

Acute hepatitis induced by insulin overdose and oral glucose administration in a child managed under a hybrid continuous care model

Judy Kattan, Kowshik Gupta, Hala Zakaria^{ORCID}, Sheikha Alshehhi, Noah Almarzooqi, Ali Hashemi and Ihsan Almarzooqi

GluCare Integrated Diabetic Center, Dubai, United Arab Emirates

Correspondence should be addressed to H Zakaria: hala@glucare.health

Summary

Acute hepatitis was reported in a 10-year-old male patient with type 1 diabetes, believed to be due to hepatic glycogenosis from insulin overdose and oral glucose administration. Liver function abnormalities, including increased ALT, AST, and GGT, were observed without any abnormality in liver ultrasound. After detailed investigation, it was discovered that the patient was dosing himself with additional insulin to induce hypoglycemia. Close monitoring by the GluCare.Health hybrid platform and CGM was done along with further education about insulin doses, hypoglycemia, and hyperglycemia treatment. No specific pharmacological treatment was needed to treat hepatitis and the patient's liver enzymes normalized with the GluCare continuous care model.

Learning points

- Importance of hybrid care models: hybrid care models allow for continuous tracking, closing the feedback loop that is currently missing from traditional clinical practice, leading to better patient outcomes through continuous engagement, monitoring, and timely adjustments.
- Risk of hepatitis from glucose overload: excessive glucose intake following a significant insulin overdose can lead to hepatitis due to the overaccumulation of glycogen.
- Balancing glucose administration: while the risk of hypoglycemia-induced neurological damage is a major concern, glucose administration should be carefully adjusted based on closely monitored blood glucose levels.
- Awareness of acute hepatitis: acute hepatitis as a complication of substantial insulin overdose and excessive glucose administration is a rare occurrence that endocrinologists should be aware of.
- Importance of monitoring liver enzymes: specific treatment may not be necessary; however, monitoring liver enzymes is essential to ensure they return to normal levels.
- Challenges in diagnosing factitious insulin use: diagnosing factitious insulin use in children and adolescents is challenging, as many patients may deny it, and parents may find it hard to believe. Careful and sensitive questioning is necessary.

Keywords: diabetes; hybrid model of care

Background

Acute hepatitis due to hepatic glycogenosis is a rare and noteworthy condition, significant to clinicians for several reasons. This case highlights the unusual pathogenesis resulting from the excessive accumulation of glycogen in the liver, often triggered by an insulin overdose and subsequent high intake of oral glucose. This pathway sheds light on the possible pathogenesis of hepatitis linked to glycogen overload. The clinical presentation begins with an insulin overdose, which induces severe hypoglycemia requiring high intake of oral or intravenous glucose for treatment, presenting a unique and challenging scenario that demands careful management. The high insulin levels stimulate the liver to uptake glucose from the blood and store it as glycogen (1). When glycogen accumulation becomes excessive, it can cause hepatic inflammation, leading to acute hepatitis. This insight into the mechanism of hepatic inflammation is valuable for understanding similar rare presentations. The rarity of this condition underscores the importance of awareness among endocrinologists and other healthcare providers. Understanding this rare complication can aid in the diagnosis and management of similar cases in clinical practice. This case not only illustrates an unusual presentation of a common therapeutic intervention but also emphasizes the need for vigilance and careful monitoring in patients receiving high doses of insulin and glucose (2).

Case presentation

A 10-year-old boy presented with significant fluctuations in blood glucose levels and severe episodes of hypoglycemia, which his parents managed with large amounts of fruit juice. He had a history of type 1 diabetes for 3 years, well-controlled with a basal-bolus regimen. Initially, both the patient and his family denied any intentional insulin misuse. However, after several in-depth history-taking sessions, the child admitted to deliberately administering insulin overdoses to avoid school and to gain access to carbohydrate-rich foods.

Over the course of a week, he experienced prolonged periods of low-grade hypoglycemia due to repeated insulin overdosing, treated with frequent high glycemic index carbohydrate. The patient was on Libre 2

continuous glucose monitoring (CGM), and his parents received alerts whenever glucose levels dropped below 70 mg/dL. In response, they would immediately give him juice, which helped prevent severe hypoglycemia but resulted in prolonged glucose fluctuations between 53 and 72 mg/dL for approximately five hours.

