Annals of Clinical Case Reports

Case Report
Published: 10 Jun, 2022

Hepar Lobatum Carcinomatosum: Risk of Underestimated Progression in a Triple Negative Metastatic Breast Cancer

*Morcet-Delattre Robin[1], Zimmermann Pierre-André[2], Lesourd Samuel[1] and Billard Felix[1], LE DU Fanny[1]**

[1]Department of Medical Oncology, Eugène Marquis Cancer Center, France

[2]Department of Nuclear Medicine, Eugène Marquis Cancer Center, France

[3]Department of Radiology, CHU, France

Abstract

A 49-year-old woman with metastatic triple-negative breast cancer with liver metastasis died, during her systemic chemotherapy treatment of a liver dysfunction (hepatic cytolysis, portal hypertension and hepatic dysmorphism) despite clear decrease in metabolism on PET-CT images. This patient suffered from a Hepar Lobatum Carcinomatosum (HL) or pseudocirrhosis which is an acquired non-cirrhotic major hepatic dysmorphism mostly observed during systemic treatments of liver metastatic breast carcinoma patients. Sinusoidal obstruction syndrome is the main mechanism of HL. The radiological aspect is well described in the literature unlike the metabolic aspect on PET-CT images as presented here with a confusing partial metabolic response.

Introduction

Hepar Lobatum (HL) is an acquired non-cirrhotic major hepatic dysmorphism. Initially described in hepatic tertiary syphilis [1,2], HL remains rare and is currently mostly observed during systemic treatments of liver metastatic breast carcinoma patients, but also in other solid metastatic tumors [3-6]. Thus, HL is currently called HL carcinomatosum or pseudocirrhosis. HL cause clinical worsening despite systemic treatment of the cancer, with liver failure and portal hypertension [7,8] leading to rapid death. In this article, we will report the case of a young woman with triple-negative metastatic breast cancer who experience fatal HL carcinomatosum during second line of metastatic systemic treatment.

Case Presentation

A 49-year-old woman, without BRCA1/2 mutation, was diagnosed in January 2020 with a non-specific infiltrating breast carcinoma. Clinical staging was T3N1M0. Axillary involvement was cytologically confirmed. PET-CT showed no evidence of distant metastases. Biopsy histological report reveals a highly proliferative triple negative breast cancer (Scarff-Bloom-Richardson grade 3, Ki-67 proliferation index of 80%). Based on multidisciplinary meeting decision, this young patient was treated with sequential neoadjuvant chemotherapy: 4 cycles of dose-dense EC (epirubicine 90 mg/m^2 and cyclophosphamide 600 mg/m^2 every two weeks) followed by 12 weekly paclitaxel (80 mg/m^2) from February 2020 to July 2020. Breast conserving surgery with lymph node dissection revealed pathological complete response both in the breast and the axilla. Adjuvant radiotherapy on the tumor bed and supraclavicular lymph node areas was performed from September to November 2020. She was then one active surveillance with trimestral clinical and biological check-up. This patient experienced intense abdominal pain during her 2021 summer holiday abroad. When she came back, biological and radiological work-up revealed a potential hepatic relapse with visceral crisis. Cytolysis was 10 times Upper Normal Limits (UNL) and associated with cholestasis and increased bilirubin up to 36 µmol/L. Multiples secondary lesions of both hepatic lobes associated with hypermetabolic retroperitoneal adenopathy, were seen on PET-CT without obvious biliary tract distension (Figure 1A). Biopsy of a suspected liver secondary lesion confirmed the relapse of the breast cancer with identical IHC characteristics (estrogen receptor 0%, progesterone receptor 0%, HER2 IHC scores 1+). Patient was immediately hospitalized to start a first line of systemic treatment with carboplatin in monotherapy (AUC 5) given the visceral crisis. After 2 cycles, physical examination revealed massive ascites with mucocutaneous icterus. Biological liver function was worsening with a cytolysis 12 times UNL and a total bilirubin dosed at 62 µmol/l. A second line of chemotherapy with 5-FUpc (continuous treatment at 300 mg/m^2 for 3 weeks, every 4 weeks)

