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Triple threat: New presentation with diabetic ketoacidosis, COVID-19, and cardiac arrhythmias

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Abstract

Patients with diabetes have increased susceptibility to infection with Severe acute respiratory syndrome-coronavirus 2 and increased morbidity and mortality from Coronavirus disease 2019 (COVID-19) infection. Mortality from COVID-19 is sometimes caused by cardiac arrhythmias. Electrolyte disturbances in patients with diabetic ketoacidosis (DKA) can increase the risk of cardiac arrhythmias. Despite these correlations, little has been reported about the co-incidence of these three conditions: COVID-19, DKA and cardiac arrhythmias. In this case report we describe two children with COVID-19, new-onset DKA and cardiac arrhythmias. These cases emphasize the importance of close cardiac and electrolyte monitoring in patients with COVID-19 infection.

1. Introduction

While COVID-19 is often a mild disease in children [1], there may be more severe manifestations in children with certain comorbidities. Adults with diabetes have increased expression of ACE 2 which may play a role in increasing susceptibility to infection with SARS-CoV-2 and increased morbidity and mortality from COVID-19 infection [2-4]. Mortality from COVID-19 can be caused by cardiac arrhythmias [5]. Electrolyte disturbances increase the risk of cardiac arrhythmias, and patients with DKA are at risk for electrolyte disturbances. Despite these correlations, little has been reported about the co-incidence of COVID-19, DKA, and cardiac arrhythmias.

2. Case 1

A healthy, 17-year-old female presented to a community hospital with one day of altered mental status, fever, nausea, and vomiting. Her labs suggested severe DKA with pH 6.84, bicarbonate 4 mEq/L, anion gap 25 mEq/L, glucose 644 mg/dL. Her initial potassium was 1.9 mEq/L. She was treated with two liters of normal saline and started on an insulin drip at the community hospital. Her SARS-CoV-2 PCR test at that time was positive.

During transport to a pediatric tertiary care center, she had worsening mental status and an abnormal rhythm. Hypertonic saline was administered by the transporting team. On emergency department arrival, her heart rate was 150 bpm with a wide QRS complex consistent with ventricular tachycardia (Fig. 1a). She was oriented to person and place, with good femoral pulses. Her blood pressure was 127/70, her oxygen saturation 97% on room air. Her initial laboratory testing is shown in Table 1. She was treated with lidocaine, magnesium, and calcium gluconate with conversion to sinus tachycardia with PVC and intermittent Mobitz type I heart block (Fig. 1b and c). She was admitted to the pediatric intensive care unit with no further arrhythmias. Her arrhythmia was presumed to be ventricular tachycardia due to severe acidosis.

3. Case 2

A 12-year-old male with a family history of type 2 diabetes presented with two days of vomiting, increased thirst, and fatigue without other infectious symptoms. He was brought to the emergency department by EMS for decreased responsiveness. Blood glucose in the field was 550 mg/dL.

On arrival, his heart rate was 130 bpm, blood pressure was 104/64, and oxygen saturation was 98% in room air. His initial laboratory testing is shown in Table 1. He was treated with lidocaine, magnesium, and calcium gluconate with conversion to sinus tachycardia with PVC and intermittent Mobitz type I heart block (Fig. 1b and c). She was admitted to the pediatric intensive care unit with no further arrhythmias. Her arrhythmia was presumed to be ventricular tachycardia due to severe acidosis.

Abbreviations: COVID-19, Coronavirus disease 2019; ACE 2, Alveolar angiotensin-converting enzyme; DKA, Diabetic ketoacidosis; SARS-CoV-2, Severe acute respiratory syndrome-coronavirus 2; PCR, Polymerase chain reaction; PVC, premature ventricular complexes; g, gram(s); mg, milligram(s).

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Fig. 1. 17-year-old presenting with new onset DKA, COVID-19 and wide complex tachycardia. A. ECG with wide QRS complex, right axis deviation and presumed ventricular tachycardia. B. ECG shortly after lidocaine and magnesium showing sinus tachycardia with diffuse ST changes. C. Telemetry rhythm strip with sinus tachycardia and Mobitz I second degree AV block. 
ECG = electrocardiogram, AV = atrioventricular.
electrophysiologist, the R-R interval was noted to be irregular, making atrial fibrillation or atrial flutter with variable atrioventricular block (2:1, 3:1) more likely. He was sedated, intubated, and cardioverted with conversion to sinus rhythm. He had no subsequent arrhythmias and was extubated during his first hospital day. His DKA resolved with insulin and fluids. His arrhythmia was presumed to be due to electrolyte disturbances.

4. Discussion

We present two cases of concurrent COVID-19 infection, DKA, and cardiac arrhythmias. This is, to the best of our knowledge, the only reported cases of these diagnoses presenting simultaneously. The relationship between cardiac rhythm disturbances and DKA has been well
established; recently, associations between COVID-19 infection and cardiovascular disease and diabetes have emerged.

COVID-19 likely unmasks existing DM and precipitates DKA. SARS-CoV-2 attaches to ACE2 receptors throughout the body, including beta cells of the pancreas, subsequently impairing insulin secretion [6]. Injury to beta cells may also occur through pro-inflammatory cytokines or by enhancing autoimmunity in genetically predisposed people [6].

