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Letter to the Editor

Hepatocellular carcinoma in Gaucher disease: Reinforcing the proposed guidelines

ARTICLE INFO

Editor: Narla Mohandas

To the Editor,

A recent international collaborative case series [1] of 16 patients with GD type 1 (GD1) showed a clear association of hepatocellular carcinoma (HCC) with splenectomy and liver cirrhosis. In a previous article [2], Regenboog and colleagues reported a high prevalence of focal hepatic lesions in GD1 patients (25%), with an apparent association with splenectomy. In that cohort, four patients were diagnosed with HCC, and eighteen with gaucheroma, making the diagnosis of the latter 4.5-fold more common than the former. However, there was one case in which the ultrasonographic image was suggestive of HCC (a hypoechoic and hypervascular nodule) but pathological examination confirmed that it was a gaucheroma, showing that it is possible for these tumours to emulate the imaging of HCC. Conversely, two confirmed cases of HCC did not present with the complete set of typical findings of arterial wash-in and venous wash-out on contrast-enhanced computed tomography (CECT). Based on these findings, the authors suggested an algorithm for the evaluation of focal hepatic lesions in GD1, in which splenectomized patients with lesions > 1 cm presenting arterial wash-in and venous wash-out on CECT should be diagnosed immediately as having an HCC. In the Gaucher Reference Centre of the Hospital de Clínicas de Porto Alegre (HCPA), we follow a 62-year-old male patient of non-Jewish descent who was diagnosed with GD1 by enzymatic and genetic assays (genotype: N370S/RecNciI). He had hepatosplenomegaly and thrombocytopenia since age 42, and a splenectomy at age 49 yielded the suspicion of GD1 upon the histological identification of Gaucher cells. During that time, a liver biopsy showed micronodular cirrhosis (classified as Child-Pugh A). His first appointment at the Gaucher clinic was at 50 years of age, and he had no thrombocytopenia (231,000 platelets/mm^3, NRV 150,000–400,000) nor anaemia (Hb 14.7 g/dL, NRV 12.5–16.0), a mildly elevated AST (53 U/dL, NRV < 42), normal ALT and high γGT (363 U/dL, NRV < 40), chitotriosidase (7271 nmol/h/mL, NRV 8.8–132), and ferritin levels (3392 ng/dL, NRV 30–300). Enzyme replacement therapy (ERT) with imiglucerase was initiated at 15 IU/kg/2 weeks when he was 52. When he was 58, a routine abdominal ultrasonography (AUS) showed a liver nodule of 1.2 cm in diameter, which was confirmed by a CECT to have an arterial wash-in without venous washout pattern that disappeared two years later. After two years, another nodule seen on AUS followed by an abdominal CECT showed two liver nodules, the bigger measuring 1.8 × 1.4 cm with both arterial wash-in and venous wash-out, suggesting HCC. A CECT performed three months later did not detect the smaller nodule but confirmed the characteristics of the bigger one (Fig. 1). Meanwhile, the patient had unintentionally lost 3.1 kg (5.7% of his body weight), what was attributed to his recent diagnosis of symptomatic primary hypolactasia. By the time of the second CT, laboratory exams showed a mildly increased AST (57 U/dL), a highly increased γGT (196 U/dL), a slightly increased alpha-fetoprotein (11.5 pg/mL, NRV < 10), a normal transferrin saturation (36.8%, NRV 25–45%), and a high, although lower than at the diagnosis, serum ferritin level (627 ng/dL). Other exams, including a comprehensive viral hepatitides panel and genotyping for hereditary haemochromatosis, were negative. Due to the absence of tumour growth in the three months between the CTs and that liver gaucheromas may mimic HCC [2], we decided to perform a percutaneous core needle biopsy of the lesion.

The biopsy showed a cirrhotic liver with multiple engorged, micro vacuolar Gaucher cells, some clumped together in groups of approximately five cells (Fig. 2), similar, except for the microvacuolation, to the aspect described by Korula and colleagues [3]. Perls staining was strongly positive in hepatocytes and Gaucher cells. No neoplastic tissue was found. Based on these findings and a previous report of micro vacuolar Gaucher cells in an extraosseous gaucheroma [4], the lesion was diagnosed as gaucheroma, and imiglucerase dosage was increased to 30 IU/kg biweekly. In the subsequent months, the mass continued to grow, reaching 2.4 cm after 9 months. As alpha-fetoprotein also rose to 36.7 pg/mL, a new biopsy was performed which showed a moderately-differentiated HCC. The patient was staged with CTs and a bone scan which detected a subpleural nodule (diagnosed by biopsy as fungal granuloma) and a 1.4 cm intrahepatic metastasis. He has now successfully undergone transarterial chemoembolization and is listed for liver transplantation.

