Radiology Case Reports 14 (2019) 1377–1381

Available online at www.sciencedirect.com

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journal homepage: www.elsevier.com/locate/radcr

Case Report

A case of primary clear cell hepatocellular carcinoma comprised mostly of clear cells

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ARTICLE INFO

Article history:
Received 10 June 2019
Revised 28 August 2019
Accepted 30 August 2019
Available online 16 September 2019

Keywords:
Clear cell hepatocellular carcinoma
Hepatocellular carcinoma
Clear cell carcinoma
Computed tomography
Magnetic resonance imaging

ABSTRACT

Clear cell hepatocellular carcinoma (CHCC) is defined as a tumor which contains more than 50% of clear cells. However, CHCC with more than 90% of clear cells are extremely rare. We report a case of a 65-year-old woman who was found to have a solitary mass, which was histologically diagnosed as clear cell hepatocellular carcinoma composed of 90% or more clear cells. The tumor presented rim arterial phase hyperenhancement in computed tomography, magnetic resonance imaging, and computed tomography during hepatic arteriography, and was classified as LR-M category according to The Liver Imaging Reporting and Data System version 2018(LI-RADS v2018). This tumor may mimic other tumors with similar radiographic features, such as intrahepatic cholangiocellular carcinoma and metastatic tumor.

Introduction

Clear cell hepatocellular carcinoma (CHCC) is a type of HCC in which clear cells, which have a clearer cytoplasm than normal HCC cells, comprise 50% or more of the tumor [1]. CHCC is a rare lesion, which has been reported to account for 7.3%-12.5% of all liver cancers. In particular, CHCC in which more than 90% of the tumor comprises clear cells is extremely rare [2]. Here we describe the radiological findings of a patient with CHCC, in which more than 90% of the tumor comprised clear cells.

Case

A liver lesion was found in a 65-year-old woman with chronic hepatitis C during a follow-up study. She had no significant family history. A liver lesion was detected in segment 7 on

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https://doi.org/10.1016/j.radcr.2019.08.021

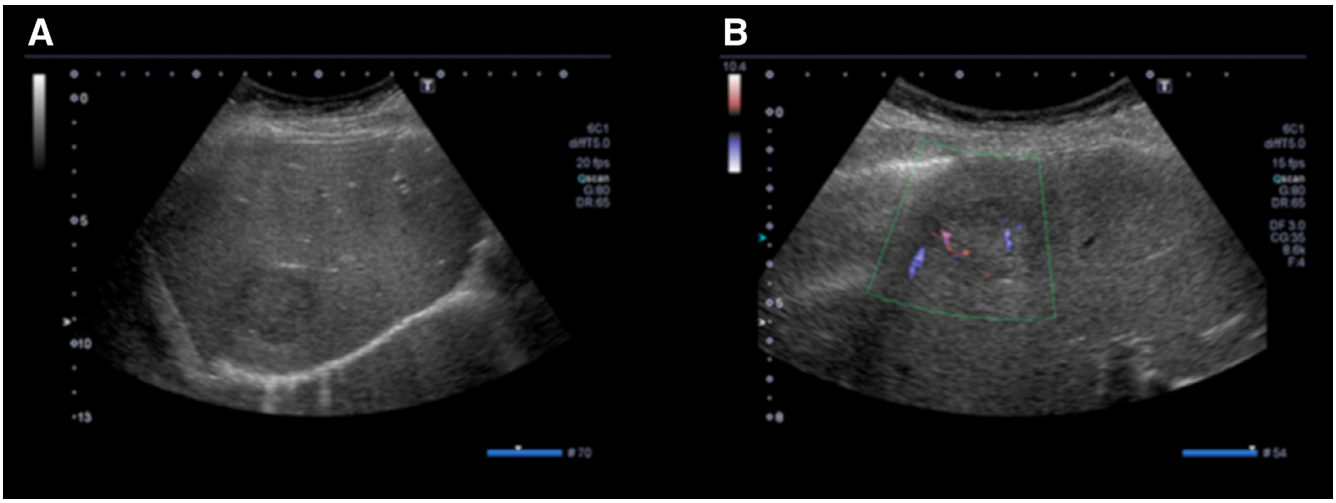

Fig. 1. – (A) Abdominal ultrasound displayed an isoechoic mass with a hypoechoic rim in segment 7, with a microlobulated surface. The lesion did not have a lateral shadow and had slightly posterior echo enhancement. (B) Color flow Doppler images displayed inflow of the blood flow signal, which indicated that the lesion was hypervascular.

