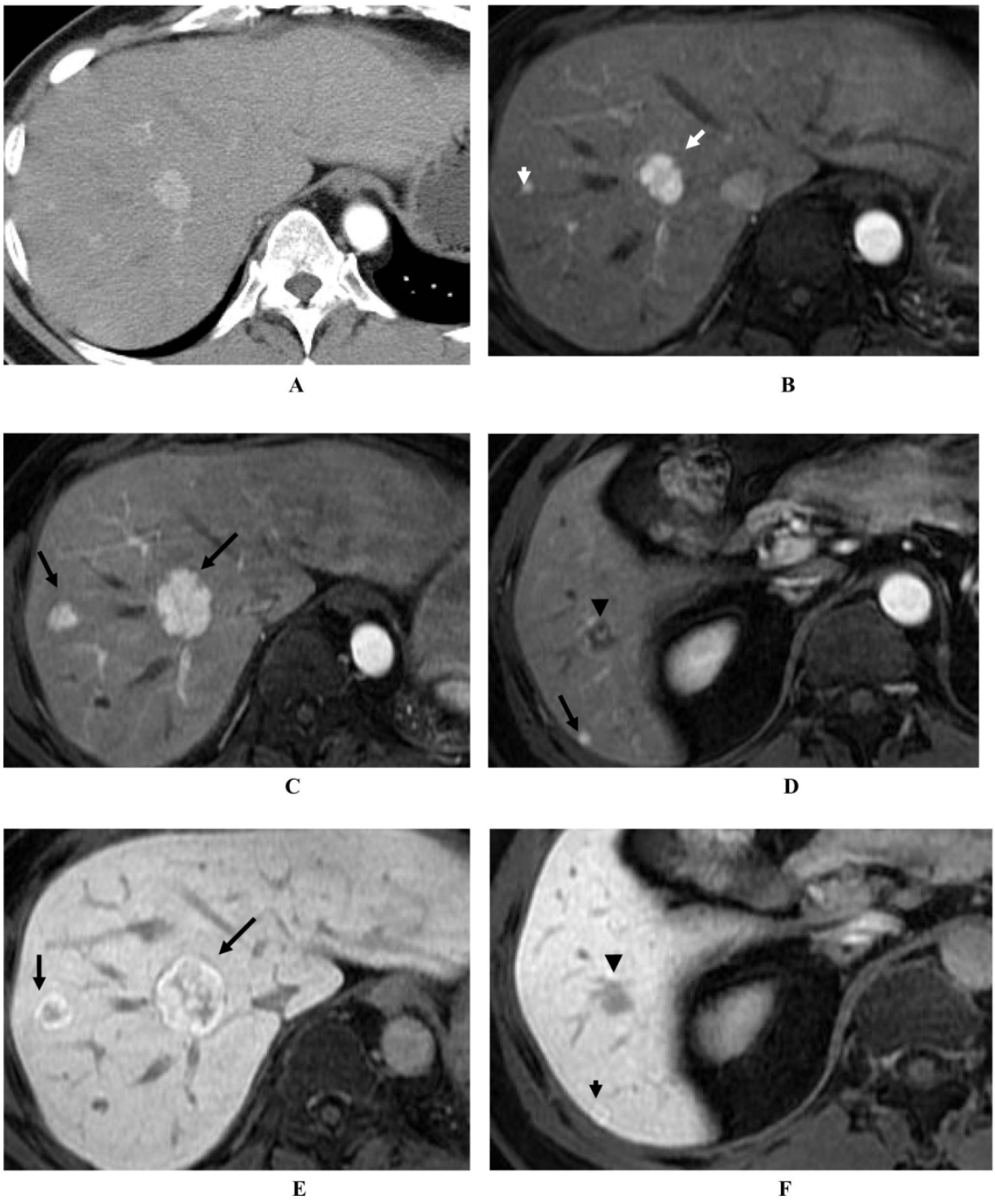

Fig. 1 Liver Imaging. **A:** CT scan upper abdomen, **B**: MRI liver, **C** and **D**: MRI with a hepatocyte specific contrast, Gd-EOB-DTPA injection; (arterial phase), **E** and **F**: MRI with a hepatocyte specific contrast, Gd-EOB-DTPA injection (hepatobiliary phase).

