SAGE Open Medical Case Reports
Volume 11: 1–4
© The Author(s) 2023
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/2050313X231190004
journals.sagepub.com/home/sco
Sage

Severe multiple organ failure as a consequence of diabetic ketoacidosis in an adolescent with new-onset type 1 diabetes: A case report

Rachel Modarelli[1], Lauren Brown[2], Jenny Boyd[2], Bradley Podd[2], Zachary Willis[3] and Amy Levenson[1]

Abstract

The initial presentation of pediatric diabetes is variable, making prompt diagnosis and treatment challenging. The overlap between type 1 and type 2 diabetes and presence of developmental delays can complicate diagnosis, resulting in delays and severe illness at presentation. Here we describe a case of a 13-year-old male with autism and attention deficit hyperactivity disorder who presented with severe diabetic ketoacidosis, multiple organ failure, and shock. Within 2 weeks of this initial presentation, he had further clinical decompensation due to an intestinal perforation. Cultures from resected gastrointestinal tissue grew mucormycosis, protracting his hospital stay and recovery. He was able to go home several months later with remarkable improvement. This case highlights the necessity of careful history taking and early testing, and how investigation for rare complications of diabetes is vital when patients do not improve as expected.

Keywords

Pediatric, diabetic ketoacidosis, multiple organ failure

Date received: 26 May 2023; accepted: 10 July 2023

Introduction

Type 1 diabetes (T1D) continues to impact the pediatric population with rising incidence.[1–3] The initial presentation of T1D in pediatric patients is quite variable, adding significant challenges to prompt diagnosis and treatment initiation.[4] Patients with diabetic ketoacidosis (DKA) presented with greater severity during the COVID-19 pandemic than prior to the pandemic.[5] Here we describe a case of an adolescent male with developmental delay who presented with severe DKA complicated by multiorgan failure, bowel perforation, and intestinal mucormycosis.

Case

A 13-year-old male with a history of autism and attention deficit hyperactivity disorder who presented with nausea, vomiting, and altered mental status was found to have severe DKA. The patient was seen 4 months prior by a pediatric endocrinologist for an elevated hemoglobin A1c of 5.9% and was recommended to make diet and lifestyle modifications. Growth parameters at that time were significant for body mass index (BMI) 27.2 kg/m^2 (>97th percentile), an increase from 25.4 kg/m^2 8 months prior. Three days prior to admission he was evaluated in an emergency department for nausea and vomiting and was sent home with supportive care. There was no laboratory investigation beyond a respiratory viral panel, which was negative. On the day of admission, he presented back to the emergency department with worsening mentation, including an initial exam notable for agitation and inability to form words clearly, but opening eyes appropriately with a Glasgow coma score of 9.[6] Vital signs were significant for heart rate 121 bpm, blood pressure 126/80 mmHg,

[1]Division of Pediatric Endocrinology, University of North Carolina School of Medicine, Chapel Hill, NC, USA
[2]Division of Pediatric Critical Care Medicine, University of North Carolina School of Medicine, Chapel Hill, NC, USA
[3]Division of Pediatric Infectious Diseases, University of North Carolina School of Medicine, Chapel Hill, NC, USA

Corresponding Author:
Rachel Modarelli, Division of Pediatric Endocrinology, University of North Carolina School of Medicine, 127 Medical Wing E, CB#7039, Chapel Hill, NC 27599, USA.
Email: rachel.modarelli@unchealth.unc.edu

Creative Commons Non Commercial CC BY-NC: This article is distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 License (https://creativecommons.org/licenses/by-nc/4.0/) which permits non-commercial use, reproduction and distribution of the work without further permission provided the original work is attributed as specified on the SAGE and Open Access pages (https://us.sagepub.com/en-us/nam/open-access-at-sage).

Table 1. Additional labs during hospitalization.

