Annals of Hepatology
The Official Journal of the Mexican Association of Hepatology, the Latin-American Association for Study of the Liver and the Canadian Association for the Study of the Liver

VIEWPOINT

Computed Tomography and Magnetic Resonance Imaging Features of Primary and Secondary Hepatic Glycogenosis

Zhi-yuan Chen,* Yu-pin Liu,* Guang-juan Zheng**

* Department of Radiology, The Second Affiliated Hospital of Guangzhou University of Chinese Medicine, Guangzhou, Guangdong Province, PR China.
** Department of Pathology, The Second Affiliated Hospital of Guangzhou University of Chinese Medicine, Guangzhou, Guangdong Province, PR China.

ABSTRACT

Glycogen storage disease type I and glycogenic hepatopathy are the most common type of primary and secondary hepatic glycogenosis, with presenting common radiological features of hepatomegaly, hepatic signal, or density change. Beyond that, glycogen storage disease type I shows hepatocellular adenomas or fatty liver, while glycogenic hepatopathy does not.

Key words. Hepatic glycogenosis. Glycogen storage disease. Glycogenic hepatopathy. Computed tomography. Magnetic resonance imaging.

Hepatic glycogenosis (HG), caused by glycogen deposition in hepatocytes, is a rare disease that can be divided into primary and secondary HG according to the etiology.[1] Primary HG, also known as glycogen storage disease (GSD), is more common and results from disorders in the enzymatic pathway for glycogen metabolism. GSD type I (GSD-I), caused by glucose-6-phosphatase deficiency, is the most common type of primary HG. Secondary HG is relatively rare and related to factors that affect glycogen metabolism, such as high-dose corticosteroid and azathioprine use, urea cycle enzyme defects, dumping syndrome, and diabetes mellitus (DM). Of these, secondary HG caused by poorly controlled DM is the most common type, and termed glycogenic hepatopathy (GH) in most papers. As a rare and under-recognized complication in poorly controlled DM patients, GH occurs predominantly in patients with DM type I (approximately 95%) and sporadically in patients with DM type II (approximately 5%).[2,3]

As a rare disease, HG is hard to differentiate from other diseases with abnormal liver enzyme and hepatomegaly and usually need liver biopsy. Staining with hematoxylin and eosin, liver biopsy shows glycogen deposition in hepatocytes, seen as diffusely swollen hepatocytes with pale cytoplasm and empty nuclei. Periodic acid-Schiff stain is positive in these hepatocytes, which disappeared after digestion with diastase. Typical histopathological presentation is helpful for the diagnosis of HG, but it is hard to distinguish GSD-I and GH because they present the similar histopathological manifestations. However, the treatments and prognoses of the two diseases are quite different. GH tends to have a much better prognosis and can be completely reversible after a period of good metabolism control, while GSD-I severely affects the body metabolism and results in life-threatening hypoglycemia and long-term complications. Some severe complications of GSD-I, such as hepatocellular adenomas (HCAs) and hepatocellular carcinoma (HCC), eventually lead to liver transplantation. Therefore, it is very important to distinguish these two diseases. To the best of our knowledge, there are no reports that simultaneously depict the radiological features of primary and secondary HG in a single article. Herein, we review the literature and summarize the computed tomography (CT) and magnetic resonance (MR) image features of the two types of HG to seek a way to differentiate these two diseases.

Manuscript received: July 16, 2018. **Manuscript accepted:** September 11, 2018.

DOI:10.5604/01.3001.0012.7189

On CT and MR images, the most common finding in GSD-I is hepatomegaly caused by glycogen and fat accumulation in hepatocytes. Fatty infiltration is very common in GSD-I because of malnutrition and lipid metabolism disorders. Hepatic density and signal intensity depend on the proportions of glycogen deposition and fatty infiltration. In cases where glycogen storage is predominant, hepatic density presents as increased attenuation on CT images, while increased fat deposition leads to decreased attenuation. A minority of GSD-I patients may exhibit focal or diffuse fatty liver through increased endogenous fatty acid synthesis, which results in focal or diffuse lowering of attenuation in the liver parenchyma on CT images. On MR images, the T2 signal in the liver parenchyma is slightly decreased when glycogen storage is dominant. The reason may be that macromolecular glycogen particles inhibit the movement of protons and lead to signal reduction. The T1 signal in the live parenchyma increases because glycogen deposition may shorten the T1 relaxation time. Fatty infiltration or fatty liver can be diagnosed on gradient-echo phase-shift images. Compared with the in-phase signal intensity, focal or diffuse fatty infiltration appears as focal or diffuse decreased signal intensity on opposed-phase images.

