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Case report

Diffuse intrasinusoidal hepatic metastasis from breast cancer: Multimodality imaging with pathology correlation

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ABSTRACT

Metastatic disease to the liver is a known and common site of breast cancer spread, classically presenting as either hypovascular or hypervascular masses. Rarely, hepatic metastatic disease may have an atypical diffuse and intrasinusoidal pattern of involvement, which may be radiographically occult or extremely challenging to diagnose even with multiphase contrast enhanced techniques. We report a case of a 28-year-old female with stage III invasive ductal carcinoma of the breast, who recently discontinued treatment due to pregnancy, presenting with progressive signs and symptoms of rapidly decompensating liver failure due to sinusoidal obstruction. Multimodality imaging was performed without evidence for focal hepatic metastatic disease; however, intrahepatic vein (IVC) compression was noted. Hepatic sinusoidal tumor infiltration was confirmed by liver biopsy. After palliative chemotherapy the disease became less infiltrative and more conspicuous on imaging, revealing itself as hepatic metastases, with decreased compression of the intrahepatic IVC and resolution of signs and symptoms of sinusoidal obstruction syndrome.

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Introduction

Intrasinusoidal hepatic metastasis is a rare condition described in several malignancies in which the liver is dif-

fusely infiltrated by metastases. Patients with this pattern of metastatic disease present with signs and symptoms of hepatic dysfunction and progressive liver failure [1–3]. Unlike discrete hepatic metastases, intrasinusoidal metastases may not be readily detectable on imaging, and often, biopsy or autopsy is required to confirm the diagnosis [3]. This pattern of liver metastases should be considered in patients with a history of malignancy who present with laboratory or clinical evidence

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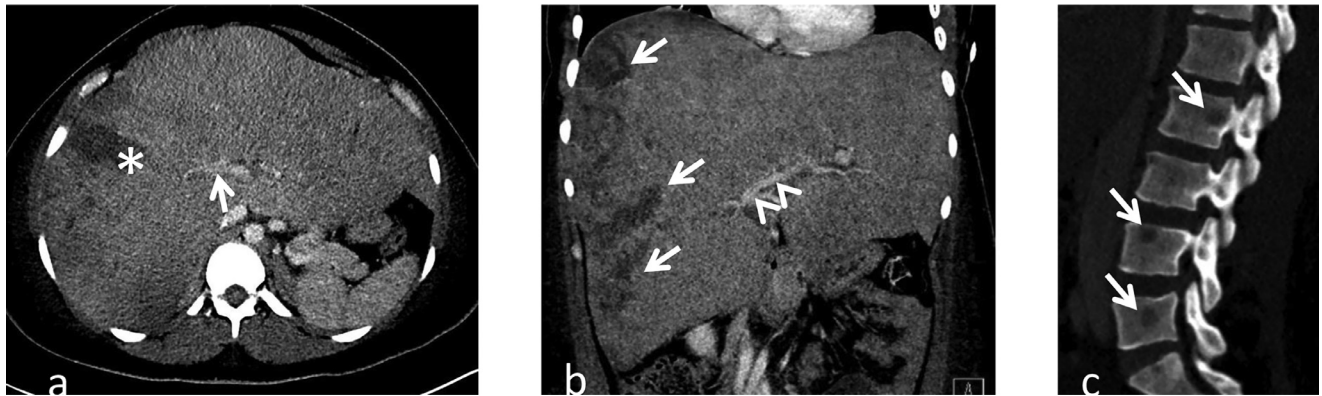


Fig. 1 – CT of the abdomen with IV contrast (100 mL of iodinated contrast/Isovue 370), portal venous phase. (A) Axial image. Massive hepatomegaly with partially necrotic mass occupying the right hepatic lobe (*) invading and occluding the posterior branch of the right portal vein (arrow). (B) Coronal image. Hypodense areas in the right hepatic lobe indicating ischemia/necrosis or tumor infiltration (arrows). Note compression and attenuation of the left portal vein (arrow head). (C) Lytic metastases were also identified in the spine (arrows).

of hepatic dysfunction and imaging findings of diffuse liver disease as highlighted on this report.

