

# Hyperglycemia in Glycogen Storage Diseases: A Case Report

**Alfateh M. Noor, Abdulrahman Alharthy, Ayman Abukhod, Hind Elshareef\*,  
Mohammed H.Lhmdi, Mohamed Abuhamdah, Abdullah Balhamar, Zohdi Farea**

Critical Care Department, King Saud Medical City, Riyadh, KSA

\*Critical Care Department, King Saud University Medical City, Riyadh, KSA

Corresponding Author: Alfateh M. Noor

## ABSTRACT

We report a rare case of diabetes in the setting of glycogen storage disease type Ia. The underlying pathogenesis for developing diabetes in these patients is unclear, and there is always fear of iatrogenic hypoglycemia which leads to unclear guidelines in the management of such patient. In this particular case we started a combination of sodium-glucose co-transporter 2 inhibitor and short acting regular insulin subcutaneously every 4 hours according to sliding scale, which was successful.

**Keywords:** Glycogen Storage Disease, hyperglycemia

## INTRODUCTION

Glycogen storage diseases are rare genetic disorders of glycogen synthesis, degradation, or metabolism. It has been categorized according to the recognition of the responsible enzyme defect<sup>(2)</sup> due to mutations of the glycogen debranching enzyme (Amylo-1,6-glucosidase) gene, located at chromosome band 1p21.2.

It has myriad of clinical presentation like exercise intolerance, myalgias, hepatomegaly, rhabdomyolysis, myoglobinuria, acute renal failure and cardiomyopathy.<sup>(3-6)</sup> Signs include Hepatosplenomegaly (sometimes liver adenoma can be seen on CT abdomen) and muscle weakness, but the feature that is shared among different types of Glycogen storage disease is hypoglycemia because of inability to produce endogenous glucose, so the development of diabetes with glycogen storage disease is extremely rare. We document this case of Glycogen Storage disease who presented with severe uncontrolled hyperglycemia.

The diagnosis is confirmed by demonstration of debrancher enzyme

deficiency on enzymatic assay. No specific treatment for GSDs, but diet therapy with nocturnal nasogastric tube feeding and cornstarch improves symptoms (especially hypoglycemia), reduces the liver size, and improves overall growth and development<sup>(1)</sup>

## CASE PRESENTATION

27-year-old, male known case of glycogen storage disease type Ia and diabetes mellitus type II on metformin tab 500 mg OD, presented to ER with fever and watery diarrhea for 5 days associated with vomiting for 2 days. His lab showed renal impairment, creatinine was 187 mmol/l BUN was 23 mmol/l. His arterial blood gas revealed high anion gap metabolic acidosis, PH 6.90 with lactate of 21, so diagnosed as severe Diabetic Keto Acidosis (DKA) with severe lactic acidosis. He was admitted to ICU for close observation and further management. We stopped metformin and DKA protocol started with insulin infusion 0.1 units /kg/hr but the patient developed hypoglycemia after four hours. So, insulin dose decreased to 0.05 units/kg/hr, even

though the acidosis improved but again the patient suffered two episodes of hypoglycemia. Therefore, insulin infusion held and human regular short acting insulin (HRI) started subcutaneously according to sliding scale, with empagliflozin (sodium-glucose co-transporter 2 inhibitor) Inhibitors 10 mg Tab OD. After few hours, PH became 7.0 but his lactate was still high 12. During his course in ICU patient became confused and agitated so electively intubated and connected to Mechanical ventilation. After CRRT started his lactate improved and became 8.1. CT abdomen requested to rule out bowel ischemia it was normal. With dialysis, fluid management and empagliflozin in addition to HRI, the patient condition continued to improve; on his 4<sup>th</sup> day in the ICU his arterial blood gas was showing normal PH and normal lactate. so he was successfully weaned from mechanical ventilation and discharged to the ward the next day.

## DISCUSSION

Glycogen storage disease type 1 (GSD-I) is a rare genetic condition that develops due to an inborn error of metabolism causing deficient activity of the enzyme, glucose 6-phosphatase <sup>(7)</sup> that hydrolyzes glucose-6 phosphate (G6P) into biochemically active glucose hence gluconeogenesis happens. Therefore, absence of this process will lead to hypoglycemia.

It is autosomal recessive disease, with an incidence of 1 out of 100,000 births. <sup>(8,9)</sup>

It is expected for a patient who is known to have Glycogen storage disease to present with hypoglycemia associated with other clinical features like rhabdomyolysis, myoglobinuria, acute renal failure and cardiomyopathy and lactic acidosis. <sup>(3-6)</sup> but hyperglycemia can be a feature as well. There are two case reports we found of patients with different subtypes of GSD who later developed DM., contributing factors were pancreatic insufficiency and insulinopenia, <sup>(10,11)</sup> this can be explained by The wide spectrum of enzymatic