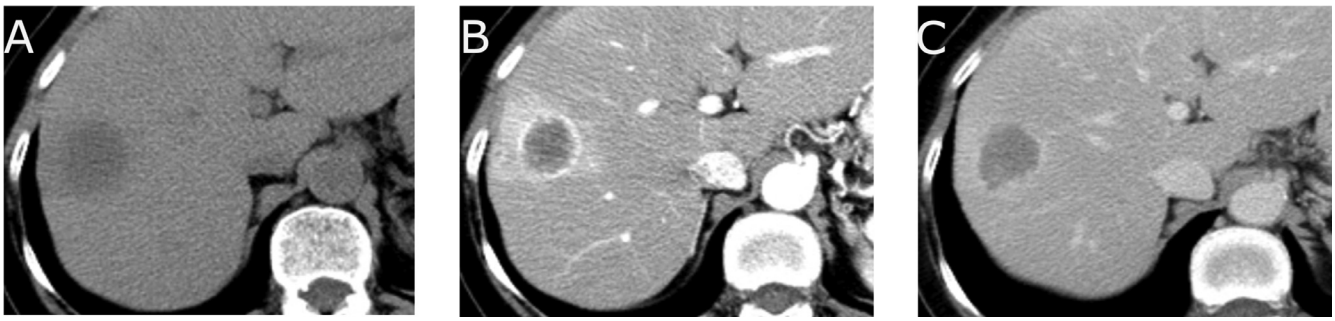

Fig. 2. – (A) Plain CT of the liver displaying a low-density mass with a maximum diameter of 30 mm on segment 7. (B) Dynamic enhanced CT displaying a ring-like enhancement in the arterial phase. (C) In the equilibrium phase, an enhancing capsule was observed, and the center of the lesion was slightly enhanced.

ultrasound. Magnetic resonance imaging was performed, and the lesion was suspected to be hemangioma; therefore, the physician decided to perform follow-up of the patient. However, the size of the lesion was found to have increased after 6 months, and additional analysis was performed. Blood analyses showed an abnormal platelet count (98,000/μL) and total protein (8.3 g/dL). The following tumor markers were increased: AFP, (26.0 ng/mL), AFP-L3 (40.7%), and PIVKA II (65 mAU/mL).

Abdominal ultrasound displayed an isoechoic mass with a hypoechoic rim in segment 7, with a microlobulated surface. The lesion did not have a lateral shadow and had slight posterior echo enhancement. Color flow Doppler images displayed internal vascularity, and these findings indicated that the lesion was hypervascular (Fig. 1).

Abdominal computed tomography (CT) displayed a low-density mass, in which the largest diameter was 30 mm on segment 7. Rim arterial phase hyperenhancement (rim APHE) was observed, and a capsule-like structure was observed in the equilibrium phase. Many small dot enhancements were displayed in the center of the lesion, and the center of the lesion was slightly stained (Fig. 2).

Abdominal magnetic resonance imaging displayed the tumor as a low-intensity region in both the in-phase and opposed-phase of T1-weighted imaging. The decreased signal intensity on chemical shift imaging was 16% [3]. T2-weighted imaging displayed the tumor as a clear high intensity lesion. Diffusion-weighted imaging showed that the lesion also had clear high signal intensity, and the Apparent Diffusion Coefficient (ADC) map showed low intensity, and these findings indicated restricted diffusion (Fig. 3). A total of 0.025 mmol/kg of gadoxetic acid was injected via the antecubital vein at 2 mL/s, followed by 40 mL of physiological saline. The dynamic study included the arterial phase, portal phase, transitional phase, and hepatobiliary phase after injecting the contrast material. The lesion showed rim APHE and hypointensity in the hepatobiliary phase.