Case summary

Twenty-eight-year-old African American female presented to the emergency room with right upper quadrant abdominal pain, abdominal distention, bilateral lower extremity edema, nausea and vomiting. Pertinent history includes stage III, ER positive, PR/HER2 negative, BRCA negative invasive ductal carcinoma of the left breast, for which, until 2 weeks prior to admission, she was on adjuvant endocrine therapy having completed neoadjuvant chemotherapy and radiation therapy over the past 3 years. Treatment was discontinued when patient was found to be 8 weeks pregnant. Initial work up including a right upper quadrant ultrasound at an outside facility showed hepatomegaly and possible acalculous cholecystitis. Hepatic enzymes were elevated, including AST 208 U/L, ALT 49 U/L, ALP 167 U/L, with normal total bilirubin of 1.1 mg/dL and albumin of 3.0 gm/dL. While undergoing a laparoscopy for possible cholecystectomy, a significantly enlarged and heterogeneous liver was noted and a frozen biopsy of the liver was positive for carcinoma, thus the procedure was aborted. Subsequent CT abdomen and pelvis revealed an enlarged and heterogeneous appearing right hepatic lobe with attenuation and possible occlusion of the posterior branch of the right portal vein and mass effect with narrowing of the left portal vein (Figs. 1A and B). Extensive osseous metastatic disease was also identified (Fig. 1C). Intraoperative biopsy of the liver showed hepatic sinusoids diffusely infiltrated by neoplastic cells with disrupted hepatic architecture due to hepatocyte compression with areas of atrophy, necrosis, and desmoplasia of involved sinusoids without frank parenchymal infiltration (Fig. 2A). Biopsy was confirmed to be metastatic carcinoma,

with additional immunostains further confirming primary breast origin (Figs. 2B and C).

After the initial presentation, the patient was discharged with follow up appointments with her oncologist; however, she re-presented to the emergency room at our institution with persistent abdominal pain, abdominal distention and lower extremity swelling. MRI of the abdomen showed liver edema and areas of parenchymal necrosis (Figs. 3A and B). The patient electively underwent termination of the pregnancy and shortly after, her clinical status started rapidly declining with new onset fever, tachycardia, shortness of breath, and worsening liver failure and lethargy. Her updated laboratory tests showed AST 381 U/L, ALT 77 U/L, ALP 152 U/L and total bilirubin of 3.8 mg/dL. CT angiogram of the chest ruled out pulmonary embolism, but demonstrated nonspecific patchy ground glass opacities, not excluding early lung metastasis. A new MRI abdomen showed massive hepatomegaly, enlarging infarcts with hepatic capsular retraction, and significant compression of the left portal vein and IVC (Figs. 4A and B). Doppler ultrasound of the liver showed patent vasculature and normal direction of blood flow, however there was lack of phasicity in the hepatic veins, consistent with downstream IVC compression and portal vein pulsatility signifying elevated hepatic sinusoidal pressure (Figs. 5A and B). Viral hepatitis serology and additional infectious investigation was negative.

Due to her clinical circumstance, the patient was started on palliative chemotherapy with weekly single-agent low-dose Adriamycin. Within a few days, the patient's liver enzymes began trending down. After 5 cycles of treatment, the patient's symptoms had resolved and her clinical status returned to baseline, with continued improvement of liver enzymes. Restaging MRI scan of the abdomen showed improved hepatomegaly, decreased compression of the intrahepatic IVC, and a more organized area of infiltrative liver hypo-enhancement, indicative of favorable treatment response (Figs. 6A-D).

