pISSN 2287-2728
eISSN 2287-285X

CMH

http://dx.doi.org/10.3350/cmh.2013.19.2.190
Clinical and Molecular Hepatology 2013;19:190-194

Liver Imaging

Pseudocirrhosis as a complication after chemotherapy for hepatic metastasis from breast cancer

Woo Kyoung Jeong[1], Seo-Youn Choi[1], and Jinoo Kim[2]

[1]Department of Radiology and Center for Imaging Science, Samsung Medical Center, Sungkyunkwan University Schoold of Medicine, Seoul, Korea; [2]Department of Radiology, Hanyang University Guri Hospital, Hanyang Univeristy College of Medicine, Gyeonggi-do, Korea

Keywords: Breast cancer; Metastasis; Chemotherapy; Pseudocirrhosis; Nodular regenerative hyperplasia

INTRODUCTION

Pseudocirrhosis is a radiologic term that describes the serial development of diffuse hepatic nodularity caused by chemotherapy for hepatic metastasis, especially from breast cancer.[1,2] It is characterized by morphologic changes mimicking liver cirrhosis following chronic liver diseases, such as multifocal capsular retraction and enlargement of the caudate lobe, and is a potential cause of portal hypertension and hepatic failure.[2,3] However, the patients with pseudocirrhosis do not unusually show the clinical features of true cirrhosis.[1] In this article, we present two cases demonstrating the radiologic features of pseudocirrhosis following chemotherapy for metastatic breast cancer.

CASE

Case 1

A 53 year-old woman visited the emergency department at our institution complaining of back pain. On physical examination, a palpable mass in the right breast was found. There were also signs of jaundice, abdominal distension, and hepatomegaly. After further examination including abdominal CT and breast ultrasonography, she was diagnosed to have multiple liver and bone metastases from breast cancer. The breast mass was proven to be an invasive ductal adenocarcinoma by biopsy. Initial abdominal CT scan showed hepatomegaly and decreased attenuation of the liver parenchyma as well as multiple hepatic metastases in both lobes. The contour of the liver was mildly lobulated and a small amount of ascites was also noted in the perihepatic space. In addition, thrombosis of bilateral intrahepatic portal veins was also seen (Fig. 1A). The patient was treated for her malignancy by combined chemotherapy using paclitaxel and trastuzumab for palliation. Blood chemistry revealed the following findings; hemoglobin, 15.0 g/dL; leukocyte count, 11,500/mm^3; platelet count, 214,000/mm^3; total protein, 5.8 g/dL; albumin 3.1 g/dL; total bilirubin 4.3 mg/dL; aspartate aminotransferase (AST), 82 IU/L; alanine aminotransferase (ALT), 385 IU/L; alkaline phosphatase (ALP), 600 IU/L; gamma-glutamyl transpeptidase (GGT), 1,152 IU/mL. Immunologic tests showed no evidence of hepatitis B or C viral infection. Assessment of her tumor markers revealed carcinoembryonic antigen (CEA) to be 680.82 ng/mL and serum carbohydrate associated antigen (CA) 19-9 to be 17,960 U/mL (normal range, 0-37 U/mL).

Abbreviations:

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CA, carbohydrate associated antigen; CEA, carcinoembryogenic antigen; GGT, gamma-glutamyl transpeptidase; INR, international normalized ratio; NRH, nodular regenerative hyperplasia

Corresponding author : Woo Kyoung Jeong
Department of Radiology and Center for Imaging Science, Samsung Medical Center, Sungkyunkwan University Schoold of Medicine, 50 Irwon-dong, Gangnam-gu, Seoul 135-710, Korea
Tel. +82-2+3410-1923, Fax. +82-2-3410-0049
E-mail; jeongwk@gmail.com

