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Case Report

Diagnostic and management challenges of glycogen storage disease type 1a in a Somali child: A case report from a low-resource setting

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Abstract

Background: Glycogen storage disease type 1a (GSD-1a) is a rare autosomal recessive metabolic disorder caused by a deficiency in the glucose-6-phosphatase enzyme. It commonly presents in infancy with fasting hypoglycemia, hepatomegaly, and metabolic disturbances. In resource-limited settings like Somalia, diagnosis and management are significantly hampered by the lack of advanced diagnostic facilities and nutritional support.

Case presentation: We describe a 16-month-old Somali boy with global developmental delay, recurrent hypoglycemia, and hepatomegaly. Initial biochemical investigations indicated hyperlactatemia, elevated transaminases, and hyperuricemia. Genetic confirmation via whole-exome sequencing identified a homozygous pathogenic variant in the *G6PC* gene, confirming GSD-1a. Empirical metabolic treatment and nutritional modification using locally available resources resulted in significant clinical improvement.

Conclusion: This case highlights the diagnostic and management challenges of GSD-1a in low-resource settings. Despite the absence of advanced diagnostic infrastructure, clinical recognition, empirical treatment, and adaptive nutritional strategies can lead to favorable outcomes.

Keywords: Glycogen storage disease type 1a, *G6PC* gene, Somalia, Metabolic disorder, Pediatric hepatomegaly, Hypoglycemia

Abbreviations: GSD-1a: Glycogen Storage Disease Type 1a; G6PC: Glucose-6-Phosphatase gene; WES: Whole-exome sequencing; AST: Aspartate Aminotransferase; ALT: Alanine Aminotransferase

Introduction

Glycogen storage diseases (GSDs) are inherited metabolic disorders that result from enzymatic defects in glycogen synthesis or degradation pathways. GSD-1a, the most common subtype, results from mutations in the *G6PC* gene that encodes the catalytic subunit of glucose-6-phosphatase, an enzyme essential for maintaining euglycemia during fasting [1,2]. Affected children often present with fasting hypoglycemia, hepatomegaly, growth retardation, hyperlactatemia, hyperuricemia, and hyperlipidemia [3].

Although GSD-1a has been extensively documented in developed countries, reports from low-income settings, particularly Sub-Saharan Africa, remain scarce. In Somalia, where healthcare infrastructure is still recovering from decades of conflict, the diagnostic and therapeutic approach to rare inherited disorders is severely constrained [4,5]. Pathogenic variants in the *G6PC* gene alter the structure of the glucose-6-phosphatase protein, reducing its catalytic efficiency and impairing

glucose release from glycogen stores. This gene-to-protein interaction underlies the metabolic imbalance characteristic of GSD-1a [1]. This case report illustrates the diagnostic odyssey, clinical decision-making, and treatment challenges of a child with GSD-1a in Somalia.

Case Presentation

A 16-month-old Somali male presented to a pediatric metabolic clinic in Mogadishu with developmental delay, poor weight gain, and recurrent episodes of fatigue and irritability. The child was the third offspring of consanguineous parents. He was born full-term by cesarean section with a birth weight of 2,100 g. His early neonatal period was complicated by prolonged jaundice, but no major illnesses were reported.

Developmentally, the child had not achieved age-appropriate milestones, he was unable to sit without support or crawl. His growth parameters were significantly below the third percentile for weight and height. Clinical examination revealed abdominal distension with palpable hepatomegaly 4 cm below the costal margin. No dysmorphic features or splenomegaly were observed.

Initial laboratory evaluation revealed fasting hypoglycemia (glucose: 47 mg/dL), elevated liver transaminases (AST: 198 U/L, ALT: 175 U/L), lactic acidosis (lactate: 12.6 mmol/L), hypertriglyceridemia (TG: 506 mg/dL), and hyperuricemia (uric acid: 8.2 mg/dL). Renal ultrasound showed bilateral nephrocalcinosis. Based on these findings, a provisional diagnosis of GSD-1a was considered.