Lab Test	Day 1	Day 7	Day 12
Glucose (74–106 mg/dL)	2,259	266	414
pH (7.32–7.43)	6.9	7.37	7.42
Bicarbonate (20–31 mmol/L)	5.6	30	27
Creatinine (0.57–0.8 mg/dL)	4.1	2.33	1.38
Alanine transaminase (ALT) 10–49 U/L)	24	2,463	157
Aspartate transferase (AST) (<34 U/L)	44	4,327	69
International normalized ratio (INR) (0.92–1.11)	1.35	2.06	1.29

respiratory rate 44, and room air SpO2 99%, temperature 36.7°C, and BMI 25 kg/m^2 (94th percentile). Blood glucose was noted to be 2259 mg/dL (74–106 mg/dL), pH 6.9 (7.32–7.43), bicarbonate 5.6 mmol/L (20–31 mmol/L), sodium 105 mmol/L (135–145 mmol/L), potassium 6.9 mmol/L (3.5–5.1 mmol/L), and creatinine 4.1 mg/dL (0.57–0.8 mg/dL). T1D was confirmed with glutamic acid decarboxylase 65 antibodies of 15.5 U/mL (0–5.0 U/mL). Additional labs are included in Table 1 for reference.

Initial management included fluid resuscitation in response to an estimated 10% fluid deficit, which is consistent with the recommended management of severe DKA via International Society for Pediatric and Adolescent Diabetes (ISPAD) guidelines.[7] While in transport to the regional pediatric intensive care unit, he developed altered mental status, lethargy, and vomiting, so was given 3% hypertonic saline for concern for cerebral injury and subsequently was intubated for airway protection. He was treated with an intravenous insulin infusion protocol per ISPAD guidelines with resolution of DKA at 65 h into the admission.[7] Within the first 24 h of admission, his high urine output added challenges in keeping up with maintaining an euvolemic state. He developed significant hypotension and poor perfusion consistent with shock despite aggressive fluid resuscitation, and multiple vasopressors and hydrocortisone were started to maintain adequate blood pressure. Despite improvement in his hyperglycemia, metabolic acidosis, and shock over the next several days, the patient developed significant transaminase elevation, hyperbilirubinemia, hyperammonemia, and coagulopathy, prompting transfer to a quaternary center for evaluation of acute liver failure. Investigation for alternative causes of liver failure was negative. Transaminases and synthetic liver function markers slowly improved, and liver injury was attributed to ischemic hepatitis secondary to profound shock state. Two weeks after the initial presentation, the patient again developed hypotension requiring vasopressors, abdominal distention with guarding, and coffee-ground emesis. He was taken to the operating room for exploratory laparotomy and found to have a right colon perforation with multiple additional areas of jejunal necrosis, prompting a right hemicolectomy and partial small bowel resection. He subsequently returned to the operating room three additional times for reexploration, and each time an additional necrotic bowel was resected. Due to progressive intestinal necrosis, resected tissue was stained for fungus, which identified mold consistent with mucormycosis. Amphotericin B was initiated. Cultures of resected intestinal tissue subsequently identified *Rhizopus*. His hospital course was further complicated by the development of abdominal abscesses, requiring drainage by interventional radiology, and prolonged feeding intolerance requiring total parenteral nutrition. He ultimately returned to the operating room for an ostomy takedown and remained hospitalized for ongoing nutrition optimization and long-term antibiotic therapy. He was maintained on intravenous amphotericin B for 4 months, and then transitioned to oral isavuconazole 1 month prior to discharge. After several months of hospital stay, he was discharged home and continues on insulin therapy with moderate control and isavuconazole for gastrointestinal mucormycosis. The patient's hospital course is outlined in Figure 1 for reference.

