DOI: 10.7860/JCDR/2018/27279.11029

Case Report

Internal Medicine Section

Glycogenic Hepatopathy in a 19-year-old Male with Uncontrolled Insulin Dependent Diabetes: Clinical Presentation and Review of Literature

DUSTIN L LITTLE[1], CRETICUS PETROV MARAK[2], ACHUTA KUMAR GUDDATI[3], WILLIAM G SIMPSON[4]

ABSTRACT

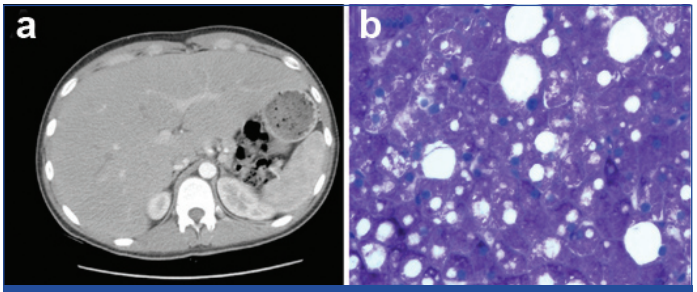
Glycogenic Hepatopathy (GH) is a rare entity encountered in patients with poorly controlled insulin-dependent diabetes. GH results from excessive accumulation of glycogen in the hepatocytes and is characterised by tender hepatomegaly and transaminitis. Hyperglycaemia in these patients leads to frequent use of high doses of insulin. High plasma levels of both serum glucose and insulin causes increased production and storage of glycogen in the hepatocytes. We present the clinical course and management of a patient who presented with hyperglycaemia and was found to have glycaemic hepatopathy. The presentation of similar cases that have been reported in medical literature has been reviewed and discussed in this review. GH is an underdiagnosed entity and should be considered in the differentials of any patient presenting with hepatomegaly and transaminitis, particularly among uncontrolled diabetics.

Keywords: Diabetes mellitus, Glycogen storage disease, Hepatomegaly

CASE REPORT

A 19-year-old American Indian male patient presented to our facility with a two week history of right upper quadrant abdominal pain. The pain was sharp and radiated to his back. He reported one episode of bilious vomiting but denied fever, cough, dyspnoea, dysuria, diarrhoea, constipation, haematemesis, melena haematochezia and haematuria. Review of systems was significant for polydipsia and polyuria. His medical history was significant for poorly controlled type 1 diabetes with recurrent Diabetic Ketoacidosis (DKA) related admissions. His home diabetic regimen included levemir 20 units twice daily and a sliding-scale novolog with meals. He was an active polysubstance abuser (nicotine, alcohol and methamphetamine) and had compliance issues with his home medications.

His blood pressure was 124/90 mmHg, heart rate 128 beats/minute, respiratory rate 16 breaths/minute, SpO_2 100% on room air, temperature 98°F and Body Mass Index (BMI) 20.6 kg/m^2. Physical examination revealed a soft, flat abdomen with mild tenderness over the right upper quadrant. The liver was firm, smooth and tender and approximately three finger breadths below the costal margin in the right midclavicular line. The remainder of the physical examination was unremarkable. Laboratory analysis revealed elevated serum glucose of 296 mg/dL, increased anion gap of 35, positive 2+ urine ketones, serum bicarbonate of 14 mmol/L, and serum lactic acid of 6.5 mmol/L with venous pH of 7.39. Liver panel showed elevated Aspartate Aminotransferase (AST) 165 U/L, Alanine Aminotransferase (ALT) 189 U/L, Alkaline Phosphatase (ALP) 186 U/L and a normal total bilirubin of 0.2 mg/dL. Both HbA1c and serum triglycerides levels were elevated at 11% and 549 mg/dL respectively. Complete blood count and coagulation profiles were within the normal reference range. Computed Tomography (CT) scan of the abdomen showed hepatomegaly of 30 cm without any focal lesions or intrahepatic ductal dilation [Table/Fig-1a]. Ultrasonography of liver revealed hepatomegaly with increased echogenicity consistent with an infiltrative process. Ultrasonography of the gall bladder and biliary system was otherwise unremarkable. The patient was admitted to the Intensive Care Unit (ICU) and treated for DKA. He subsequently underwent a liver biopsy and the histopathologic findings were consistent with GH [Table/Fig-1b]. After resolution of DKA, he was restarted on his home insulin regimen consisting of levemir 20 units BID and insulin coverage based on a sliding scale glucose level. His glucose levels were well controlled on this regimen. Since, his blood sugar level was reasonably well-controlled on the insulin regimen that was supposed to be at home, we concluded that medication non compliance was the reason for his poorly controlled diabetes and associated hepatopathy. Extensive diabetic education was provided to him during his short hospital stay. The plan was to monitor his diabetes and the underlying liver disease as an outpatient. However, he did not keep his outpatient follow up appointments and was subsequently lost to follow up.



