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Radiological Patterns of Hepatocellular Cancers Vis-À-Vis Histopathological Differentiation: A Radiological Appraisal

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Abstract

Aims and Objectives: The objective of our study is to determine the degree of radio-pathological correlation of HCC according to our experience at our institution.

Methods: Radiological parameters: All patients underwent a dynamic imaging study by CT and/or MRI, including at least one image acquisition in the arterial phase and another in the portal phase.

Pathological parameters: The 63 patients presented histological confirmation of HCC, obtained by means of a biopsy with a thick needle of 18 G or in a surgical specimen.

In all of them, the histological grade of the tumor was assessed according to the WHO classification, which distinguishes 4 grades: well differentiated (BD), moderately differentiated (MD), poorly differentiated (PD) and undifferentiated. These last two were grouped into a single group.

Conclusion: Characteristics of HCC helps in the estimation of the histological grade: arterial phase enhancement, washing, heterogeneity of the lesions, regularity of the contours and the presence of fat deposits and intratumoral vessels.

Keywords Imaging; Radiology; Histopathology; Liver; Cancer

Introduction

Hepatocarcinoma (HCC) is the most common cancer in the liver, and accounts for one fifth of all malignancies in the body. The incidence of HCC in the Asian countries is approximately 5-10 cases per 100,000 inhabitants, the most frequent etiology being chronic alcoholic liver disease, followed by chronic hepatitis C virus infections [1].

The radiological imaging study plays a fundamental role in the diagnosis of HCC. According to the updated criteria of the American Association for the Study of Liver Diseases (ASSLD), the presence of at least one lesion larger than 1cm that presents a typical enhancement pattern in the dynamic study of computed tomography (CT) or magnetic resonance (MRI), with enhancement in arterial phase and portal phase lavage, is considered diagnostic in patients with established liver cirrhosis, and histological confirmation is not necessary [2].

The greatest contribution in the irrigation of the healthy liver occurs at the expense of the portal circulation. Less important is vascularization dependent on the hepatic artery. During the development of HCC, this pattern is reversed, which results in the typical pattern described above [3].

The histological grade is, among others, an important prognostic factor, being inversely proportional to the degree of differentiation [4]. There are several studies in which the correlation between the histological grade and the radiological characteristics of the lesion is established. In this way, a close correlation has been described in moderately differentiated tumors with the typical behaviour of HCC in the dynamic tests of Diagnostic Imaging (Wash-in / Wash-out) [5].

Material and Methods

Radiological parameters

All patients underwent a dynamic imaging study by CT and / or MRI, including at least one image acquisition in the arterial phase and another in the portal phase.

Pathological parameters

The 63 patients presented histological confirmation of HCC, obtained by means of a biopsy with a thick needle of 18 G or in a surgical specimen. In all of them, the histological grade of the tumor was assessed according to the WHO classification, which distinguishes 4 grades: well differentiated (BD), moderately differentiated (MD), poorly differentiated (PD) and undifferentiated. These last two were grouped into a single group.

Radiographic variables of the study

The radiological findings of the HCC that we valued were the following:

1. Typical and atypical enhancement pattern

Those that showed enhancement in arterial phase and lavage in portal and late phase were calcified as typical; and as atypical those who did not show this pattern in any of the phases.

2. Tumor size

It was distinguished between greater than >3 cm and smaller than 3 cm.

3. Number of injuries

HCC that at the time of diagnosis presented: single lesion, multiple lesions or diffuse infiltration.

4. Radiological pattern in acquisition without contrast

Hypercaptant, isocaptant or hypocaptant lesion with respect to the hepatic parenchyma in acquisition without contrast.

5. Type of enhancement in arterial phase

Hypercaptant, isocaptant or hypocaptant lesion with respect to the hepatic parenchyma in the arterial phase.

6. Type of enhancement in the portal phase

Washing of the lesion was observed or not.

7. Tumor heterogenicity

Lesions of density and /or homogeneous or heterogeneous intensity.

8. Capsule/Pseudocapsule

Presence or not of well-defined peripheral enhancement in the portal phase.

9. Contour

Regular or irregular edges.

10. Intratumoral vessels

Presence of neovascularization inside the lesion (more evident in the arterial phase).

11. Tumor necrosis

Heterogeneity that mainly affects the center of the tumor.

12. Fat deposit

Signal fall inside the tumor in fat saturation sequences in MRI.

13. Portal thrombosis

Depletion defect in portal vessels.

The correlation between the different histological grades and the typical or atypical radiological pattern of HCC was analysed. The association between the histological grade and the morphological and dynamic findings characteristic of HCC in imaging techniques was also assessed.

