Clinics in Surgery

Case Report
Published: 18 Apr, 2024

Liver Transplantation Subsequent to Liver Resection for Collision Tumors in VHC Cirrhotic Patient

Cadar R[1,2], Năstase A[1], Trofin AM[1,2], Zabara M[1,2], Ciobanu D[2,3], Vasiluta C[1], Blaj M[2,4], Vlad N[1,2], Ursulescu-Lupașcu C[2,5] and Lupașcu C[1,2]*

[1]II General Surgery and Liver Transplant Clinic, University Hospital "Saint Spiridon" Iasi, Romania

[2]University of Medicine and Phamacy "Grigore T. Popa" Iasi, Romania

[3]Histopathology Clinic, University Hospital "Saint Spiridon" Iasi, Romania

[4]Department of Anesthesia and Intensive Care, University Hospital "Saint Spiridon" Iasi, Romania

[5]Radiology Clinic, University Hospital "Saint Spiridon "Iasi, Romania

Abstract

Liver transplantation is a well-established indication for hepatocarcinoma developed in end-stage liver disease; however, the indications for liver transplantation still controversial. This combined type of tumor lesion follows an aggressive clinical course with an unfavorable prognosis. The clinical outcome of orthotopic liver transplantation in patients with Hepatocellular Carcinoma (HCC) is well defined, but its role in the management of cHCC-CC remains largely unknown. Herein, we present the case of a 50-year-old female patient with Hepatitis C virus-related cirrhosis who received antiviral treatment two years prior to admission to a surgical clinic where she was admitted for an imagistic finding of two focal hepatic lesions measuring 4.5 cm and 1.5 cm, in the liver segments 6. At the admission the patient presented low level of thrombocytes (102,000 mm^3 and slightly elevated alpha-fetoprotein serum level (31.3 ng/ml) and she was classified as score Child-Turcotte – Pugh A6. After surgery, the patient was listed for liver transplant, and one year later, a proper donor was found. The liver transplant procedure was uneventful. Histopathological examination of the cirrhotic liver revealed a recurrence of hepatocellular carcinoma. In conclusion, liver transplantation should be considered for combined cholangiocarcinoma and hepatocarcinoma after liver resection because of the risk of tumor recurrence.

Keywords: Liver transplantation; Cholangiocarcinoma; Hepatocarcinoma; Recurrence; Collision tumor

OPEN ACCESS

Correspondence:
Nutu Vlad, II General Surgery and Liver Transplant Clinic, University Hospital "Saint Spiridon" Iasi, Romania,

Received Date: *18 Mar 2024*
Accepted Date: *03 Apr 2024*
Published Date: *18 Apr 2024*

Citation:
Cadar R, Năstase A, Trofin AM, Zabara M, Ciobanu D, Vasiluta C, et al. Liver Transplantation Subsequent to Liver Resection for Collision Tumors in VHC Cirrhotic Patient. Clin Surg. 2024; 9: 3699.

Introduction

Intrahepatic Cholangiocarcinoma (CCI) and Hepatocellular Carcinoma (HCC) are some liver tumors that rarely develop simultaneous. The frequency of this tumor association is reported by some authors to have an incidence that varies from 0.8% to 6.5% in primary liver carcinoma [1]. These tumors exhibit histological features of both the hepatocellular and biliary epithelial cell types. It had been reported that some useful methods in differentiation of Intrahepatic Cholangiocarcinoma (ICC) and Hepatocellular Carcinoma (HCC) is Contrast-Enhanced Ultrasound (CEUS), contrast-enhanced Magnetic Resonance Imaging (MRI) that can help accurately in characterize the most focal hepatic lesions [2,3]. Although liver resection remains the only curative treatment for combined hepatic tumors, its long-term prognosis is disappointing because the survival rate is depending on age, the tumor cell grade, TNM stage, size of the tumor, tumor vascular invasion, comorbidity and oral antiviral therapy as reported by Chen et al. [4].

