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A 57-year-old woman with chronic hepatitis B and left hepatic nodularity unmasking intrahepatic hilar adenocarcinoma: A diagnostic case report

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Case Report

ABSTRACT

Metastatic breast cancer involving the biliary tract is a rare case with an incidence rate of 1.49 per 100.000 persons. Chronic hepatitis B virus (HBV) infection is associated with tumor development and migration and promotes metastasis. While hepatocellular carcinoma is the most common primary liver cancer, cholangiocarcinoma is a rarer malignancy originating from epithelial cells in various parts of the bile ducts. Intraluminal adenocarcinoma of the common hepatic duct (CHD) is an exceptionally uncommon hepatic tumor. We reported that a 57-year-old female has been complaining of abdominal pain on the upper right side for 1 year, accompanied by nausea and icterus. The patient had a history of breast cancer in 1995 and chronic hepatitis B for 20 years on Tenovofir 1x300 mg. No abnormalities were found on physical examination. However, Magnetic Resonance Cholangiopancreatography (MRCP) revealed bilateral dilatation of the intrahepatic bile duct (IHBD), common hepatic duct (CHD), ductus cysticus, and common bile duct (CBD) distal to proximal, suggesting an intraluminal mass likely due to a tumor. A plastic stent was then placed, which reduced the lesion size. Immunohistochemistry (IHC) test confirmed adenocarcinoma, in which CK-7 and mammaglobin were positive, indicating metastatic breast cancer. A thoracic MSCT revealed multiple lytic lesions in the T1, T7, T9–T12, and L2–L3 vertebral bodies. The patient was diagnosed with intraluminal adenocarcinoma of the CHD, representing metastatic Stage I triple-negative breast cancer with biliary, pulmonary, and osseous involvement, along with chronic hepatitis B. The chemotherapy regimen included carboplatin 370 mg and paclitaxel 260 mg, continued with Taceral 500 mg 2x3 in two weeks and Zometa every 6 weeks. Post-chemotherapy MRCP evaluation showed a solid intraluminal liver lobe lesion with partial obstruction. Metastatic adenocarcinoma of the CHD caused by breast cancer is a highly unusual clinical problem. In such cases, IHC plays a vital role in identifying the primary tumor site.

INTRODUCTION

Breast cancer stands as the most prevalent cancer among women worldwide. Thanks to advancements in comprehensive, multi-faceted treatment approaches, patients with early-stage breast cancer have seen significant improvements in their long-term prognosis. For instance, Caucasian women now experience a five-year survival rate of approximately 88.8%. However, metastasis remains a major cause of mortality, accounting for about 30% of breast cancer–related deaths..[1,2] Breast cancer commonly spreads to the skeletal system, pulmonary tissues, hepatic structures, and cerebral regions, while gastric metastasis is rare and requires confirmation through IHC[3] Metastatic involvement in the biliary tract is a rare case with an incidence rate of

1.49 per 100.000 persons. By contrast, hepatocellular carcinoma is a common primary liver cancer. Cholangiocarcinoma is a rare epithelial malignancy of the bile ducts; however, intraluminal adenocarcinoma of the common hepatic duct is an exceptionally uncommon hepatic tumor.[4]

Mammaglobin, a 93–amino acid glycoprotein in the secretoglobin-uteroglobin family, was first identified as a breast cancer–specific marker. This glycoprotein shares structural similarities with other members of its protein family. In the realm of breast cancer diagnostics, the presence of cytokeratin 7 (CK-7) is generally considered a characteristic feature. The vast majority of breast cancer cases exhibit positive CK-7 expression. However, medical literature does include rare instances where breast cancer has been found to lack CK-7 expression. These uncommon CK-7 negative cases represent exceptions to the typical pattern, highlighting the complexity and variability in breast cancer's molecular profile. Most previous studies on CK-7 negative breast malignancies showed metastatic disease from unknown origin tumors or large tissue microarrays with many breast carcinomas.[5–7]

Chronic HBV infection is a pathogenic condition that leads to long-term liver damage, characterized by immune alterations and liver inflammation. As an oncogenic virus, HBV contributes through several mechanisms that support tumor cell growth and migration. First, HBV directly promotes the colonization of the liver by breast cancer cells. It binds to the HBV X-interacting protein (HBXIP), which is expressed in breast cancer. Chronic HBV infection causes immunological tolerance in the liver, fostering the survival of cancer cells. Long-term chronic HBV antigenic stimulation exhausts virus-specific T lymphocytes and impairs their activity. Pathway activation produces regulatory T cells (Treg), which suppress CD4/CD8 T cells by releasing IL-10 and TGF-β. Together, these combinations result in immune tolerance, which allows tumor cells to colonize without immune clearance.[8–10]