[Table/Fig-1]: a) CT scan of the abdomen showing hepatomegaly without any focal liver lesions; b) Hepatocytes with glycogen overload seen on periodic acid-schiff (PAS) staining.

DISCUSSION

Glycogenic hepatopathy was first described by Mauriac in 1930 in an uncontrolled type 1 diabetic child as a component of Mauriac syndrome (growth failure, hyperlipidaemia, delayed puberty, hepatomegaly and cushingoid appearance) and has been reported in handful of case reports [1,2]. However, GH has also been described in patients without the extra-hepatic manifestations of Mauriac syndrome [3]. The prevalence of GH in patients with hepatomegaly and transaminitis is close to 80% among uncontrolled diabetics [4]. Yet this entity remains largely underdiagnosed and therefore, under reported consequently, the overall prevalence of GH is not known exactly.

Non Alcoholic Fatty Liver Disease (NAFLD) commonly presents with hepatomegaly and transaminitis, as a result it is commonly assumed

to be the diagnosis. Non Alcoholic Steatohepatitis (NASH), GH and other causes of acute or chronic hepatitis must be considered in the differentials when these patients present with transaminitis. NAFLD is the most common chronic liver disease worldwide with reported global prevalence of 25% [5]. Discriminating between these diseases is important because the prognosis are different. Glycogenic hepatopathy is completely reversible with institution of glucose control; in contrast NAFLD may lead to fibrosis and cirrhosis. Ultrasonography, CT and Magnetic Resonance Imaging (MRI) cannot differentiate between NAFLD and GH and a definitive diagnosis of GH can only be made by liver biopsy [6].

NAFLD is the most common liver disorder worldwide especially in the western industrialised nations. NAFLD is characterised by fatty infiltration and elevated transaminases; whereas, NASH also has signs of inflammation. There is no good correlation between glycaemic control and the degree of steatosis [7]. Furthermore, a negative ultrasound does not exclude steatosis; thus, necessitating a biopsy to diagnose or assess the degree of fibrosis [8,9].

Patients with NAFLD, acute hepatitis and GH may present with fatigue, abdominal pain, acute transaminitis and hepatomegaly. NASH and hepatitis may progress to cirrhosis or hepatocellular carcinoma; in contrast, GH is caused by poor glucose control and has been shown to be completely reversible with stabilisation of glycaemic control [5,10]. While, GH has also been reported in diabetics with poorly controlled type 2 insulin-dependent diabetes, it has also been described in various circumstances involving poor glycaemic control: a type 2 diabetic patient who attempted suicide by injecting 180 units of insulin glargine, in non diabetics including a toddler with dumping syndrome associated with gastrostomy feeding and three children treated with high-dose glucocorticoid therapy [11-13].

Hyperglycaemia causes inhibition of the glycogen phosphorylase flux; whereas, hyperinsulinemia cause stimulation of the glycogen synthase flux. Both these steps occurring simultaneously cause a major suppression in the hepatic glycogen cycling and an increase in the hepatic glycogen synthesis [14]. This mechanism is thought to underlie the pathogenesis of GH in young diabetics with poorly controlled diabetes. Recently, a mutation in the catalytic subunit of liver glycogen phosphorylase kinase has been attributed to the development of GH [15]. Strict glycaemic control must be obtained in order to treat GH and reverse the hepatomegaly and transaminitis [10]. The converse has also been reported three patients who were diagnosed with GH demonstrated complete reversal of symptoms without intense glucose control, their HbA1c levels being 11%, 13% and 15%, respectively [16].