Despite established screening measures for the early detection of liver cancer among at-risk patients, non-specific symptoms of these types of cancer often result in late detection, precluding curative treatment options [5,6].

The aim of this study is to report a case of liver transplantation performed in a patient with concomitant resected hepatocarcinoma and cholangiocarcinoma.

Case Presentation

We report the case of a 50-year-old female patient with Hepatitis C virus-related cirrhosis who received antiviral treatment 2 years prior to admission to a surgical clinic where she was admitted

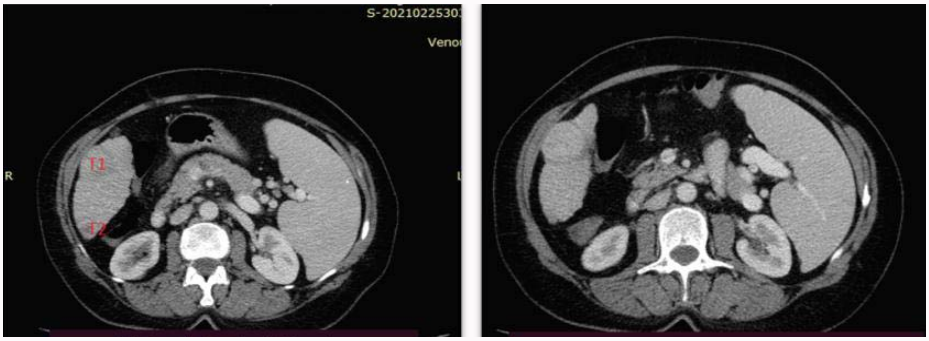

Figure 1: CT scan aspects of liver tumors.

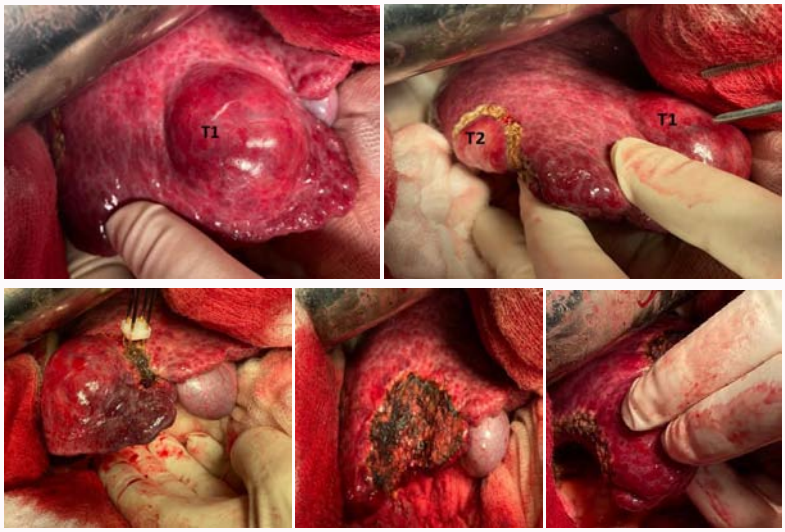

Figure 2: Intraoperative aspect of the hepatic tumors and post-resection scar.

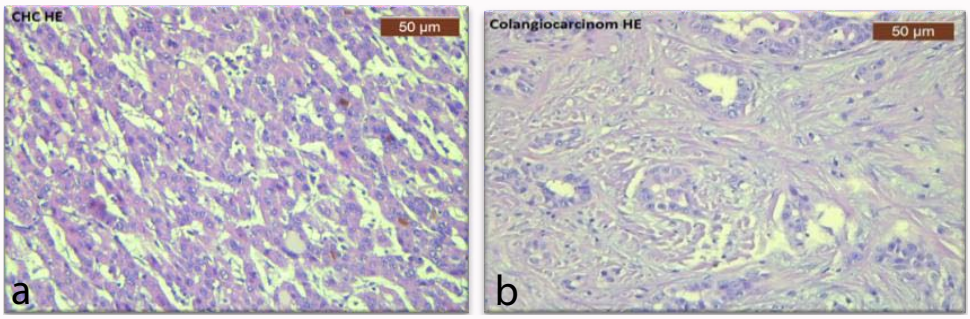

Figure 3: Histological aspects hepatocellular carcinoma (a) and cholangiocarcinoma (b).