Statistical Analysis

The data obtained were processed using the statistical software SPSS® version 20.0.0 Statistical analysis was performed using the Fisher exact test and the Chi-square test.

Results

Of the 63 HCC studied, 38% had a BD histological grade, 33% MD and 29% PD. 51% had a typical pattern, while 49% showed an atypical pattern. Classifying by tumor size, 70% of the HCC presented at least one lesion greater than 3 cm, while in 30% all lesions were less than 3 cm. Regarding the number of lesions, 46% were unique, 41% multiple and 13% diffusely infiltrated the liver. In the radiological pattern in the acquisition without contrast, 8% had hyper-uptake, 25% isocaptation and 33% were hyperactive. 34% of the studies did not present acquisition without contrast. In the arterial phase, 71% of HCC showed hyper-uptake, 18% had hypo-uptake while 11% were isodense with respect to the adjacent hepatic parenchyma.

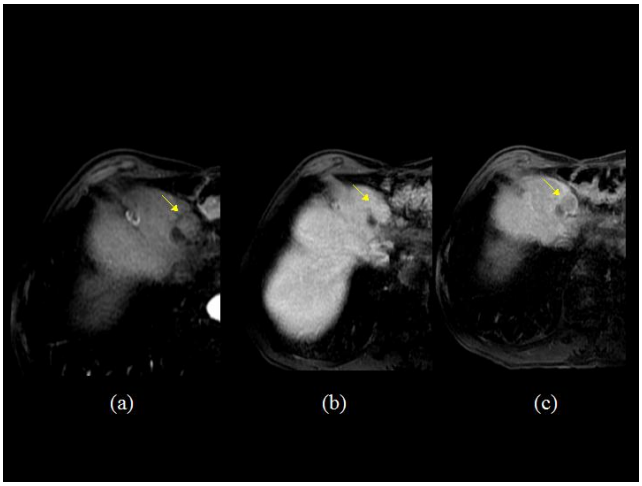

Figure 1: Single 1.6 cm nodule corresponding to a BD-grade HCC. The dynamic contrast-enhanced CT study shows an atypical enhancement, isointense with respect to the hepatic parenchyma in the arterial phase (a), hyperintense in the portal phase (b), and washing of the lesion in the late phase (c).

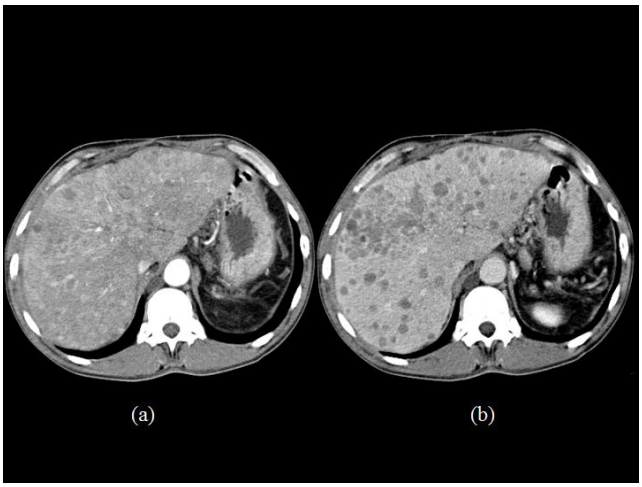

Figure 2: Dynamic contrast-enhanced CT of a patient with diffuse HCC, in which multiple nodules are visualized, most of which are enhanced in the arterial phase (a) and washed in the portal phase (b). The histological grade corresponded to a poorly differentiated HCC.

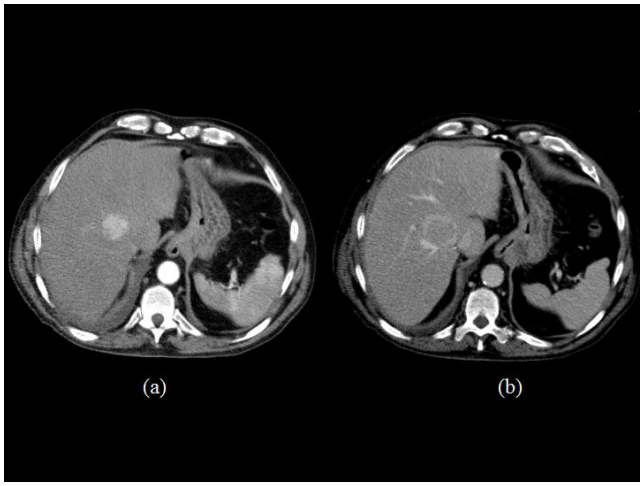

Figure 3: HCC showing a typical enhancement pattern in the dynamic CT study, with enhancement in arterial phase (a) and portal phase lavage (b). Its edges are regular and shows capsule. The histological grade of the lesion corresponded to a well differentiated one.