CT during hepatic arteriography displayed rim APHE, and neovascularity was observed in the center of the lesion. Corona enhancement was also observed around the tumor

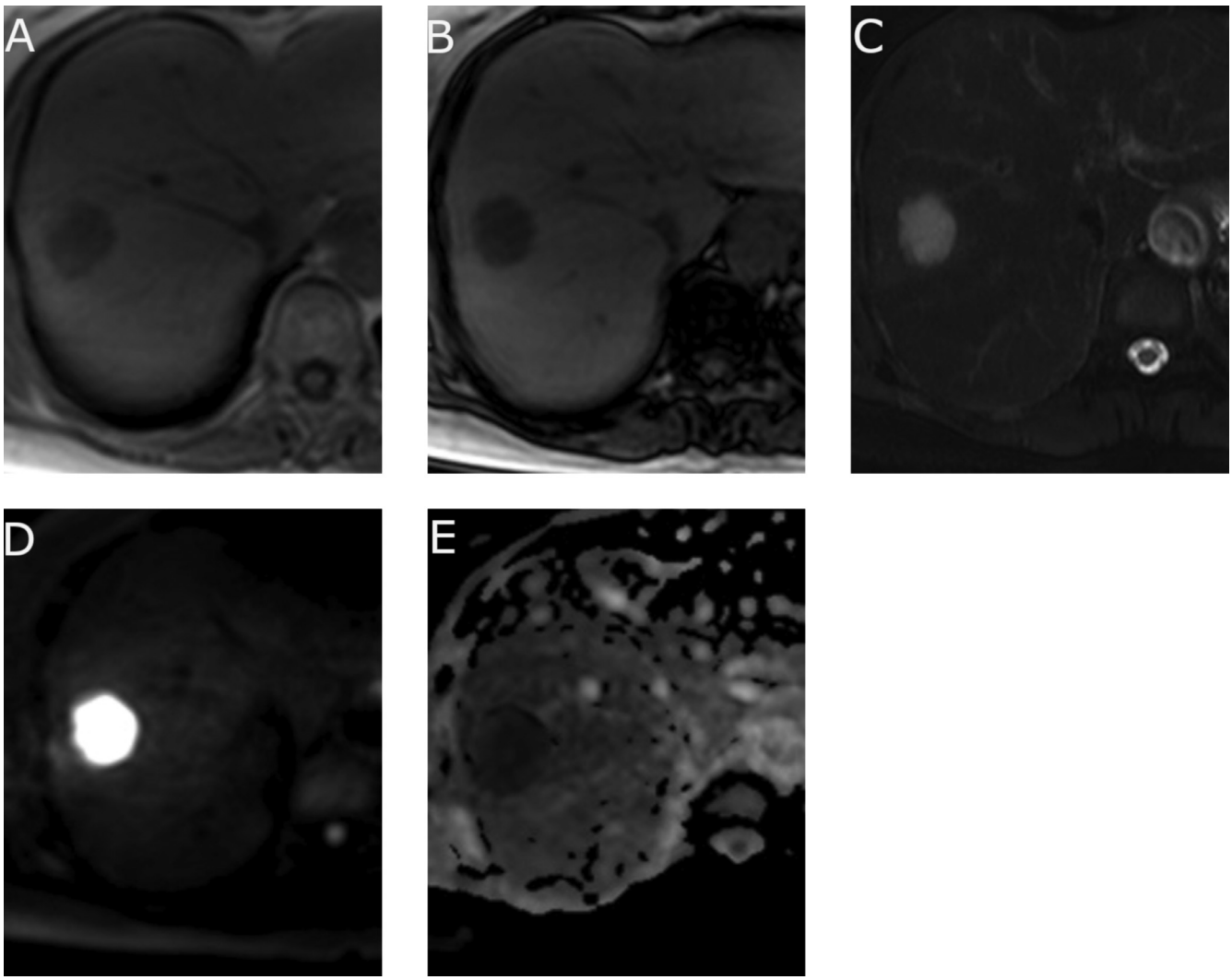

Fig. 3. – Nodule hypointensity displayed on in-phase (A) and opposed-phase T1WI (B). The lesion is displayed as a clear high intensity area on T2WI (C). DWI displays the lesion as an area of clear hyperintensity (D), and the ADC map displays the lesion as an area of hypointensity (E).