Age/Sex (years)	Presentation	Time to normalisation	HbA1c	Reference
21 M	New-onset fulminant T1DM with DKA, HM	Improvement at discharge	6.2%	[6]
20 F	T1DM, HM, transaminitis	Improvement at five-month follow up	13.3%	[10]
30 F	T2DM, HM, transaminitis, dietary indiscretion	Resolution at one month follow up		[11]
02 M	Dumping syndrome, no steroids or DM	n/a		[12]
10 F	T1DM, RUQ pain, HM, transaminitis	Persistent HM at two months		[17]
15 M	T1DM, DKA, HM, transaminitis	Persistent HM at five years	9.6%	[18]
18 F	T1DM, DKA, lactic acidosis, HM	Persistent lactic acidosis at six months	11.4%	[19]
21 F	T1DM, tender HM, transaminitis	Seven weeks	8.1%	[20]
19 F	T1DM, HM, DKA	Resolution 10 weeks after CSII	14.6%	[21]
29 F	T1DM, HM, anorexia nervosa	n/a		[22]
41 M	T2DM, HM, insulin overdose (SI), hypoglycemia	Began to resolve in eight days	10.6%	[23]
22 F	AN, transaminitis	n/a		[24]
26 F	AN, abdominal pain, transaminitis	Persistently transaminitis		[25]
22 M	T1DM, HM, transaminitis, anorexia	Improved with better glycaemic control	11.3%	[26]
18 F	T1DM, DKA (multiple episodes of DKA)	10 days	8.2%	[27]
13 M	T1DM, DKA, ischemic hepatopathy	16 days	10.4%	[28]
19 F	T1DM, transaminitis	Resolution at A1C of 9.1%	10.1%	[29]
17 F	T1DM, CD, HM, transaminitis	Resolved at one year follow up	12.0%	[30]
22 M	T1DM, AAT deficiency (ZZ), HM, transaminitis	Resolved with better glycaemic control	14.6%	[31]
16 M	T1DM, over insulinisation with dietary indiscretion, HM	Four weeks	11.1%	[32]
19 F	T1DM, occurred four weeks after treatment for DKA, HM			[33]
21 F	T1DM, CD, HM, lactic acidosis, transaminitis	One week	13.3%	[34]
18 M	T1DM, abdominal pain, HM, lactic acidosis	Resolved at three-month follow up	11.0%	[35]
33 F	T1DM, transaminitis, diarrhoea	Normal at one year follow up	13.7%	[36]
8 M	T1DM, painful HM, transaminitis	Days	14.0%	[37]
27 M	T1DM, RUQ pain, HM, transaminitis	Resolution at three months	15.0%	[38]
19 M	T1DM, HM, transaminitis	Began to resolve in three weeks		[39]
13 M	T1DM, HM, transaminitis			[40]
13 F	T1DM, HM, transaminitis	Began to resolve in four weeks	10.7%	[41]
12 F	Labile T1DM, HM, transaminitis	Began three weeks after CSII	8.4%	[42]
14 F	T1DM, RUQ pain, transaminitis		14.3%	[43]
13 M	T1DM, HM, DKA	Improved at three months		[44]
13 M	T1DM, ketosis, HM			[45]
19 M	T1DM, RUQ pain, HM, transaminitis, DKA, lactic acidosis		11%	Current report

[Table/Fig-2]: Cases of glycogenic hepatopathy, presentation and time to normalisation of liver size and liver function tests (LFT).
T1DM: type 1 diabetes mellitus, T2DM: type 2 diabetes mellitus, HM: hepatomegaly, DKA: diabetic ketoacidosis, CD: celiac disease, AN: anorexia nervosa, AAT: alpha-1-antitrypsin deficiency, SI: suicidal ideation (attempt), CSII: continuous subcutaneous insulin infusion.

