

## Clear Cell Hepatocellular Carcinoma with Associated Tuberculosis-A Case Report

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### Abstract

Clear cell hepatocellular carcinoma (CCHCC) is a rare variant of classical hepatocellular carcinoma (CHCC). Most of these cases pose a histological diagnostic dilemma with broad range of differentials of tumor with clear cell morphology. Use of immunostains or presence of classical hepatocellular carcinoma morphology focally aids in accurate diagnosis of these lesions.

We report a case of a 62-year-old male who presented with loss of appetite and altered bowel habits for last 3 months. On investigation he was found to be HCV positive with genotype 1a and viral load of 3853865 IU/ml. His CECT revealed a well-defined hyper dense lesion of size 38 x 34 mm in segment V with a thin hypo dense rim. Contrast studies were suggestive of hepatocellular carcinoma with chronic liver disease. His PET CT revealed an FDG avid lesion in lung, biopsy from which showed caseating epithelioid granulomas. He underwent living donor related liver transplant. Explant liver tissue examined showed CCHCC with cirrhosis and several epithelioid granulomas.

Occurrence of CCHCC with tuberculosis is a rare with no similar case has been reported in indexed English literature till date. We herein report the first case of CCHCC with coincidental Tuberculosis in an elderly male.

**Keywords:** Clear cell carcinoma; Liver; Tuberculosis

### Introduction

Hepatocellular carcinoma has several variants histologically including fibro lamellar, schirrous, pseudoglandular, steatohepatitic and clear cell HCC. The variants are independent prognostic factor of HCC. CCHCC is a less malignant subtype of HCC with later intrahepatic recurrences and a better prognosis. As compared to CHCC, CCHCC often show pseudocapsules and are less involved with vascular invasion. These tumours are frequently found to be associated with HCV related chronic liver disease. We herein describe a case of CCHCC in a patient with HCV cirrhosis and along with tuberculosis.

### Case Report

We report a case of a 62-year-old male who was apparently alright 3 months back when he developed loss of appetite and irregular bowel habits. He was an occasional alcoholic which he had stopped 2 years back. His weight was 63 kg, height 169 cm, BMI 22.1, Haemoglobin 14.6 (13 g/dl to 17 g/dl), TLC 7.2 (4000/ml to 10000/ml), DLC polymorphs 54/e-02/l-34/m-00/b-00, platelet-1.33, PT/INR-23.6/2.01, Bilirubin total/direct-0.94/0.32 mg/dl, fibrinogen-262, SGOT-73 (15 U/L to 37 U/L, SGPT-125 U/L (30 U/L to 65 U/L), Alkaline phosphatase 107-U/L (50 U/L to 136 U/L), GGT-223 U/L (5 U/L to 85 U/L) Total proteins-7.7 g/dl (6.4 g/dl to 8.2 g/dl) albumin-3.8 g/dl (3.4 g/dl to 5 g/dl) BUN-17 g/dl (6 g/dl to 20 mg/dl), creatinine-0.96 g/dl (0.9 g/dl to 1.3 mg/dl), Na-137 mmol/l (136 mmol/l to 145 mmol/l), potassium-4.45 mmol/l (3.5 mmol/l to 5.1 mmol/l), magnesium 1.7 mg/dl (1.8 mg/dl to 2.4 mg/dl). His HbsAg,

HIV I, II negative, AFP 12.10 ng/ml (2-9 ng/ml) CEA 1.93 ng/ml Non-smoker <2.5 ng/ml, smoker <5.0 ng/ml) CA 19.931.49 (<1.20 U/ml to 30.9 U/ml). On investigations he was found to be HCV positive with genotype 1a and a viral load of 3853865 IU/ml.

