Centrally-located Sclerosing Hepatocellular Carcinoma: A Case Report with Imaging Findings before and after Transcatheter Arterial Chemoembolization

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Sclerosing hepatocellular carcinoma is a rare subtype of hepatocellular carcinoma (HCC), characterized by intense fibrous stroma separating cords of tumor cells. It has a different imaging presentation from that of ordinary HCC. We report this uncommon subtype of HCC around the hepatic hilum in a 55 year-old female. The lesion showed hypervascularity in the peripheral portion and prolonged enhancement in the central fibrous portion on both dynamic computed tomography (CT) scan and angiography. The tumor was resistant to the transcatheter arterial chemoembolization therapy, and peripheral globular Lipiodol retention was noted in the tumor site of liver on the follow-up CT scan.

Key words: Sclerosing hepatocellular carcinoma, Hepatocellular carcinoma, Computer Tomography (CT), Transcatheter arterial chemoembolization (TACE) therapy

Edmondson described a variant of hepatocellular carcinoma (HCC) as “a carcinoma of the liver with dense stroma” in 1958 [1]. Then in 1976, Peters briefly described it as a subclass “sclerosing liver carcinoma” from 247 liver tumors in 38586 autopsies in the Los Angeles area [2]. The tumor cells in sclerosing HCC are embedded in abundant fibrous stroma, instead of in the prominent sinusoid seen in patients with ordinary HCC. Although the fibrolamellar HCC also has intense fibrous stroma, it is different from the sclerosing HCC in clinicopathological findings. Fibrolamellar HCC is usually seen in young patients and has a much more favorable prognosis than the other types of HCC [3]. Histologically, tumor cells are composed of eosinophilic polygonal hepatocytes in fibrolamellar HCC. The imaging features of sclerosing HCC have been presented in less than 100 cases in the literature. The features include the absence of a tumor capsule, focal atrophy, homogeneous architectures, hypervascularity, arterial encasement, and delayed enhancement due to fibrous component of tumor [4-6].

CASE REPORT

A 55 year-old female, who is a HBV carrier, came to our hospital with complaints of abdominal fullness and occasional nausea for 2 months. Physically, only epigastric tenderness was noted. The laboratory studies showed abnormal liver function (ALT: 118 u/l, AST: 165 u/l, ALK-P: 340 u/l, γ-GT: 378 u/l), positive HBs antigen and negative anti-HCV antibody, and markedly
elevated α-fetoprotein (AFP: 50607 ng/ml). The serum calcium level (10.1 mg/ml) was within normal limit.

Abdominal sonography revealed a hypoechoic mass in liver. Dynamic CT scan of the liver further demonstrated a 10 × 11 × 9 cm hypodense tumor with geographic margins at the central portion of segment I, IV, and VIII of liver (Fig. 1a). The tumor was densely enhanced at its periphery in the arterial phase (Fig. 1b) and prolonged enhancement at its center in the late phase (Fig. 1c). Enlarged lymph nodes were also

Figure 1. Dynamic CT scan: a. A hypodense tumor with geographic margin in segment I, IV, VIII of liver was depicted in precontrast scan b. In arterial phase, the peripheral part of the tumor enhanced densely. In addition, the right portal vein was engulfed by the tumor. c. The central part of the tumor was enhanced in the portal phase.

Figure 2. Microscopic pathology (H & E stain, 100X) of the two specimens a. Biopsy from peripheral part of the tumor revealed grade II HCC with trabecular and occasional glandular patterns. b. Biopsy from central part of the tumor showed dense fibrous stroma separating cords of tumor cells.
depicted at the hepatic hilum. The intrahepatic bile ducts were not dilated. The main portal vein and its branches were patent, though the tumor engulfed the right portal vein. Sclerosing HCC was proven using the results of pathologic tests obtained during a sono-guided biopsy, which revealed grade II HCC with trabecular and occasional glandular patterns (Fig. 2a), and dense fibrous stroma was noted between tumor nests (Fig. 2b). The non-tumorous liver tissue showed portal fibrosis and sinusoidal fibrosis.

Angiography revealed a hypervascular tumor with fine tumor vessels around the hepatic hilum, and there was neither tumor encasement of the hepatic arteries nor any portal vein involvement (Fig. 3). Transcatheter arterial chemoembolization (TACE) was performed with infusion of 15 ml Lipiodol and 30 mg Adriamycin into the proper hepatic artery. Follow-up AFP dropped to 661 ng/ml 2 months after treatment, while abdominal CT scan showed a decrease in the tumor size to 8 cm at the largest area. Globular Lipiodol retained in the peripheral part and the central part was spared with enhancement in late phase (Fig. 4). The second TACE was performed 2 months after the first one. Through the right and left hepatic arteries, 10 ml Lipiodol and 30 mg Adriamycin were infused. The central part of the tumor was still resistant to the embolization therapy depicted on the follow-

Figure 3. a. Superselective proper hepatic arteriography revealed a hypervascular tumor around the hepatic hilum, with fine tumor vessels noted. b. Superior mesenteric arterial portography demonstrated patency of bilateral main portal veins and their branches.

