

CASE NOTE

Stepwise carcinogenesis of hepatocellular carcinoma in a nodule surrounded by hyperplastic and hypervascular liver tissue

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Stepwise carcinogenesis of hepatocellular carcinoma (HCC) in the cirrhotic liver has been well described pathologically and radiologically.^{1,2} It is accompanied by sequential hemodynamic changes in the nodules.^{3,4} The dysplastic nodule (DN, adenomatous hyperplasia) and early HCC frequently include portal tract structures without arterial neovascularization. In contrast, advanced HCC is characterized by abundant arterial neovascularization. Therefore, late-stage hepatic nodules are enhanced at the arterial phase of various imagings and early-stage nodules are not.

We describe a unique case in which we could observe stepwise carcinogenesis of HCC in a nodule surrounded with hyperplastic and hypervascular liver tissue.

CASE REPORT

A 59-year-old man was referred to us for the management of a hepatic lesion. Abdominal ultrasonography, performed as a follow-up examination for chronic hepatitis B and C, revealed a hypoechoic lesion 1 cm in size.

Results of biochemical investigations showed mild elevations in plasma levels of α -fetoprotein and transaminases. Plasma levels of albumin and the prothrombin time were within normal limits. There was mild leukopenia and thrombocytopenia, and elevated plasma levels of type VI collagen and hyaluronic acid.

Computed tomography (CT) with contrast showed the lesion in segment 5 of the liver in the pre-enhanced, arterial and parenchymal phases as an iso- and hypodense area with a branch of portal tract on the rim, respectively (Fig. 1A). In the arterial phase, there was an arteriportal shunt-like obscure high-density area around the lesion. The lesion was diagnosed as a DN or an early HCC.

Another CT scan, obtained 6 months after the original referral, showed a tiny high-density spot in the lesion on the arterial phase. The lesion was shown as a slightly low-density area on plain CT (Fig. 1B). Three months later, the high-density spot in the lesion had increased to 1 cm in size and almost replaced the lesion with a surrounding thin, low-density area. The surrounding shunt-like area was recognized as an obvious high-density area (Fig. 1C). The lesion was diagnosed as an early advanced HCC with a surrounding uncertain tumour-like area. The patient underwent the partial resection of the liver.

The resected specimen yielded a central 9-mm tumour with uninvolved margins and a surrounding 2-cm tumour-like lesion with obscure margins. Pathological examination revealed that the surrounding area was hyperplastic liver tissue, and the central lesion was a moderately differentiated HCC surrounded by a thin rim of well-differentiated HCC with extranodular growth