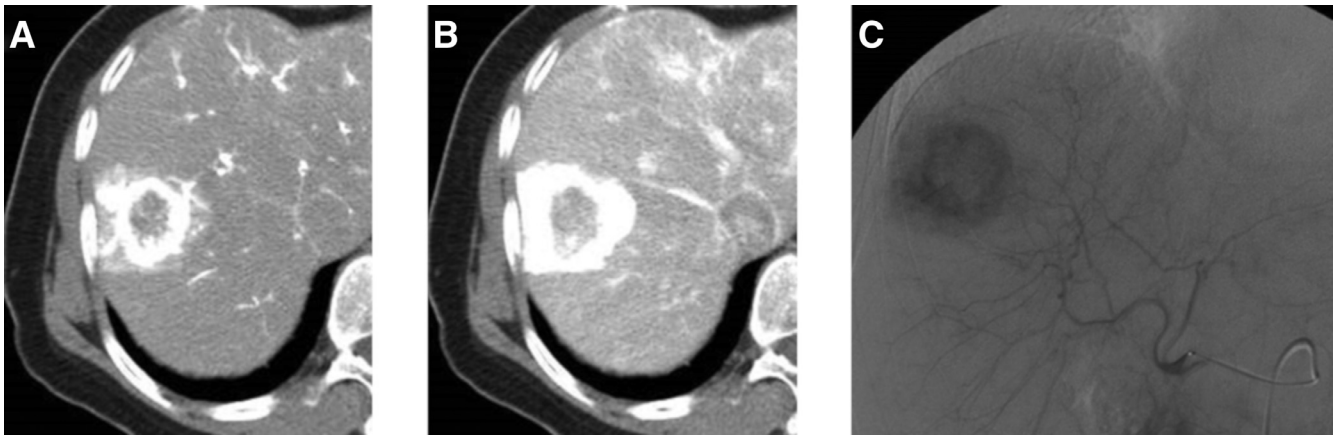

Fig. 4. – (A) CT during hepatic arteriography displayed rim APHE, and neovascularity was observed in the center of the lesion. (B) Corona enhancement was also observed around the tumor. (C) Common hepatic arteriography displayed rim enhancement.