Number	Summary	Resolution	Reference
2	Newly diagnosed males T1DM, HM (both)	Weeks	[3]
3	Ages 8-12, two females, HM (all), high dose steroids, no DM	n/a	[13]
3	Ages 20-26, three females, T1DM, GH with persistent transaminitis, mean A1C 13.4% (±0.47)	Four to eight weeks, still poor DM control	[16]
14	Ages 8-25, nine males, T1DM, abdominal pain, transaminitis, HM	Three months (three patients)	[46]
2	18/F and 21/M with labile T1DM, HM (both)	Cure with pancreas transplant	[47]
11	Ages 13-70, median age 23, seven females T1DM (all), HM (nine), transaminitis (six)	Two weeks	[48]
3	Adolescents, two males, T1DM, HM, transaminitis	Resolved with better glycaemic control	[49]
3	Ages 13-14, two females, T1DM, HM (all), mean A1C 12.5% (±1.35)	Two weeks	[50]
4	Ages 17-20, median age 19, three females, T1DM, lactic acidosis (all), HM (all), mean A1C 12.5% (±2.14)	Normalized with glucose control (case four)	[51]
4	Ages 21-29, median age 21.5, three females, T1DM, DKA (three), HM (all), mean A1C 11.4% (±2.95)	Resolved with improved glycaemic control	[52]
4	Ages 19-29, median age 22.5, three females, T1DM, HM, transaminitis, mean A1C 13.2% (±2.46)	LFTs improved in one month	[53]
4	Ages 12-18, median age 13, three females, T1DM with multiple episodes of DKA, mean A1C 11.9% (±1.80)	Four weeks	[54]

[Table/Fig-3]: Summary of glycogenic hepatopathy case reports involving multiple patients.

Review of literature indicated that there were 124 reported cases of GH, the details of which are summarised in [Table/Fig-2,3,4]. The median age was 19±10.6 years (range 2-70 years). Most of the patients were uncontrolled type 1 diabetics (93.7%), only two were type 2 diabetics (1.6%) and six (4.7%) were not diabetic. Only 11 (8.7%) presented with acute DKA. The most common physical finding was hepatomegaly with 63 patients (49.6%) having a palpable hepatomegaly at presentation. Forty patients (31.5%) had severely elevated AST and ALT (defined as >3x ULN). The median HbA1c was 11.7%±2.7 (n=47, range 6.2-22.2%), with the lowest HbA1c finding occurring in a patient with new-onset fulminant type 1 diabetes mellitus who was found in cardiac arrest. The median AST, ALT, ALP and Gamma-glutamyltransferase (GGT) values were 363±1451 U/L (n=55, range 9-6720); 346±505 U/L (n=59, range 14-2549); 199±240 U/L (n=30, range 79-933) and 187±319 U/L (n=25, range 15-1467), respectively. Total bilirubin was found to be elevated in eight patients (6.3%) and eight patients had lactic acidosis. Of the reported cases, 104 patients (81.9%) underwent liver biopsy, all were positive for GH; however, 21 also had steatosis and another 15 also had fibrosis.

Summary of GH Case Reports	
Total number of patients	**N=124**
Diabetes mellitus	118 (95.1%)
Type 1	116
Type 2	2
Non-diabetic	6 (4.9%)
Diabetic ketoacidosis (at presentation)	11 (8.8%)
Hepatomegaly (physical examination)	63 (50.8%)
Biopsy	104
Glycogenic hepatopathy	104 (100%)
Steatosis	21 (20.2%)
Fibrosis	15 (14.4%)
Inflammation	1 (1%)
Hepatitis	1 (1%)
Elevated liver enzymes (peak)	
AST (40 U/L=ULN)	
Mild (<3x ULN)	10 (8%)
Severe (>3x ULN)	40 (32.2%)
ALT (40 U/L=ULN)	
Mild (<3x ULN)	14 (11.3%)
Severe (>3x ULN)	40 (32.2%)
ALP (130 U/L=ULN)	
Mild (<3x ULN)	23 (18.5%)
Severe (>3x ULN)	9 (7.2%)
GGT (45 U/L=ULN)	
Mild (<3x ULN)	9 (7.2%)
Severe (>3x ULN)	14 (11.3%)
Total bilirubin (>1.0 mg/dL)	8 (6.4%)
Elevated lactic acid (>2.2 mmol/L)	8 (6.4%)

[Table/Fig-4]: Summary of GH case reports.