OPEN ACCESS

Correspondence:
Fanny LE DU, Department of Medical Oncology, Eugène Marquis Cancer Center, Rennes, France, Tel: (+33)299252956; E-mail: f.ledu@rennes.unicancer.fr

Received Date: *21 Apr 2022*
Accepted Date: *03 Jun 2022*
Published Date: *10 Jun 2022*

Citation:
Robin M-D, Pierre-André Z, Samuel L, Felix B, Fanny LD. Hepar Lobatum Carcinomatosum: Risk of Underestimated Progression in a Triple Negative Metastatic Breast Cancer. Ann Clin Case Rep. 2022; 7: 2217.

ISSN: 2474-1655

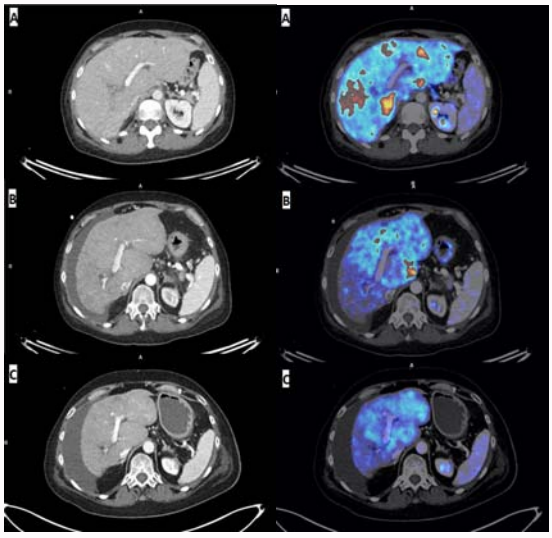

Figure 1: Series of abdominal CT and metabolic images showing the evolution of hepatic dysmorphism and the appearance of signs of portal hypertension. A) PET scanner of September 2021, B) PET scanner of December 2021, appearance of caudate lobe enlargement, heterogeneous liver parenchyma and ascites C) PET scanner of January 2022, major atrophy of the liver as a whole and particularly of the right liver, the area initially most affected by metastases.

was started in emergency - due to the deterioration of the general condition - and corticosteroids increased. After 2 months of 5FU-pc, patient experienced acute asthenia (ECOG-performance status 2) and worsening of the ascites. Liver dysfunction improved with a decrease total bilirubin to 35 µmol/L and a reduced cytolysis at 9 times UNL. PET scanner was in favor of a partial metabolic response with a decrease in the heterogeneity of hepatic parenchyma uptake in particular in the right liver and almost completes radiologic and metabolic regression of the retroperitoneal adenopathy (Figure 1B). However, an increase in peritoneal effusion was observed. It was then decided to continue 5FUpc and add metronomic endoxan (50 mg/day) in order to improve efficacy. A month later (less than 6 months after diagnosis of metastatic disease), the clinical situation deteriorates with a performance status of 3, appearance declivity edema, increased abdominal ascites requiring weekly punctures. The ascitic liquid was analyzed: The total protein level was 13 g/L, which suggested transudative ascites due to the presence of portal hypertension, even if, cytology of the ascitic fluid also revealed carcinomatous cells compatible with a mammary origin. However, PET-CT found a complete morpho-metabolic response of liver metastasis compared to the previous FDG PET and CT scan. CT sequences of PET-CT shows an apparent tumor regression of all liver metastases and progressively revealed a heterogeneous liver parenchyma with regional changes (segmental hypertrophy involving segment I and atrophy of the right lobe), ascites and signs of portal hypertension (Figure 1C). After multidisciplinary discussion, it was concluded a Hepar Lobatum carcinomatosum. Additional work-up (liver MRI or biopsy) was not permitted due to the rapid patient's condition deterioration who died few days after the last PET-CT of liver failure with encephalopathy.