CECT abdomen showed normal sized liver with mildly irregular margin. A well defined hyper dense lesion of size 38 x 34 mm was noted in segment V of right lobe. The lesion shows a thin hypodense rim. On post contrast study the lesion show mild enhancement on arterial phase with intense enhancement on delayed arterial/ portal phase. On delayed scan it shows complete washout of contrast. The features were suggestive of Chronic liver disease with a hyperdense lesion in segment V of right lobe suggestive of mitotic activity most likely HCC.

PET CT showed an FDG avid lesion in left lung lower lobe. CT guided biopsy from the lesion showed caseating epithelioid granuloma.

Patient thus had child A liver cirrhosis, with early esophageal varices suggestive of increase portal pressure, required liver transplant as the best option in that setting in which partial resection is not a feasible option. BCLC was early stage A, CLIP stage 0, T1N0M0 stage is of the lesion. HCV was not treated before liver transplant because with new DAA it is very easy to treat HCV after transplant with better tolerability and effective results.

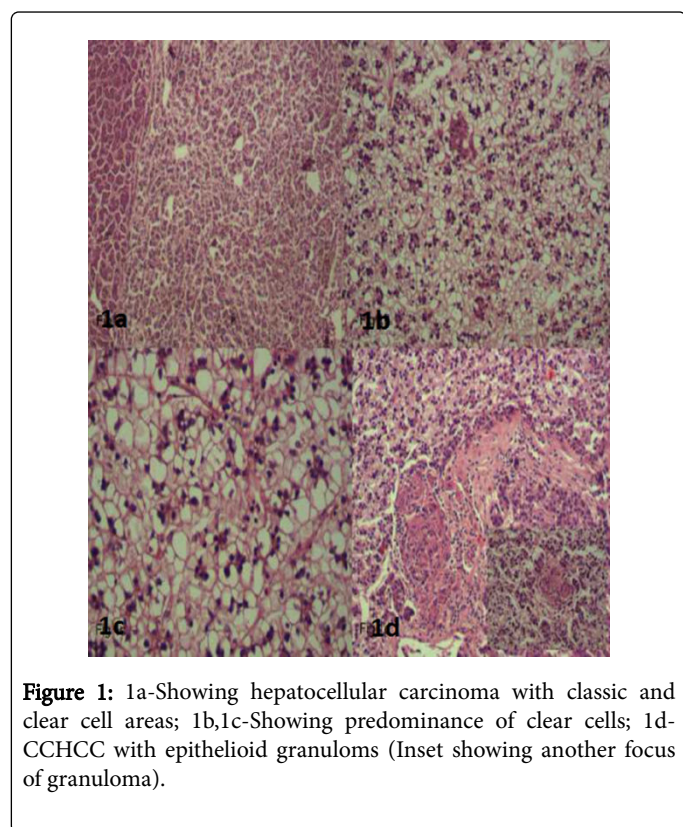
As tubercular infection was not active, as there are no constitutional systemic symptoms. We treated tuberculosis immediately after transplant by regimen including Rifampicin and maintaining adequate level of tacrolimus with the knowledge of rifampicin-tacrolimus drug interactions.

There was no indication for any antiretroviral therapy.

The patient underwent Living donor related living transplant.

**Explant liver** -The liver Explant weighed 1340 gm and measured 22 × 13 × 10 cm. The liver was firm. External surface is brownish nodular, margins were irregular. The liver was serially sectioned at 0.5 cm to 1cm interval to show a tan brownish colour diffusely multinodular cut surface, with nodules ranging from 0.2 cm to 0.6 cm in diameter. There was a well defined tumor in right lobe with a pseudocapsule in segment V measuring 3.5 × 3 × 2.5 cm. Tumor is 5.5 cm away from the hilum.

Microscopy from the tumor mass showed a moderately differentiated carcinoma Edmondson and Steiner Grade II, composed of thick trabeculae of neoplastic hepatocytes near the periphery of tumor along with diffuse sheets of clear cells with hyperchromatic nuclei. Around 80% of the tumor was composed of neoplastic clear cells. There was also presence of several large epithelioid granulomas (Figure 1). No lymphovascular emboli noted. Adjacent liver tissue showed cirrhosis.