Summary	Reference
N=31 (16 males) with GH. Median age 15.1 years. Liver biopsy was done showing GH. 17 children improved on follow up.	[2]
N=692 (333 males) with T1DM. Mean age 9.7 years. 60 (8.7%) of the 692 studied had either hepatomegaly, increased ALT, positive HCV antibody or abnormal liver US. Biopsy showed GH in three cases.	[55]

[Table/Fig-5]: List of cohort studies reviewed involving glycogenic hepatopathy.

[Table/Fig-5] summarises the clinical characteristics of two cohort studies. In the large cohort, which assessed the prevalence of liver dysfunction in 692 children with type 1 diabetes mellitus, 60 (8.7%) had one or more abnormalities hepatomegaly, increased ALT, positive anti-HCV antibody and abnormal USG. These abnormalities were reported to resolve in 37 of the 60 with improved glycaemic control. Of these, we only included the three biopsy confirmed cases; although, more are suspected. The second cohort examined the liver of 31 children with Mauriac syndrome and GH, of which 19 had biopsies performed. All the biopsies were positive for GH.

Our case is the only documented case of active methamphetamine use which has also been shown to cause GH; although, the mechanism is not completely understood. Our patient also presented with lactic acidosis. Generally, resolution of hepatomegaly and transaminitis occurs quickly, most often between two to four weeks. Strict glycaemic control must be obtained in order treat GH and reverse the hepatomegaly and transaminitis. However, two patients with persistent hepatomegaly one at two months and the other at five years have been described [17,18]. One of the cases also had persistent lactic acidosis [19]. Until more is known about this entity; we would emphasise good glycaemic control for patients with GH as it would also reduce other complications related to diabetes.

CONCLUSION

Non-alcoholic fatty liver disease, NASH, chronic hepatitis and GH may all present with right upper quadrant pain, hepatomegaly and transaminitis. Liver biopsy is the gold standard for diagnosis as imaging by ultrasound cannot reliably distinguish between them. NAFLD, NASH and chronic hepatitis can lead to fibrosis and eventually progress to cirrhosis and hepatocellular carcinoma; whereas, GH has a good prognosis and completely resolves on institution of adequate glycaemic control.

ACKNOWLEDGEMENTS

We wish to thank Dr. Laura Van Newkirk, MD for her assistance in providing the microscopic slides.