Here, we report a rare case of intrahilar hepatic adenocarcinoma in a patient with chronic hepatitis B, who presented with obstructive jaundice. The condition was caused by metastatic breast cancer involving the common hepatic duct, despite a normal physical examination. A comprehensive evaluation of the patient, including medical history, physical examination, laboratory analyses, and histopathological studies, revealed an intraluminal adenocarcinoma within the common hepatic duct, originating from a Stage I triple-negative breast cancer. This primary cancer had metastasized to multiple sites, including the biliary system, lungs, and bones. Additionally, the patient was diagnosed with chronic hepatitis. This case stands out due to its atypical clinical presentation. Metastatic adenocarcinoma in the hepatic duct is an exceptionally rare condtion, often leading to diagnostic delay and treatment challenges. The patient has given informed consent for this publication.

CASE DESCRIPTION

A 57-year-old female came to the gastroenterohepatology outpatient clinic with complaints of abdominal pain on the upper right side for 1 year, accompanied by nausea and jaundice. She had a history of breast cancer in 1995 and chronic hepatitis B for 20 years on Tenovofir 300 mg daily. Physical examination revealed no specific abnormalities. Initial MRCP (Figure 1) showed intra- and extrahepatic biliary obstruction with bilateral IHBD dilatation, involvement of the CHD and cystic duct, and changes extending from the distal to proximal CBD. An intraluminal filling defect suggestive of a mass was observed, with the lesion size decreasing during the study. A plastic stent was placed. Subsequent ERCP (Figure 2) confirmed biliary obstruction due to a CHD mass and a CBD stone, and the plastic stent was replaced with a metallic stent. Histopathological examination of the bile duct tissue confirmed adenocarcinoma. IHC demonstrated CK-7 positivity, CK-20 negativity, mammaglobin positivity, ER negativity, and HER-2 positivity (Figure 3). Based on these findings, the bile duct lesion was concluded to represent metastatic breast carcinoma.

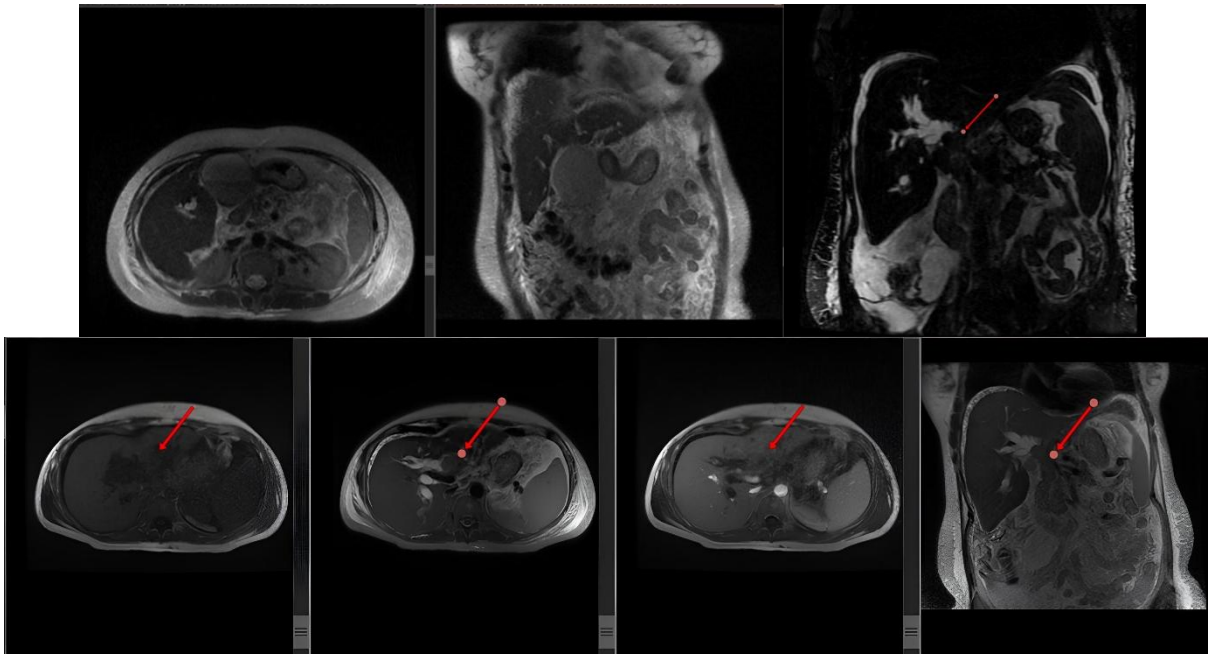

Figure 1. Initial MRCP showing intra- and extrahepatic biliary obstruction with bilateral IHBD dilatation