Patients post-operative course was uneventful and was started on immunosuppression as per protocol. 15 days after surgery antitubercular drugs (Etambutol 1 g and Rcin 150 mg orally once a day) were also started. Patient is doing well after an year of followup.

## Discussion

Hepatocellular carcinoma (HCC) is the most common primary malignancy of liver. Most cases arise in cirrhotic liver. There are several histological variants of HCC like fibro lamellar, schirrous, pseudoglandular, steatohepatic and clear cell HCC.

Clear cell hepatocellular carcinoma is a rare variant of HCC. The incidence of clear cell HCC varies from 5% in western world to [1] to around 40% in Japanese countries [2].

These tumor have a strong association with cirrhosis [2] and are frequently seen with HCV related chronic liver disease [3] as compared to classical HCC as was also seen in our case.

In a series on 41 patients by Li et al most cases of CCHCC are seen in males with a male to female ratio of 3:1. The median age of diagnosis is 56 years [4]

Majority of these tumours have serum alpha-fetoprotein (AFP) levels of ≤ 20 ng/ml [5]. Similar findings were noted in our patient who was 62-year-old male and whose AFP was 12 ng/ml.

Radiologically most cases present as solitary intra-parenchymal mass lesions which have well-defined borders. On pre-contrast CT scans, they mostly show hypo-attenuation and occasionally as isointense to the adjacent liver parenchyma. On post-contrast CT scans, most lesions show avid enhancement on the hepatic arterial phase, and show slightly hyper-attenuation or iso-attenuation on the portal venous phase images. All lesions demonstrated hypointensity on the equilibrium phase. As compared to usual HCC, CCHCC often show pseudocapsules and are less involved with vascular invasion, could be useful in differentiating from common type hepatocellular carcinoma (CHCC) [5] as was also noted in our case.

Cytologically, most cases show hypercellular smears with loosely cohesive clusters and individually scattered malignant cells demonstrating anisonucleosis, nuclear hyperchromasia and irregularity, prominent nucleoli, and abundant finely vacuolated to clear cytoplasm [6].

Clear Cell variant of HCC is a histological diagnosis. Though there are no uniform criteria on to the percentage of clear cells usual cut off of 50% is taken as clear cell HCC. Few authors have classified them as focal or diffuse clear cell HCC. Diffuse CCHCC as greater than 50% clear cells and focal when 10% to 50% clear cells. Focal clear cell change is classified as HCC with focal clear cell change rather than as CCHCC. Tumors with <10 % clear cells is a common finding in common HCC and are not classified separately [7].

Difference from classical HCC-CCCL is a less malignant subtype of HCC than CHCC, patients with CCHCC likely have later intrahepatic recurrences and a better prognosis. Edmondson grade predicts survival of patients with CCHCC after curative resection; those with higher Edmondson grades may require more careful follow-up and aggressive post-hepatectomy therapy [8].

Ultra structurally clear cell hepatocellular carcinoma shows abundant cytoplasmic lipid and swollen mitochondria [9,10].

Clear cell hepatocellular carcinoma is morphologically similar to other clear cell tumours. The differential diagnosis included metastatic clear cell renal cell carcinoma, primary clear cell cholangiocarcinomas, epithelioid angiomyolipoma (pecoma) and metastatic adrenal cortical carcinoma. Immunohistochemical stain plays an important role in reaching to accurate diagnosis. Primary clear cell hepatocellular carcinoma (HCC) are positive with Hep Par 1 and Arginase, metastatic renal cell carcinoma are positive with PAX 8, CD10, epithelioid angiomyolipoma show Melan A and HMB-45 positivity. Primary clear cell cholangiocarcinoma usually positive for CK7 and CK19, negative for CK20. Adrenal cortical carcinoma is positive with Melan A and SF-1 is a recently described marker and usually positive

in tumor arising from adrenal glands. Murakata et al. did immunohistochemical analysis of CCHCC and metastatic RCC and found that HepPar 1 has high sensitivity and specificity for diagnosing CCHCC [11,12].

