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Fibrolamellar hepatocellular carcinoma treated with chemotherapy and immunotherapy: a rare entity with unique characteristics

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Keywords: Hepatocellular carcinoma. Genomics. Immunotherapy.

Dear Editor,

We present the case of a 21-year-old male diagnosed with stage IV fibrolamellar hepatocellular carcinoma (FL-HCC) (Fig. 1A), tested with the Oncomine™ Comprehensive Assay genomic sequencing panel and treated with chemotherapy and immunotherapy.

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Discussion

Conceptually, FL-HCC is a rare entity with distinctive and unique characteristics and is not a subtype of hepatocellular carcinoma (HCC) (1-4). It represents less than 1 % of all primary liver cancer cases and typically affects younger adults and adolescents. There is no consensus regarding its etiopathogenesis, although FL-HCC often develops in the absence of underlying chronic liver disease (1-5).

In addition to its histological features (Fig. 1B), we identified the DNAJB1-PRKACA fusion (Fig. 1C), a genomic alteration present in more than 90 % of all cases of FL-HCC and intrinsically related to its pathogenesis, now considered as a unique diagnostic biomarker for FL-HCC (1-5). Most cases of FL-HCC present are at an advanced stage at the time of diagnosis. However, up to 70 % of patients with FL-HCC could benefit from potentially curative therapeutic options, such as surgical resection and liver transplantation (3,4). Regarding systemic treatment options, no combination of cytostatic agents has been sufficiently validated as standard first-line treatment through prospective clinical trials. The limited data available allow us to conclude that FL-HCC is a poorly chemosensitive tumor for which platinum-based chemotherapy combinations are preferable to drugs administered as monotherapy (2-5).

Immunotherapy does not offer better results. High tumor mutational burden (TMB), high levels of PD-L1 or microsatellite instability (MSI) are considered to be predictive biomarkers of response to immunotherapy. However, consistent with many other cancer types diagnosed in younger adults and adolescents, FL-HCC is characterized by low TMB. It is also rare to find high levels of PD-L1 and MSI in these tumors. In any case, the best response data so far in FL-HCC have been obtained with the anti-PD-L1 agent nivolumab (2,4,5). On the other hand, recent clinical trials with vaccines suggest that the DNAJB1-PRKACA fusion could emerge in the coming years as a promising therapeutic target (2,4). Unfortunately, eight months after diagnosis and after nine cycles of a combination based on cisplatin, 5-fluorouracil, adriamycin and nivolumab, the patient passed away.

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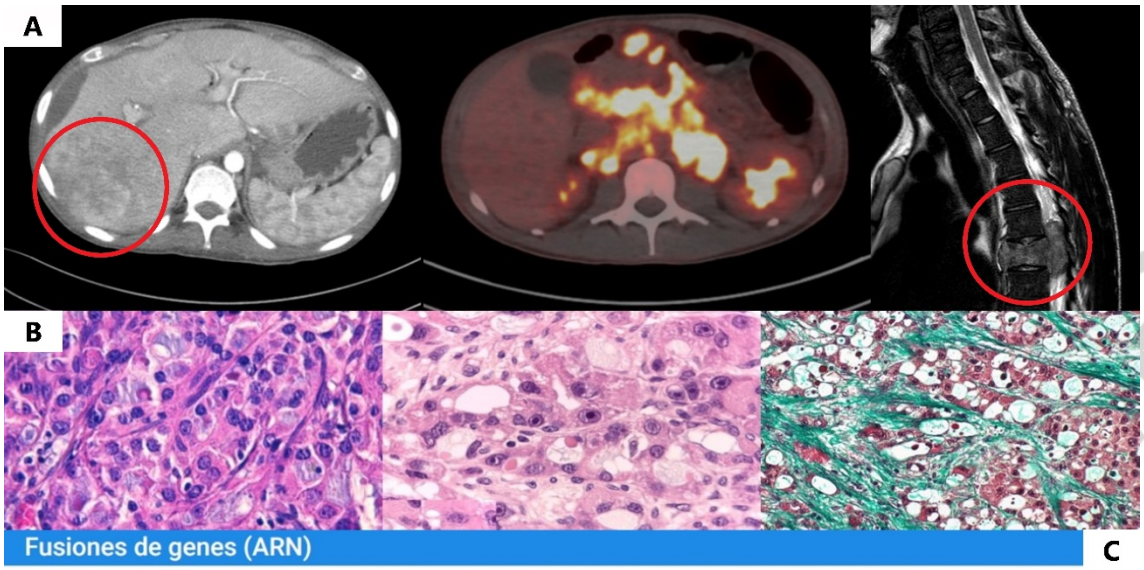

Fig. 1. A. Fibrolamellar hepatocellular carcinoma with extensive metastatic disease at the retroperitoneal lymph node and bone level with destruction of the vertebral body of T6 and compression of the spinal canal. B. Well-differentiated malignant hepatocytes with trabecular arrangement, surrounded by a fibrous stromal meshwork, vesicular nuclei with one or more macronucleoli, large granular and eosinophilic cytoplasm. C. Finding of a DNAJB1-PRKACA fusion by genomic sequencing.