Another common radiological feature in GSD-I is HCAs. Despite a broad range of incidence from 22% to 75% in the literature,[4] HCAs are widely considered to be a frequent secondary complication to GSD-I and to occur by the second or third decade of life.[5] Unlike HCAs in females that mainly occur with long-term use of oral contraceptives or anabolic steroids, HCAs secondary to GSD-I tend to be dominant in males with a male-to-female ratio of 2:1.[6] Generally, HCAs in patients using oral contraceptives or exogenous androgens tend to be large, single, and encapsulated, while those in GSD-I patients tend to be small, multiple, and non-encapsulated. On plain CT images, most HCAs manifest as multiple, well-defined, round, isoattenuating, or hypoattenuating masses. Some HCAs are surrounded by a fibrous pseudocapsule formed by compression of the adjacent liver tissue. The density of these masses is frequently heterogeneous because large and multiple HCAs are prone to spontaneous hemorrhage, necrosis, fatty degeneration, and sometimes rupture. After contrast agent injection, most HCAs present as heterogeneous or uniformly hyperattenuating on hepatic arterial phase images, followed by a slow wash-out in the portal venous phase. On MR images, HCAs show quite variable appearances. Most HCAs are slightly hyperintense or hypointense relative to the liver parenchyma on unenhanced T1-weighted images, but generally appear heterogeneously hyperintense on T2-weighted images. On in-phase and out-phase MR images, signal loss is common because of fatty components within the HCAs. Hemorrhage and necrosis are other common complications of HCAs and present their respective MR features. HCAs in GSD-I have greater potential to undergo malignant transformation, which was reported in about 10% of patients.[7] However, the diagnosis of malignant transformation is very difficult on CT and MR images. In rare cases, patients with GSD-I can have HCC or focal nodular hyperplasia (FNH) without HCAs. HCC and FNH in these patients have similar CT and MR features to those in patients without GSD-I.

The common CT and MR features in GH are hepatomegaly and density or intensity changes in the liver parenchyma. Similar to GSD-I, GH always presents a clearly enlarged liver with a vertical diameter exceeding 15 mm, or even 18 mm in severe cases. GH scarcely exhibits fatty liver, although some specimens may show a little fatty infiltration. The density of the liver parenchyma is increased compared with the spleen because of the glycogen deposition. GH presents the same MR features as GSD-I without fatty infiltration, being hypointense or isointense on T2-weighted images and hyperintense on T1-weighted images. Rarely, ascites are seen in some cases and can be improved by good control of the blood glucose level. Unlike GSD-I, there are no case reports of HCAs, HCC, or FNH occurring in GH patients in the literature.

In summary, the common CT and MR features of GSD-I and GH are hepatomegaly, hepatic signal, or density change. Beyond that, patients with HCAs or fatty liver are inclined toward GSD-I, while patients with DM history are more likely to be GH.

ABBREVIATIONS

- **CT:** computed tomography.
- **DM:** diabetes mellitus;
- **FNH:** focal nodular hyperplasia.
- **GH:** glycogenic hepatopathy.
- **GSD:** glycogen storage disease.
- **GSD-I:** glycogen storage disease type I.
- **HCAs:** hepatocellular adenomas.
- **HCC:** hepatocellular carcinoma.
- **HG:** hepatic glycogenosis.
- **MR:** magnetic resonance.

CONFLICT OF INTEREST

The authors declares that there is no conflict of interest regarding the publication of this article.

ACKNOWLEDGMENTS

The authors thank Alison Sherwin, PhD, from Liwen Bianji, Edanz Group China (www.liwenbianji.cn/ac) for editing the English text of a draft of this manuscript.

REFERENCES

1. Vyas M, Zhang X, Morrow JS, Jain D, Salem RR, West AB. Focal hepatic glycogenosis associated with metastatic insulinoma presenting as mass lesions. *Pathol Res Pract* 2016; 212: 59-62.
2. TorresM, López D. Liver glycogen storage associated with uncontrolled type 1 diabetes mellitus. *J Hepatol* 2001; 35: 538.
3. van den Brand M, Elving LD, Drenth JP, van Krieken JH. Glycogenic hepatopathy: a rare cause of elevated serum transaminases in diabetes mellitus. N*eth J Med* 2009; 67: 394-6.
4. Lee PJ. Glycogen storage disease type I: pathophysiology of liver adenomas. *Eur J Pediatr* 2002; 161: S46-S49.
5. Franco LM, Krishnamurthy V, Bali D, Weinstein DA, Arn P, Clary B, Boney A, et al. Hepatocellular carcinoma in glycogen storage disease type Ia: a case series. *J Inherit Metab Dis* 2005; 28: 153-62.
6. Bianchi L. Glycogen storage disease type I and hepatocellular tumours. *Eur J Pediatr* 1993; 152: S63-S70.
7. Katabathina VS, Menias CO, Shanbhogue AK, Jagirdar J, Paspulati RM, Prasad SR. Genetics and imaging of hepatocellular adenomas: 2011 update. *Radiographics* 2011; 31: 1529-43.

Correspondence and reprint request:
Yu-pin Liu, M.D.
Department of Radiology, The Second Affiliated Hospital of Guangzhou University of Chinese Medicine, No. 55, Neihuanxi Road, Guangzhou Higher Education Mega Center, Panyu District, Guangzhou City, Guangdong Province, PR China.
Tel.: +86-13580449707
E-mail: MDLIUYUPIN@163.com