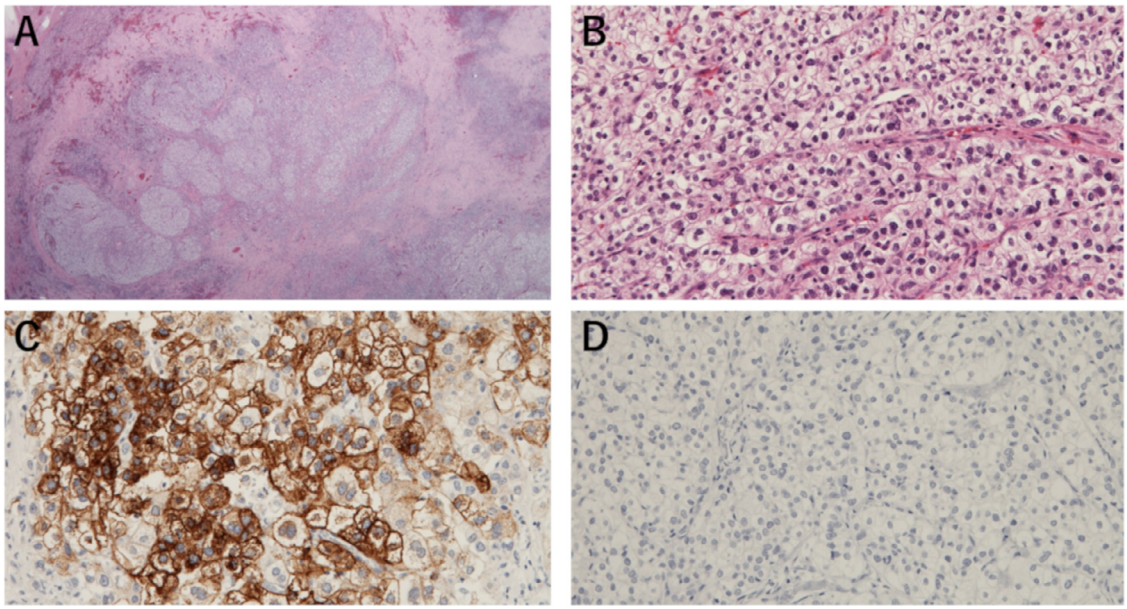

Fig. 5. – Hematoxylin and eosin staining demonstrating that the lesion is surrounded by a fibrous capsule structure (A, × 10 magnification), and more than 90% of the tumor is comprises clear cells (B, × 200 magnification). Immunohistochemical staining demonstrated that the tumor was positive for glypican 3 (C, × 200 magnification), but negative for HepPar-1 (D, × 200 magnification).

(Fig. 4). Common hepatic arteriography displayed rim enhancement (Fig. 4).

Partial hepatectomy was performed based on the diagnosis of malignant tumor. The fibrous capsule structure was confirmed pathologically. More than 90% of the tumor comprised clear cells, and clear cells formed an alveolar structure that was surrounded by vascular stroma. The cytoplasm of the clear cells contained a large amount of stored glycogen and few fat vacuoles. Immunohistochemical analyses showed that following characteristics: glypican 3 (+), Hepatocyte Paraffin 1 (HepPar-1) (–), and epithelial membrane antigen (–). These pathological findings and the absence of a primary lesion elsewhere by radiological analysis supported the diagnosis of primary CHCC (Fig. 5). Background liver tissue corresponded to F2 of the New Inuyama classification.

Discussion

Cases of CHCC in which clear cells comprise more than 90% of the tumor are extremely rare. CHCC is more frequent in females than classical HCC, and 90% of patients with CHCC are reported to have cirrhosis. Almost all of the patients had hepatitis B or hepatitis C, and the CHCC was pathologically classified into the moderately differentiated type in most patients [2]. Clayton et al reported that CHCC in which clear cells comprise more than 90% of the tumor was associated with the absence of cirrhosis [4]. Our present case was similar with this previously reported case.

CHCC has been reported to generally show similar findings to classical HCC [5–7], such as hypervascularity in the arterial phase, washout in the portal phase, and a pseudocapsule. The present patient also showed a pseudocapsule, as well as atypical findings, such as rim APHE in the arterial phase. Diffusion-weighted imaging showed hyperintensity and the ADC map showed hypointensity. We assumed that the restricted diffusion in this case was owing to the high proportion of clear cells and small amount of interstitial space. CT during arteriography showed corona enhancement [8]. Corona enhancement is an imaging feature described in The Liver Imaging Reporting and Data System version 2018(LI-RADS v2018), and is an ancillary feature characteristic of malignancy in general, but not HCC in particular. Corona enhancement is a periobservational enhancement occurring in the late arterial phase or early portal phase, which is attributable to venous drainage from a tumor. It does not refer to periobservational enhancement attributable to arterioportal shunting, which indicates that the drainage vein is the portal vein. The drainage vessel of almost all liver tumors, except for HCC, is the hepatic vein. In our present patient, we were able to diagnose the lesion as HCC from the pseudocapsule and corona enhancement, although some characteristics of the LR-M category, such as rim APHE, were observed. This radiographic feature mimics intrahepatic cholangiocellular carcinoma and metastatic tumor.

Our present patient reminded us of the importance of ultrasound, as the ultrasound images displayed typical HCC findings [9]. Additional information from contrast-enhanced ultrasonography would enable easier qualitative diagnosis [10].

CHCC is usually difficult to distinguish from metastatic clear cell carcinoma from the kidney, ovary, and adrenal gland. Immunohistochemical staining of molecules, such as

glypican-3 and HepPar-1, is useful for confirming the liver origin clear cell carcinoma [2,11].

The tumor of the present patient was glypican 3 (+), HepPar-1 (–), and epithelial membrane antigen (–), and these findings were atypical for CHCC. Most cases of CHCC are positive for HepPar-1 [11]. We assumed that HepPar-1 was negative in our patient owing to the small number of cytoplasmic organelles in the tumor cells. Sakhuja et al reported a similar case to our case, and they discussed that HepPar-1 was probably negative owing to the low number of cytoplasmic organelles [12]. Furthermore, we radiologically confirmed the absence of a primary lesion in the kidney, ovary, and adrenal gland of our patient.