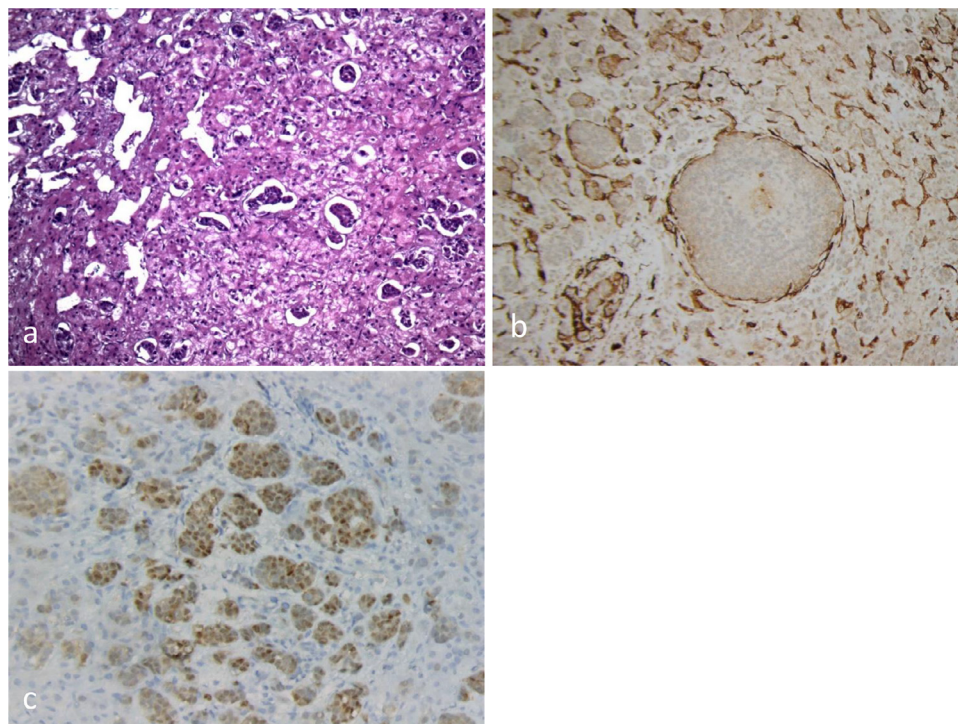


Fig. 2 – (A) Hematoxylin and eosin (HE) image of the liver tissue intraoperative biopsy revealing diffuse infiltration of the hepatic sinusoids by metastatic carcinoma (HE, original magnification x100). (B) Immunohistochemical stain for CD31, a vascular marker shows the presence of tumor emboli inside distended hepatic sinusoids (original magnification x200). (C) Immunohistochemical stain for estrogen receptor reveal nuclear positivity in the tumor cells. This finding is consistent with the patient’s primary breast carcinoma estrogen receptor positivity (original magnification x200).

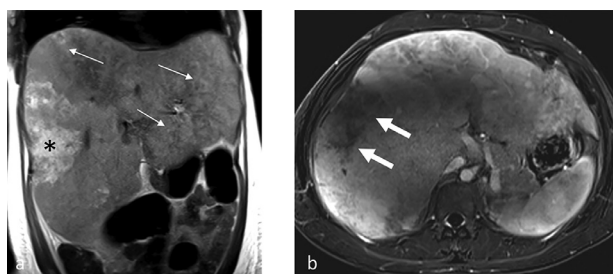


Fig. 3 – MRI of the abdomen, 1.5 Tesla. (A) Coronal T2 weighted image demonstrates diffusely increased T2 signal in the right and left hepatic lobes (thin arrows). Note more confluent areas of increased signal in the right hepatic lobe indicating edema/necrosis (*). (B) Axial T1 post contrast (7.5 mL of Gadavist) image shows heterogeneous enhancement of the liver with areas of hypo-enhancement indicating ischemia or necrosis (thick arrows).

Discussion

The liver is the most common site of metastatic disease for many cancers, including breast carcinoma, with 40-50% of breast cancer patients presenting with liver metastases [1]. The most common pattern of disease is the development of

multiple, distinct hypovascular or hypervascular masses. Although metastatic disease to the liver is common, acute hepatic failure due to metastatic disease is rare occurrence [1,3]. Rarely, tumor infiltrates and spreads along the hepatic sinusoids instead of forming discrete masses, making the disease radiographically occult. This process allows extensive disease to spread through the parenchyma without becoming radiologically apparent, until obstruction of hepatic sinusoids occurs which can lead to acute liver failure [2]. This diffuse intrasinusoidal metastatic pattern is the most common method associated with acute liver failure. It has been reported most commonly for hematologic malignancies, but it can also be associated with solid tumors, including small cell lung cancer, breast cancer and gastric cancer [3].

