JURNAL KEDOKTERAN DIPONEGORO
(*DIPONEGORO MEDICAL JOURNAL*)
Online http://ejournal3.undip.ac.id/index.php/medico
E-ISSN : 2540-8844
DOI : http://10.14710/jkd (dmj).v12i2.36748
JKD (DMJ), Volume 12, Number 2, March 2023 : 80-84

CASE REPORT : NON-CIRRHOTIC HEPATOMA BCLC-C WITH VERTEBRAE METASTASIS

Bonfilio Neltio Ariobimo*[1], Nurun Nujum[1], Daniel Ponco Harto Saputro[2]
[1]General Practitioner, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia
[2]General Surgeon, Surgery Department, St.Vincentius a Paulo Catholic Hospital, Surabaya, Indonesia
*Corresponding Author : E-mail: neltioario@gmail.com

ABSTRACT

Background: Hepatocellular carcinoma (HCC) can arise from either cirrhosis or non-cirrhosis of the liver. HCC in non-cirrhotic livers is still uncommon and can present insidiously in patients. HCC may develop in people with non-cirrhotic chronic liver illness, such as chronic hepatitis B virus infection and chronic HCV infection. More than half of non-cirrhotic individuals with HCC may not exhibit any symptoms, and the disease is frequently detected when it is advanced and incurable. **Case Report:** Here we presented a 47-year-old man went to the emergency room complaining of upper right side abdominal discomfort that suddenly arose and spread to the back and right shoulder. He also experiencing upper right abdominal fullness for the past two months, along with a sense of a lump growing larger and harder. Hepatic stigmata were not discovered, whole blood revealed a thrombocytosis and significant rising AFP from the expected result of 71,000 ng/dL, with hepatitis B testing was positive. Abdominal ultrasound revealed hepatomegaly and several hypo-hyperechoic nodules. CT scan revealed multiple solid lesions and lytic lesions of the vertebrae bodies. The patient recieved palliative treatment.. **Conclusion:** This case study demonstrates a non-cirrhotic hepatoma that came at an80 tan advanced stage and was more likely to be asymptomatic than a cirrhotic hepatoma that showed signs of liver failure, such as hepatic stigmata and other physiologic abnormalities. This case report demonstrates the This case study demonstrates the importance of strengthening general HHC preventative measures in order to lower non-cirrhotic HHC's incidence and fatality rate
Keywords: *AFP, Hepatitis B, Hepatocellular Carcinoma, Non-Cirrhotic Liver*

INTRODUCTION

The most typical form of primary liver cancer is hepatocellular carcinoma (HCC). There are 600,000 newly diagnosed patients worldwide each year.[1–3] HCC in non-cirrhotic livers is still uncommon and can present insidiously in patients.[4] More than half of non-cirrhotic individuals with HCC may not exhibit any symptoms, and the disease is frequently detected when it is advanced and incurable.[5,6] HCC incidence in individuals without cirrhosis varied from 0.1 to 0.8 per 100 person-years, but it ranged from 2.2 to 4.3 per 100 person-years in patients with cirrhosis.[3,6,7] Less than 0.3% of inactive HBV carriers who do not have liver cirrhosis (LC) develop HCC each year. It is unclear how certain HBV genotypes or mutations affect the development of hepatocarcinogenesis.[8,9] HCC may develop in people with non-cirrhotic chronic liver illness, such as chronic hepatitis B virus infection and chronic HCV infection, even though liver cirrhosis is the predominant risk factor for this malignancy.[7,10] Here, we have a case of insidiously advanced HCC in a patient without liver cirrhosis.

CASE PRESENTATION

A 47-year-old man who had never been hospitalized before went to the emergency room complaining of upper right side abdominal discomfort that suddenly arose and spread to the back and right shoulder. Continuous abdominal discomfort that is not relieved by shifting positions. The patient had been experiencing upper right abdominal fullness for the past two months, along with a sense of a lump growing larger and harder without experiencing any discomfort. During the same time, the patient was also reported to have dropped 10 kg of weight with a decrease in appetite. He also complained of intermittent back pain, but he did not worry about it since he believed he was just worn out from work. Patient acknowledged of smoking and having risky sexual encounters in the past. There was no prior history of gallstones, hematemesis, melena, altered consciousness, or swelling of the face or extremities. He denied having ever had high blood pressure or diabetes. The patient denied having ever used injectable drugs, drank alcohol, received blood transfusions, or had hepatitis in the past. There is no family history of HCC or liver disease.

