CASE REPORT

Radiographically occult intrasinusoidal liver metastases leading to hepatic failure in a case of breast cancer

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Accepted 28 January 2016

SUMMARY

The liver is one of the commonest sites of metastatic involvement in breast cancer, usually evident as focal lesions on imaging tests. Rarely, the pattern of metastatic spread is so diffuse that it remains radiologically occult. Such patients usually present with signs of hepatic insufficiency without any focal lesions on liver imaging. In such cases, liver biopsy is required to make a definitive diagnosis. We report a case of a 56-year-old postmenopausal woman with metastatic breast cancer who presented with subacute progressive liver failure. Repeated imaging of the liver was normal or non-descript. Liver biopsy finally established the diagnosis of intrasinusoidal metastases from breast cancer.

CASE SUMMARY

A 56-year-old woman was diagnosed with metastatic breast cancer with bone involvement, in 2009. Histopathology revealed infiltrating ductal carcinoma with a prominent lobular-like growth pattern with positive estrogen receptor and progesterone receptor, and negative human epidermal growth factor receptor 2 (HER2) receptor. She was treated on a clinical trial with paclitaxel and bevacizumab for 16 cycles. She had disease progression in the form of new lung lesions in June 2010, and was started on tamoxifen. She had partial response and continued tamoxifen until April 2014, when she had anaemia and thrombocytopaenia with increasing bone lesions, and histopathologically proven bone marrow metastases. At this point, the anaemia and thrombocytopaenia were due to the bone marrow involvement. She received palliative radiation to symptomatic bone sites followed by three cycles of doxorubicin and cyclophosphamide. Her blood counts stabilised after three cycles but she refused further chemotherapy and was hence started on exemestane. In April 2015, after having been on exemestane for 10 months, she presented with weakness and fatigue. Physical examination showed jaundice and mild hepatomegaly, and investigations revealed deranged liver functions: Aspartate transaminase (AST) 223 U/L, alanine transaminase (ALT) =105 U/L, bilirubin=0.76 mg/dL and normal alkaline phosphatase. Markers for hepatitis A, E, B and C were negative. Contrast-enhanced CT scan of the abdomen showed a normal liver. The patient followed up again after 6 weeks, with worsened liver functions: AST=982, ALT=230, bilirubin=8.98 mg/dL (direct=4.23 and indirect=4.73 mg/dL) and alkaline phosphatase=99 U/L. An ultrasound scan

of the abdomen showed mild hepatomegaly with no focal lesions. Work up for autoimmune conditions was inconclusive with negative anti-dsDNA antibody and positive smooth muscle antigen (SMA) antibody. The patient was started on prednisolone. Her general condition continued to deteriorate and she was admitted to our hospital in July 2015, with abdominal distention, deep icterus and Eastern Cooperative Oncology Group (ECOG) performance status of 4. On physical examination, she had hepatomegaly with ascites. Investigations showed severely deranged liver functions: bilirubin=35 mg/dL, AST=423 U/L, ALT=99 U/L, alkaline phosphatase=158 (UNITS U/L), serum albumin=2.6 g/dL and a deranged coagulation profile. A repeat ultrasound scan showed a normal liver with no focal lesion and no evidence of bile duct obstruction. A contrast CT scan also confirmed a normal liver (figure 1A, B). A transjugular liver biopsy was performed, which revealed intrasinusoidal metastasis of adenocarcinoma compatible with known primary in the breast (figure 2A, B). In view of her poor general condition, the patient was started on anastrozole plus fulvestrant. Her general condition gradually improved and liver function tests (LFT) started improving with bilirubin 3.24 mg/dL, AST-81 U/L and ALT-17 U/L. She was discharged on the same treatment. She has completed 3 months of fulvestrant plus anastrozole with improvement in her general condition and normal bilirubin.

DISCUSSION

About 40–50% of women with metastatic breast cancer have liver involvement during the course of their disease. Hepatic involvement is usually evident as focal lesions on imaging tests. On CT scan, they appear as low attenuation lesions on contrast-enhanced images, and on ultrasonography they appear as target lesions.¹ Other atypical appearances of liver metastases include fatty liver, hypervascular metastasis² and metastatic disease mimicking cirrhosis.³ Rarely, the pattern of metastatic spread can be so diffuse that it remains radiographically occult.⁴ Such patients usually present with signs of hepatic insufficiency without any focal lesions on liver imaging, as was seen in our patient. In such cases, liver biopsy is required to make a definitive diagnosis.

There are several points of note in our case. First, the patient presented with subacutely progressive liver failure, which is not a common scenario in patients with breast cancer with liver

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To cite: Gulia S, Khurana S, Shet T, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2015-214120

Figure 1 (A) CT of the liver showing a normal liver without focal infiltrates. (B) CT of the liver showing a normal liver without focal infiltrates.

metastases.⁵ Second, liver imaging tests on repeated occasions were normal or nondescript. Third, to our knowledge, this is only the second *ante mortem* case of breast cancer with an intrasinusoidal pattern of liver metastases with no apparent liver abnormality on imaging. In one previous report, three breast cancer cases with a similar intrasinusoidal pattern were described *post mortem*, all of whom had liver failure followed by rapid progression and death.⁶ It is possible that liver failure associated with an intrasinusoidal pattern of liver metastases is due to extensive hepatocellular necrosis resulting from pressure atrophy and interference of the vascular supply.⁷ Fourth, it is interesting that our patient had a prominent lobular component in her invasive carcinoma, which is known to have a somewhat distinct clinical pattern in the metastatic setting, characterised by predilection for peritoneal, meningeal and bone marrow involvement with histopathologically diffuse infiltration of serosa, muscularis propria, submucosa and mucosa by carcinoma cells.⁸⁻⁹ Loss of E cadherin in lobular carcinomas facilitates this type of infiltration.¹⁰ It is plausible that the intrasinusoidal, radiographically occult pattern of liver metastases in our patient was a reflection of lobular histology. Finally,

Figure 2 Core biopsy of the liver. (A) Liver biopsy with metastatic adenocarcinoma. Liver tissue is diffusely infiltrated by malignant cells; intrasinusoidal metastasis (H&E stain). Core biopsy of the liver. (B) Immunohistochemistry showing ER positivity. ER, estrogen receptor.

it is worth noting that intrasinusoidal, radiographically occult liver metastases have rarely been reported in other malignancies, including small cell lung cancer, bladder carcinoma, melanoma and prostate cancer.¹¹

In conclusion, clinicians should be aware of the possibility of a rare pattern of intrasinusoidal liver metastases in patients with metastatic breast cancer with progressive derangement of liver functions associated with normal liver imaging.

Learning points

- ▶ Hepatic involvement in metastatic breast cancer is usually evident as focal lesions on imaging studies.
- ▶ Rarely, the pattern of metastatic spread can be so diffuse that it remains radiographically occult.
- ▶ Such patients present with signs of progressive hepatic insufficiency without any focal lesions on liver imaging.
- ▶ Liver biopsy is required in such cases to make the definitive diagnosis.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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