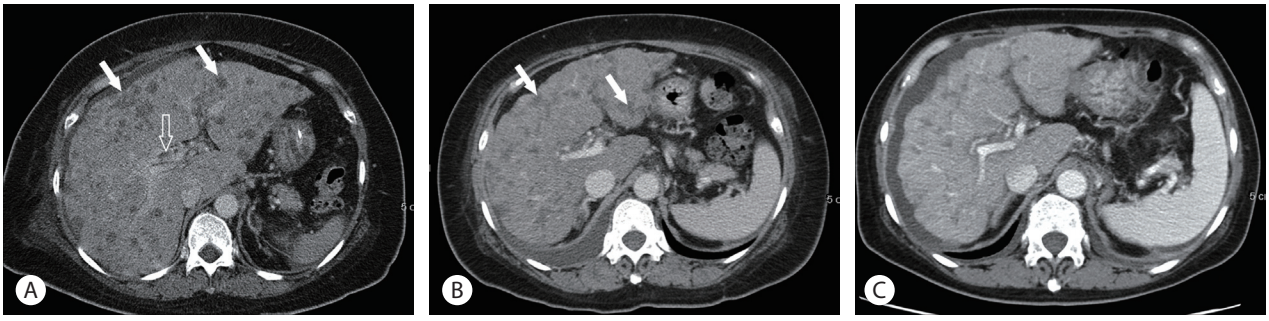

Figure 1. A 53-year-old woman with hepatic metastasis from right breast cancer. (A) An initial CT scan shows multiple metastatic nodules in the whole liver (arrows). Hepatomegaly is also noted, and the parenchymal attenuation is somewhat decreased. Small thrombus (open arrow) in the right portal vein is seen. (B) One and half month later, follow-up CT scan shows that metastatic nodules are coalesced and less prominent (arrows). The volume of liver is decreased, and capsular retraction is more prominent. The thrombus in the portal vein disappears. (C) Seven months later, the last follow-up CT scan shows that the volume loss and capsular retraction of the liver is more and more prominent. Ascitic fluid around perihepatic space and splenomegaly are newly developed, and suggests the signs of portal hypertension.

After six cycles of chemotherapy, a follow-up CT scan was performed. It showed decreased hepatic volume and enlargement of the caudate lobe. The metastatic lesions in the liver either decreased in size or coalesced with one another and portal vein thrombosis was seen to resolve. The hepatic surface also became more lobulated (Fig. 1B). The results of a follow-up of the blood chemistry was as follows: hemoglobin, 9.4 g/dL; leukocyte count, 8,100/mm^3; platelet count, 146,000/mm^3; total protein, 4.4 g/dL; albumin 2.7 g/dL; total bilirubin 1.5 mg/dL; AST, 43 IU/L; ALT, 14 IU/L; ALP, 180 IU/L; GGT, 98 IU/mL; prothrombin time of 87% and international normalized ratio (INR), 1.09. CEA level had decreased to 6.10 ng/mL. However, a metastatic lesion was subsequently discovered in the cerebellum for which she underwent radiation therapy and palliative chemotherapy consisting of doxorubicin and cyclophosphamide. On the follow-up CT performed after 7 months, shrinkage of liver volume and surface nodularity were more prominent. The amount of perihepatic ascites also increased compared with the previous CT scan (Fig. 1C).

Finally, she expired due to multi-organ failure and worsening metastasis 17 months after initial hospitalization.

Case 2

A 25 year-old woman was diagnosed with invasive ductal adenocarcinoma of the left breast (stage T3N2M0). She was initially treated with neoadjuvant chemotherapy using doxorubicin and cyclophosphamide and received left modified radical mastectomy. She underwent four cycles of adjuvant chemotherapy using the same regimens, and followed by radiation therapy combined with chemotherapy using paclitaxel and hormonal therapy using tamoxifen. After 24 months, the patient developed multiple hepatic lesions that had metastasized from the breast cancer. Blood chemistry revealed the following findings at the time; hemoglobin, 10.9 g/dL; leukocyte count, 3,110/mm^3; platelet count, 227,000/mm^3; total protein, 8.2 g/dL; albumin 4.3 g/dL; total bilirubin 0.9 mg/dL; AST, 110 IU/L; ALT, 64 IU/L; ALP, 127 IU/L. Tumor analysis revealed a CA15-3 level of 206 U/mL (normal range, 0-28 U/mL). She was immunologically negative for hepatitis B and C viral infection. Combined chemotherapy using docetaxel and cisplatin was initiated. A follow-up CT performed after 2 months revealed the development of hepatomegaly and decreased parenchymal attenuation of the liver suggesting fatty infiltration. Some metastatic lesions in the liver coalesced while others decreased (Fig. 2B). A follow-up of the blood chemistry revealed the following: hemoglobin, 8.5 g/dL; leukocyte count, 530/mm^3; platelet count, 50,000/mm^3; total protein, 5.1 g/dL; albumin 2.7 g/dL; total bilirubin 2.4 mg/dL; AST, 233 IU/L; ALT, 74 IU/L; ALP, 476 IU/L. CA15-3 had increased to 560 U/mL. CT performed after 5 months showed that the liver volume had decreased, while hypertrophy of the left liver was noted. In addition, the hepatic surface had become more lobulated (Fig. 2C). On the final follow-up CT performed after 9 months, the shrinkage of the liver was more prominent and perihepatic ascites had developed (Fig. 2D). Follow-up blood chemistry showed that the total bilirubin level and hepatic enzymes had decreased (total bilirubin, 1.2 mg/dL; AST, 93 IU/L; ALT, 66 IU/L), and that CA15-3 had also decreased to 140 U/mL. Thereafter, fulminant hepatic failure developed at which time her serum bilirubin level increased to 32.3 mg/dL. She expired a year after initial detection of hepatic metastasis.