Regarding the enhancement in the portal phase, 56% had a wash compared to 44% that did not wash. The heterogeneity of the HCC was present in 82% of the studies, compared to 18% in which homogeneity of the lesion was appreciated (Figures 1-12 and Table 1).

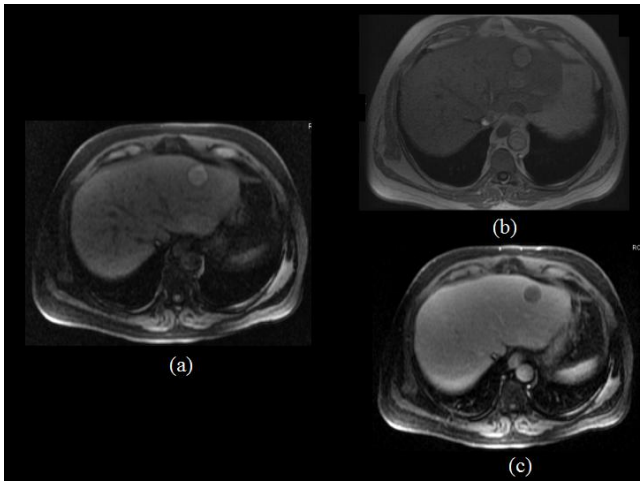

Figure 4: Dynamic MRI study, in which a well-defined nodule is identified, with a capsule, showing a hyperintense enhancement in the non-contrast phase (a), enhanced after the administration of contrast in arterial phase (b), and lava in portal phase (c). The anatomopathological study confirmed that it was a well-differentiated HCC.

The HCC with capsule represented 33% while the rest, 67%, did not have a capsule. In 44% of the HCC the contours were regular. In contrast, 54% were irregular. The presence of intratumoral vessels was found in 52% of the lesions; in 48% they were not found. The characteristic of "necrosis" was found in 74% of the HCC, while in 26% no signs of it were found.

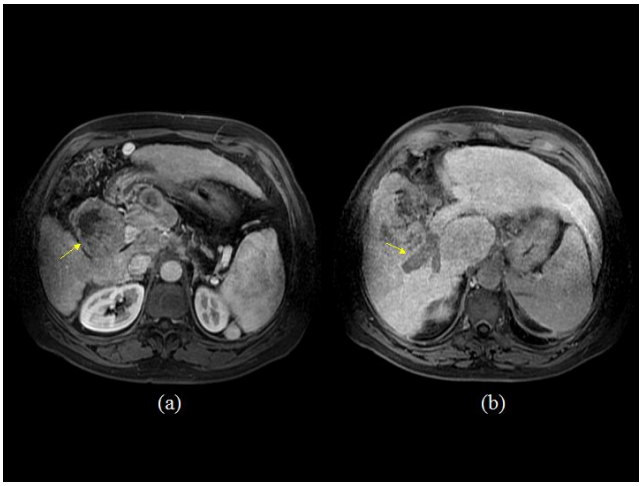

Figure 5: CT image of HCC in portal phase. A subhepatic, heterogeneous mass is observed, with areas of intratumoral necrosis (a). In upper sections identifies secondary portal thrombosis (b). The histological grade, confirmed by biopsy, was moderately differentiated.

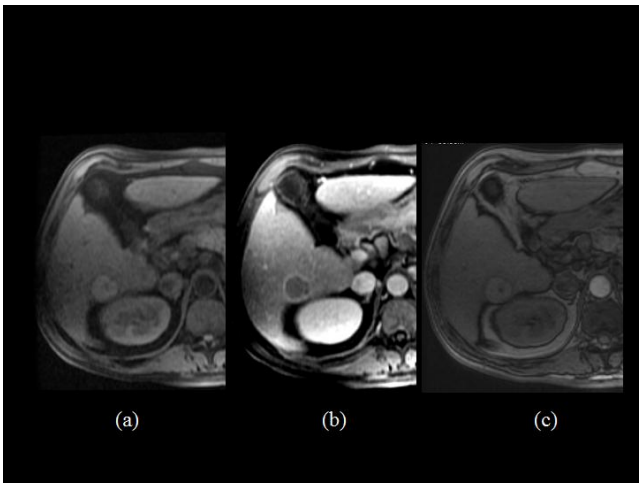

Figure 6: Dynamic MRI study of HCC. There is a nodule with regular edges, capsule and fat inside. It shows a typical pattern, with enhancement in arterial phase (a) and intense washing in portal phase (b). Anatomopathologically, it corresponded to a well-differentiated HCC.