Discussion

Even if liver is a frequent site of metastasis development in breast cancer patients, carcinomatous cirrhosis remains rare. In this observation, the diagnosis of HLC was retained in view of the association of breast cancer with hepatic metastases under chemotherapy, and rapid onset of hepatic dysmorphism, portal hypertension and clinical deterioration. There was no history of alcohol abuse, metabolic syndrome or viral hepatitis. In retrospective cohorts, ascites was demonstrated in 68%, portal hypertension in 11%, and splenomegaly in 8% of patients with HLC [9]. As in other case reports, the histological diagnosis is missing due to clinical deterioration of the patient, although the biopsy seems essential for such diagnosis [10-14]. Here, the diagnosis was initially difficult because of the discrepancy between a complete hepatic metabolic response and the appearance of hepatic dysmorphism with rapid deterioration of the clinical state. Histologically, the most frequently type of breast cancer associated to HLC is invasive ductal carcinoma and triple negative specificity [9]. The appearance corresponds to a Sinusoidal Obstruction Syndrome (SOS) [10-13]. Indeed, metastatic invasion of portal venules by tumor cells and tumor extension into the sinusoids with perivascular fibrosing desmoplastic reactions have been observed in other cases of HLC [15]. SOS could be responsible of heterogeneous liver perfusion with hepatic atrophy [16]. Anti-cancer treatments (alkyling agents [i.e., carboplatin], anti-metabolites [i.e., 5FU] have also been reported to be associated with SOS [17,18]. Objective imaging of major capsular retractions developed rapidly (less than 3 months), in our case, as described in the literature [9,17]. Indeed, the most frequent radiological signs of HLC described are nodular hepatic contour (98%), capsular retraction (83%), caudate lobe enlargement (67%) and segmental or lobar volume loss (62%) [19]. In a retrospective analysis of 374 metastatic breast cancer patients, Oliai demonstrate that 55% of patients with liver metastasis will developed pseudocirrhosis CT signs and that 100% of patients with pseudocirrhosis had liver metastases, even if some of them seems occults at the initial diagnosis [9,17]. HLC is negative prognostic factor with an overall survival in all types of breast cancer of 69 months *vs.* 189 months in presence of liver metastasis without HLC evolution [9]. In the literature, HLC often occurs in heavily pretreated patients, which is not the case of our patient [9]. There is really limited data in the literature regarding the associated metabolic response as described. The metabolic response described in this case, can potentially be explained by fibrous replacement of cancerous tissue. Sass et al. reported results regarding the role of PET-CT scan in the liver of a patient with autopsy evidence of diffuse infiltration by tumor cells. In their case of diffuse desmoplastic metastatic breast cancer simulating cirrhosis, PET-CT scans showed inhomogeneous uptake consistent with cirrhosis, but no focal areas of increased uptake suggestive of FDG-avid malignancy [15]. Moreover, there is no specific treatment described because of the rapid death apart from palliative treatments such as TIPS (Transjugular Intrahepatic Portosystemic Shunt) [20].

Conclusion

HL is rare but life-threatening evolution of the disease. It requires increased morphological monitoring of the liver parenchyma in patients with liver metastases from breast cancer. This case report illustrates the need to remain attentive to the clinical and radiological data despite a complete metabolic response on the PET scanner. Given the frequency of pseudocirrhotic lesions in patients with liver metastases and the dramatic prognosis, it is necessary to identify the first signs, to supplement with examinations such as biopsy and MRI and to quickly adapt the treatment.

References

1. Tiliakos N, Shamma'a JM, Nasrallah SM. Syphilitic hepatitis. Am J

Gastroenterol. 1980;73(1):60-1.