dysfunction that can occur; while some patients have no functional G6PC, others might have partial specially type Ia. <sup>(12)</sup> In this case, there might be remnant enzymatic activity, in addition of other environmental factors that contributed to metabolic syndrome which documented by study by Melis et al. to be associated with type Ia GSD. <sup>(10)</sup> and this could lead to the dilemma of treating the hyperglycemia carefully without risking a common incidence of hypoglycemic episodes that is caused by nature of the disease and its overresponse reaction to insulin. Other explanation that could contribute to the incidence of hyperglycemia is the fact that type 1 GSD patients showed delayed insulin secretion response when they eat which result in post-prandial hyperglycemia. <sup>(11)</sup> Unfortunately, no clear protocols exist in managing such patient, and use of insulin could pose a risk of hypoglycemia. Therefore, clinicians depend on other hypoglycemic agents. In our case the patient was receiving metformin which lowers blood glucose in multiple ways, including suppression of hepatic gluconeogenesis, increased peripheral insulin-mediated glucose uptake, decreased fatty acid oxidation, and increased intestinal glucose consumption. <sup>(13)</sup> But metformin can cause lactic acidosis <sup>(14)</sup> specially in the presence of renal impairment like in our patient, even if the patient doesn't have renal impairment, while therapy with metformin may improve the patient blood glucose, GSD already has a propensity for lactic acidosis, so it is additional risk of euglycemic diabetic ketoacidosis with the use of such medication. In our case, the best option was to stop metformin and insulin infusion and to start sodium-glucose co-transporter 2 inhibitor in addition to insulin subcutaneously in sliding scale dose every four hours with close observation of glucose level.

## CONCLUSION

Glycogen Storage Disease is a rare disorder. Furthermore, its unusual

presentation with diabetes is confusing and this could lead to disastrous treatment results if we are not familiar with the subtypes of the disease. So, close observation is a necessity and more research needs to be done in order to come up with a clear guideline in the management of such cases.

#### Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

#### Declaration of conflicting interest

The authors declare no conflicts of interest in preparing this article.

#### Ethical approval

The study was approved by the Ethics committee of the hospital. Written informed consent was obtained from the patient.

#### REFERENCES

1. Smit GPA, Rake JP, Akman HO, DiMauro S: Inborn Metabolic Diseases: Diagnosis and Treatment. Edited by: Fernandes John Saudubray Jean-Marie Van Den Berghe Georges Walter John H. 2006, Springer, 108-109. 4
2. Burda P, Hochuli M. Hepatic glycogen storage disorders: what have we learned in recent years? *Curr Opin Clin NutrMetab Care*. 2015;18(4):415–421. doi: 10.1097/MCO.000000000000181.
3. Bollig G, Mohr S, Raeder J. McArdle's disease and anaesthesia: case reports. Review of potential problems and association with malignant hyperthermia. *Acta Anaesthesiol Scand*. 2005;49(8): 1077–1083. doi: 10.1111/j.1399-6576.2005.00755.x.
4. McMillan MA, Hallworth MJ, Doyle D, Douglas Briggs J, Junor BJR. Acute renal failure due to McArdle's disease. *Ren Fail*. 1989;11(1):23–25. doi: 10.3109/08860228909066942.
5. Davis PJ, Brandom BW. The association of malignant hyperthermia and unusual disease: when you're hot you're hot or maybe not. *AnesthAnalg*. 2009;109(4):1001–1003. doi: 10.1213/ane.0b013e3181b493d4.
6. Reid CJ, Hebert D. Acute renal failure complicating liver transplantation in twin sisters with glycogen storage disease type Ia. *Transplant Proc*. 1996;28(6):3629–3631.
7. Rajas F, Labrune P, Mithieux G. Glycogen storage disease type 1 and diabetes: learning by comparing and contrasting the two disorders. *Diabetes Metab*. 2013;39(5):377–87. doi: 10.1016/j.diabet.2013.03.002.
8. Rajas F, et al. Lessons from new mouse models of glycogen storage disease type 1a in relation to the time course and organ specificity of the disease. *J Inherit Metab Dis*. 2015;38(3):521–7. doi: 10.1007/s10545-014-9761-0.
9. Froissart R, et al. Glucose-6-phosphatase deficiency. *Orphanet J Rare Dis*. 2011;6:27. doi: 10.1186/1750-1172-6-27.
10. Melis D, et al. Glycogen storage disease type Ia (GSDIa) but not Glycogen storage disease type Ib (GSDIb) is associated to an increased risk of metabolic syndrome: possible role of microsomal glucose 6-phosphate accumulation. *Orphanet J Rare Dis*. 2015;10(1):91. doi: 10.1186/s13023-015-0301-2.
11. Lockwood DH, et al. Insulin secretion in type I glycogen storage disease. *Diabetes*. 1969;18(11):755–8. doi: 10.2337/diab.18.11.755.
12. Bali DS, Chen YT, Austin S, et al. Glycogen storage disease type I. 2006 Apr 19 (Updated 2016 Aug 25). In: Pagon RA, Adam MP, Ardinger HH, et al., editors. *GeneReviews*® [Internet]. Seattle: University of Washington; 1993-2017.
13. Bailey CJ, Turner RC. Metformin. *N Engl J Med*. 1996;334(9):574–579.
14. Correia CS, Bronander KA. Metformin-associated lactic acidosis masquerading as ischemic bowel. *Am J Med*. 2012; 125(5): e9.

How to cite this article: Noor AM, Alharthy A, Abukhod A et.al. Hyperglycemia in glycogen storage diseases: a case report. *Int J Health Sci Res*. 2020; 10(8):281-283.

\*\*\*\*\*