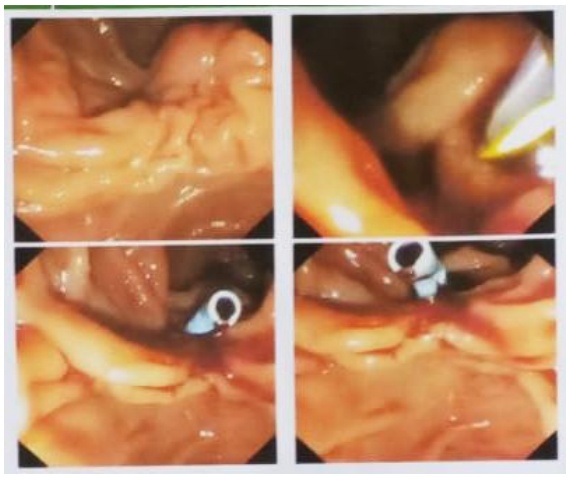

Figure 2. ERCP showing biliary obstruction due to a CHD mass and a blood clot in the CBD.

Bone survey examination revealed no visible bone metastases in the evaluated skeletal system. A biliary stent was also noted projecting from the T12 to L3 vertebral level on the right side (Figure 4). However, thoracic MSCT showed left pleural effusion associated with subpleural pulmonary metastases. Multiple bone metastases were identified as lytic lesions involving the vertebral bodies of T1, T7, T9–T12, and L2–L3. Additional findings included multiple suspicious paraaortic lymphadenopathies and thoracolumbar spondylosis. Incidental findings revealed a borderline solid lesion with irregular margins in the CHD, showing post-contrast enhancement consistent with a mass, along with the presence of a biliary tube terminating in the distal CHD (Figure 5)

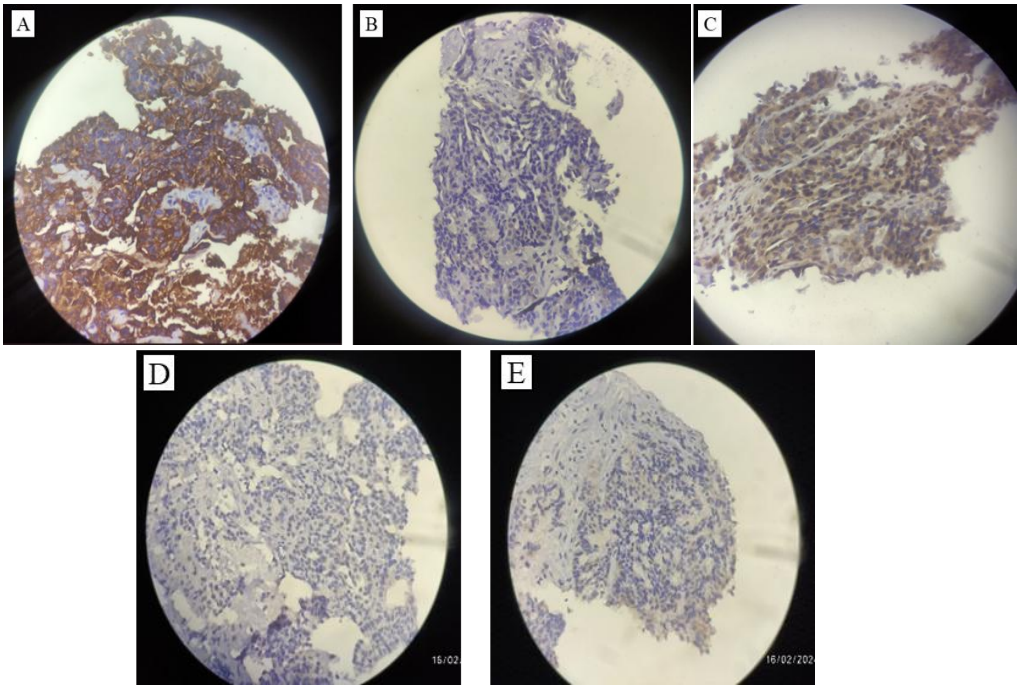

Figure 3. Histopathological IHC showed (A) CK-7 positive, (B) CK-20 negative, (C) mammoglobin positive, (D) ER negative, (E) HER-2 positive.