Surgery offers adequate cure in most patients and there is no obvious role of post-operative chemotherapy in these patients. Clear cell ratio, capsule formation, preoperative liver function, and vascular invasion were independent risk factors for prognosis [3,4,13].

CCHCC with Tuberculosis-There is a single case report of lipid-rich clear-cell hepatocellular carcinoma in a 67-year-old Japanese female with a past history of tuberculosis, appendicitis, ischaemic heart disease, and non-insulin-dependent diabetes mellitus non-alcoholic steatohepatitis along with diabetes mellitus [14].

There is no case report of simultaneous occurrence of clear cell HCC with tuberculosis in indexed English literature till date.

## Conclusion

CCHCC are rare variant of HCC. Most cases are associated with HCV infection and with cirrhosis. They follow a good prognosis course as compared to classical HCC.

## References

1. Buchanan TF, Huvos AG (1974) Clear cell carcinoma of the liver. A clinicopathologic study of 113 patients. *Am J Clin Pathol* 61: 529-539.
2. Yang SH, Watanabe J, Nakashima O (1996) Clinicopathologic study on clear cell hepatocellular carcinoma. *Pathol Int* 46: 503-509.
3. Liu Z, Ma W, Li H, Li Q (2007) Clinicopathological and prognostic features of primary clear cell carcinoma of the liver. *Hepatol Res* 38: 291-299.
4. Li ZY, Bi XY, Zhao JJ, Zhao H, Zhou JG, et al. (2013) Clinicopathological and prognostic analysis of primary clear cell carcinoma of the liver. *Zhonghua Zhong Liu Za Zhi* 35: 140-143.
5. Wang H, Tan B, Zhao B, Gong G, Xu Z (2014) CT findings of primary clear cell carcinoma of liver: with analysis of 19 cases and review of the literature. *Abdom Imaging* 39: 736-743.
6. Singh HK, Silverman JF, Geisinger KR (1997) Fine-needle aspiration cytomorphology of clear-cell hepatocellular carcinoma. *Diagn Cytopathol* 17: 306-310.
7. Hepatocellular carcinoma in Surgical pathology of liver tumors. Taofic M, Vishal SC, Michael ST (editors).
8. Xu W, Ge B, Liao W, Ren J, Yang H, et al. (2016) Edmondson grade predicts survival of patients with primary clear cell carcinoma of liver after curative resection: A retrospective study with long-term follow-up. *Asia Pac J Clin Oncol*.
9. Clayton EF, Furth EE, Ziober A, Xu T, Yao Y, et al. (2012) A case of primary clear cell hepatocellular carcinoma in a non-cirrhotic liver: an immunohistochemical and ultrastructural study. *Rare Tumors* 4: e29.
10. Wu PC, Lai CL, Lam KC, Lok ASF, Lin HJ (1983) Clear cell carcinoma of liver. An ultrastructural study. *Cancer* 52: 504-507.
11. Murakata LA, Ishak KG, Nzeako UC (2000) Clear Cell Carcinoma of the Liver: A Comparative Immunohistochemical Study with Renal Clear Cell Carcinoma. *Mod Pathol* 13: 874-881.
12. Ji SP, Li Q, Dong H (2010) Therapy and prognostic features of primary clear cell carcinoma of the liver. *World J Gastroenterol* 16: 764-769.
13. Orikasa H, Ohyama R, Tsuka N, Eyden BP, Yamazaki K (2001) Lipid-rich clear-cell hepatocellular carcinoma arising in non-alcoholic steatohepatitis in a patient with diabetes mellitus. *J Submicrosc Cytol Pathol* 33: 195-200.