Empirical metabolic therapy was initiated using L-carnitine, thiamine, and oral uncooked cornstarch every 4 hours. Genetic confirmation was later achieved via external referral for whole-exome sequencing, which revealed a homozygous pathogenic variant c.G193C (p.A65P) in the *G6PC* gene. Nutritional guidance was adapted using locally available carbohydrate-rich meals due to the unavailability of medical-grade cornstarch. Within three months, the patient demonstrated clinical improvement: increased activity, reduction in hepatomegaly, normalized blood glucose and transaminases, and improved weight gain.

Discussion

GSD-1a is characterized by impaired gluconeogenesis and glycogenolysis, leading to an array of metabolic complications. In this case, the classic triad of hepatomegaly, hypoglycemia, and lactic acidosis was evident and, combined with laboratory markers, enabled a clinical suspicion prior to molecular confirmation [6–8].

Early diagnosis is crucial to prevent complications such as nephropathy, hepatic adenomas, and growth retardation [9]. However, in Somalia, limited diagnostic facilities and low awareness of inborn errors of metabolism often result in delayed or missed diagnoses. Our patient benefitted from strong clinical suspicion, despite the lack of local genetic testing capabilities, a common challenge in low-resource countries [10,11]. Chronic complications of GSD-1a include hepatic adenomas, which may undergo malignant transformation into hepatocellular carcinoma if metabolic control remains poor. Secondary renal disease and growth impairment are also recognized sequelae that require long-term monitoring.

Uncooked cornstarch therapy remains the cornerstone of GSD-1a management, offering a sustained source of glucose to prevent fasting-induced metabolic crises [12]. Due to cost and availability barriers, we employed a locally adapted dietary plan, which proved effective. The use of L-carnitine and thiamine, although not standard in GSD-1a protocols, provided empirical metabolic support in the absence of targeted supplements. Molecular modeling techniques can also be used to simulate G6PC enzyme conformations and predict the structural impact of novel mutations, providing insights for future therapeutic strategies and safe molecular interventions tailored to regional genetic backgrounds.

Furthermore, cell culture systems derived from patient hepatocytes or induced pluripotent stem cells can serve as valuable models for investigating glucose-6-phosphatase deficiency and evaluating candidate therapeutic compounds [14].

This case highlights the need for increased clinical training in pediatric metabolic diseases, establishment of cross-border laboratory collaborations, and integration of genetic counseling services. It also emphasizes that even in fragile health systems, meaningful interventions are possible with family engagement and context-sensitive care plans.

Neurological manifestations are not typical features of GSD-1a; however, recurrent severe hypoglycemia can transiently affect cognitive function. Management is mainly dietary, focusing on maintaining normoglycemia and preventing metabolic derangements through frequent carbohydrate intake and cornstarch therapy [15].

Conclusion

This case illustrates the feasibility of diagnosing and managing a rare metabolic disorder like GSD-1a in Somalia, even without comprehensive diagnostic tools. With heightened clinical awareness, nutritional innovation, and strategic international partnerships, children with inherited metabolic diseases in low-resource settings can achieve meaningful health improvements. Strengthening local capacity for early diagnosis and sustainable care remains a public health imperative. Emerging technologies, including artificial intelligence (AI), hold promise in improving early detection of inherited metabolic disorders through pattern recognition of biochemical profiles and genetic data. Although AI cannot prevent genetic diseases, its integration into newborn screening and diagnostic algorithms could support timely diagnosis and counseling in settings such as Somalia

Ethical Approval and Participant Consent

Not applicable to this study.

Consent for Publication

A written informed consent to publish/present this case was obtained from the patient's parents.

Data Availability

Not applicable to this study.

Competing Interests

The author declares no conflicts of interest related to this study.

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Author Contributions

Abdullahi Hassan Elmi was solely responsible for the conception and design of the study, data collection, analysis, interpretation, and drafting of the manuscript. The author approves the final version and agrees to be accountable for all aspects of the work.

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