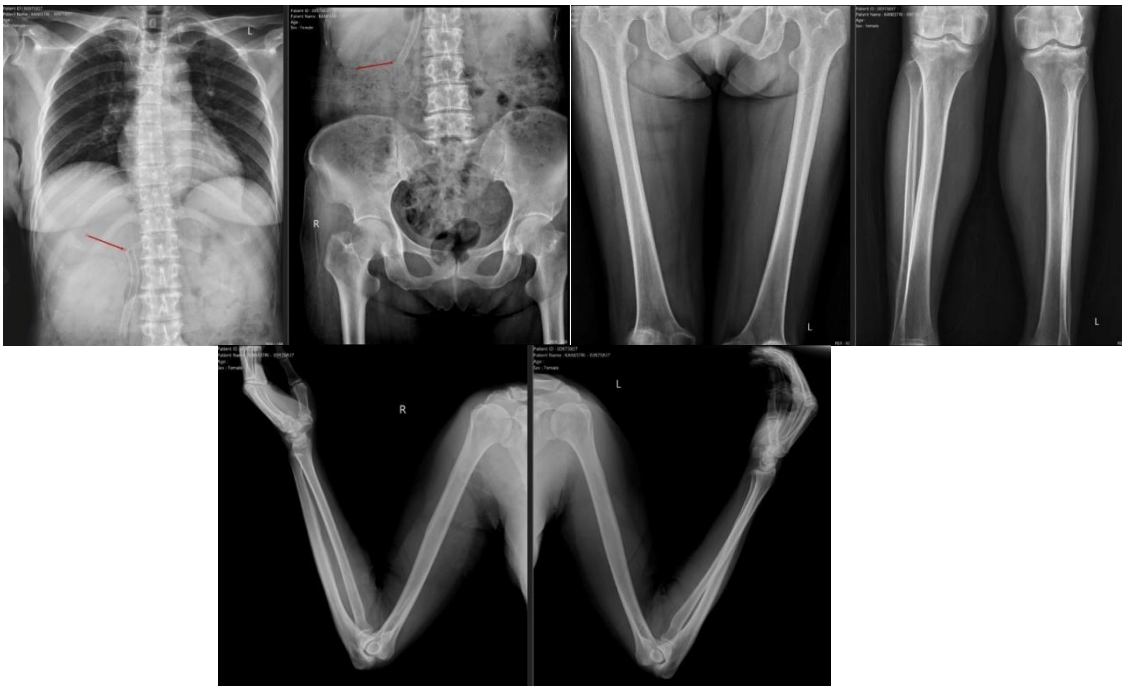

Figure 3. A bone survey showed projection of the biliary stent

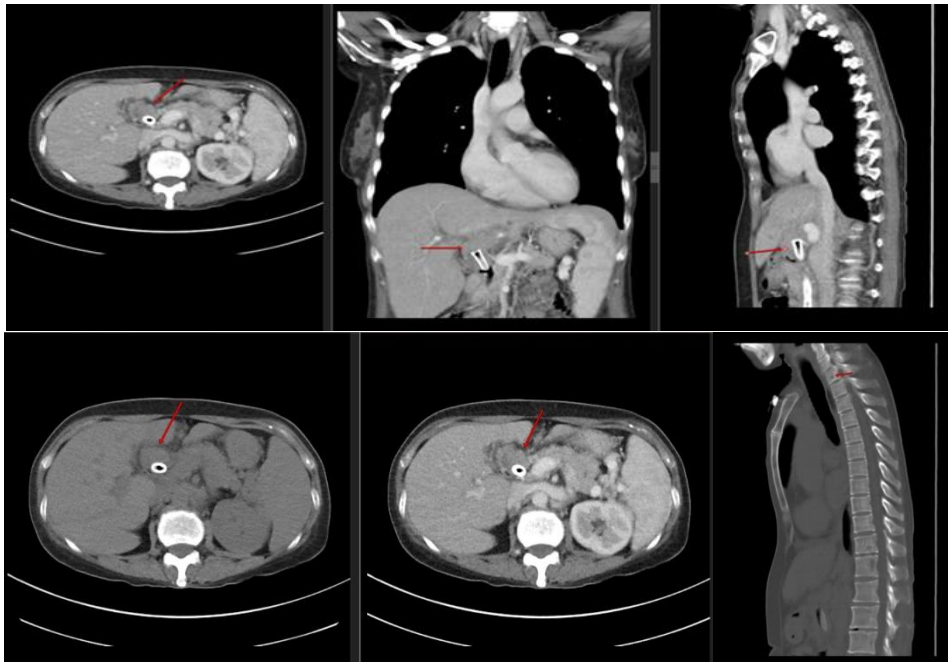

Figure 5. Thoracic MSCT showing multiple lytic bone metastases and a solid lesion with irregular margins in the common hepatic duct.