JURNAL KEDOKTERAN DIPONEGORO
(*DIPONEGORO MEDICAL JOURNAL*)
Online http://ejournal3.undip.ac.id/index.php/medico
E-ISSN : 2540-8844
DOI : http://10.14710/jkd (dmj).v12i2.36748
JKD (DMJ), Volume 12, Number 2, March 2023 : 80-84

On physical examination, the patient scaled a PS score of 1-2 and the VAS pain level of 7. The patient's sclera was not icterus, and there was no evidence of jaundice. During the abdominal exam, it was discovered that the right upper quadrant of the patient had a solid mass that was palpable four fingers from the right costal arch, suggesting hepatomegaly. Hepatic stigmata such erythema palmaris, ascites, splenomegaly, spider nevi, caput medusa, gynecomastia, or quickly falling out axillary hair were not discovered. A normal neurological examination revealed no hepatic encephalopathy symptoms. The results of other physical exams were normal.

Laboratory analysis of whole blood revealed a thrombocytosis of 661x103/uL, hemoglobin 13.5 g/dL, WBC 13.35x109/L, PPT 13.9, aPTT 25.9 seconds. There was a rise in the transaminases ALT 107 U/L and AST 173 U/L. The levels of albumin and bilirubin were normal. Alpha Feto Protein (AFP) analysis revealed a significant rise from the expected result of 71,000 ng/dL. Hepatitis B testing was positive, anti-HCV testing was negative, and HIV testing was negative. An abdominal ultrasound revealed a larger liver and several hypo-hyperechoic nodules in the right lobe. CT scan of the abdomen with and without contrast showed an enlarged liver size (midclavicular craniocaudal length ± 23.6 cm) and revealed multiple solid lesions in the right and left lobes of the liver, as well as early wash in (82 HU) in the arterial phase, early wash out (61 HU) in the venous phase, and delay. There was no thrombus and no arteriovenous fistula. Right inguinal nodules measured 1 cm, left inguinal nodules 0.6 cm, peritumoral nodules 0.8 cm, and paraorta nodules 1.2 cm. There were lytic lesions of the VTh 8 and VL 1 bodies. Hepatoma with Barcelona Clinic Liver Cancer (BCLC) class C was the patient's diagnosis, and he consented to accept palliative treatment.

