Case Report

Spontaneous complete necrosis of hepatocellular carcinoma caused by feeding vessel occlusion outside the tumour capsule

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ABSTRACT

A 64-year-old man began treatment for chronic hepatitis C with peg-interferon and ribavirin. His hepatitis C virus ribonucleic acid (HCV-RNA) results turned negative. Just after the treatment, a computed tomography (CT) scan revealed a hypovascular mass in the segment 8. We performed a right hemihepatectomy as HCC. Upon macroscopic examination, the tumour was yellow and firm with a fibrous capsule. A wedge-shaped necrotic area was located at the top of an artery and a portal vein of segment 8. Necrosis was observed not only in the tumour but in the adjacent parenchyma. A histopathological examination showed that the tumour had been completely replaced by necrosis. This tumour was surrounded by capillary vessels and fed by several thick arteries, but organized thrombi were not detected. No viable cells were found. The histopathological diagnosis was a spontaneous complete necrosis of HCC caused by the occlusion of feeding vessels outside the capsule.

Keywords: Spontaneous Necrosis, Hepatocellular Carcinoma, Vascular Occlusion.

Spontaneous necrosis or regression of neoplasms occurs in 1 in 60,000 to 100,000 of all tumours [1]. The spontaneous complete necrosis of hepatocellular carcinoma (HCC) is quite rare, with a frequengy of 1 in 140,000 cases of HCC [2]. Possible causes of necrosis include feeding vessels thrombosis, oxygen deprivation due to bleeding, and cessation of exposure to noxious agents, such as alcohol and tobacco smoke [3]. HCCs are generally fed only by the hepatic artery; hence, they shrink easily due to ischemia included by degreased arterial blood flow. In contrast, some immunological mechanisms, such as lymphocyte infiltration and various cytokines are related to the spontaneous necrosis of HCC [3-7]. However, the mechanism of the spontaneous necrosis and regression of HCC remains unclear.

Here, we report the spontaneous complete necrosis of HCC by feeding artery or portal venous occlusion, as demonstrated by a histological examination.

CASE REPORT

A 64-years-old man began treatment for chronic hepatitis C with peg-interferon and ribavirin in October 2011. His blood hepatitis C virus ribonucleic acid (HCV-RNA) level decreased to below the measurable range 12 weeks later. After the interruption of treatment 53 weeks later due to pancytopenia, an abdominal computed tomography (CT) scan revealed a tumour in the liver. The serum concentrations of proteins induced by vitamin K absence or antagonism-2 (PIVKA-2) and that of alpha-fetoprotein (AFP) were not elevated, but that of cancer

antigen 19-9 (CA19-9) was slightly elevated (43 IU/ml). The patient was referred to our hospital for surgery.

A dynamically enhanced multi-detector-row CT (MDCT) images revealed a hypovascular mass measuring 41 mm in the segment 8 of liver. An arterial phase image showed a capsule-like enhancement around the mass. This enhancement was unremarkable and continued in the delayed phase without wash-out. The inside of the mass took in little material, but slight intake by the intratumoral nodule appeared in the delayed phase (**Fig. 1**). Gadolinium ethoxybenzyl diethylenetriaminepentaacetic acid (Gd-EOB-DTPA) - enhanced magnetic resonance imaging (MRI) showed that the mass structure was more remarkable than that demonstrated by the CT scan, with a thick capsule and internal nodule. In contrast to the CT findings, the capsule and nodule were slightly enhanced from the early phase to the delayed phase. In the hepatocyte phase, the triangular enhancement of the parenchyma around the mass was absent (**Fig. 2**).

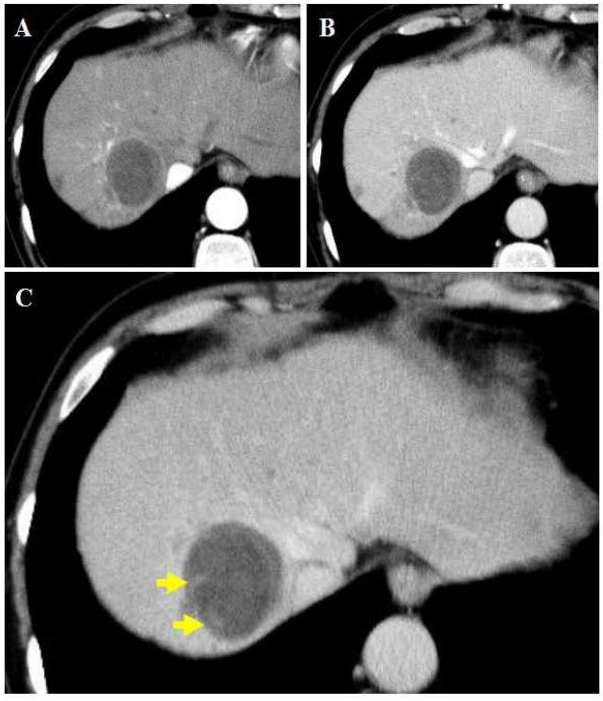

Figure 1: Dynamically enhanced MDCT image A) Arterial phase, B) portal phase, and C) delayed phase. A hypovascular mass was present in the anterior segment. A capsule-like enhancement around the mass continued from the arterial phase to the delayed phase. Slight intake by an intratumoral nodule appeared in the delayed phase (yellow arrows).