The patient was diagnosed with intraluminal adenocarcinoma of the CHD, representing metastatic Stage I triple-negative breast cancer with biliary, pulmonary, and osseous involvement, along with chronic hepatitis B. She received six cycles of chemotherapy with Carboplatin 370 mg and Paclitaxel 260 mg, continued with Taceral 500 mg 2x3 in 2 weeks and Zometa every 6 weeks. Post-chemotherapy MRCP evaluation (Figure 6) revealed a solid lesion in hepatic segment I infiltrating the CHD lumen and extending from the proximal to distal CBD. This resulted in partial obstruction at that level and dilatation of the proximal, medial, and distal CBD, cystic duct, CHD, right IHBD, and gallbladder hydrops, suggesting a metastatic process. Hepatosplenomegaly was also noted.

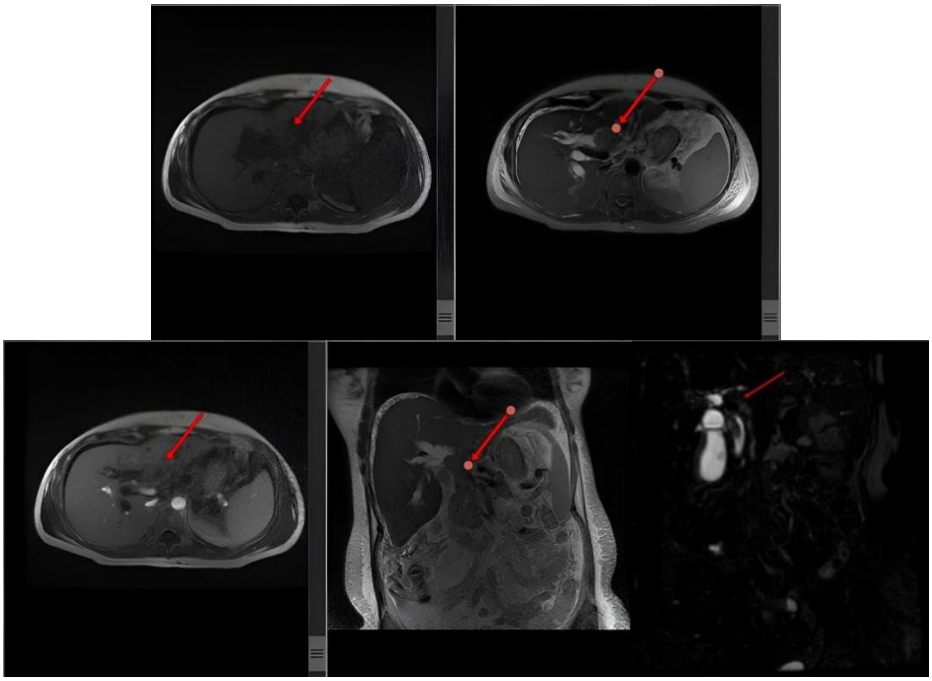

Figure 4. MRCP abdomen showed a solid intraluminal liver lobe lesion with partial obstruction.

DISCUSSION

Breast cancer frequently metastasizes to the liver, ranking it as the third most common site after bone and lung. The prognosis for patients with liver metastases is generally poor, with a median survival of about four months and a very low five-year survival rate. However, a small subset of patients with breast cancer (approximately 5%) present with isolated liver metastases that are amenable to surgical intervention. For these carefully selected individuals, complete resection of the metastatic lesion (margin-negative hepatectomy) is safe and can provide benefits beyond standard chemotherapy alone.[11]

Patients with breast cancer liver metastases (BCLM) often experience decreased hepatic function as the tumor burden increases, which poses a risk to cancer patients' lives. Without treatment, the survival rate is limited to 4–8 months. Current treatment options include chemotherapy, immunotherapy, targeted systemic therapies—such as endocrine therapy for luminal subtypes and HER2-directed therapy for HER2-enriched disease—radiotherapy, and palliative measures. However, patients with BCLM frequently have high mortality rates and limited response to current therapy.[12]