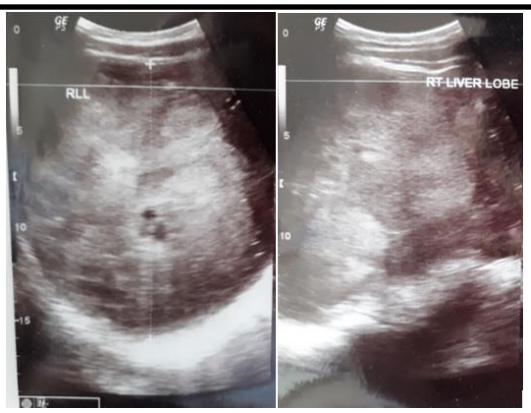

Figure 1. Abdominal Ultrasonography on Right Hepatic Lobe

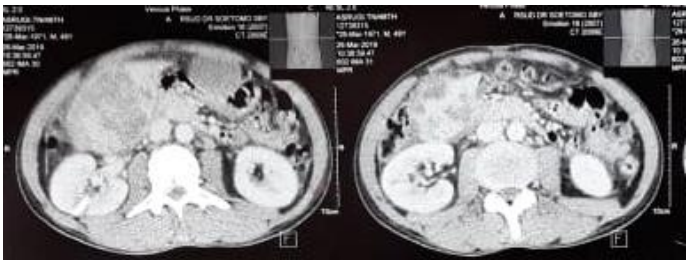

Figure 2. Multiple Solid Lesion on Hepatic Lobe

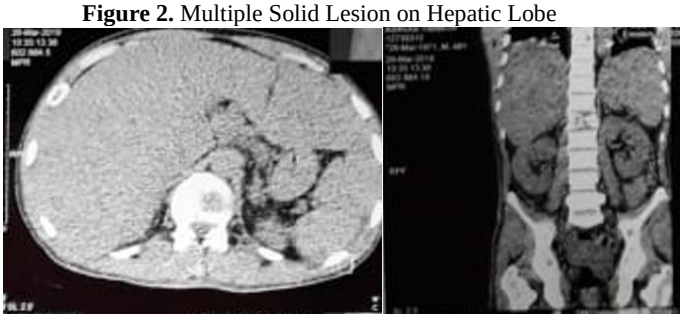

Figure 3. Osteolytic Lesion on Corpus Vertebrae

DISCUSSION

It was about 90% of primary tumor involved in liver was hepatocellular carcinoma (HCC).[1] In this scenario, HCC is more common in individuals with liver cirrhosis, although in 20% of cases it can arise without liver cirrhosis being present first, a condition whose occurrence is still not well recorded.[2] The bimodal age distribution of patients showed a peak for HCC cases that were not preceded by liver cirrhosis between the second and seventh decades.[1,2] Non-alcoholic fatty liver disease (NAFLD), viral hepatitis, germline mutations, hereditary illnesses, and genotoxic chemicals are among the factors that contribute to the occurrence of HCC.[2] Hepatitis B virus infection is linked to up to 30% of instances of HCC without liver cirrhosis.[4] Less than 0.3% of people with dormant hepatitis B carriers get non-

JURNAL KEDOKTERAN DIPONEGORO
(*DIPONEGORO MEDICAL JOURNAL*)
Online http://ejournal3.undip.ac.id/index.php/medico
E-ISSN : 2540-8844
DOI : http://10.14710/jkd (dmj).v12i2.36748
JKD (DMJ), Volume 12, Number 2, March 2023 : 80-84

cirrhotic HCC each year.[5] Because HBV is a double-stranded DNA virus that may integrate into host cells and operate as a mutagenic agent producing chromosomal damage and genomic instability, it is likely that HBV can produce HCC without cirrhosis. Additionally, HBx protein gene transactivation can alter the balance between DNA repair and death, promote cell proliferation, and dysregulate cell cycle regulation.[8]

Most liver cirrhosis patients who develop HCC have symptoms of portal vein hypertension and hepatic failure sign, such as jaundice, hepatic encephalopathy, ascites, hematemesis, and melena from gastrointestinal bleeding, peripheral edema from hypoalbumin, immunosuppression, muscle atrophy, spider naevi, palmar erythema, caput medusa, and gynecomastia.[1,9] In the examples we mentioned, these weren't discovered. HCC without liver cirrhosis frequently develops covertly and does not demonstrate disease progression.[7] Most of the time, HCC is asymptomatic in the early stages, making early detection challenging. When it manifests, as in this patient's case, it is well advanced and incurable.[10] Abdominal pain complaints are the most prevalent in 52% of illnesses that already produce symptoms, followed by abdominal distension, weight loss, malaise, anorexia, weakness, chronic diarrhea, jaundice, chest discomfort, and fever of unclear origin.[2] The patient we described experienced right upper abdominal discomfort that had suddenly started, along with symptoms of weight loss and a lumpy, hard feeling in the upper right abdomen. Although relatively uncommon, paraneoplastic syndromes such as hypoglycemia, demyelination, pemphigus vulgaris, thrombocytosis, hypercalcemia, hypercholesterolemia, and erythrocytosis can be caused by HCC.[7,11] Thrombocytosis was discovered in this patient. HCC is susceptible to metastatic dissemination, and extrahepatic extension is more prevalent in noncirrhotic HCC.[12] The lung, portal vein, local lymph nodes, and bone are the locations where HCC metastases most often.[13,14] Patient also complained of back discomfort that was considered to be caused by bone metastases as evidenced by the lysis of the vertebral bodies.