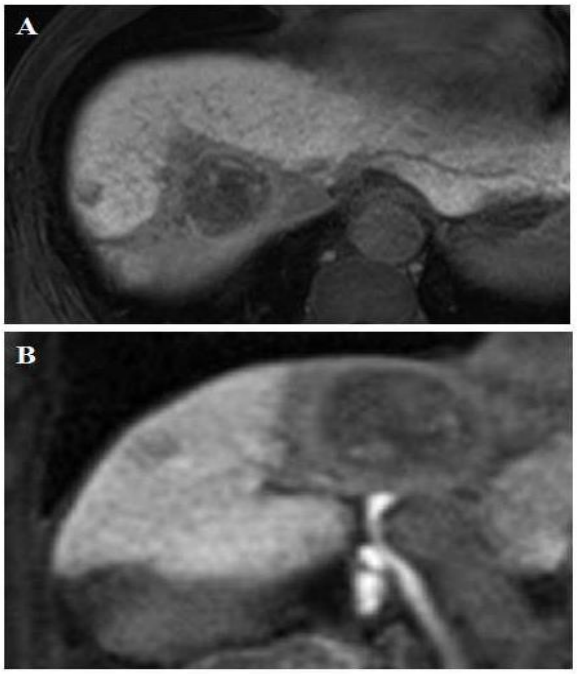

Figure 2: Gd-EOB-DTPA-enhanced MRI image of hepatocyte phase A) Axial and B) coronal images. The thick capsule and internal nodule were more remarkable than shown by CT and continually enhanced. The enhancement of the parenchyma around the mass was absent in triangular shape.

We diagnosed the lesion as HCC or a combined hepatocellular and cholangiocarcinoma lesion due to the imaging findings and the patient's history of hepatitis C. We performed a right hemihepatectomy in December 2012 (operation time 465 min. blood loss 6536 ml). The patient was discharged on the 20th day after the operation. No recurrence was detected at 30 months after the operation.

Upon macroscopic examination, the tumour was yellow and firm with a fibrous capsule. The wedge-shaped necrotic area was located at the top of an artery and a portal vein that fed the tumour and segment 8. These vessels were approximately 2 cm away from the HCC capsule. Necrosis was observed not only in HCC itself, but also in the adjacent parenchyma (**Fig. 3**). The histo-pathological examination showed that the tumour in the cirrhotic liver had been completely replaced by central coagulative necrosis, which consisted of linearly-arranged large cells, similar to hepatocytes, and a few inflammatory cells. This coagulative necrosis was found not only in this tumour, but also in adjacent regenerative nodules. This tumour was surrounded by capillary vessels and was fed by several thick arteries, but no organised thrombi or

tumour cells in the hepatic artery were detected. No viable cells were found in this tumour (**Fig. 4**). The histopathological diagnosis was a spontaneous complete necrosis of HCC, possibly caused by the occlusion of feeding vessels outside the capsule.

DISCUSSION

The spontaneous regression of cancer is defined as the partial or complete disappearance of a malignant tumour in absence of all treatments or in presence of a therapy that is considered inadequate to exert a significant influence on neoplastic disease [8]. According to a report by Huz et al. in 2012 that reviewed 75 studies on spontaneous HCC regressions published in the English language, the common mechanisms of spontaneous regression of HCC were tumour hypoxia (n=21, 28.0%), a systemic inflammatory response (n=25, 33.3%) and unknown causes (n=29, 38.7%) [9]. These authors also noted that hypoxia resulted not only from direct ischemia, such as arterial or portal obstruction, but also from hypoperfusion, such as hypotension associated with variceal bleeding.