In 65% of the tumors fat deposits were not appreciated, in 28% yes. 7% did not have an acceptable study for the evaluation of this variable.

Finally, 26% had radiological signs of portal thrombosis compared to 74% who did not have them. Correlation between the histological grade and the radiological enhancement pattern of HCC. In 32 of the 63 patients (50.8%) a characteristic vascular pattern was observed with hypervascularity in the arterial phase and portal lavage.

Figure 7: CT image of HCC in the arterial phase, showing enhancement of the parenchymal lesions, as well as the presence of intratumoral vessels inside the dominant lesion.

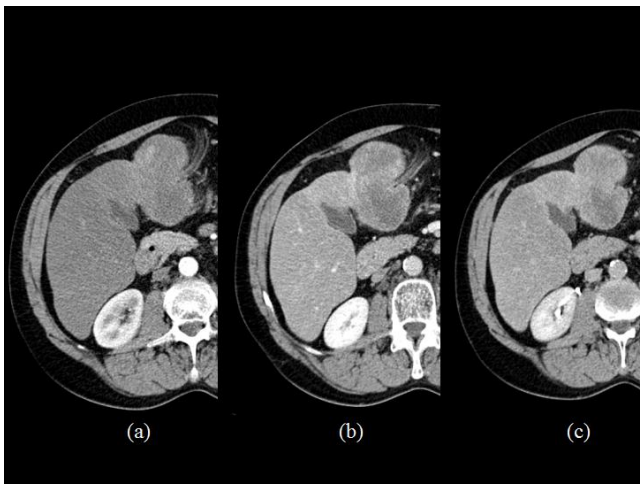

Figure 8: Dynamic CT in the study of a poorly differentiated HCC. It presents an atypical pattern after the administration of contrast, with isointense enhancement with respect to the healthy hepatic parenchyma in the arterial phase (a) and that barely washed in the portal (b) and delayed (c) phases.

We found a statistically significant correlation (p=0.008) between type of enhancement and degree of histological differentiation; the HCC with typical enhancement, were more frequently MD and the HCC with atypical enhancement BD and PD.

Influence of the histological grade on the radiological characteristics of HCC. Although the three histological grades showed mostly enhancement in the arterial phase, hypovascular behaviour was more frequent in PDs (27%).

Portal phase lavage was greater in MD. No washing was observed in 55% and 53% of the HCC BD and PD respectively. The presence of intratumoral vessels and contour of the lesion showed significant differences (p<0.005) according to the degree of differentiation. Within the HCC PD 12 (80%) showed irregular contours. In the BD HCC more than half, 17 (58.6%) showed smooth contours.

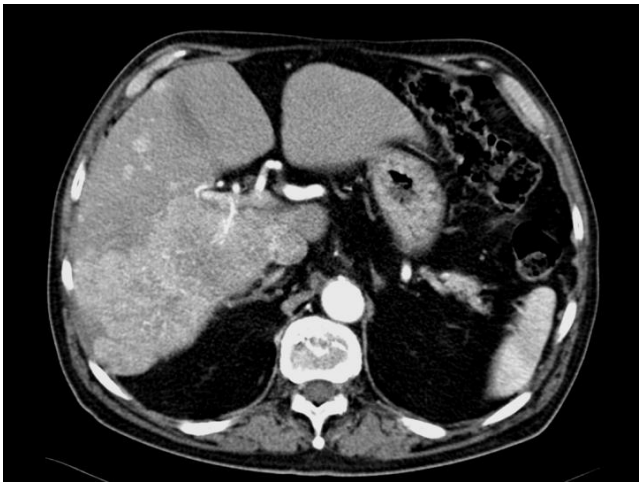

Figure 9: CT scan image with contrast in arterial phase, where a large hyperintense hepatic mass is identified in the right lobe, with irregular borders. The biopsy confirmed that it was a well-differentiated HCC.