The tumor-node-metastasis (TNM) classification, which is determined during surgery by pathological inspection of the resected material, is the most used staging method for solid tumors. Since cirrhosis is a significant contributing factor to instances, the prognosis is influenced by the severity of liver failure and the patient's physical appearance as well as the size and number of tumors present in the body. The optimum therapy may be chosen by using the liver disease stage determined using a variety of clinical parameters.[1,15] The TNM classification for staging HHC cannot measure the degree of hepatic dysfunction and appearance status of the patient that is required in HHC to determine the choice of therapy in HHC.[9] It is advised to stage HHC using the Barcelona Clinic Liver Cancer (BCLC) criteria since it takes into account the patient's appearance status, liver functioning, and tumor size. Additionally, BCLC have been verified for populations in Europe, America, and Asia.[1,5] The BCLC categorization of this patient's stage is BCLC-C based on the assessment of appearance status PS score 2, liver function status exhibiting Child-Pugh A, and evidence of extrahepatic invasion of lymph nodes, bone, and peritumoral. The size of the tumor, the existence of satellite lesions, the integrity of the tumor capsule, vascular invasion, stage, partial resection, and HBV infection all affect a patient's prognosis with non-cirrhotic HCC.[2,8] With a 3-year survival rate for patients with vascular invasion of 9% and 35% if no vascular invasion is identified, the presence of vascular invasion and the growth of tumors are poor prognostic indicators.

CONCLUSION

HHC is an uncommon condition that can develop in persons without cirrhosis, but it can be brought on by a number of factors and result in the development of cancer in an otherwise healthy liver. Clinically, cirrhosis-preceded HHC patients will exhibit indications of liver malfunction and portal vein hypertension, allowing for monitoring and treatment to be started before malignant degeneration or early cancer treatment. Since the majority of HHC patients are asymptomatic, it might be challenging to track the disease's course in those in whom cirrhosis is not present first. This case study demonstrates the importance of strengthening general HHC preventative measures in order to lower non-cirrhotic HHC's incidence and fatality rate.

JURNAL KEDOKTERAN DIPONEGORO
(*DIPONEGORO MEDICAL JOURNAL*)
Online http://ejournal3.undip.ac.id/index.php/medico
E-ISSN : 2540-8844
DOI : http://10.14710/jkd (dmj).v12i2.36748
JKD (DMJ), Volume 12, Number 2, March 2023 : 80-84

DECLARATIONS

Informed consent was obtained from patient included in the study. The authors affirm that research participants provided informed consent.