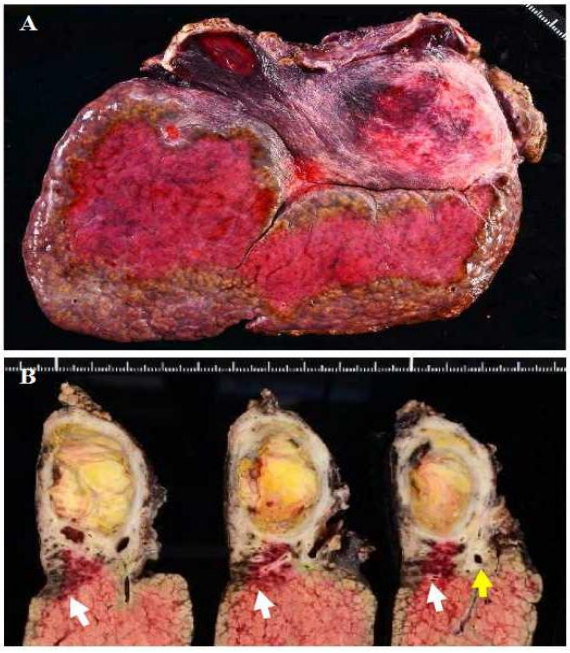

Figure 3: Macroscopic findings of the specimen A) Resected liver and B) cut side of the tumour. The tumour was yellow and firm with a fibrous capsule. The wedge-shaped necrotic area was located at the top of vessels feeding the tumour and segment 8 (yellow arrow). Necrosis was observed not only in the tumour itself, but also in the adjacent parenchyma (white arrows).

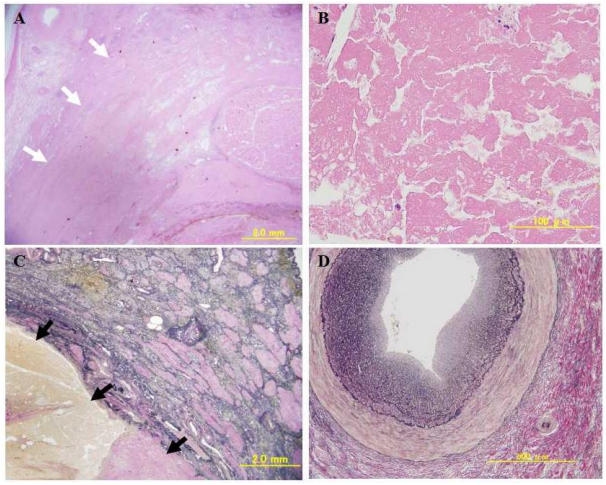

Figure 4: Histopathological examination A,B) Hematoxylin-Eosin stain, and C,D) Elastica van Gieson stain. A) The tumour covered by thick fibrous capsule (white arrows) had been completely replaced by central coagulative necrosis, B) which consisted of linearly-arranged large cells similar to hepatocytes and a few inflammatory cells. C) This coagulative necrosis (black arrows) was found not only in this tumour, but also in adjacent regenerative nodules. D) This tumour was surrounded by several thick arteries, but organized thrombi in the hepatic artery were not detected.

As most previous cases have suggested, during vascular occlusion, arteries feeding necrotic HCCs become markedly narrowed and obstructed at the point at which they penetrate HCC capsules. Thick fibrous capsules around HCC stop the blood supply, resulting in necrosis. Theses occlusions have also originated from a thick fibrous medial membrane or a hyaline thrombus in the arterial wall. However, the adjacent tissues outside the capsule were nearly intact. Therefore, the occlusion was considered to have occurred in the vessels penetrating the HCC capsule.

In the present case, we found an unusual histopathological result of spontaneous necrosis of HCC. A wedge-shaped necrotic area was located at the top of an artery and a portal vein that fed the HCC and segment 8. These vessels were distant from the capsule, and necrosis was observed not only in the HCC itself, but also in the adjacent parenchyma. This finding suggests that the occlusion of the vessels could have occurred at this point, particularly at the feeding artery, as though transcatheter arterial or portal venous embolisation had been performed before the operation. However, no emboli, such as thrombi, were detected in the vessels. Neither HCCs nor

inflammatory cells had invaded these vessels. No reports exist that describe their similar histological findings.

We believe that some type of vascular obstruction, such as a spasm, occured in the present case. Regarding the start of necrosis, it is reasonable that the HCC was already present when this patient was medicated for hepatitis C. Two possible causes exist for this speculation. One cause is the cessation of smoking. The patient stopped smoking immediately before hepatitis C treatment. Changes in a vasoactive substance, such as nicotine or nitrogen oxide, cause an arterial occlusion [5]. The other cause is the medication that was administered for chronic hepatitis C. The administration and interruption of peg-interferon and ribavirin might have stimulated an immunoreaction in the patient's liver to cause necrosis, despite no previous report mentioning this effect.

Although surgical case reports of the spontaneous regression and necrosis of HCC are increasing in frequency, but the detailed mechanism of necrosis remains unclear. Most of these cases include a partial resection; thus, the discussion of histopathological findings including adjacent parenchyma, are insufficient. Additional case reports of anatomical hepatectomy with detailed histopathological findings, such as those of Tomino, Yokoyama and Lee [10-12], are needed to investigate this necrotic mechanism.

CONCLUSION

We observed a rare case of spontaneous necrosis of HCC with specific histopathological findings. Additional case reports of anatomical hepatectomy are needed to clarify this phenomenon.

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