The association between the proportion of clear cells and the prognosis of CHCC is controversial [2,13,14]. A recent study reported a more favorable prognosis in patients with higher proportions of clear cells. Our present patient had a tumor with a high proportion of clear cells, and therefore, a favorable prognosis can be expected. However, the postoperative course of our patient has not been followed, and hence the clinical outcome remains unknown.

Conclusion

We reported an extremely rare case of CHCC in which clear cells comprise more than 90%. The tumor presented rim APHE and was classified as LR-M category according to LI-RADS v2018. It may mimic other tumors with similar radiographic features, such as intrahepatic cholangiocellular carcinoma and metastatic tumor.

REFERENCES

[1] Takahashi A, Saito H, Kanno Y, Abe K, Yokokawa J, Irisawa A, et al. Case of clear-cell hepatocellular carcinoma that developed in the normal liver of a middle-aged woman. World J Gastroenterol 2008;14(1):129–31.

[2] Yang SH, Watanabe J, Nakashima O, Kojiro M. Clinicopathologic study on clear cell hepatocellular carcinoma. Pathol Int 1996;46(7):503–9.

[3] Jhaveri KS, Elmi A, Hosseini-Nik H, Hedgire S, Evans A, Jewett M, et al. Predictive value of chemical-shift MRI in distinguishing clear cell renal cell carcinoma from non-clear cell renal cell carcinoma and minimal-fat angiomyolipoma. AJR Am J Roentgenol 2015;205(1):W79–86.

[4] Clayton EF, Furth EE, Ziober A, Xu T, Yao Y, Hwang PG, et al. A case of primary clear cell hepatocellular carcinoma in a non-cirrhotic liver: an immunohistochemical and ultrastructural study. Rare tumors 2012;4(2):e29.

[5] Tan Y, Xiao EH. Rare hepatic malignant tumors: dynamic CT, MRI, and clinicopathologic features: with analysis of 54 cases and review of the literature. Abdom Imaging 2013;38(3):511–26.

[6] Wang H, Tan B, Zhao B, Gong G, Xu Z. CT findings of primary clear cell carcinoma of liver: with analysis of 19 cases and review of the literature. Abdom Imaging 2014;39:736–43.

[7] Liu QY, Li HG, Gao M, Lin XF, Li Y, Chen JY. Primary clear cell carcinoma in the liver: CT and MRI findings. World J Gastroenterol 2011;17(7):946–52.

[8] Ueda K, Matsui O, Kawamori Y, Nakanuma Y, Kadoya M, Yoshikawa J, et al. Hypervascular hepatocellular carcinoma: evaluation of hemodynamics with dynamic CT during hepatic arteriography. Radiology 1998;206(1):161–6.

[9] Nino-Murcia M, Ralls PW, Jeffrey RB Jr, Johnson M. Color flow Doppler characterization of focal hepatic lesions. AJR Am J Roentgenol 1992;159(6):1195–7.

[10] D'Onofrio M, Crosara S, De Robertis R, Canestrini S, Mucelli RP. Contrast-enhanced ultrasound of focal liver lesions. AJR Am J Roentgenol 2015;205(1):W56–66.

[11] Murakata LA, Ishak KG, Nzeako UC. Clear cell carcinoma of the liver: a comparative immunohistochemical study with renal clear cell carcinoma. Mod Pathol 2000;13(8):874–81.

[12] Sakhuja P, Mishra PK, Rajesh R, Sharma AK, Gondal R, Singh M. Clear cell hepatocellular carcinoma: back to the basics for diagnosis. J Cancer Res Ther 2015;11(3):656.

[13] Ji SP, Li Q, Dong H. Therapy and prognostic features of primary clear cell carcinoma of the liver. World J Gastroenterol 2010;16(6):764–9.

[14] Liu Z, Ma W, Li H, Li Q. Clinicopathological and prognostic features of primary clear cell carcinoma of the liver. Hepatol Res 2008;38(3):291–9.