On March 6, 2024, his glucose levels ranged widely, fluctuating between 40 and 322 mg/dL over a 7 h period. Blood tests performed the following day as part of the hypoglycemia workup revealed that his liver enzymes were elevated compared to 2 months prior: ALT increased from 11.8 U/L to 280 U/L, AST from 17.9 U/L to 167 U/L, and gamma-glutamyl transferase (GGT) from 13 U/L to 50 U/L. A metabolic panel and abdominal ultrasound were normal. Upon introducing the patient to a hybrid care model that included continuous engagement, monitoring, and adjusting insulin and glucose intake, the severe hypoglycemic events ceased, and his liver enzymes returned to normal. Typically, this would have been missed under traditional episodic care.

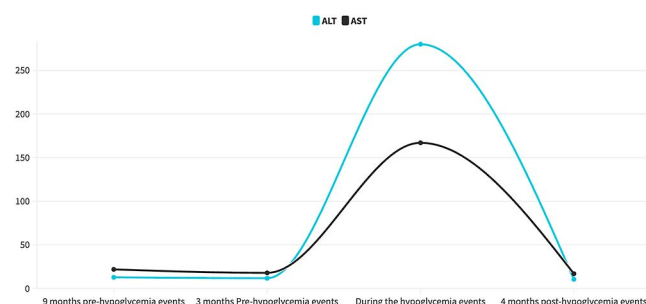
Investigation

During the investigation, laboratory tests and imaging studies were conducted to assess the patient's condition. Table 1 presents the clinical progression of the patient's laboratory tests, specifically focusing on liver enzymes and other markers at different time points: 9 months before, 3 months before, the day of, and 4 months after the hypoglycemia events. Notably, there was a marked elevation in alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels during the hypoglycemia events, reaching 280.0 U/L and 167.0 U/L, respectively, compared to much lower levels in the pre- and post-event periods. GGT also showed a significant increase during the hypoglycemia events, while hemoglobin A1c (HbA1c) levels remained relatively stable. An abdominal ultrasound performed during the hypoglycemia events revealed normal findings, with the liver appearing normal in shape, size, and echogenicity, and no signs of intrahepatic biliary radical dilatation. The gallbladder, common bile duct (CBD), portal vein, pancreas, spleen, kidneys, aorta, and inferior vena cava (IVC) were all observed to be within normal limits, with no evidence of structural abnormalities or pathology.

Table 1 Clinical presentation of the patient's laboratory tests (pre, during, and post the hypoglycemia events).

Lab test	9 months PHE	3 months PHE	Day of HE	4 months POHE
ALT (U/L)	12.8	11.8	280.0	10.5
AST (U/L)	21.9	17.9	167.0	16.9
GGT (U/L)	12.0	13.0	50.0	-
HbA1c (%)	6.60	5.9	6.1	5.9

ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; HbA1c, hemoglobin A1c; PHE, pre-hypoglycemic events; HE, hypoglycemic events; POHE, post-hypoglycemic events.

**Figure 1**

Fluctuations in liver enzymes pre, during, and post hypoglycemia events.

Figure 1 illustrates the fluctuations in liver enzyme levels, highlighting the significant elevations during the hypoglycemia episodes and subsequent normalization post-event. Despite the transient enzyme elevations, the ultrasound findings showed no abnormalities, indicating no structural issues within the abdominal organs. Furthermore, imaging was recommended only if liver function tests continued to show abnormal results.

Ultrasound findings

The abdominal ultrasound revealed normal findings for various organs (during the hypoglycemia events):

- Liver: normal shape, size, and echogenicity. No signs of intrahepatic biliary radical dilatation. Measures 12.13 cm in craniocaudal dimension.
- Gallbladder: normal appearance with an echo-free lumen and smooth wall. No pericholecystic fluid noted.
- CBD and portal vein: not dilated. CBD measures 1.2 mm, and portal vein measures 6 mm.
- Pancreas: normal echotexture with no dilation of the main pancreatic duct.
- Spleen: normal shape, size (approximately 8.2 cm), and echogenicity.
- Kidneys: both kidneys are normal in shape, size, echogenicity, and location. Corticomedullary differentiation is maintained. No hydronephrosis or calculus disease observed. Right kidney measures approximately 8.5 × 4.8 cm, and the left kidney measures approximately 8.0 × 5.2 cm.
- Aorta and IVC: unremarkable.
- Overall impression: no obvious abnormalities were noted in the study. Furthermore, imaging is recommended if liver function tests remain abnormal.