The mechanisms underlying each stage of the metastasis are complex and remain only partially understood. However, recent developed engineered models have clarified some important aspects of the metastatic cascade which involves six key steps: (a) Invasion of the basement membrane and cell migration and; (b) intravasation into vasculature or the surrounding lymphatic system; (c) survival in the circulation; (d) extravasation from the vasculature into the secondary tissues; (e) further proliferation at distant sites; and (f) colonization of secondary tumor sites. A critical cellular remodeling process event during the first local invasion is the epithelial-to-mesenchymal transition. In this process, the basement membrane breaks apart, and the epithelial cells lose their polarized orientation during this transition. The cells then migrate, become invasive, and ultimately transform into highly migratory mesenchymal cells. These actions promote metastatic expansion for distant site proliferation during the reversal process, or the mesenchymal-to-epithelial transition.[13,14]

For this patient, treatment included a chemotherapy regimen of Carboplatin 370 mg and Paclitaxel 260 mg for six cycles. Carboplatin is a common chemotherapy drug for solid malignant tumors, which is used to treat breast cancer and other malignant tumors.. When used in conjunction with chemotherapy, carboplatin can enhance the immune response and offer specific therapeutic advantages to patients with early-stage breast cancer who test positive for HER-2. One taxane that has anticancer efficacy is docetaxel, which can cause cell cycle stalling in G2/M, which can lead to cytotoxicity and apoptosis. In current medical practice, docetaxel plays a significant role as a component of initial combination therapy for individuals diagnosed with metastatic breast cancer. These drug, along with two others (not specified in the given text), forms a treatment protocol that has demonstrated favorable outcomes in managing both early-stage and advanced breast cancer cases. Clinical experience with this three-drug regimen has shown promising results. Patients generally tolerate the treatment well, and it has demonstrated a robust safety profile. Importantly, long-term follow-up has not revealed any significant lasting toxic effects. These characteristics make this combination therapy an attractive option for oncologists treating breast cancer patients across various stages of the disease.[15] The patient was also given a regimen of Zometa (zoledronic acid) for 6 weeks and Taceral (capecitabine) 500mg in a dose of 3x2 tablets.

Diagnosing metastatic adenocarcinoma of the biliary tract is challenging, requiring a meticulous approach to differentiate it from primary hepatobiliary malignancies. A comprehensive workup is essential, beginning with a detailed patient history, including prior breast cancer and chronic HBV infection, which can raise clinical suspicion for metastasis.[8]Imaging modalities such as MRCP and MSCT are crucial to identify the location and extent of the tumor within the biliary system.[11] Ultimately, histopathology and IHC are indispensable to confirm the diagnosis and pinpoint the primary tumor site. In this case, IHC results (CK-7+, Mammaglobin+) definitively established the origin as metastatic breast cancer.[6]

In cases of metastatic adenocarcinoma to the CHD, identifying the primary tumor site is

crucial, making IHC an indispensable tool for pathologists. As the case report emphasizes, 'Pathologists are routinely asked to identify the major tumor site, and IHC must be informative'. In this case, IHC findings of CK-7 and Mammaglobin positivity were pivotal in confirming the diagnosis of metastatic breast cancer. The diagnostic value of these markers is well supported in the literature, underscoring the importance of IHC in establishing tumor origin and guiding appropriate treatment planning.[6]

The treatment regimen for this case of metastatic breast cancer to the CHD included a combination of Carboplatin, Paclitaxel, Taceral, and Zometa. This combination reflects current evidence-based practices in managing advanced breast cancer with potential bone involvement. Carboplatin and Paclitaxel are well-established chemotherapy agents for metastatic breast cancer, while Zometa is used to prevent skeletal-related complications in patients with bone metastases.[16–20]

Bisphosphonates are widely used to manage tumor-related osteolysis by inhibiting osteoclastic bone resorption and reducing tumor cell adhesion to the bone matrix. Among them, zoledronic acid (zoledronate, Zometa), a third-generation bisphosphonate, is approved in adults with solid tumors. It has the strongest anti-resorptive activity in its class, reduces the incidence of skeletal-related events, and has also been reported to exert anti-tumor effects by inhibiting cancer cell migration. Potential adverse effects include hypocalcemia, hypophosphatemia, bone fractures, flu-like syndrome, and ototoxicity. However, there were no orthopedic-related complications, except in female patients and patients over 40 years of age.. Additionally, zoledronate improves wound healing.[16,20]