In a core needle liver biopsy, only about one-fifty-thousandth of the total liver volume is sampled [5], which implicates that inevitable sampling errors tend to occur. Because of this, we advocate that any nodule in patients with GD1 and at high risk of developing HCC, such as splenectomy and cirrhosis as in our patient's should be managed as HCC, regardless the possibility of being a gaucheroma. Therefore, we support the algorithm proposed by Regenboog and colleagues, hoping that it may help to avoid unnecessary delay in the management of such patients.

Declaration of interests

None.

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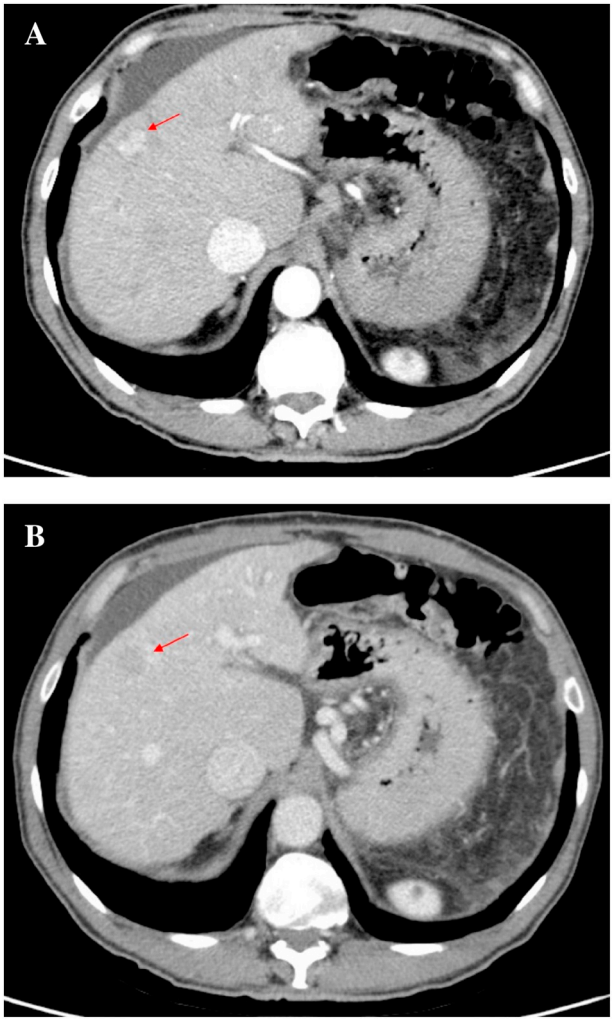

Fig. 1. CECT findings. A: arterial phase showing a discrete lesion in the left lobe of the liver (red arrow) with contrast wash-in. B: venous phase showing complete wash-out of contrast in the same lesion (red arrow). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

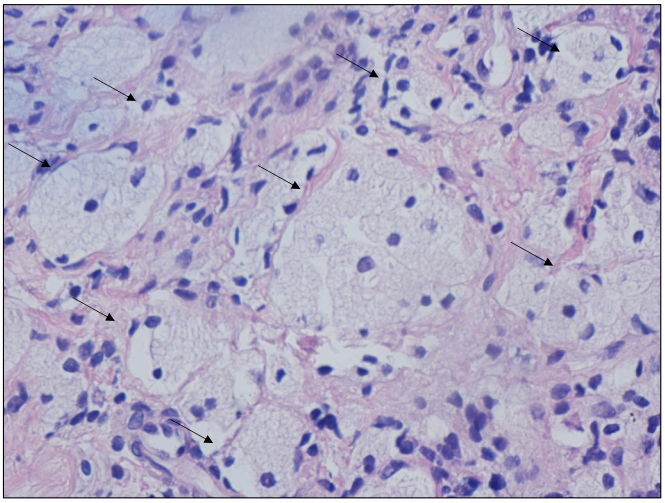

Fig. 2. Photomicrograph, haematoxylin and eosin, 400×. Fibrotic liver tissue with individual and grouped plump, microvacuolar macrophages (black arrows) diagnosed as atypical Gaucher cells in a gaucheroma.

Contribution

RTS, FPV, ADD and IVDS participated in the patient care in the Medical Genetics Service. RTS wrote the first version of the manuscript. FPV and IVDS reviewed the first version of the manuscript and co-wrote with RTS the next versions. CTSC performed the histological diagnoses and participated in the radiographical-pathological correlation. RTS and CTSC reviewed the literature on the liver histology of Gaucher disease. MRAS participated in the patient care at the Gastroenterology and Hepatology Service. MRAS, RTS, FPV, ADD, and IVDS reviewed the literature on hepatocellular carcinoma in Gaucher disease and on liver gaucheromas, and gathered to form a consensus opinion. ADD, CTSC, MRAS and IVDS reviewed the manuscript. All authors approve the final manuscript.

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