REFERENCES

[1] Kim MS, Quintos JB. Mauriac syndrome: growth failure and type 1 diabetes mellitus. Pediat Endocrinology Rev. 2008;4:989-93.
[2] Fitzpatrick E, Cotoi C, Quaglia A, Sakellariou S, Ford-Adams ME, Hadzic N. Hepatopathy of Mauriac syndrome: a retrospective review from a tertiary liver centre. Archives of Disease in Childhood. 2014;99(4):354-57.
[3] Carcione L, Lombardo F, Messina MF, Rosano M, De Luca F. Liver glycogenosis as early manifestation in type 1 diabetes mellitus. Diabetes Nutr Metab. 2003;16(3):182-84.
[4] Stone BG, Van Thiel DH. Diabetes mellitus and the liver. Semin Liver Dis.1985;5(1):08-28.
[5] Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M. Global epidemiology of nonalcoholic fatty liver disease meta-analytic assessment of prevalence, incidence, and outcomes. Hepatology. 2016;64(1):73-84.
[6] Murata F, Horie I, Ando T, Isomoto E, Hayashi H, Akazawa S, et al. A case of glycogenic hepatopathy developed in a patient with new-onset fulminant type 1 diabetes: the role of image modalities in diagnosing hepatic glycogen deposition including gradient-dual-echo MRI. Endocr J. 2012;59(8):669-76.
[7] Silverman JF, O'Brien KF, Long S, Leggett N, Khazanie PG, Pories WJ, et al. Liver pathology in morbidly obese patients with and without diabetes. Am J Gastroenterol. 1990;85(10):1349-55.
[8] Scatarige JC, Scott WW, Donovan PJ, Siegelman SS, Sanders RC. Fatty infiltration of the liver: ultrasonographic and computed tomographic correlation. J Ultrasound Med. 1984;3(1):09-14.
[9] Leevy CM. Fatty liver: a study of 270 patients with biopsy proven fatty liver and review of the literature. Medicine (Baltimore). 1962;41:249-76.
[10] Hudacko RM, Manoukian AV, Schneider SH, Fyfe B. Clinical resolution of glycogenic hepatopathy following improved glycemic control. J Diabetes Complications. 2008;22(5):329-30.
[11] Nakamuta M, Ohashi M, Goto K, Tanabe Y, Hiroshige K, Nawata H. Diabetes mellitus-associated glycogen storage hepatomegaly: report of a case and review of the Japanese literature. Fukuoka Igaku Zasshi. 1993;84(7):354-58.
[12] Resnick JM, Zador I, Fish DL. Dumping syndrome: a cause of acquired glycogenic hepatopathy. Pediatr Dev Pathol. 2011;14(4):318-21.
[13] Iancu TC, Shiloh H, Dembo L. Hepatomegaly following short-term high-dose steroid therapy. J Pediatr Gastroenterol Nutr. 1986;5(1):41-46.
[14] Ferrer JC, Favre C, Gomis RR, Fernandez-Novell JM, Garcia-Rocha M, de la Iglesia N, et al. Control of glycogen deposition. FEBS Lett. 2003;546(1):127-32.
[15] MacDonald MJ, Hasan NM, Ansari IU, Longacre MJ, Kendrick MA, Stoker SW. Discovery of a Genetic Metabolic Cause for Mauriac Syndrome in Type 1 Diabetes. Diabetes. 2016;65(7):2051-59.
[16] Cha JH, Ra SH, Park YM, Ji YK, Lee JH, Park SY, et al. Three cases of glycogenic hepatopathy mimicking acute and relapsing hepatitis in type I diabetes mellitus. Clinical and Molecular Hepatology. 2013;19(4):421-25.
[17] Jin HY, Kang D-Y, Choi JH. Hepatic glycogenosis in a patient with poorly controlled type 1 diabetes mellitus. Korean J Pediatr. 2009;52(11):1279-82.
[18] Kant R, Loper HB, Verma V, Malek R, Drachenberg CB, Munir KM. Glycogenic hepatopathy with persistent hepatomegaly in a patient with uncontrolled type 1 diabetes. Journal of Endocrinology and Metabolism. 2015;5(1-2):189-91.
[19] Deemer KS, Alvarez GF. A rare case of persistent lactic acidosis in the icu: glycogenic hepatopathy and mauriac syndrome. Case Reports in Critical Care. 2016;2016:6072909.
[20] Torres M, Lopez D. Liver glycogen storage associated with uncontrolled type 1 diabetes mellitus. J Hepatol. 2001;35(4):538.
[21] Imtiaz KE, Healy C, Sharif S, Drake I, Awan F, Riley J, et al. Glycogenic hepatopathy in type 1 diabetes: an underrecognized condition. Diabetes Care. 2013;36(1):e6-e7.
[22] Van den Brand M, Elving LD, Drenth JP, van Krieken JH. Glycogenic hepatopathy: a rare cause of elevated serum transaminases in diabetes mellitus. Neth J Med. 2009;67(11):394-96.
[23] Tsujimoto T, Takano M, Nishiofuku M, Yoshiji H, Matsumura Y, Kuriyama S, et al. Rapid onset of glycogen storage hepatomegaly in a type-2 diabetic patient after a massive dose of long-acting insulin and large doses of glucose. Intern Med. 2006;45(7):469-73.
[24] Komuta M, Harada M, Ueno T, Uchimura Y, Inada C, Mitsuyama K, et al. Unusual accumulation of glycogen in liver parenchymal cells in a patient with anorexia nervosa. Intern Med. 1998;37(8):678-82.
[25] Kransdorf LN, Millstine D, Smith ML, Aqel BA. Hepatic glycogen deposition in a patient with anorexia nervosa and persistently abnormal transaminase levels. Clinics and Research in Hepatology and Gastroenterology. 2016;40(2):e15-e18.
[26] Park J, Song D, Park JS, Nam JY, Kim CS, Kim DM, et al. A case of hepatomegaly due to diabetic glycogenosis reversed by glycemic control. J Korean Soc Endocrinol. 2004;19(2):223-28.
