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Clinical Image

# Mutation at Codon 249 of the TP53 Gene in Hepatocellular Carcinoma: MD-CT and Pathologic Features

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## 1. Abstract

Aflatoxin B1 is a mycotoxin produced by the Aspergillus Flavus fungus that contaminates many sources of food. This mycotoxin has its metabolism into the liver. So, Aflatoxin B1 metabolites create a DNA mutation at the third base of codon 249 in the TP53 tumor suppressor gene, inducing a G to T trasversion (AGG to AGT), which replace an arginine "R" to a serine "S".

**2. Keywords:** Liver; Hepatocellular carcinoma; Mutation; Gene; Computed tomography

## 3. Clinical Image

Two West Africa (Senegal) male patients (38 and 40-year-old) were sent to our hospital for evaluation of possible liver nodular mass. At the time of their presentation a clinical history of chronic hepatitis B virus (HBV) infection and arrival in Italy from Senegal (one and three years respectively) has been evaluated. Abdominal multi-detector computed tomography (MD-CT) revealed in bought patient a singular liver nodular mass, with a diameter of 8.1 and 3.6 cm respectively (Figure 1-2). No radiological signs of liver cirrhosis, other thoraco-abdominal nodules or lymph nodes were noted. Patients underwent surgical resection of the liver nodular mass.

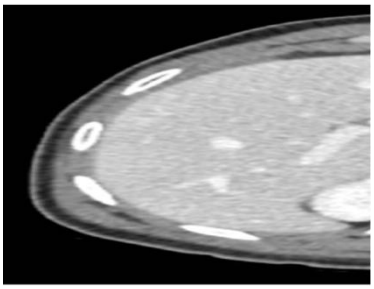

**Figure 1:** Contrast-enhanced Multi-Detector Computed Tomography axial image of 38-year-old man that show at the level of the left liver lobe (II and III segment) (*) a focal nodular mass, with low density, with partial vascular enhancement, well-delimited margins and a diameter of 8.1 cm.

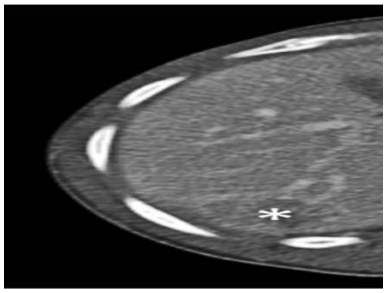

**Figure 2:** Contrast-enhanced Multi-Detector Computed Tomography axial image of 40-year-old man that show at the level of the right liver lobe (VII segment) (*) a focal nodular mass, with low density, well-delimited margins and a diameter of 3.6 cm.

Histopathological evaluation demonstrated unconventional type HepatoCellular Carcinomas (HCC). The poorly differentiated carcinoma was characterized by great variation in nuclear size, hepatoid morphology and chromatin structure. Cytoplasm was slightly eosinophilic. Numerous atypical mitosis has been noted. Large areas of tumour cell necrosis and hemorrhage were present (patient 40-year-old). Immunohistochemistry revealed the hepatocellular carcinomas were strongly positive for cytokeratin 20 (clone SP33, prediluited, Ventana). In particular, TP53 gene accumulation of mutant was observed at codon 249 in both hepatocellular carcinomas. The morphological and immunohistochemical features were consistent with diagnosis of Cytokeratin 20 positive hepatocellular carcinoma with the accumulation of mutant p53 (Figure 3-4).

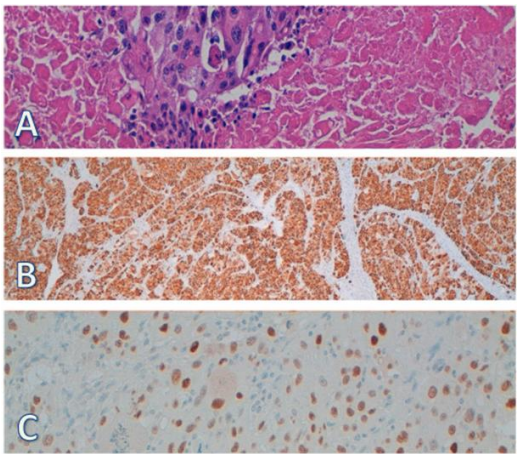


**Figure 3:** Histopathological evaluation of 38-year-old man that shows: A) Hepatocellular carcinoma showing a solid pattern with infiltrate inflammatory chronic (Hematoxylin-eosin staining magnification 20x), B) Immunohistochemical cytokeratin 20 slide showing diffuse and intense positive of tumour cells (cytokeratin 20, magnification 4x), C) Hepatocellular carcinoma : immunostaining with p53 showing diffuse and intense positive nuclear (p53, magnification 20x).

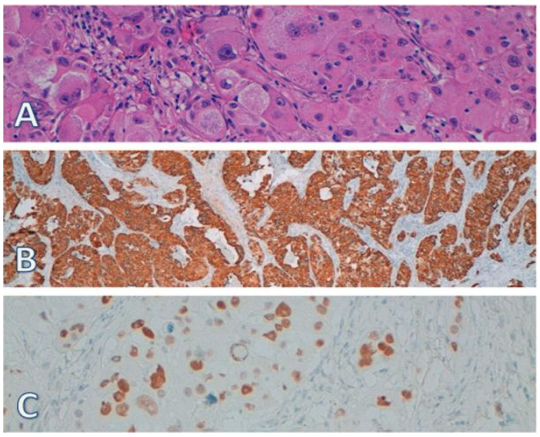


**Figure 4 :** Histopathological evaluation of 40-year-old man that shows. A) Hepatocellular carcinoma showing a mixed trabecular and acinar pattern with necrosis (Hematoxylin-eosin staining magnification 20x), B) Immunohistochemical cytokeratin 20 slide showing diffuse and intense positive of tumour cells (cytokeratin 20, magnification 4x), C) Hepatocellular carcinoma: immunostaining with p53 showing diffuse and intense positive nuclear (p53, magnification 20x).

Given the malignant diagnosis, patients have been enrolled in clinical, laboratory and imaging follow-up program. At 28 months mean follow-up none of the two patients showed signs of recurrence or new liver nodular disease.

HCC is one of the major causes of cancer in many parts of the world. In West Africa, including Senegal, the two main risk factors for liver carcinogenesis include aflatoxin B1 (AFB1) and HBVinfection [1]. Other risk factors as hepatitis C virus (HCV) and alcohol have a minor role in these countries [2].

AFB1 is a mycotoxin produced by the Aspergillus Flavus fungus that contaminates many sources of food in hot and tropical areas, including Senegal. This mycotoxin has its metabolism into the liver. So, AFB1 metabolites create a DNA mutation at the third base of codon 249 in the TP53 tumor suppressor gene, inducing a G to T trasversion (AGG to AGT), which replace an arginine "R" to a serine "S" [1, 3-5]. This mutation was confirmed in about 75% of HCC cases in high incidence areas [4]. Furthermore, this type of mutation has not been observed in cases of HCC in areas not contaminated by AFB1 [1-4].

## References

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