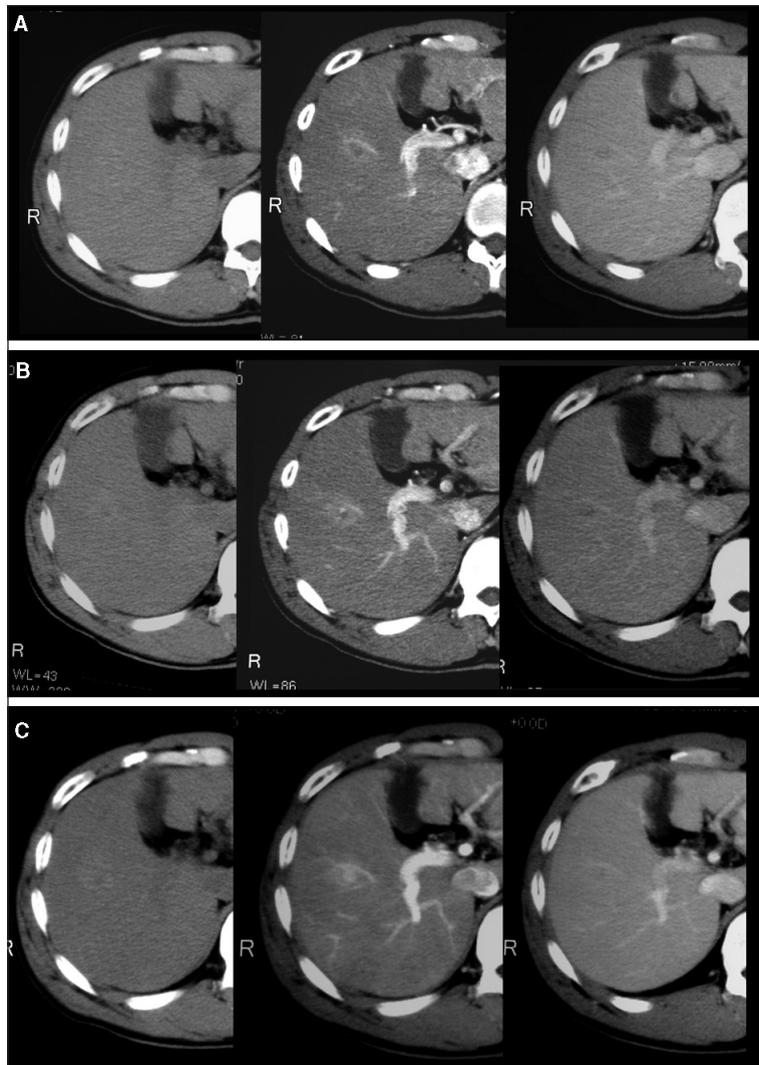


Fig. 1. Findings of computed tomography (CT) with contrast at the time of referral (A), 6 months (B) and 9 months after original referral (C). Left = pre-enhanced phase, middle = arterial phase, right = parenchymal phase. (A) The lesion in liver segment 5 was described as an iso- and hypodense area with a branch of portal tract on the rim in pre-enhanced, arterial and parenchymal phases, respectively. In the arterial phase, there was an arterioportal shunt-like obscure high-density area around the lesion. (B) The lesion was shown as a slightly low-density area on plain CT. A tiny high-density spot inside the lesion appeared in the arterial phase. (C) The high-density spot in the lesion has increased to 1 cm in size and has almost replaced the lesion; there was a thin low-density area around the lesion. The surrounding shunt-like area was recognized as an obvious high-density area.

(Fig. 2). A small branch of the portal vein had been invaded by moderately differentiated HCC cells and hemosiderin deposits, which suggested obstruction of the vessel by tumour invasion. The lesion was diagnosed as an early-advanced HCC, accompanied by surrounding hyperplastic liver tissue (focal nodular hyperplasia, FNH).

DISCUSSION

The theory that describes stepwise carcinogenesis of HCC in the cirrhotic liver and accompanying sequential

hemodynamic changes has been established recently. The central part of the present lesion was well explained by the theory. First, atypism of the cells occurred in regenerative nodules in the cirrhotic liver and a DN developed. In the nodule, the spot of higher malignant grade cells arose and expanded to replace the nodule with one of higher malignancy. In our case, we observed this developing step from DN–early HCC to advanced HCC.

The surrounding area of hyperplasia could not be differentiated from DN (adenomatous hyperplasia) pathologically. Although the resected specimen resembled a DN