for imaging findings of two focal hepatic lesions. At admission, the patient presented with a low level of thrombocytes (102,000 mm^3 and slightly elevated alpha-fetoprotein serum level (31.3 ng/ml), and she was classified as Child-Turcotte –Pugh A6. Computed Tomography (CT) revealed an enlarged liver, with an irregular outline, presenting in segment VI a tumor mass of 43/36/44 mm, hyperdense arterial time and isodense venous time, and another mass of 15/16 mm isodense in the arterial and late exposure time but discretely hyperdense in venous time (Figure 1). The portal vein was dilated to 17 mm and was permeable. In addition, the CT scan confirmed the absence of free intraperitoneal fluid and described a tumor located on the left side of the uterus measuring 44/43 mm, with a peripheral calcification imagistic aspect suggestive of fibroma.

The patient underwent atypical resection of the two tumors *via* laparotomy using a 4× electrode radiofrequency device (Habib device), with minimal blood loss (Figure 2).

Histological examination revealed the coexistence of two different types of tumor cells and confirmed the presence of an early-stage well-differentiated hepatocellular carcinoma developed on liver cirrhosis pT1bNxG1 L0V0Pn0 at the site of T1 and an intrahepatic cholangiocarcinoma with small ductal structures and moderately differentiated pT1NxG2 L0V0Pn0 at the T2 site (Figure 3a, 3b). Immunohistochemistry analysis was performed to differentiate

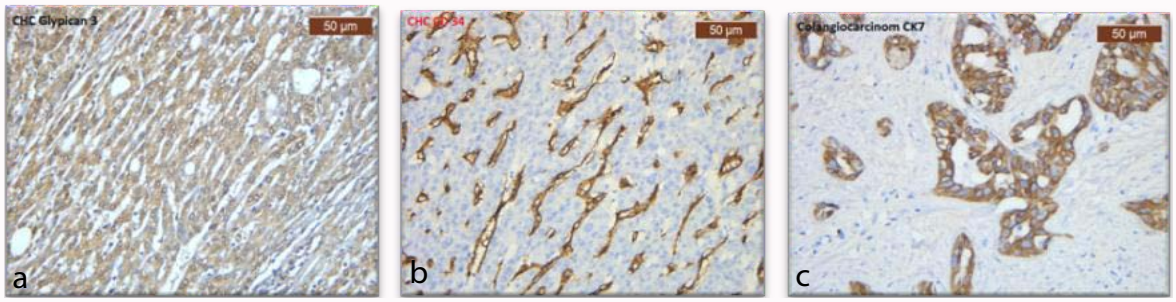

Figure 4: Immunohistology staining for confirmation of hepatocellular carcinoma (a, b) and cholangiocarcinoma (c).