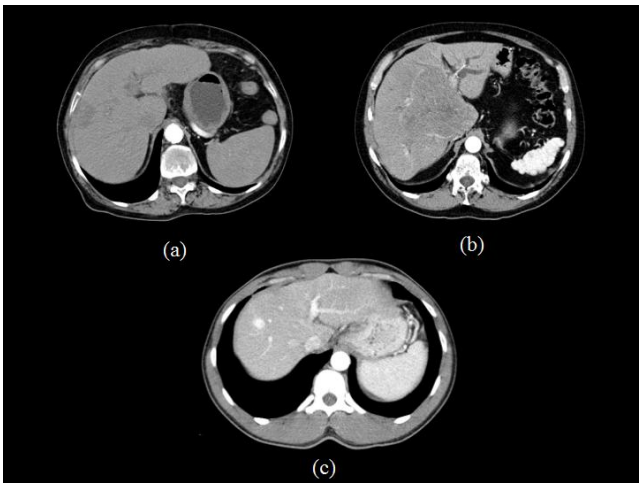

Figure 10: Dynamic CT images in the arterial phase of three patients, showing the three different types of HCC enhancement. In (a) a hypointense peripheral nodule was observed that corresponded with a poorly differentiated HCC. In (b) there is a mass that occupies almost the entire right hepatic lobe, pseudoencapsulated, isointense with the adjacent hepatic parenchyma, which also corresponded with poorly differentiated HCC. The last image (c) shows a lesion in the right hepatic lobe with typical hyperintense enhancement, which corresponded with a moderately differentiated HCC.

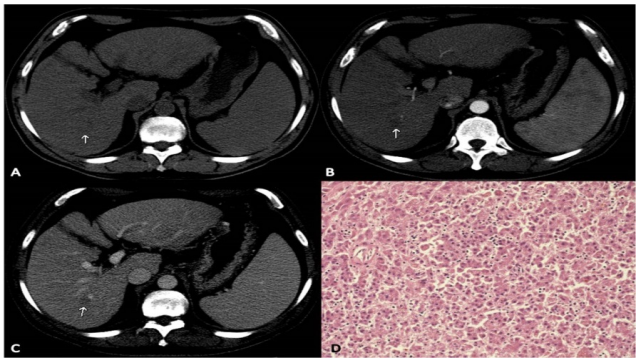

Figure 11: It shows a hypovascular nodule (as shown by white arrows A-C) and the histopathology slide proven to be as hepatocellular cancer -grade 1 (Image D).

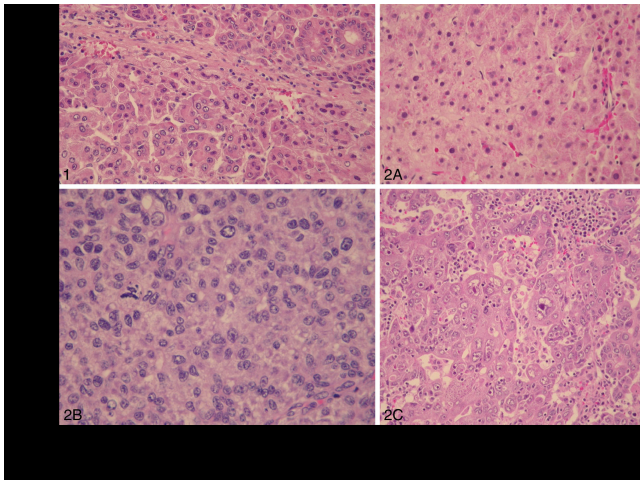

Figure 12: Histopathology slides: (H&E) stain demonstrating the increasing grades of HCC from 1-2c.

Classification Parameter	Definition
Class	
TX, NX, MX	Not assessed
T0, N0, M0	Not found
T1	One nodule ≤ 1.9 cm
T2	One nodule 2.0-5.0 cm; two or three nodules, all <3.0 cm
T3	One nodule >5.0 cm; two or three nodules, at least one >3.0 cm
T4a	Four or more nodules, any size
T4b	T2,T3, or T4 a plus gross intrahepatic portal or hepatic vein involvement
N1	Regional (portal hepatitis) node involvement
M1	Metastatic disease, including extrahepatic portal or hepatic vein involvement
Stage	
I	T1
II	T2
III	T3
IVA1	T4a
IVA2	T4b
IVB	Any N1, any M1

Table 1: Showing the TNM staging of HCC.

The existence of intratumoral vessels was evidenced in the majority of the HCC PD 10 (66.7%), whereas in the HCC BD the absence of the same 19 (65.5%) was predominant. Tumor heterogeneity was most frequently identified in MD (94%) and PD (87%) and the presence of fat in BD (31%) and MD (35%).

There was no significant correlation in terms of size, number of lesions, radiological pattern in the non-contrast acquisition and the presence or absence of capsule, necrosis or thrombosis.

Conclusion

In HCC imaging, a typical enhancement pattern suggests a lesion with moderately differentiated histological grade [6-8].

Likewise, other characteristics of HCC can also help in the estimation of the histological grade: arterial phase enhancement, washing, heterogeneity of the lesions, regularity of the contours and the presence of fat deposits and intratumoral vessels [9,10].

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