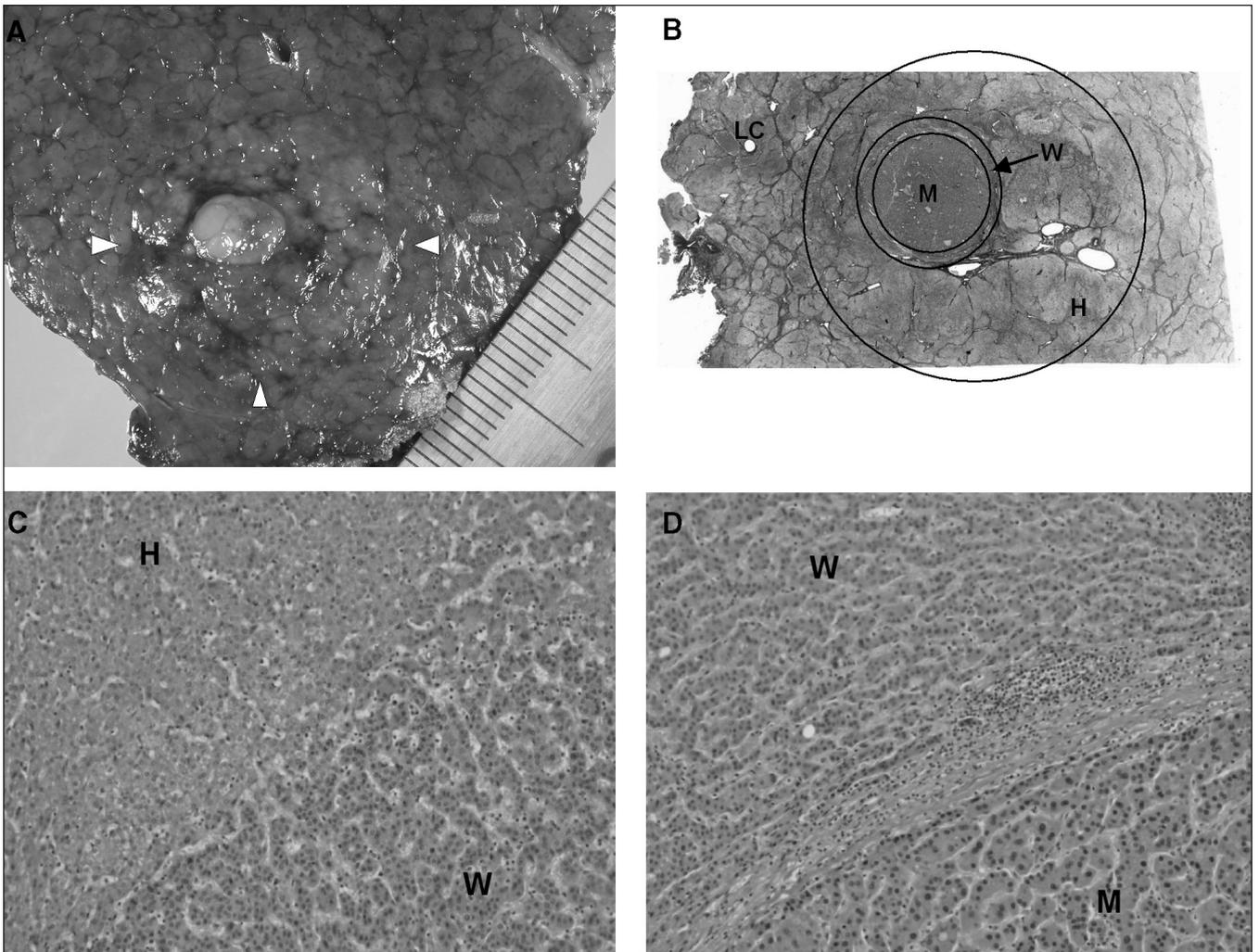


Fig. 2. Findings from the resected specimen. (A) There is a central 9-mm whitish tumour with uninvolved margins and a surrounding 2-cm tumour-like lesion with an obscure margin (arrowheads). (B–D) Pathological examination revealed that the surrounding area was hyperplastic liver tissue (H) and the central lesion was a moderately differentiated hepatocellular carcinoma (M) surrounded by a thin rim of well-differentiated hepatocellular carcinoma (W). (B: alcian blue stain, original magnification $\times 1$. C and D: hematoxylin-eosin stain, original magnification $\times 400$.)

surrounding a nodule of HCC, we diagnosed the surrounding area as FNH, not DN. The central scar of FNH contains a vascular lesion, and the main cause of developing FNH is thought to be a nonspecific response to abnormal blood flow.⁵ Mechanical effects of tumours on blood flow and tumour-associated angiogenic factors were among the various factors suggested as the cause of local hyperperfusion and following hepatocellular hyperplasia. In our case, the findings suggested the existence of abnormal blood flow due to the tumour. At first, the surrounding area was described as an obscure shunt-like lesion, which developed to an obvious area subsequently. Although DN is usually hypovascular, the area was described as a hypervascular lesion throughout the course. Although the nodule of well-differentiated HCC was replaced by moderately differentiated HCC, the area of hyperplasia was not replaced by HCC. We believe that these facts point to a surrounding area FNH not a DN.

Competing interests: None declared.

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