[27] Lee SH, Kwon HS, Shin JA, Kim WC, Kim JH, Choi YH, et al. A case of hepatic glycogenosis in a patient with uncontrolled type 1 diabetes mellitus. J Korean Diabetes Assoc. 2006;30(1):82-86.
[28] Martin J, Tomlinson P. Hepatic complications in poorly controlled type 1 diabetes mellitus: a case report. The New Zealand Medical Journal. 2014;127(1392):95-97.
[29] Bassett JT, Veerappan GR, Lee DH. Glycogenic hepatopathy: a rare cause of increased aminotransferase levels in a diabetic patient. Clin Gastroenterol Hepatol. 2008;6(11):A26.
[30] Bua J, Marchetti F, Faleschini E, Ventura A, Bussani R. Hepatic glycogenosis in an adolescent with diabetes. J Pediatr. 2010;157(6):1042.
[31] Xu J, Dhall D, Sundaram V. An enlarging liver in a young diabetic male. Gastroenterology. 2015;149(6):e8-e10.
[32] Abaci A, Bekem O, Unuvar T, Ozer E, Bober E, Arslan N, et al. Hepatic glycogenosis: a rare cause of hepatomegaly in Type 1 diabetes mellitus. Journal of Diabetes and its Complications. 2008;22(5):325-28.
[33] Tomihira M, Kawasaki E, Nakajima H, Imamura Y, Sato Y, Sata M, et al. Intermittent and recurrent hepatomegaly due to glycogen storage in a patient with type 1 diabetes: genetic analysis of the liver glycogen phosphorylase gene (PYGL). Diabetes Res Clin Pract. 2004;65(2):175-82.
[34] Parmar N, Atiq M, Austin L, Miller RA, Smyrk T, Ahmed K. Glycogenic Hepatopathy: Thinking Outside the Box. Case reports in gastroenterology. 2015;9(2):221-26.
[35] Saadi T. Glycogenic hepatopathy: a rare disease that can appear and resolve rapidly in parallel with glycemic control. Isr Med Assoc J. 2012;14(4):269-70.
[36] Saxena P, Turner I, McIndoe R. Education and Imaging. Hepatobiliary and pancreatic: Glycogenic hepatopathy: a reversible condition. J Gastroenterol Hepatol. 2010;25(3):646.
[37] Lecomte M, Gottrand F, Stuckens C, Lecomte-Houcke M. Acute steatosis in an 8-year-old boy with insulin-dependent diabetes mellitus. Journal of Pediatric Gastroenterology and Nutrition. 1997;25(1):98-100.
[38] Sweetser S, Kraichely RE. The bright liver of glycogenic hepatopathy. Hepatology. 2010;51(2):711-12.
[39] Atmaca M, Ucler R, Kartal M, Seven I, Alay M, Bayram I, et al. Glycogenic Hepatopathy in Type 1 Diabetes Mellitus. Case reports in Hepatology. 2015;2015:236143.
[40] Aljabri KS, Bokhari SA, Fageeh SM, Alharbi AM, Abaza MA. Glycogen hepatopathy in a 13-year-old male with type 1 diabetes. Ann Saudi Med. 2011;31(4):424-27.
[41] Jeong HR, Shim YS, Kim YB, Lee HS, Hwang JS. Glycogenic hepatopathy in a Korean girl with poorly controlled type 1 diabetes mellitus. Annals of Pediatric Endocrinology and Metabolism. 2014;19(1):49-52.
[42] Chung IH, Jeong SJ, Cho YA, Kim GI, Yoo EG. Liver dysfunction due to hepatic glycogenosis in a girl with type 1 diabetes. J Korean Soc Pediatr Endocrinol 2009;14(2):174-78.
[43] Jung IA, Cho WK, Jeon YJ, Kim SH, Cho KS, Park SH, et al. Hepatic glycogenosis in type 1 diabetes mellitus mimicking Mauriac syndrome. Korean J Pediatr. 2015;58(6):234-37.
[44] Ruschhaupt DG, Rennert OM. Recurrent hepatomegaly and transient alteration of liver functions in an adolescent with diabetic acidosis. Clinical Pediatrics. 1970;9(2):122-24.
[45] Weitzman S, Lehman E, Lischinsky M. Transient hepatomegaly with glycogen deposition in transient juvenile diabetes with ketosis. Harefuah. 1974 ;86(11):556-57.
[46] Torbenson M, Chen YY, Brunt E, Cummings OW, Gottfried M, Jakate S, et al. Glycogenic hepatopathy: an underrecognized hepatic complication of diabetes mellitus. Am J Surg Pathol. 2006;30(4):508-13.
[47] Fridell JA, Saxena R, Chalasani NP, Goggins WC, Powelson JA, Cummings OW. Complete reversal of glycogen hepatopathy with pancreas transplantation: two cases. Transplantation. 2007;83(1):84-86.
[48] Chatila R, West AB. Hepatomegaly and abnormal liver tests due to glycogenosis in adults with diabetes. Medicine (Baltimore). 1996;75(6):327-33.
[49] Munns CF, McCrossin RB, Thomsett MJ, Batch J. Hepatic glycogenosis: reversible hepatomegaly in type 1 diabetes. J Paediatr Child Health. 2000;36(5):449-52.
[50] Flotats BM, Miserachs BM, Ricart CA, Clemente LM, Gussinyer CM, Yeste F, et al. Hepatomegaly due to glycogen storage disease and type 1 diabetes mellitus. Anales de Pediatria. 2007;67(2):157-60.
[51] Brouwers MC, Ham JC, Wisse E, Misra S, Landewe S, Rosenthal M, et al. Elevated lactate levels in patients with poorly regulated type 1 diabetes and glycogenic hepatopathy: a new feature of Mauriac syndrome. Diabetes Care. 2015;38(2):e11-e12.
[52] Silva M, Marques M, Cardoso H, Rodrigues S, Andrade P, Peixoto A, et al. Glycogenic hepatopathy in young adults: a case series. Rev Esp Enferm Dig. 2016;108(10):673-76.
[53] Ikarashi Y, Kogiso T, Hashimoto E, Yamamoto K, Kodama K, Taniai M, et al. Four cases of type 1 diabetes mellitus showing sharp serum transaminase

