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Case Report

Focal hepatic glycogenosis associated with metastatic insulinoma presenting as mass lesions

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ABSTRACT

One of the important functions of the liver is glycogen storage. Most processes associated with increased hepatic glycogen, or glycogenoses, are metabolic and affect the entire liver leading to diffuse glycogenosis. We present a case in which the liver contained multiple small pale nodules that on initial assessment were recognized to be composed of glycogenated hepatocytes. Most of the known causes of hepatic glycogenosis were not pertinent to this case. After cutting many deeper levels and obtaining additional sections, small foci of insulinoma were revealed in the center of each of these lesions. The glycogenosis surrounding the foci of insulinoma can be best explained as a local effect of insulin on the hepatocytes, a phenomenon that has been previously described in primate models, but not in human subjects. Here, we report the first case of metastatic insulinoma causing local hepatic glycogenosis.

1. Introduction

The liver and glycogen metabolism are intricately associated. The liver stores about 1/3rd of the total body glycogen and is responsible for blood glucose homeostasis by converting glycogen to glucose and *vice versa* [1]. Glycogen accumulation in the hepatocytes is termed hepatic glycogenosis. The primary glycogenoses are due to disorders in the enzymatic pathways of glycogen metabolism, *i.e.* the glycogen storage disorders [2]. Acquired or secondary glycogenoses are due to factors influencing glycogen metabolism such as drugs and diseases. The latter include insulin and glucagon mediated disorders of glucose metabolism, urea cycle disorders and dumping syndrome [3–6]. Of these, glycogenic hepatopathy due to diabetes mellitus is the most common [5]. Drugs such as azathioprine and high dose steroids also cause focal liver glycogenosis [7–9]. Glycogen accumulation has also been implicated as a preneoplastic change in hepatic carcinogenesis [10]. Glycogenosis can be diffuse or focal depending on the process involved. Glycogen accumulation can sometimes result in "ground-glass" inclusions within hepatocytes. The causes of such inclusions include polyglucosan inclusions, as seen in Lafora's disease, cyanamide aversion therapy in alcohol abuse, type IV glycogen storage disease and immunosuppressive therapy in transplant patients. The etiology in all these processes remains altered glycogen metabolism [11]. Such inclusions can also be seen in fibrinogen storage disease [11].

2. Case report

The patient was a 41 year old man with an established diagnosis of MEN 1 syndrome. He had undergone partial pancreatectomy for pancreatic neuroendocrine tumor 20 years ago. Details of this tumor were not available at the time of initial assessment. The patient was normoglycemic and serum levels of all the pancreatic hormones were normal at this presentation. During his present admission to hospital, he underwent completion pancreatectomy for removal of multifocal enlarging pancreatic neuroendcrine tumor. These tumors showed negative staining for gastrin, insulin and glucagon. Post-operatively, the patient was insulin dependent for control of his rising blood glucose. The post-operative course was complicated and he died three weeks later following a massive intra-abdominal hemorrhage. A complete autopsy was performed.

3. Pathologic findings

At autopsy, the liver showed multiple pale yellow lesions up to 1 cm in diameter (Fig. 1A and B). On microscopy, these lesions