Discussion

Diagnosing new-onset diabetes in the pediatric population can be challenging for multiple reasons. This patient's initial presentation to the pediatric endocrinology clinic was most concerning for insulin resistance, which often precedes type 2 diabetes (T2D); thus, additional workup such as antibody testing was not performed. The presence of an elevated BMI often leads clinicians to suspect T2D, although 20–40% of patients with new-onset T1D present with an elevated BMI.[4] An increase in adiposity is suggested to increase pancreatic β-cell fragility and a decreased cell mass.[8] Furthermore, insulin resistance is associated with an increased risk of developing clinical diabetes compared to those without insulin resistance.[9] An additional consideration for this patient is his neurodevelopment disorder (NDD) and the challenges in obtaining a reliable history. There is limited data on patients with NDD and their initial diagnosis of T1D, though research does show patients with T1D and NDD have higher hemoglobin A1c values, potentially due to impaired executive function.[10] Effort to avoid missed diagnoses requires thorough investigation when patients present to the acute care setting and are unable to provide additional history. Lastly, the patient's clinical course took place during the COVID-19 pandemic years. Literature has emphasized an increase in the incidence of both T1D and T2D cases, pointing to a variety of possible causes including patient delay in seeking care, behavioral and environmental changes, and the increasing prevalence of obesity.[8,11–13] All these factors require further thought and caution when evaluating pediatric patients for possible diabetes.

This patient encountered profound complications during his hospital course, including suspected cerebral edema, shock, coagulopathy, and multiorgan failure, each associated with increased mortality.[14] The pathogenesis of DKA

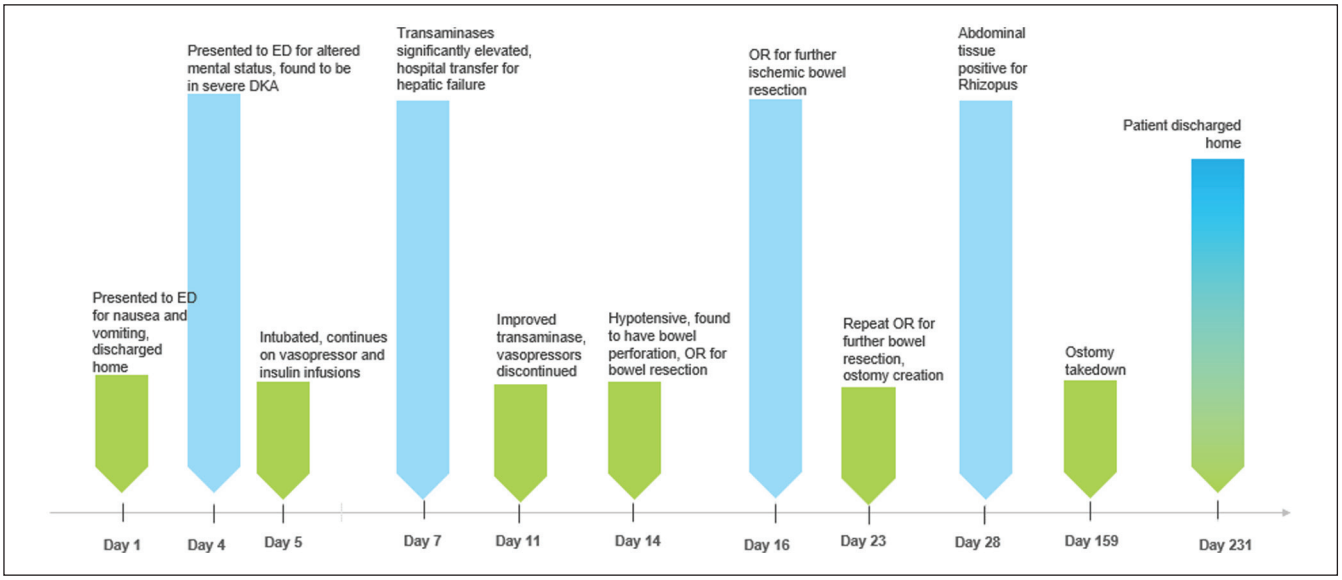

Figure 1. Timeline of the patient's hospital course.