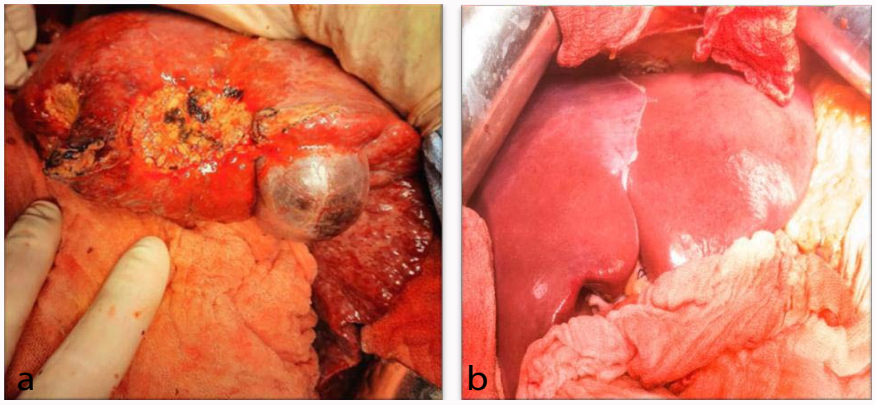

Figure 5: Intraoperative aspect of cirrhotic liver (a) and transplanted liver (b).

the two histological types using CD34, CD7 and Glycan 3 staining (Figures 4a-4c).

Three months after the surgery, the patient had no signs of tumor recurrence, serum levels of AFP decreased to 6 ng/ml, and she was listed for liver transplantation.

One year after the surgery, a deceased donor liver transplant at laparotomy showed no signs of macroscopic tumors, but two post-resection scars on the liver surface. The procedure was uneventful (Figure 5a, 5b). Histological analysis of the explanted liver revealed a background of viral cirrhosis in the area corresponding to the previous intervention aspects of well-differentiated hepatocellular carcinoma.

Postoperative immunosuppression included tacrolimus (3 mg bid) and mycophenolate mofetil (1000 mg bid). At the 3-, 6- and 9-months follow, the patient had good liver performance, with normal levels of alpha-fetoprotein (2.4–2.5) and no imagistic evidence of tumor recurrence.

Discussion

Hepatocellular Carcinoma (HCC) is the most common type of primary liver cancer, accounting for approximately 90% of all cases [7]. It typically arises in the context of liver cirrhosis, which is often caused by chronic viral Hepatitis B or C, alcohol abuse, or non-alcoholic fatty liver disease [8]. Intrahepatic Cholangiocarcinoma (ICC), on the other hand, accounts for about 15% of primary liver cancers. It arises from the bile ducts within the liver and is often associated with chronic inflammation and scarring of the liver [8,9].

Both HCC and ICC are aggressive malignancies with poor prognoses, and the optimal management of these cancers remains a challenge. Treatment options may include surgery, radiation therapy, and chemotherapy, but the choice of therapy depends on the stage of cancer and the patient's overall health status [10,11].

Combined hepatocellular carcinoma and cholangiocarcinoma are rare forms of primary liver cancer [1,12]. The first reported case of CHC associated with CCI dates back to 1903 and was documented by Wells. Allen and Lisa categorized the CHC-CCI associations into three types. Type A is characterized by CHC and CCI growing independently in different parts of the same liver, but with clear boundaries. Type B is characterized by CHC and CCI originating from different cells and mixing as they grow, but there are still some boundaries between the two populations. Type C involves CHC, and CCI is completely integrated within the same tumor [13,14].

Moeini et al. conducted a molecular analysis of 18 cases of Hepatocellular Carcinoma (HCC) associated with Intrahepatic Cholangiocarcinoma (CCI). Their findings revealed that the mixed CHC-CCI type demonstrated a more aggressive nature and a poorer prognostic outcome, whereas the solitary type exhibited a common cell lineage for both the CHC and CCI components from a molecular perspective [12,15].

Patients with combined hepatocellular carcinoma and cholangiocarcinoma exhibit distinct clinical and pathological features compared to those with solitary Hepatocellular Carcinoma (HCC) [16,17]. Two retrospective studies conducted in Taiwan and Turkey over a period of eight years involving 710 patients with living and cadaveric donor liver transplants revealed that out of 377 transplants for HCC, 11 (2.92%) were diagnosed with combined HCC-CCIs. The findings indicated an overall survival rate of 80% at one year for combined CHC-CCI in comparison to 97.2% in HCC, while the three-year survival rate for CHC-CCI was 46.7% as opposed to 92.5%

in pure hepatocellular carcinoma. Additionally, this study confirmed the high risk of tumor recurrence in the biliary epithelial component of the new liver graft [1,5,18].