Taceral, a targeted therapy containing capecitabine, was included in this patient's regimen based on the tumor profile. Despite these interventions, the prognosis for BCLM remains poor, with untreated BCLM having a median survival duration of approximately 4-6 months, highlighting the aggressive nature of this condition and the urgent need for effective treatment strategies.[18,21] Capecitabine, an oral pyrimidine analogue, is frequently used in conjunction with other medications to treat metastatic and advanced breast and colorectal cancers. While generally well tolerated, it may cause transient elevations in aminotransferases and, rarely, clinically apparent acute liver injury. Studies have shown that capecitabine is effective both as monotherapy and in combination regimens. In particular, when combined with taxanes, it has demonstrated a feasible, well-tolerated, and effective approach for managing breast cancer, including in early-stage disease.[17]

CONCLUSION

Metastatic adenocarcinoma of the CHD secondary to breast cancer is a rare clinical problem. In such cases, IHC is an indispensable tool for pathologists in identifying the primary tumor site.

CONFLICT OF INTEREST

The authors of this study affirm that they have no conflicts of interest that could influence the content or conclusions presented. Additionally, the patient involved in this case report has provided informed consent for the publication of their medical information, with the understanding that their personal details will remain confidential to protect their privacy.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are not publicly available due to the inclusion of sensitive patient information and examination results that are subject to privacy and confidentiality restrictions. Access to the data may be granted by the corresponding author upon reasonable request, subject to institutional and ethical approval, and in compliance with applicable data protection regulations.

SUPPLEMENTARY MATERIAL(S)

There are no supplementary material in this paper

AUTHORS CONTRIBUTIONS

TAG, TYP performs in observing, researching, and compiling manuscripts. AD, DP, AJ provided input in therapy for patient comorbidities. BW carries out histopathological examinations according to his field.

DECLARATION OF USING AI IN THE WRITING PROCESS

This manuscript was prepared entirely by the authors without the use of artificial intelligence (AI) tools for writing, editing, or data analysis

LIST OF ABBREVIATIONS

BCLM : Breast cancer liver metastases, HBV : Hepatitis B Virus, IHBD : Intrahepatic bile duct , CHD : Common Hepatic Duct, CBD : Common Bile Duct , VTh : Vertebrae Thoracal, MRCP : Magnetic Resonance Cholangiopancreatography, MSCT : Multislice Computerized Tomography, IHC : Immunohistochemistry, CK : Cytokeratin, HBXIP : HBV X-interacting protein

REFERENCES

1. Łukasiewicz S, Czeczelewski M, Forma A, Baj J, Sitarz R, Stanislawek A. Breast Cancer-Epidemiology, Risk Factors, Classification, Prognostic Markers, and Current Treatment Strategies-An Updated Review. Cancers (Basel). 2021;13(17):4287. DOI: 10.3390/cancers13174287.
2. Kosmidis C, Varsamis N, Anthimidis G, Baka S, Valoukas D, Koletsa T, et al. Primary hepatocellular carcinoma in a patient with history of treated breast cancer: A case report with challenging diagnosis and treatment. Int J Gen Med. 2018;11:399-403. DOI: 10.2147/IJGM.S176052.
3. Rodrigues MV, Tercioti-Junior V, Lopes LR, Coelho-Neto JDS, Andreollo NA. Breast cancer metastasis in the stomach: When the gastrectomy is indicated? Arq Bras Cir Dig. 2016;29(2):86-9. DOI: 10.1590/0102-6720201600020005.
4. Bruix J, Ayuso C. Diagnosis of hepatic nodules in patients at risk for hepatocellular carcinoma: LI-RADS probability versus certainty. Gastroenterology. 2019;156(4):860-862. DOI: 10.1053/j.gastro.2019.02.008.
5. Moatamed NA, Wu A, Sarah K, Apple SK. Cytokeratin 7 negative invasive breast carcinoma: Clinicopathological and immunohistochemical analysis of 14 cases with clinical follow-up. J Clin Pathol. 2015;68(6):484-7. DOI: 10.1136/jclinpath-2014-202729. Erratum in: J Clin Pathol. 2015;68(7):e2. DOI: 10.1136/jclinpath-2014-202729corr1.
6. Milosevic B, Stojanovic B, Cvetkovic A, Jovanovic I, Spasic M, Stojanovic MD, et al. The enigma of mammaglobin: Redefining the biomarker paradigm in breast carcinoma. International Journal of Molecular Sciences. 2023; 24(17):13407. DOI: 10.3390/ijms241713407
7. Wang Z, Spaulding B, Sienko A, Liang Y, Li H, Nielsen G, et al. Mammaglobin, a valuable diagnostic marker for metastatic breast carcinoma. Int J Clin Exp Pathol. 2009;2(4):384-9.
8. Yu P, Liu P, Li N, Xie X, Tang H, Wu J, et al. Hepatitis B virus infection specially increases risk of liver metastasis in breast cancer patients: a propensity-matched analysis. Transl Cancer Res. 2020;9(3):1506-1517. DOI: 10.21037/tcr.2020.01.63.
9. Zha Y, Yao Q, Liu JS, Wang YY, Sun WM. Hepatitis B virus X protein promotes epithelial-