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0344-0338/

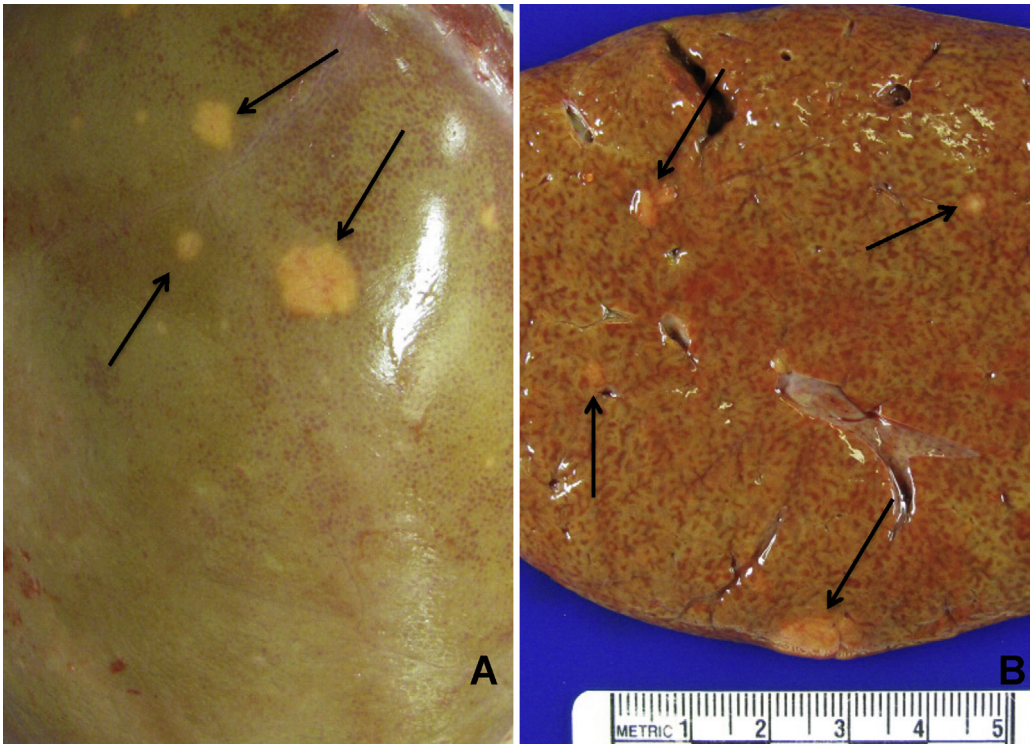

Fig. 1. (A and B) Liver with multiple yellow, nodular subcapsular and intra-parenchymal deposits (indicated by arrows).

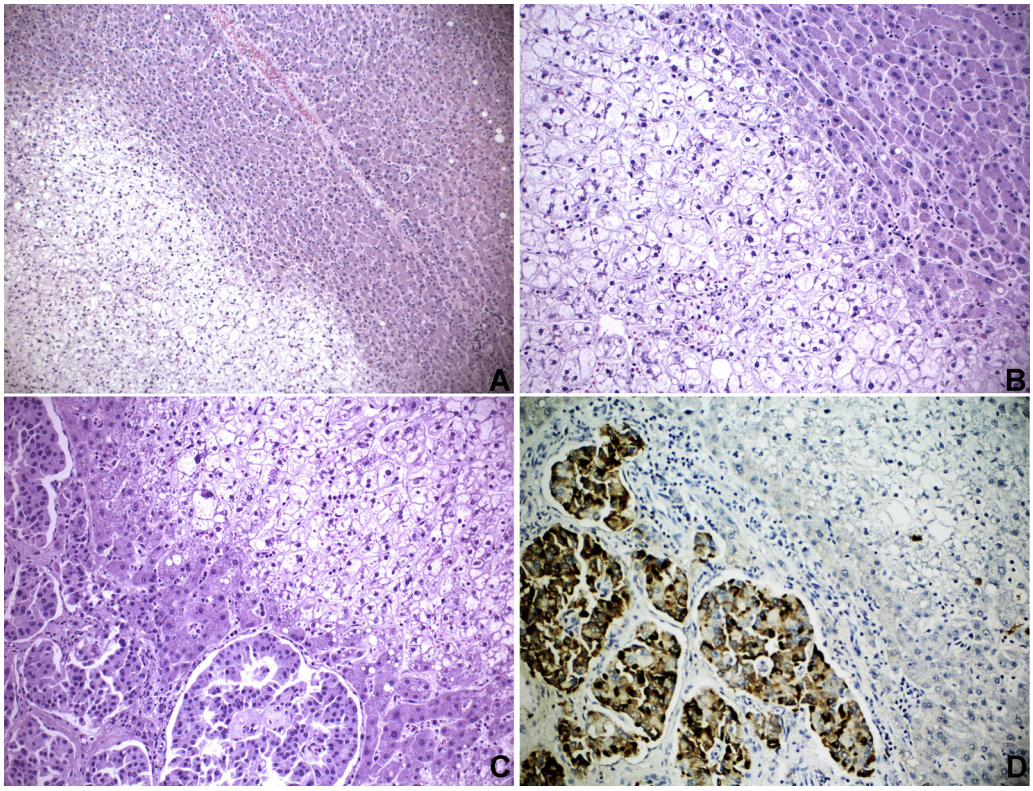

Fig. 2. (A) Microscopic section of the yellow nodules shows nodules composed of pale, clear parenchyma (as compared the adjacent liver parenchyma) (H&E, 100X). (B) Higher magnification of the same nodule shows benign hepatocytes with abundant clear cytoplasm (H&E, 200X). (C) Deeper sections of the nodules reveal a tumor in the center of the clear cell nodules. The tumor has a nested, organoid architecture and is composed of cells with abundant eoisinophilic cytoplasm and round nucleus with granular "salt and pepper" chromatin (H&E, 200X). (D) The tumor cells show strong cytoplasmic positivity for insulin (insulin immunohistochemistry, 200X).