A Case of Hepatopulmonary Syndrome as a Complication of Metastatic Breast Cancer to the Liver

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Abstract
Many patients with metastatic breast cancer develop liver metastases. A rare complication of this is hepatopulmonary syndrome (HPS), which is associated with exertional dyspnea and intrapulmonary shunting. We present a patient who presented with HPS as a consequence of liver metastases and subsequently treated with chemotherapy leading to resolution of her symptoms.

Introduction

Patients with metastatic breast cancer develop liver metastases in up to 50\% of cases [1]. The clinical course can range from asymptomatic disease to fulminant liver failure and death [1, 2]. Recent advances in the locoregional and systemic management of patients with metastatic triple-negative breast cancer with liver metastases have been made [3, 4]. Despite these improvements, optimal patient selection and evaluation of prognostic factors are currently being investigated [3, 5]. One rare complication of metastatic triple-negative breast cancer with liver metastases is hepatopulmonary syndrome (HPS), which is typically characterized by exertional dyspnea and hypoxemia caused by intrapulmonary vascular dilations [6, 7]. Here we present a unique case of patient with breast cancer metastasized to liver who developed HPS, and highlight the challenges in its management.
Case Report/Case Presentation

A 39-year-old woman with a history of Stage IA breast cancer (ER weakly positive, PR negative, HER-2 negative) treated with bilateral nipple-sparing mastectomies 3 years prior, presented to the emergency department with 3 weeks of progressive dyspnea on exertion. Pulse was 108 and oxygen saturation (SpO2) on room air was 91% and 84% with ambulation requiring up to 3 L of supplemental oxygen via nasal canula. Physical exam was notable for a decrease in SpO2 while sitting upright which improved with lying in the supine position. Laboratory values were notable for platelet count of 89,000 K, calcium 11.2 mg/dL, alkaline phosphatase 627 U/L, aspartate aminotransferase 148 U/L, and alanine aminotransferase 143 U/L. Computed tomography of the chest with intravenous contrast pulmonary embolism protocol was negative for pulmonary embolism, but revealed numerous hepatic lesions and numerous sclerotic osseous lesions. Trans-thoracic echocardiogram (TTE) with saline contrast and bubble study revealed lack of bubbles in the left ventricle after cough and the presence of bubbles after 7 heartbeats, suggestive of a transpulmonary shunt (as shown in Fig. 1, 2). The patient underwent an ultrasound-guided biopsy of a liver lesion and was diagnosed with metastatic breast cancer (ER weakly positive, PR negative, HER-2 negative). She was started on chemotherapy with weekly paclitaxel at a dose of 60 mg/m². After completion of a 3-week cycle.
of treatment, her hypoxia and supplemental oxygen needs resolved, and she had a significant reduction in her transaminases (as shown in Table 1).

**Discussion/Conclusion**

HPS typically presents with dyspnea and hypoxemia and is thought to be caused by increased release of nitrous oxide, leading to intrapulmonary vascular distensions. It is typically diagnosed by the presence of transpulmonary shunting seen on contrast-enhanced TTE and is most often observed in patients awaiting liver transplant in up to 32% of cases [7]. Liver metastases from breast cancer and other solid tumors have been described, although this is a very rare complication of a relatively common disease state [6, 8].

Our patient presented with dyspnea, platypnea-orthodeoxia, and hypoxemia in the setting of newly metastatic breast cancer to the liver. Contrast-enhanced TTE revealed transpulmonary shunt. This is a reported case of HPS cause by liver metastases which resolved with systemic chemotherapy.

Owing to its rarity, no specific guidelines exist for the management of HPS from liver metastases in metastatic breast cancer, as is highlighted by the novelty of our case. Although it should be noted as with our patient, those who present in visceral crisis are often treated with systemic chemotherapy. This poses an opportunity for further investigation with a focus on improving patient outcomes and identifying those patients who might respond to specific therapies. Recent research has suggested that our patient would likely not have responded to locoregional therapy with selective internal radiation therapy due to her elevated liver enzymes [3]. Furthermore, while she was eventually treated with combined chemoimmunotherapy based on accepted guidelines at the time of treatment due to her tumor being PD-L1 positive, newer data suggest that she may not have been predicted to respond to immune-checkpoint blockade, demonstrating the need for future clarification of which patients are most likely to respond to this sort of therapy [4]. This case represents a rare yet relevant clinical presentation of a disease commonly seen in the oncology field and highlights the need for further research into improving outcomes for patients in this clinical scenario.

**Statement of Ethics**

Ethics approval was not required per the Rush University Medical Center IRB. Unfortunately, the patient passed away, and written informed consent was obtained from the patient’s next of kin for publication of the details of their medical case and any accompanying images.

| Table 1. Laboratory values at time of diagnosis of HPS, and 3 weeks after initiation of chemotherapy |
|-------------------------------------------------|-------------------------------------------------|----------------------------------|
| Lab value                                      | Cycle 1 day 1 of weekly paclitaxel | After completion of 1 cycle of weekly paclitaxel |
| Total bilirubin                                | 1.2                                | 0.7                                |
| ALP                                            | 768                                | 438                                |
| AST                                            | 190                                | 45                                 |
| ALT                                            | 151                                | 41                                 |
| Reference range                                | 0.2–1.3 mg/dL                      | 30–125 U/L                        |
| ALP, alkaline phosphatase; AST, aspartate aminotransferase; ALT, alanine aminotransferase. | 3–44 U/L                           | 0–40 U/L                          |
Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

James Coggan: conceptualization, data collection, draft writing, and manuscript editing and review. Adam Morin: data collection, draft writing, and manuscript editing and review. Ruta Rao: draft writing, manuscript editing and review, and study oversight.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

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