2. Gensci G. Five cases of syphilitic hepar lobatum with portal obstruction. Proc R Soc Med. 1961;54(11):973-5.
3. Teke Z, Nessar G, Kiremitci S, Aksoy E, Elbir OH. Hepar lobatum carcinomatosum associated with metastatic rectal carcinoma: An unusual cause of liver dysmorphy. Med Princ Pract. 2011;20(1):93-6.
4. Hwang YT, Chen PJ, Kao JH, Wang TD, Wang HH, Chu JS, et al. Rapid hepatic failure associated with a contracted liver mimicking cirrhosis in a case of nasopharyngeal carcinoma with liver metastasis. Liver. 1996;16(4):283-7.
5. Chin NW, Chapman I, Jimenez FA. Complete chemotherapeutic regression of hepatic metastases with resultant hepar lobatum. Am J Gastroenterol. 1987;82(2):149-51.
6. Robinson SM, Wilson CH, Burt AD, Manas DM, White SA. Chemotherapy-associated liver injury in patients with colorectal liver metastases: A systematic review and meta-analysis. Ann Surg Oncol. 2012;19(13):4287-99.
7. Cervoni J-P, Dobrin A, Sailley N, Chaigneau L, Thevenot T, Richou C, et al. [Hepar lobatum carcinomatusum: A rare cause of portal hypertension complicating hepatic metastases in breast cancer]. Gastroenterol Clin Biol. 2008;32(8-9):740-4.
8. Mathis G, Felli E, Mutter D, Pessaux P. Hepar lobatum carcinomatosum: A rare cause of portal hypertension. Clin Case Rep. 2020;8(10):2082-3.
9. Oliai C, Douek ML, Rhoane C, Bhutada A, Ge PS, Runyon BA, et al. Clinical features of pseudocirrhosis in metastatic breast cancer. Breast Cancer Res Treat. 2019;177(2):409-17.
10. Honma K. Hepar lobatum carcinomatosum due to metastatic breast carcinoma. Virchows Arch A Pathol Anat Histopathol. 1987;410(6):465-9.
11. Graber I, Dumortier J, Poncet G, Queneau PE, Mathevet P, Scoazec JY. Hepar lobatum carcinomatosum revealing an occult metastatic lobular carcinoma of the breast. Ann Diagn Pathol. 2010;14(6):438-42.
12. Nakajima T, Sekoguchi S, Nishikawa T, Takashima H, Watanabe T, Minami M, et al. Multifocal intraportal invasion of breast carcinoma diagnosed by laparoscopy-assisted liver biopsy. World J Gastroenterol. 2005;11(15):2360-3.
13. DeLeve LD, Shulman HM, McDonald GB. Toxic injury to hepatic sinusoids: Sinusoidal obstruction syndrome (Veno-Occlusive Disease). Semin Liver Dis. 2002;22(1):027-42.
14. Alberti N, Bechade D, Dupuis F, Crombe A, Neuville A, Debled M, et al. Hepar lobatum carcinomatosum associated with liver metastases from breast cancer: Report of five cases. Diagn Interv Imaging. 2015;96(1):73-8.
15. Sass DA, Clark K, Grzybicki D, Rabinovitz M, Shaw-Stiffel TA. Diffuse desmoplastic metastatic breast cancer simulating cirrhosis with severe portal hypertension: a case of « pseudocirrhosis ». Dig Dis Sci. 2007;52(3):749-52.
16. Maeda S, Nakagawa H. Roles of E-cadherin in Hepatocarcinogenesis. In: Nakao K, Minato N, Uemoto S, editors. Innovative Medicine: Basic Research and Development. Tokyo: Springer; 2015.
17. Hoshina H, Takei H, Nakamura M, Nishimoto F, Hanamura S. Carcinomatous cirrhosis as radiographically occult liver metastases of breast cancer: A systematic literature review. Cancer Treat Res Commun. 2021;28:100388.
18. Yamamoto M, Ikeda M, Kubo S, Tsukioki T, Nakamoto S. [Liver atrophy and failure associated with paclitaxel and bevacizumab combination therapy for metastatic breast cancer]. Gan to Kagaku Ryoho. 2016;43(7):869-73.
19. Gopalakrishnan D, Shajihan A, Purysko AS, Abraham J. Pseudocirrhosis in breast cancer – experience from an academic cancer center. Front Oncol. 2021;11:679163.
20. Geeroms B, De Hertogh G, Vanslembrouck R, Wildiers H, Nevens F, Maleux G. Transjugular intrahepatic portosystemic shunt for the treatment of portal hypertension-induced refractory ascites due to metastatic carcinomatous liver disease. J Vasc Interv Radiol JVIR. 2018;29(12):1713-6.