begins with an insulinopenic environment that induces a catabolic state, triggering glycogenolysis, gluconeogenesis, and lipolysis.[14] Recent studies report that around 10–36% of children with new-onset T1D require intensive care due to DKA.[15,16] Complications of DKA can arise with prolonged and untreated ketoacidosis. Documented complications include pancreatitis, pulmonary edema, renal failure, and most commonly cerebral edema.[14] A less commonly described complication is hepatic failure. A recent case report describes an 11-year-old patient who presented with new-onset T1D and, after 4 days of treatment for DKA, developed significant hepatic failure and hepatomegaly and ultimately died despite aggressive therapies.[17] Autopsy findings were consistent with hypoxic hepatitis, which is described as the combination of "passive congestion, poor oxygen utilization, and reperfusion injury."[17] A possible contributor of the acute hepatic failure could be the challenges in maintaining euvolemia early in the hospital course. Treatment is focused on supporting the underlying disease process, such as DKA, and maintaining appropriate vital parameters to ensure adequate tissue perfusion to the vital organs.[17] The incidence of hypoxic hepatitis is unknown in the pediatric population but should be considered in patients with DKA who are demonstrating worsening liver function.

Mucormycosis is a frequently fatal fungal infection that has a known correlation with poorly controlled diabetes but is less commonly reported with new-onset diabetes.[18] The most common type of mucormycosis in children with diabetes is rhino-orbito-cerebral form, with less common forms being cutaneous, pulmonary, renal, and gastrointestinal.[19] Gastrointestinal (GI) mucormycosis is especially rare, and in a review of 176 cases of adults and children with GI mucormycosis, there was a 67.5% mortality despite therapy.[20] Risk factors for infection include immunosuppression, ketosis, and prolonged hyperglycemia, which provides an ideal environment for the germination of spores.[21] In this patient, the finding of GI mucormycosis occurred about 2 weeks following presentation, though it is difficult to determine how long this infection had been present. We suspect that with prolonged hyperglycemia during the prior months and the extensive amount of bowel involvement, his infection was present at the time of his presentation in severe DKA. Treatment of mucormycosis can also be variable, with the total duration variable depending on the patient and extent of disease.[22] Given that our patient required several months of antifungal treatment, this suggests that the extent of disease was significant. There are limited cases reported with pediatric patients developing mucormycosis at or around the time of developing diabetes,[19,21] but this case is a reminder to fully investigate any abdominal symptoms occurring after DKA has resolved in any patient with diabetes.

Conclusion

Delays in diagnosing pediatric diabetes can have several consequences. This report highlights the uncommon complications of new-onset T1D including multiple organ failure with severe hepatic failure and an extremely rare case of gastrointestinal mucormycosis. Given the life threatening complications despite a common presentation of the prodromal stage, this case emphasizes the need for a high index of suspicion for the development of severe disease among children with developmental or behavioral differences.

Acknowledgements

The authors thank the family for allowing this case to be published.

Author contributions

R.M. and L.B. drafted the article. J.B., B.P., Z.W., and A.L. revised the article. All authors contributed to the conception of the article, gave final approval, and agreed to be accountable for all aspects of the article.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Ethics approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed consent

Written informed consent was obtained from a legally authorized representative for anonymized patient information to be published in this article.