In our case of a 28-year-old female with breast cancer, the patient’s clinical status rapidly declined with progressive signs and symptoms of liver failure, including hepatomegaly, right upper quadrant pain, jaundice, and ascites. Imaging findings on CT abdomen and Doppler ultrasound of the liver did not show the typical masses expected for metastatic disease, but instead demonstrated hepatomegaly, hepatic infarcts, and compression of the intrahepatic IVC. Areas of hepatic infarcts and necrosis, as seen in our case, is a frequently associated imaging finding with intrasinusoidal spread of tumor and is thought to be due to spread of tumor cells along the hepatic and portal veins, causing intravascular stenosis or obstruction and ischemia [3,4]. Another associated finding is a heterogeneous appearance of the liver driven by a desmoplastic reac-

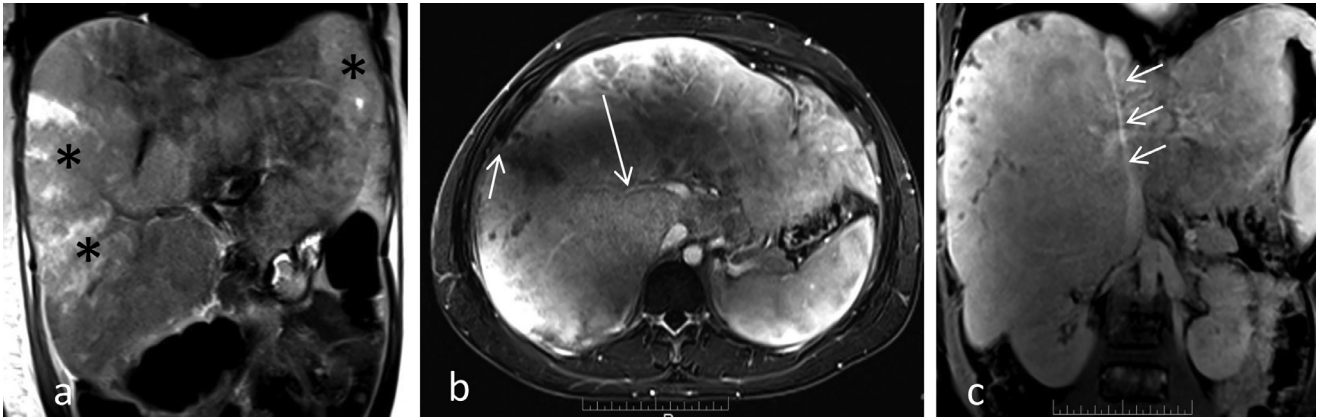


Fig. 4 – MRI of the abdomen, 1.5 Tesla. (A) T2 weighted coronal image shows hepatomegaly with diffuse abnormal signal of the liver (*). (B) T1 weighted axial image with Gadavist contrast portal venous phase shows area of capsular retraction in the right lobe (short arrow) and significant compression of the right portal vein (long arrow). (C) T1 weighted coronal image portal venous phase post-contrast shows severe compression of the intrahepatic IVC (arrows).