Early detection of tumors during the asymptomatic phase and curative resection are crucial for achieving optimal survival rates [19-21]. In the last two decades, advancements have been made in the management of Cholangiocarcinoma (CCI), and the outcomes of liver transplantation after neoadjuvant treatment have shown promise [17,22].

Consequently, some centers now consider CCI as an indication for liver transplantation [11,23,24]. Furthermore, recent research has demonstrated promising results after liver transplantation in patients with early stage CCI [11].

Intraparenchymal cholangiocarcinoma is considered a relative indication for liver transplantation in most centers because of the contradictory results associated with liver transplantation in this condition [25-27].

This case serves as a reminder of the risk of recurrence of liver tumors and highlights the importance of postoperative surveillance. Furthermore, post-liver transplant follow-up is crucial for assessing the risk of recurrence of cholangiocarcinoma or hepatocellular carcinoma.

Acknowledgment

Surgical resection is the preferred and most efficacious treatment modality for concomitant primary liver malignancies, especially in non-cirrhotic patients. However, in patients with cirrhosis, the extent of resection should be restricted while ensuring oncological clearance. Although liver transplantation can be performed for combined hepatocellular carcinoma and cholangiocarcinoma, there is a lack of sufficient data regarding its long-term curative efficacy.

References

1. Chang CC, Chen YJ, Huang TH, Chen CH, Kuo FY, Eng HL, et al. Living donor liver transplantation for combined hepatocellular carcinoma and cholangiocarcinoma: Experience of a single center. Ann Transplant. 2017;22:115-20.
2. Chen LD, Xu HX, Xie XY, Xie XH, Xu ZF, Liu GJ, et al. Intrahepatic cholangiocarcinoma and hepatocellular carcinoma: differential diagnosis with contrast-enhanced ultrasound. Eur Radiol. 2010;20(3):743-53.
3. Al Hamoudi W, Khalaf H, Allam N, Al Sebayel M. Coincidental occurrence of hepatocellular carcinoma and cholangiocarcinoma (Collision Tumors) after liver transplantation: A case report. Hepat Mon. 2012;12(10 HCC):e5871.
4. Chen PD, Chen LJ, Chang YJ, Chang YJ. Long-term survival of combined hepatocellular-cholangiocarcinoma: A nationwide study. The Oncol. 2021;26:e1774-85.
5. Takahashi K, Obeid J, Burmeister CS, Bruno DA, Kazimi MM, Yoshida A, et al. Intrahepatic cholangiocarcinoma in the liver explant after liver transplantation: Histological differentiation and prognosis. Ann Transplant. 2016;21:208-15.
6. Jarnagin WR, Weber S, Tickoo SK, Koea JB, Obiekwe S, Fong Y, et al. Combined hepatocellular and cholangiocarcinoma: Demographic, clinical, and prognostic factors. Cancer. 2002;94:2040-6.
7. Llovet JM, Kelley RK, Villanueva A, Singal AG, Pikarsky E, Roayaie S, et al. Hepatocellular carcinoma. Nat Rev Dis Primers. 2021;7(6).
8. El-Diwany R, Pawlik TM, Ejaz A. Intrahepatic cholangiocarcinoma. Surg Oncol Clin N Am. 2019;28(4):587-99.
9. Tickoo SK, Zee SY, Obiekwe S, Xiao H, Koea J, Robiou C, et al. Combined hepatocellular cholangiocarcinoma: A histopathologic, immunohistochemical, and in situ hybridization study. Am J Surg Pathol. 2002;26:989-97.
10. Gores GJ. Liver transplantation for cholangiocarcinoma. Liver Transpl. 2015;21(Suppl 1):S32-S33.