ORCID iD

Rachel Modarelli https://orcid.org/0000-0001-6058-144X

References

1. Divers J, Mayer-Davis EJ, Lawrence JM, et al. Trends in incidence of type 1 and type 2 diabetes among youths—selected counties and Indian Reservations, United States, 2002–2015. *MMWR Morb Mortal Wkly Rep* 2020; 69: 161–165.
2. Lawrence JM, Divers J, Isom S, et al. Trends in prevalence of type 1 and type 2 diabetes in children and adolescents in the US, 2001-2017. *JAMA* 2021 326: 717.
3. Gregory GA, Robinson TI, Linklater SE, et al. Global incidence, prevalence, and mortality of type 1 diabetes in 2021 with projection to 2040: a modelling study. *Lancet Diabetes Endocrinol* 2022; 10: 741–760.
4. Siller AF, Tosur M, Relan S, et al. Challenges in the diagnosis of diabetes type in pediatrics. *Pediatr Diabetes* 2020; 21: 1064–1073.
5. Rahmati M, Keshvari M, Mirnasuri S, et al. The global impact of Covid-19 pandemic on the incidence of pediatric new-onset type 1 diabetes and ketoacidosis: a systematic review and meta-analysis. *J Med Virol* 2022; 94: 5112–5127.
6. Mehta R and Chinthapalli K. Glasgow Coma Scale explained. *BMJ* 2019; 365: l1296.
7. Glaser N, Fritsch M, Priyambada L, et al. ISPAD clinical practice consensus guidelines 2022: Diabetic ketoacidosis and hyperglycemic hyperosmolar state. *Pediatr Diabetes* 2022; 23: 835–856.
8. Modarelli R, Sarah S, Ramaker ME, et al. Pediatric diabetes on the rise: trends in incident diabetes during the COVID-19 pandemic. *J Endocr Soc* 2022; 6: bvac024.
9. Fourlanos S, Narendran P, Byrnes GB, et al. Insulin resistance is a risk factor for progression to type 1 diabetes. *Diabetologia* 2004; 47: 2247–2247.
10. Liu S, Kuja-Halkola R, Larsson H, et al. Neurodevelopmental disorders, glycemic control, and diabetic complications in type 1 diabetes: a nationwide cohort study. *J Clin Endocrinol Metab* 2021; 106: e4459–e4470.
11. Passanisi S, Salzano G, Aloe M, et al. Increasing trend of type 1 diabetes incidence in the pediatric population of the Calabria region in 2019-2021. *Ital J Pediatr* 2022; 48: 66.
12. Vlad A, Serban V, Timar R, et al. Increased incidence of type 1 diabetes during the COVID-19 pandemic in Romanian children. *Medicina* 2021; 57: 973.
13. Unsworth R, Wallace S, Oliver NS, et al. New-onset type 1 diabetes in children during COVID-19: multicenter regional findings in the U.K. *Diabetes Care* 2020; 43: e170–e171.
14. Castellanos L, Tuffaha M, Koren D, et al. Management of diabetic ketoacidosis in children and adolescents with type 1 diabetes mellitus. *Pediatr Drugs* 2020; 22: 357–367.
15. Lah Tomulić K, Matko L, Verbić A, et al. Epidemiologic characteristics of children with diabetic ketoacidosis treated in a pediatric intensive care unit in a 10-year-period: single centre experience in Croatia. *Medicina* 2022; 58: 638.
16. Passanisi S, Salzano G, Basile P, et al. Prevalence and clinical features of severe diabetic ketoacidosis treated in Pediatric Intensive Care Unit: a 5-year monocentric experience. *Ital J Pediatr* 2023; 49: 58.
17. Buczkowski K, Oóg-Zabolska I, Gulczyski J, et al. Hypoxic hepatitis as a complication of newly diagnosed type 1 diabetes in a teenager. *Autops Case Rep* 2022; 12: e2021372.
18. Moye J, Rosenbloom AL and Silverstein J. Clinical predictors of mucormycosis in children with type 1 diabetes mellitus. *J Pediatr Endocrinol Metab* 2002; 15: 1001–1004.
19. Jevalikar G, Sharma R, Raghunathan V, et al. Intestinal mucormycosis complicated by iliac artery aneurysm and ureteric rupture in a child with new-onset type 1 diabetes mellitus. *J Paediatr Child Health* 2021; 57: 1117–1119.
20. Kaur H, Ghosh A, Rudramurthy SM, et al. Gastrointestinal mucormycosis in apparently immunocompetent hosts—a review. *Mycoses* 2018; 61: 898–908.
21. Jevalikar G, Sudhanshu S, Mahendru S, et al. Cutaneous mucormycosis as a presenting feature of type 1 diabetes in a boy – case report and review of the literature. *J Pediatr Endocrinol Metab* 2018; 31: 689–692.
22. Francis JR, Villanueva P, Bryant P, et al. Mucormycosis in children: review and recommendations for management. *J Pediatric Infect Dis Soc* 2018; 7: 159–164.