REFERENCES

1. Desai A, Sandhu S, Lai JP, Sandhu DS. Hepatocellular carcinoma in non-cirrhotic liver: A comprehensive review. World J Hepatol [Internet]. 2019 Jan 27;11(1):1–18. Available from: https://dx.doi.org/10.4254/wjh.v11.i1.1
2. Galle PR, Forner A, Llovet JM, Mazzaferro V, Piscaglia F, Raoul JL, et al. EASL Clinical Practice Guidelines: Management of hepatocellular carcinoma. J Hepatol [Internet]. 2018;69(1):182–236. Available from: https://doi.org/10.1016/j.jhep.2018.03.019
3. Yen YH, Cheng YF, Wang JH, Lin CC, Wang CC. Characteristics and etiologies of hepatocellular carcinoma in patients without cirrhosis: When East meets West. PLoS One [Internet]. 2021;16(1 January):1–12. Available from: http://dx.doi.org/10.1371/journal.pone.0244939
4. Gaddikeri S, McNeeley MF, Wang CL, Bhargava P, Dighe MK, Yeh MMC, et al. Hepatocellular carcinoma in the noncirrhotic liver. Am J Roentgenol [Internet]. 2014;203(1):34–47. Available from: https://dx.doi.org/10.2214/AJR.13.11511
5. Giannini EG, Marenco S, Bruzzone L, Savarino V, Farinati F, Del Poggio P, et al. Hepatocellular carcinoma in patients without cirrhosis in Italy. Dig Liver Dis [Internet]. 2013;45(2):164–9. Available from: http://dx.doi.org/10.1016/j.dld.2012.08.018
6. Zhang Y, Wang C, Xu H, Xiao P, Gao Y. Hepatocellular carcinoma in the noncirrhotic liver: A literature review. Eur J Gastroenterol Hepatol [Internet]. 2019;31(7):743–8. Available from: http://dx.doi.org/10.1097/MEG.0000000000001419
7. Schütte K, Schulz C, Poranzke J, Antweiler K, Bornschein J, Bretschneider T, et al. Characterization and prognosis of patients with hepatocellular carcinoma (HCC) in the non-cirrhotic liver. BMC Gastroenterol [Internet]. 2014;14(1):1–10. Available from: http://dx.doi.org/10.1186/1471-230X-14-117
8. Marrero JA, Kulik LM, Sirlin CB, Zhu AX, Finn RS, Abecassis MM, et al. Diagnosis, Staging, and Management of Hepatocellular Carcinoma: 2018 Practice Guidance by the American Association for the Study of Liver Diseases. Hepatology [Internet]. 2018;68(2):723–50. Available from: http://dx.doi.org/10.1002/hep.29913
9. Omata M, Cheng AL, Kokudo N, Kudo M, Lee JM, Jia J, et al. Asia–Pacific clinical practice guidelines on the management of hepatocellular carcinoma: a 2017 update. Hepatol Int [Internet]. 2017;11(4):317–70. Available from: http://dx.doi.org/10.1007/s12072-017-9799-9
10. Gómez Rodríguez R, Romero Gutiérrez M, González de Frutos C, de Artaza Varasa T, de la Cruz Perez G, Ciampi Dopazo JJ, et al. Características clínicas, estadificación y tratamiento de los pacientes con carcinoma hepatocelular en la práctica clínica. Estudio prospectivo de una serie de 136 pacientes. Gastroenterol Hepatol [Internet]. 2011;34(8):524–31. Available from: https://dx.doi.org/10.1016/j.gastrohep.2011.06.009
11. Newman NB, Jabbour SK, Hon JDC, Berman JJ, Malik D, Carpizo D, et al. Hepatocellular Carcinoma Without Cirrhosis Presenting With Hypercalcemia: Case Report and Literature Review. J Clin Exp Hepatol [Internet]. 2015;5(2):163–6. Available from: http://dx.doi.org/10.1016/j.jceh.2015.04.001
12. Sanyal AJ, Yoon SK, Lencioni R. The Etiology of Hepatocellular Carcinoma and Consequences for Treatment. Oncologist [Internet]. 2010;15(S4):14–22. Available from: https://dx.doi.org/10.1634/theoncologist.2010-s4-14
13. Liu CJ, Chen BF, Chen PJ, Lai MY, Huang WL, Kao JH, et al. Role of hepatitis B virus precore/core promoter mutations and serum viral load on noncirrhotic hepatocellular carcinoma: A case-control study. J Infect Dis [Internet]. 2006;194(5):594–9. Available from: https://dx.doi.org/10.1086/505883
14. Castán A, Navarro Y, Sarría L, Larrosa R, Serradilla M, Serrablo A. Radiological diagnosis of hepatocellular carcinoma in non-

JURNAL KEDOKTERAN DIPONEGORO
(*DIPONEGORO MEDICAL JOURNAL*)
Online http://ejournal3.undip.ac.id/index.php/medico
E-ISSN : 2540-8844
DOI : http://10.14710/jkd (dmj).v12i2.36748
JKD (DMJ), Volume 12, Number 2, March 2023 : 80-84

cirrhotic patients. Hepatoma Res [Internet]. 2017;3(1):1. Available from: https://dx.doi.org/10.20517/2394-5079.2015.62

15. Mansour D, McPherson S. Management of decompensated cirrhosis. Clin Med J R Coll Physicians London [Internet]. 2018;18:s60–5. Available from: https://dx.doi.org/10.7861/clinmedicine.18-2-s60