Figure 4. Follow-up CT scan 2 months after the first TACE revealed that: a. Globular Lipiodol retained in the periphery, with sparing of the central part of the tumor. b. The central part of the tumor became more densely enhanced in the portal phase.
up CT scan. The patient received the third TACE 5 months after the first one, with result of incomplete obliteration of the tumor stains supplied from right and middle hepatic arteries, and no further embolization due to her intolerance to the epigastralgia. Concurrent systemic chemotherapy was given twice with EPFL regimen (etopoxide, prednisolone, 5-FU, leukovorin). CT scan obtained 12 months after the first TACE showed Lipiodol resorption and progressively enlarged tumor to 10 cm in diameter, associated with portal vein encasement, biliary obstruction and IVC invasion. The patient refused further treatment and was lost of follow-up.

**DISCUSSION**

Sclerosing HCC is a rare subtype of HCC, also named as scirrhous HCC, characterized by intense fibrous stroma separating cords of tumor cells. It is often seen following radiation, chemotherapy or infarction [1]. However, varying degrees of the sclerosing HCC are also found in HCCs without any known etiologic factors [7].

Histopathologically, tumor necrosis and hemorrhage are extremely rare. Extrahepatic metastasis is frequent, and the two most common sites are porta hepatis lymph node and lung [2]. Clinically, sclerosing HCC is associated with a high incidence of hypercalcemia, and parathyroid hormone-related protein production by the tumor has been reported in some cases [2, 8]. There was no hypercalcemia in our patient. The imaging presentation of patients with sclerosing HCC is different from that of patients with ordinary HCC. It shows both hypervascularity and prolonged enhancement on angiography or dynamic CT scan, corresponding to vascular (carcinoma cell) and fibrous (stroma) components of the tumor [3]. The prolonged enhancement is probably due to slow washout of extravascular contrast agents in the fibrous stroma [3], which is also present in other fibrous tumors, such as cholangiocarcinoma, metastatic adenocarcinoma from the colon [9]. However, they are usually less vascular in the arterial phase, which can be differentiated from sclerosing HCC. Fibrolamellar HCC also shows delayed or prolonged enhancement in its central fibrous scar. However, in addition to the clinicopathological differences, fibrolamellar HCC has other imaging features different from sclerosing HCC, including calcification and heterogeneous architecture with necrosis [10]. In our patient, the neoplastic and fibrous components of the tumor appeared to be somehow separated, since hypervascularity mainly in the periphery and prolonged enhancement in the central portion of the tumor were depicted. In addition, peripheral globular Lipiodol retention was noted after TACE. These observations correlated with the pathologic findings of liver biopsy obtained from the central and peripheral parts of the tumor. Though the tumor was large around the hilum, portal vein and hepatic artery, they were not encased or invaded and no bile duct obstruction was found initially. Other characteristics of sclerosing HCC, such as focal atrophy and arterial encasement have been reported [4,5]. However, they were not seen in the initial imaging presentation of this patient.

In this patient, each TACE showed temporary obliteration of the tumor stain, then central viable tumor and Lipiodol retention in the peripheral rim were noted on follow-up CT scan. The findings reflect that sclerosing HCC is very resistant to chemoembolization. It could be explained by poor Lipiodol accumulation in the fibrous part, where some residual neoplastic tissues were still embedded. Thereafter, the neoplastic tissues spread outward and became infiltrative. Recently, microwave coagulation has been applied to treat sclerosing HCC with efficacy [11]. However, the candidates reported in most of the cases in the literature were peripherally-located sclerosing HCC. Centrally-located sclerosing HCC including that found in our patient is not suitable for this therapy, since the heat is easily carried away by great vessels at hepatic hilum.

In conclusion, the imaging presentation of the centrally-located sclerosing HCC in our patient includes homogeneous density on non-contrast CT scan, absence of tumor capsule, no encasement of hepatic artery, portal vein and bile ducts until the late stage, hypervascularity, lymphadenopathy in the porta hepatis, prolonged enhancement and resistance to TACE. The last two findings are considered due to the presence of intense fibrous stroma, and are not usually found in patients with ordinary HCC.

**REFERENCES**

中心位置硬化性肝細胞癌於動脈栓塞治療前後之影像學發現：一病例報告

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硬化性肝細胞癌是一種罕見的肝細胞癌亞型，特徵在於有豐富的纖維性基質。它的影像學表現不同於一般的肝細胞癌。我們報告一例五十五歲女性病人長有此種罕見的肝癌亞型在肝門周圍，電腦斷層及血管攝影發現此腫瘤的周圍部份呈現高血管性，而中心纖維部份呈現延遲顯影。它對經導管動脈栓塞治療效果不佳，治療後電腦斷層攝影發現油性碘Lipiodol 呈球粒狀沉積在腫瘤周邊。

關鍵詞：硬化性肝細胞癌，肝細胞癌，電腦斷層攝影，經導管動脈栓塞治療