 http://dx.doi.org/10.3350/cmh.2013.19.2.190

CMH
Clin Mol Hepatol
Volume 19 Number 2 June 2013

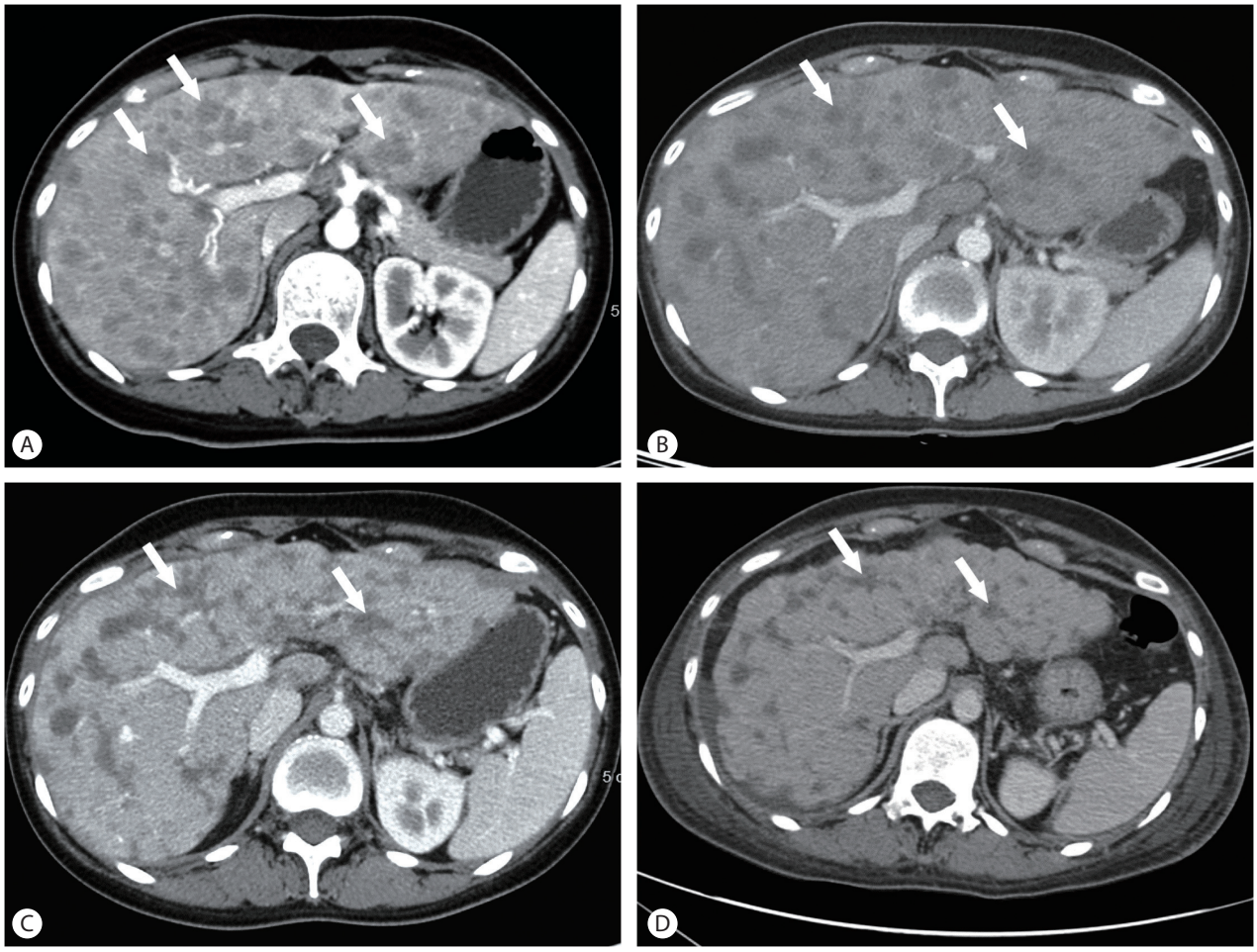

Figure 2. A 25-year-old woman with multiple hepatic metastases from left breast cancer. (A) On the initial CT scan, numerous metastases (arrows) scattered in the whole liver are noted, and neither decreased volume nor capsular retraction of the liver is seen. (B) Two months later, the metastases are decreased and coalesced (arrows). The liver volume is increased, and the contour of the liver becomes lobulated. The parenchymal attenuation is decreased due to fatty change. (C) On 5 months from the initial CT, the follow-up CT shows geographic lesions around coalesced metastatic lesions are developed. Decreased hepatic volume and capsular retraction are noted. (D) On the last follow-up after 9 months, the shrinkage of the liver is more prominent and perihepatic ascites is developed.

DISCUSSION

Pseudocirrhosis refers to the morphologic changes of the liver resembling features of macronodular cirrhosis on imaging studies including features such as capsular retraction, decreased hepatic volume and caudate lobe enlargement after chemotherapeutic treatment of hepatic metastasis.[4,5] Most of the cases reported in the literature were found in patients with metastatic breast cancer, but occasionally some cases were associated with pancreatic cancer, thyroid cancer, and gastrointestinal cancer including esophageal cancer.[4,6,7]

The pathogenesis of pseudocirrhosis associated with chemotherapy is still unclear, but a theory has been previously proposed that pseudocirrhosis may be related to nodular regenerative hyperplasia (NRH) caused by chemotherapy-induced hepatic injury. It is thought to be attributed to ischemic atrophy with secondary nodular hyperplasia in regions with favorable blood flow.[8] According to a report which investigated the pathologic findings of pseudocirrhosis, most of the cases demonstrated histologic features of NRH. NRH is characterized by widespread transformation of normal liver parenchyma into hyperplastic regenerative nodules without bridging fibrosis, a feature that distinguishes this entity from liver cirrhosis. However, NRH can also develop portal hypertension. Bissonnete et al studied the results from the measurement of the pressure gradients between the hepatic and portal veins for NRH patients with symptomatic portal hypertension, and they

http://dx.doi.org/10.3350/cmh.2013.19.2.190

suggested that the mechanism of portal hypertension was associated with portal venopathy and compression of sinusoids by the regenerative nodules.[9] There were also suggestions that it was associated with venoocclusive disease involving small hepatic veins or terminal branches of portal veins.[10] Various chemotherapeutic agents have been associated with the formation of NRH.[9,11,12] Oxaliplatin is a well-known causative drug for the development of NRH, and is known to induce vascular injury such as sinusoidal ballooning, microvascular injury, formation of NRH, and long-term fibrosis. Furthermore, paclitaxel, capecitabine, doxorubicin, and trastuzumab are also known to be causative chemotherapeutic agents.