increases and hepatomegaly due to glycogenic hepatopathy. Hepatol Res. 2017;47(3):e201-e209.
[54] Vo HTD, Klein GW, Loizides A, Zhou P, Liu Q, Pan DH. Glycogen hepatopathy in children with poorly controlled type 1 diabetes. International Journal of Case Reports and Images. 2011;2(9):01-04.
[55] El-Karaksy HM, Anwar G, Esmat G, Mansour S, Sabry M, Helmy H, et al. Prevalence of hepatic abnormalities in a cohort of Egyptian children with type 1 diabetes mellitus. Pediatric Diabetes. 2010;11(7):462-70.

PARTICULARS OF CONTRIBUTORS:
1. DO, Department of Family Medicine, Tahlequah City Hospital, Tahlequah, Oklahoma, USA.
2. MD, Department of Critical Care, Tahlequah City Hospital, Tahlequah, Oklahoma, USA.
3. MD, PhD, Department of Haematology and Oncology, SUNY Downstate Medical Center, Brooklyn, New York, USA.
4. MD, Department of Gastroenterology, Tahlequah City Hospital, Tahlequah, Oklahoma, USA.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Achuta Kumar Guddati,
450, Clarkson Avenue, Brooklyn, New York, USA.
E-mail: drgakumar@yahoo.com

FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Feb 04, 2017**
Date of Peer Review: **Mar 10, 2017**
Date of Acceptance: **Nov 10, 2017**
Date of Publishing: **Jan 01, 2018**