11. Mehta N, Yao FY. Hepatocellular cancer as indication for liver transplantation: Pushing beyond Milan. Curr Opin Organ Transplant. 2016;21:91-8.
12. Moeini A, Sia D, Zhang Z, Camprecios G, Stueck A, Dong H, et al. Mixed hepatocellular cholangiocarcinoma tumors: Cholangiolocellular carcinoma is a distinct molecular entity. J Hepatol. 2017;66:952-61.
13. Alen RA, Lisa JR. Combined liver cell and bile duct carcinoma. Am J Pathol. 1949;25:647-55.
14. Zhang G, Chen BW, Yang XB, Wang HY, Yang X, Xie FC, et al. Prognostic analysis of patients with combined hepatocellular-cholangiocarcinoma after radical resection: A retrospective multicenter cohort study. World J Gastroenterol. 2022;28(41):5968-81.
15. Gastaca M, Sapisochin G. Mixed hepatocellular and cholangiocarcinoma: the difficulty of finding the right answer. HPB (Oxford). 2017;19:558.
16. Pillai A. Mixed hepatocellular-cholangiocarcinoma: is it time to rethink consideration for liver transplantation? Liver Transpl. 2018;24:1329-30.
17. Jung D-H, Hwang S, Song G-W, Ahn CS, Moon DB, Kim KH, et al. Clinicopathological features and prognosis of intrahepatic cholangiocarcinoma after liver transplantation and resection. Ann Transplant. 2017;22:42-52.
18. Weimann A, Varnholt H, Schlitt HJ, Lang H, Flemming P, Hustedt C, et al. Retrospective analysis of prognostic factors after liver resection and transplantation for cholangiocellular carcinoma. Br J Surg. 2000;87:1182-7.
19. Adam R, Bhangui P, Vibert E, Azoulay D, Pelletier G, Duclos-Vallée JC, et al. Resection or transplantation for early hepatocellular carcinoma in a cirrhotic liver: does size define the best oncological strategy? Ann Surg. 2012;256:883-91.
20. Tribillon E, Barbier L, Goumard C, Irtan S, Perdigao-Cotta F, Durand F, et al. When should we propose liver transplant after resection of hepatocellular carcinoma? A comparison of salvage and de Principe strategies. J Gastrointest Surg. 2016;20:66-76.
21. Ravaioli M, Grazi GL, Piscaglia F, Trevisani F, Cescon M, Ercolani G, et al. Liver transplantation for hepatocellular carcinoma: Results of down-staging in patients initially outside the Milan selection criteria. Am J Transplant. 2008;8:2547-57.
22. Yao FY, Xiao L, Bass NM, Kerlan R, Ascher NL, Roberts JP. Liver transplantation for hepatocellular carcinoma: Validation of the UCSF-expanded criteria based on preoperative imaging. Am J Transplant. 2007;7:2587-96.
23. Park SE, Lee SH, Yang JD, Hwang HP, Hwang SE, Yu HC, et al. Clinicopathological characteristics and prognostic factors in combined hepatocellular carcinoma and cholangiocarcinoma. Korean J Hepatobiliary Pancreat Surg. 2013;17:152-6.
24. Goldaracena N, Gorgen A, Sapisochin G. Current status of liver transplantation for cholangiocarcinoma. Liver Transpl. 2018;24:294-303.
25. Chan AC, Lo CM, Ng IO, Fan ST. Liver transplantation for combined hepatocellular cholangiocarcinoma. Asian J Surg. 2007;30:143-6.
26. W u D, Shen ZY, Zhang YM, Wang J, Zheng H, Deng YL, et al. Effect of liver transplantation in combined hepatocellular and cholangiocellular carcinoma: A case series. BMC Cancer. 2015;15:232.

27. Sotiropoulos GC, Kaiser GM, Lang H, Molmenti EP, Beckebaum S, Fouzas I, et al. Liver transplantation as a primary indication for intrahepatic cholangiocarcinoma: a single center experience. Transplant Proc. 2008;40:3194-5.