mesenchymal transition and metastasis in hepatocellular carcinoma cell line HCCLM3 by targeting HMGA2. Oncol Lett. 2018;16(5):5709-5714. DOI: 10.3892/ol.2018.9359.
10. Lin N, Yin W, Miller H, Byazrova MG, Herrada AA, Benlagha K, et al. The role of regulatory T cells and follicular T helper cells in HBV infection. Front Immunol. 2023;14:1169601. DOI: 10.3389/fimmu.2023.1169601.
11. Ozaki K, Higuchi S, Kimura H, Gabata T. Liver metastases: Correlation between imaging features and pathomolecular environments. Radiographics. 2022;42(7):1994-2013. DOI: 10.1148/rg.220056.
12. Lian D, Chen MM, Wu H, Deng S, Hu X. The Role of oxidative stress in skeletal muscle myogenesis and muscle disease. Antioxidants (Basel). 2022;11(4):755. DOI: 10.3390/antiox11040755.
13. Zuo Q, Park NH, Lee JK, Erdogan ZM. Liver metastatic breast cancer: Epidemiology, dietary interventions, and related metabolism. Nutrients. 2022;14(12):2376. DOI: 10.3390/nu14122376.
14. Rashid NS, Grible JM, Clevenger CV, Harrell JC. Breast cancer liver metastasis: current and future treatment approaches. Clin Exp Metastasis. 2021; 263-277. DOI: 10.1007/s10585-021-10080-4.
15. Wu D, Xiong L. Efficacy analysis of trastuzumab, carboplatin and docetaxel in HER-2-positive breast cancer patients. Oncol Lett. 2020;19(3):2539-2546. DOI: 10.3892/ol.2020.11277.
16. Li S, Chen P, Pei Y, Zheng K, Wang W, Qiu E, et al. Addition of zoledronate to chemotherapy in patients with osteosarcoma treated with limb-sparing surgery: A phase III clinical trial. Med Sci Monit. 2019 ;25:1429-1438. DOI: 10.12659/MSM.913236.
17. Xu D, Chen X, Li X, Mao Z, Tang W, Zhang W, et al. Addition of capecitabine in breast cancer first-line chemotherapy improves survival of breast cancer patients. J Cancer. 2019;10(2):418-429. DOI: 10.7150/jca.29739.
18. O'Carrigan B, Wong MH, Willson ML, Stockler MR, Pavlakis N, Goodwin A. Bisphosphonates and other bone agents for breast cancer. Cochrane Database Syst Rev. 2017;10(10):CD003474. DOI: 10.1002/14651858.CD003474.pub4.
19. Wang Q, Yu Q, Zeng P, Ai W. Efficacy and safety of annual infusion of zoledronic acid and weekly oral alendronate in the treatment of primary osteoporosis: A meta-analysis. J Clin Pharmacol. 2023;63(4):455-465. DOI: 10.1002/jcph.2181.
20. Stopeck AT, Lipton A, Body JJ, Steger GG, Tonkin K, de Boer RH, et al. Denosumab compared with zoledronic acid for the treatment of bone metastases in patients with advanced breast cancer: a randomized, double-blind study. J Clin Oncol. 2010;28(35):5132-9. DOI: 10.1200/JCO.2010.29.7101.
21. Leone BA, Vallejo CT, Romero AO, Machiavelli MR, Pérez JE, Leone J, et al. Prognostic impact of metastatic pattern in stage IV breast cancer at initial diagnosis. Breast Cancer Res Treat. 2017;161(3):537-548. DOI: 10.1007/s10549-016-4066-7.