COVID-19 also produces a broad range of cardiovascular effects including myocarditis, myocardial infarction, cardiomyopathy, arrhythmias, and cardiac arrest [7,8]. Arrhythmias may occur in the setting of viral illness due to hypoxia, inflammatory stress, or abnormal metabolism [9]. Additionally, viral myocarditis can elicit cardiac conduction disease [10]. Increased cytokines and inflammation of conduction tissue may lead to subsequent arrhythmias. Arrhythmias have been reported in up to 17% of patients with COVID-19 [11,12]. Electrolyte abnormalities, particularly hyperkalemia, seen in DKA may precipitate dysrhythmias through decrease in action potential upstroke and increase junctional resistance within the myocardium [13,14].

In both cases described above, the patients presented with significant acidosis and electrolyte abnormalities, which were thought to be contributing factors in precipitating their arrhythmias. Standard treatment of DKA includes fluid resuscitation, potassium repletion, and insulin replacement. It is important to note that in case one, the patient did not receive potassium repletion prior to fluid resuscitation and insulin replacement, which may have precipitated the arrhythmia. While in patients with DKA and COVID-19 the treatment remains largely the same [15], patients with COVID-19 may have higher insulin needs [16]. In addition, the concomitant use of vasopressors or steroids can impact insulin requirements [17].

In these patients with COVID-19, DKA, and an arrhythmia, deciphering whether the arrhythmia was caused by the potential cardiovascular effects of COVID-19 infection and inflammation of conducting cardiac myocytes or the acidosis and electrolyte abnormalities from DKA was challenging, and multidisciplinary evaluation and management needed be aimed at both underlying pathologies. It is also possible that, in the absence of respiratory symptoms and high community spread, a positive COVID test may have been incidental and not necessarily contributory to the pathology.

5. Conclusion

Described here are two pediatric patients with arrhythmias in the setting of new onset DKA and COVID-19. Systemic inflammation in COVID-19 can trigger DKA and a predisposition to arrhythmias, and metabolic derangement in DKA can also result in arrhythmias. These cases emphasize the importance of close cardiac and electrolyte monitoring for critically ill patients with COVID-19.

Author statement

Dr. Howard, conceptualized the report, drafted the original manuscript, and reviewed and edited the manuscript.

Dr. Basu conceptualized the report, and reviewed and edited the manuscript.

Dr. Sherwin conceptualized the report, and reviewed and edited the manuscript.

Dr. Cohen conceptualized the report, drafted the original manuscript, and reviewed and edited the manuscript.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Funding

No funding was secured for this study.

Declaration of Competing Interest

The other authors have no example conflicts of interest to disclose.

References

[1] Coronavirus Disease. In children — United States, February 12–April 2, 2020. U.S. Department of Health and Human Services; 2019 Accessed April 21, 2020.

[2] Fang L, Karakiulakis G, Roth M. Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection? Lancet Respir Med. 2020;8(4):e21. https://doi.org/10.1016/S2213-2600(20)30116-8.

[3] Bello-Chavolla OY, Bahena-López JP, Antonio-Villa NE, et al. Predicting mortality due to SARS-CoV-2: a mechanistic score relating obesity and diabetes to COVID-19 outcomes in Mexico. J Clin Endocrinol Metab. 2020;105(8). https://doi.org/10.1210/clinem/dgaa346.

[4] Singh AR, Gillies CL, Singh R, et al. Prevalence of co-morbidities and their association with mortality in patients with COVID-19: a systematic review and meta-analysis. Diabetes Obes Metab. 2020;22(10):1915–24. https://doi.org/10.1111/dob.14124.

[5] Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA. 2020;323(11):1061–9.

[6] Sathish T, Tapp RJ, Cooper ME, Zimmet P. Potential metabolic and inflammatory pathways between COVID-19 and new-onset diabetes. Diabetes Metab. 2020;101204.

[7] Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus Disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. JAMA. 2020;S23:13; 1239–42.

[8] Li B, Yang J, Zhao F, et al. Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China. Clin Res Cardiol. 2020;109(5):531–8.

[9] Baksi AJ, Kanaganaagayam CS, Prasad SK. Arrhythmias in viral myocarditis and peri-carditis. Card Electrophysiol Clin. 2015;7(2):269–81.

[10] Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA. 2020;323(11):1061–9.

[11] Goyal P, Chai J, Pinheiro LC, et al. Clinical characteristics of Covid-19 in New York City. N Engl J Med. 2020;382(24):2372–4.

[12] Colon CM, Bartos JG, Chiles JW, et al. Atrial arrhythmias in COVID-19 patients. JACC Clin Electrophysiol. 2020;6(9):1189–90.

[13] Kagiymana Y, Hill JL, Gettes LS. Interaction of acidosis and increased extracellular potassium on action potential characteristics and conduction in Guinea pig ventricular muscle. Circ Res. 1982;51(5):614–23.

[14] Bergmann KR, Whitcomb V. Ventricular tachycardia in an adolescent with severe diabetic ketoacidosis. Am J Emerg Med. 2020 Online ahead of print.

[15] Palermo NE, Sadhu AR, McDonell ME. Diabetic ketoacidosis in COVID-19: unique concerns and considerations. J Clin Endocrinol Metab. 2020;105:8.

[16] Finucane FM, Davenport C. Coronavirus and obesity: could insulin resistance mediate the severity of Covid-19 infection? Front Public Health. 2020;8:184.

[17] Moghissi ES, Korytkowski MT, DiNardo M, et al. American Association of Clinical Endocrinologists and American Diabetes Association consensus statement on inpatient glycemic control. Endocr Pract. 2009;15(4):353–69.