Hepatocellular carcinoma in an adult patient with type IV glycogen storage disease

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To the editor,

Type IV glycogen storage disease (type IV GSD), also known as Andersen disease or amylopectinosis, is a rare autosomal-recessive disorder caused by deficiency of the glycogen branching enzyme (1). The classic form is characterized by progressive hepatic fibrosis resulting in hepatosplenomegaly and failure to thrive and death by the age of 5 years. Few patients do not develop hepatic failure and survive to adulthood (2). Here we report a case of hepatocellular carcinoma (HCC) in a young adult with GSD IV and chronic liver disease following a 20 year period with no apparent disease progression.

A 21-year-old woman had been diagnosed with GSD type IV at the age of 1 year. At that time, she presented with hepatosplenomegaly and nephromegaly. Laboratory examination showed anemia and elevation of liver enzymes. Family history revealed that a female sibling with hepatosplenomegaly had died from heart failure at the age of 14 months. A liver biopsy demonstrated periodic acid-Schiff (PAS)–positive, diastase-resistant, coarsely clumped, granular and fibrillary material typical of amylopectin (Fig. 1). Iodine staining formed a characteristic complex with a distinctive blue color. There was prominent bridging fibrosis. The findings were consistent with the diagnosis of GSD type IV. A repeat biopsy revealed micronodular cirrhosis when she was 9-year-old. During follow up she had no complication of cirrhosis except for several episodes of oesophageal variceal bleeding necessitating sclerotherapy. When she was 21-year-old, a 25 mm lesion was detected in the left hepatic lobe by ultrasonography which was performed as part of a surveillance program. The liver was diffuse nodular with irregular borders. Magnetic resonance imaging of the lesion was compatible with HCC or atypical regenerative nodule. At that time laboratory examination revealed normal transaminases, albumin and bilirubin. Alpha-fetoprotein was 1.54 ng/mL. Our patient did not have any other risk factors for HCC including hepatitis B and C infection, chronic alcohol consumption, diabetes, steatosis or obesity. An ultrasound guided fine-needle aspiration of the mass showed atypical hepatocytes. She had a living-related donor and she underwent liver transplantation. Histological examination of the hepatectomy specimen confirmed the diagnosis of HCC (Fig. 2, 3).

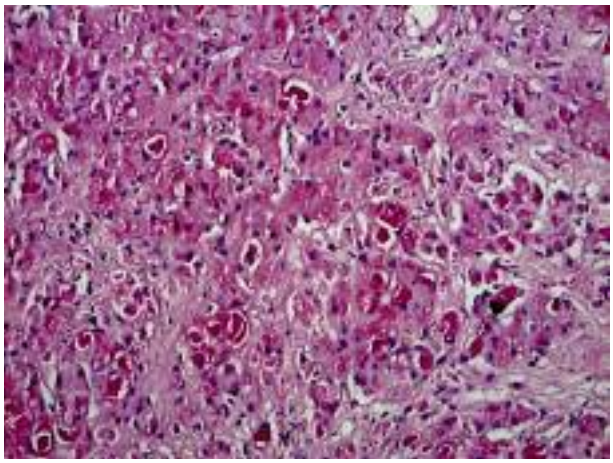

Fig. 1. — Glycogen storage disease type IV. Liver biopsy stained with periodic acid-Schiff (PAS) after diastase treatment (× 100). Presence of PAS positive, diastase-resistant, coarsely clumped material representing the accumalated abnormal glycogen.

HCC has previously been described in patients with GSD type I, III, VI and IX (3) but in the literature more cases have been reported in association with type I and III (4,5). The transformation of adenomata into HCC has been documented in approximately 10% of GSD type I patients (6). In the absence of preexisting adenoma HCC has been reported in only one patient having also hepatitis B virus infection (4). Persistent peripheral hypoglycemia has been proposed to play a role in the adenoma formation by constant hormonal stimulation (6). Meticulous adherence to a dietary regimen may prevent hypoglycemia and reduce liver size. On the other hand, the mechanism for tumorgenesis in GSD III appears different than

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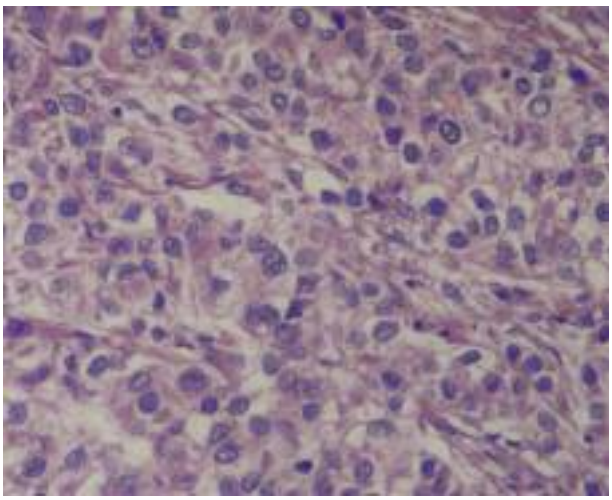

Fig. 2. — The clear cell variant of hepatocellular carcinoma : the clarity of the cytoplasm has been shown by the PAS method to be due to excess glycogen. HE, ×200.

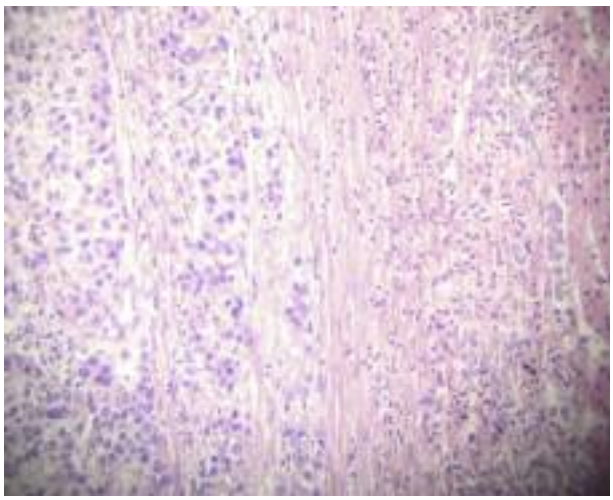

Fig. 3. — The liver tissue with hepatocellular carcinoma is seen on the left side and the adjacent normal tissue is on the right side of the histologic section. HE, ×100.

in GSD I, which is believed to be an adenoma-carcinoma sequence. Because adenomas are not as common in patients with GSD III (4.4%) as GSD I (22-75%) and in the patients with HCC adenomas do not coexist most of the time (5). Long standing cirrhosis could explain for the increased incidence of HCC in these patients. The association of GSD IV with adenoma has been reported but not as frequently as GSD type I (7). Hypoglycemia is rarely seen in GSD IV and this may partly explain for this observation. Few patients with GSD IV survive to adulthood. This may also be the reason why there have been rare cases of adenoma and only one case of HCC (8). The authors presented a male with GSD IV and HCC who died at age of 13 because of hepatic failure (8). To the best of our knowledge our report includes the first case of hepatocellular carcinoma in an adult patient with type IV GSD.

Ten of thirteen patients with GSD IV who underwent liver transplantation because of progressive liver cirrhosis had a follow up period of 13.5 years (9). Liver transplantation should be considered a treatment option for those patients with GSD who develop liver malignancy or failure. Despite successful transplantation the disease may progress in heart, skeletal muscle and nervous system.

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