The radiographic features of pseudocirrhosis are similar to liver cirrhosis: nodularity of the liver contour with capsular retraction, decreased size of the liver, confluent fibrosis, and enlargement of the caudate lobe. The signs of portal hypertension such as ascites, splenomegaly, and varices may be also seen. Qayyum et al said that about 75% of the patients with breast cancer with metastases to the liver receiving chemotherapy demonstrated various degrees of hepatic contour abnormalities from limited retraction to diffuse nodularity, and that about 9% of these patients developed portal hypertension.[2] They also stated that such morphologic change was seen after a median follow-up interval of 15 months. Because pseudocirrhosis progresses rapidly compared with 'true' liver cirrhosis, it is not difficult to detect serial changes of the liver morphology on imaging studies. At first, the initial CT shows a smooth hepatic surface with metastases which focally bulge out. With time, capsular retraction and confluent fibrosis become prominent, after which the metastatic foci seen as low attenuated lesions initially shade off.

There are several other conditions other than pseudocirrhosis that mimic the radiological features of liver cirrhosis.[1] Miliary metastases can present with diffuse surface nodularity. According to a study which evaluated the sonographic features of hepatic metastasis, surface irregularity was observed in 7%. Sarcoidosis can also mimic liver cirrhosis on imaging with diffuse granular heterogeneity and fine surface nodularity.[13]

In both cases presented in this article, serial CT imaging showed typical features of pseudocirrhosis described above: decreased liver volume, lobular margins, diffuse heterogeneity associated with confluent fibrosis, and caudate lobe enlargement without focal lesions. Serial review of the clinical features of the two cases herein disclosed several radiologic and laboratory signs of hepatic injury that eventually led to the development of pseudocirrhosis. Hepatomegaly and diffuse fatty change of the liver parenchyma were initially seen, followed by a reduction in the hepatic volume along with capsular retraction while the attenuation of liver parenchyma normalized. The laboratory results revealed an initial decrease in the serum levels of hepatic enzymes which normalized or increase slightly around the time when pseudocirrhosis developed. Tumor markers did not increase during the period of pseudocirrhosis, indicating that progression of metastasis was unlikely. The second case in which the patient died from rapid progression of hepatic failure rather than from tumor progression reflects the clinical significance of pseudocirrhosis, an entity that deserves as much recognition as the underlying malignancy.