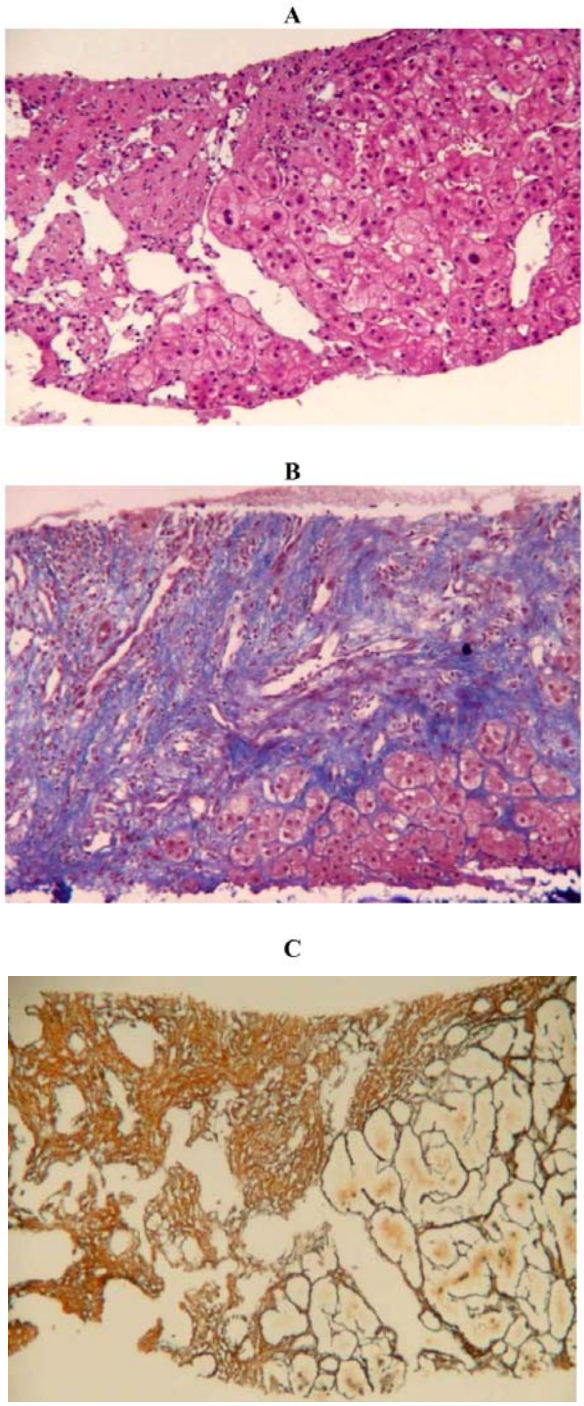

Fig. 2 Pathology view. **A**: H & E staining, **B**: Trichome staining, **C**: Reticulin staining.

useful when the size of the nodule is large. Finally, a pathological examination of the lesion may be required in establishing the accurate diagnosis of this entity.

The authors declare that they have no competing interests.

Abreviations

CT = Computerised tomography,
CEA = Carcinoembryonic antigen,
5-FU = Fluoropyrimidine,
anti-HBc IgG = anti-hepatitis B core IgG antibody
anti-HBsAg = anti-hepatitis B surface antibody,
HBsAg = hepatitis B surface antigen,
MRI = Magnetic resonance imaging,
FDG-F18 PET/CT = fluorodeoxyglucose Fluorine-18 positron emission tomography/ computerized tomography,
Gd-EOB-DTPA = contrast agent gadolinium 3, 6, 9-triaza-3, 6, 9-tris (carboxymethyl)-4-(4-ethoxybenzyl)-undecandicarboxylic acid,
FNH = Focal nodular hyperplasia,
HBV infection = hepatitis B virus infection,
FDA = Food and Drug Administration.

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