Treatment

Upon discovering the cause of the severe hypoglycemia events, several interventions were implemented to manage the condition effectively:

- Social support:** social support was provided for the child and his family to address any underlying psychosocial issues and to ensure a supportive home environment.
- Insulin dose adjustment:** adjustments were made to the patient's insulin doses to better manage his blood glucose levels. This involved careful recalibration of his basal-bolus regimen to prevent further episodes of hypoglycemia, considering the challenges posed by carb counting for precise insulin dosing.
- Education:** the family received comprehensive education on how to manage hypoglycemia, including recognizing early signs, administering appropriate amounts of glucose, and when to seek medical help.

No specific pharmacological treatments were necessary beyond the adjustments to the insulin regimen. Over time, with these measures in place, the patient's liver enzyme levels returned to normal, and the episodes of severe hypoglycemia ceased.

Outcome and follow-up

Over the next 3 months, the patient received continuous monitoring, with glucose levels tracked using CGM and access to professional healthcare through the GluCare.Health care model. During this period, no further episodes of severe hypoglycemia occurred. The patient's parents became more knowledgeable about managing hypoglycemic events, contributing to his improved condition. His liver enzyme levels returned to normal, and his time in range improved to 77%, with an average glucose level of 113 mg/dL. This outcome demonstrates the importance and effectiveness of continuous monitoring, appropriate education, and social support in managing complex medical conditions, emphasizing that continuous monitoring in this case was crucial for preventing further complications and achieving optimal patient outcomes.

Discussion

Acute hepatitis following a massive insulin overdose and excessive glucose administration is a rare complication, which any endocrinologist should be aware of since it demands careful consideration. This case highlights several critical aspects of this condition. The pathogenesis of hepatitis in this context involves the excessive accumulation of hepatic glycogenosis. Insulin overdose leads to profound hypoglycemia, which necessitates the administration of large amounts of glucose to restore normoglycemia. High insulin levels stimulate hepatic glycogen synthesis, leading to the

overaccumulation of glycogen and subsequent liver inflammation (1, 3).

Clinical presentation

Patients may present with signs of hepatic dysfunction, including elevated liver enzymes, hepatomegaly, and sometimes jaundice. In this case, the patient's transaminase levels were significantly elevated, but he did not show any symptoms of hepatitis, and liver ultrasound was normal (1).

Management

Management focuses on the careful titration of insulin and glucose administration to avoid further glycogen accumulation while treating hypoglycemia. Education here is very important to know how to avoid hypoglycemia and how to treat it. CGM is essential for maintaining optimal blood glucose levels and preventing both hypoglycemia and hyperglycemia. This case demonstrated the effectiveness of CGM in closely monitoring and adjusting glucose therapy (4). In this case, there was no specific pharmacological treatment for hepatitis; however, discontinuation of excessive glucose infusion typically results in rapid resolution of clinical and laboratory abnormalities. Regular monitoring of liver enzymes is crucial until they return to normal levels, as observed in this patient (1, 4).

Challenges in diagnosis

Identifying factitious insulin use in children and adolescents poses significant challenges due to denial by the patient and disbelief from the parents. Careful and sensitive questioning is essential to uncovering the truth and initiating appropriate treatment. In this case, thorough clinical evaluation and history-taking were key to diagnosing insulin overdose as the cause of hepatitis (3).

Expectation

This case emphasizes the rarity but potential severity of acute hepatitis following insulin overdose and excessive glucose administration. It highlights the importance of

multidisciplinary care, vigilant monitoring, and patient and caregiver education in managing such complex scenarios. Future research and case reports will help elucidate the best practices for preventing and treating this condition, improving outcomes for affected patients.

Declaration of interest

The authors declare that there are no conflicts of interest that could be perceived as prejudicing the impartiality of the case reported.

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Patient consent

Written informed consent for publication of their clinical details and/or clinical images was obtained from the parent of the patient.

Author contribution statement

SA was responsible for investigation and writing the original draft. JK contributed to conceptualization and validation and helped in writing the original draft. KG was the primary physician and was responsible for data curation. HZ managed project administration, performed data analysis, and contributed to writing review and editing. NA contributed to writing review and editing. AH helped in writing review and editing. IA assisted in validation and contributed to writing review and editing.

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