In conclusion, hepatic pseudocirrhosis following chemotherapy for hepatic metastasis associated with breast cancer is a rare but significant complication. Despite its name, 'pseudocirrhosis', its clinical significance is equivalent to that of 'true' liver cirrhosis.

SUMMARY

Pseudocirrhosis is a radiologic term to describe the development of diffuse hepatic nodularity caused by chemotherapy for hepatic metastasis, especially from breast cancer. It is characterized by morphologic changes mimicking liver cirrhosis following chronic liver diseases. Despite its name, 'pseudocirrhosis', its clinical significance is equivalent to that of 'true' liver cirrhosis. The morphologic changes on sequential radiologic imaging studies are characteristic and early recognition of these features potentially allows appropriate, timely management.

Conflicts of Interest

The authors have no conflicts to disclose.

REFERENCES

1. Jha P, Poder L, Wang ZJ, Westphalen AC, Yeh BM, Coakley FV. Radiologic mimics of cirrhosis. AJR Am J Roentgenol 2010;194:993-999.
2. Qayyum A, Lee GK, Yeh BM, Allen JN, Venook AP, Coakley FV. Frequency of hepatic contour abnormalities and signs of portal hypertension at CT in patients receiving chemotherapy for breast cancer metastatic to the liver. Clin Imaging 2007;31:6-10.
3. Sonnenblick A, Appelbaum L, Peretz T. Liver failure on the background of pseudocirrhosis in patients with liver metastasis from breast cancer, who responded to treatment. Onkologie

2011;34:199-201.
4. Kang SP, Taddei T, McLennan B, Lacy J. Pseudocirrhosis in a pancreatic cancer patient with liver metastases: a case report of complete resolution of pseudocirrhosis with an early recognition and management. World J Gastroenterol 2008;14:1622-1624.
5. Young ST, Paulson EK, Washington K, Gulliver DJ, Vredenburgh JJ, Baker ME. CT of the liver in patients with metastatic breast carcinoma treated by chemotherapy: findings simulating cirrhosis. AJR Am J Roentgenol 1994;163:1385-1388.
6. Harry BL, Smith ML, Burton JR Jr, Dasari A, Eckhardt SG, Diamond JR. Medullary thyroid cancer and pseudocirrhosis: case report and literature review. Curr Oncol 2012;19:e36-e41.
7. Kobashigawa C, Nakamoto M, Hokama A, Hirata T, Kinjo F, Fujita J. Pseudocirrhosis in metastatic esophageal cancer. South Med J 2010;103:488-489.
8. Wanless IR. Micronodular transformation (nodular regenerative hyperplasia) of the liver: a report of 64 cases among 2,500 autopsies and a new classification of benign hepatocellular nodules. Hepatology 1990;11:787-797.
9. Bissonnette J, Généreux A, Côté J, Nguyen B, Perreault P, Bouchard L, et al. Hepatic hemodynamics in 24 patients with nodular regenerative hyperplasia and symptomatic portal hypertension. J Gastroenterol Hepatol 2012;27:1336-1340.
10. Liu CH, Chao TY. Education and imaging. Hepatobiliary and pancreatic: Pseudocirrhosis after chemotherapy. J Gastroenterol Hepatol 2011;26:788.
11. Rosen AA, Iseri O, Fishbein G, Knodell RG. Nodular regenerative hyperplasia: a cause of ascites and hepatomegaly after chemotherapy for leukemia. Am J Gastroenterol 1991;86:86-88.
12. Wicherts DA, de Haas RJ, Sebagh M, Ciacio O, Levi F, Paule B, et al. Regenerative nodular hyperplasia of the liver related to chemotherapy: impact on outcome of liver surgery for colorectal metastases. Ann Surg Oncol 2011;18:659-669.
13. Scott GC, Berman JM, Higgins JL Jr. CT patterns of nodular hepatic and splenic sarcoidosis: a review of the literature. J Comput Assist Tomogr 1997;21:369-372.

http://dx.doi.org/10.3350/cmh.2013.19.2.190