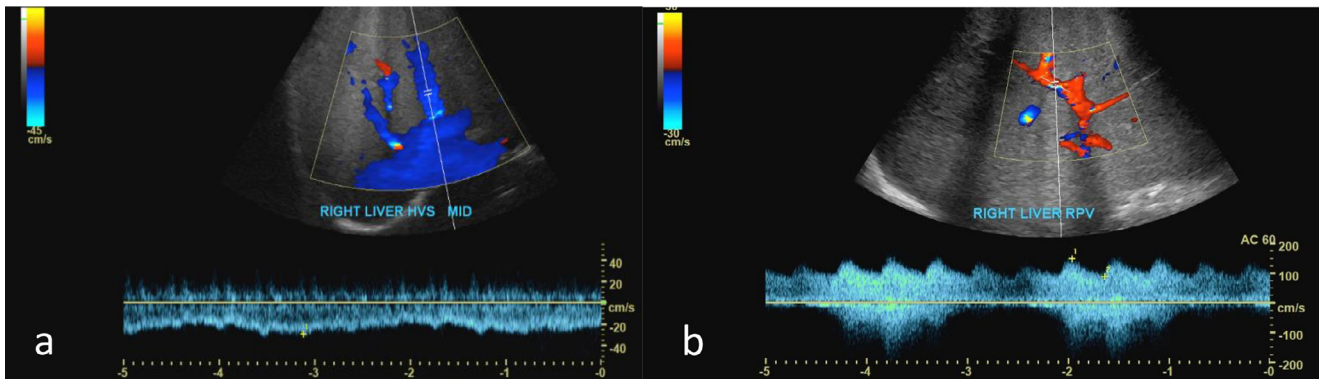


Fig. 5 – Doppler Ultrasound of the Liver with sinusoidal obstruction findings. (A) Color and Spectral Doppler of the middle hepatic vein demonstrates normal direction of flow with loss of triphasic waveforms. (B) Color and spectral Doppler of the right portal vein shows normal direction of flow with portal vein pulsatility.

tion to the infiltrative tumor cells, which was also observed in our patient during aborted laparoscopic cholecystectomy [3,4,5]. Due to invasion and obstruction of the hepatic sinusoids, typical features of hepatic veno-occlusive disease or sinusoidal obstruction syndrome was clinically apparent in our patient with rapidly progressing signs and symptoms of liver failure. Along with compression and obstruction of the sinusoids as an etiology for this syndrome, intrahepatic IVC compression is also a known etiology which was present in our case [6]. For our patient, the intrasinusoidal pattern of disease spread was confirmed with tissue biopsy, illustrating diffuse infiltration of the sinusoids without frank invasion of tumor cells into the parenchyma. A clinicopathologic study published by Allison et. al showed that case reports that described the histologic type of the primary breast carcinomas, 8 were infiltrating ductal type and 3 were described as “scirrhous,” but no primary tumors were described as having a lobular phenotype [4].

In conclusion, the diffuse infiltrating intrasinusoidal metastatic disease pattern of malignancy can be a radiographically occult cause of acute liver failure, associated with a

rapid clinical decline and poor prognosis. Due to the infiltrative pattern of tumor spread, the disease can show non-specific imaging findings and thus should be regarded with high suspicion in the appropriate clinical setting and confirmed with liver biopsy. In our case, the combination of imaging findings indicating an infiltrative liver process with areas of infarct and necrosis with intrahepatic flow changes were very helpful to indicate the severity of disease and establish an imaging baseline before treatment. Prompt recognition of this metastatic pattern and treatment are keys to improve patient outcomes and survival as demonstrated in our patient.

Teaching point

Diffuse intrasinusoidal pattern of hepatic metastasis should be suspected in patients with a history of malignancy who present with rapidly progressive hepatic dysfunction in the absence of discrete hepatic lesions on imaging.



Fig. 6 – MRI of the abdomen, 1.5 Tesla, T1 weighted post Gadavist contrast portal venous phase axial (A) and coronal (C), 9-month follow-up MRI with Eovist contrast portal venous phase axial (B) and coronal (D) images. (A) axial T1 image shows hepatomegaly with heterogeneous liver enhancement (short arrows). Follow-up MRI axial T1 image (B) shows more circumscribed area of hypo enhancement in the right hepatic lobe, indicating treatment response (long arrows). Initial Coronal T1 (C) and follow-up images (D) show resolution of hepatomegaly (*) and improved caliber of the IVC (arrow heads).

Common Imaging findings of Diffuse Intrasinusoidal Hepatic metastases include parenchymal heterogeneity with areas of infarcts or necrosis on CT and MRI as well as Doppler changes in the liver such as portal vein pulsatility and loss of hepatic vein phasicity, mostly secondary to obstruction of the hepatic sinusoids and compression of the large hepatic vasculature.

Patient consent

Patient consent is obtained.

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