Clinical Dilemma of Diabetic Ketoacidosis and COVID-19 Infection

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ABSTRACT

The COVID-19 Pneumonia with diabetic ketoacidosis is a dreadful health condition. Diabetic ketoacidosis is one of the severe metabolic complications and it can be precipitated by infection. We presented a case of 48 years female with no known comorbidities who presented with COVID-19 symptoms and with Diabetic Ketoacidosis. The case presented with elevated inflammatory markers, high anion gap metabolic acidosis with type I respiratory failure. During admission, the oxygen saturation had marked drop, later her improvement was steady followed by gradual tapering of the oxygenation. Marked improvement was noticed in the subsequent follow-up. COVID-19 infection can be precipitated by preexisting diabetes or newly diagnosed diabetes and the severity of COVID-19 infection is more pronounced in patients with diabetes mellitus, thus should be managed timely and accordingly. The scarce studies among the COVID-19 cases with diabetic ketoacidosis reflect the need for further studies for the availability of a wider range of information.

KEY WORDS

Diabetic ketoacidosis, Metabolic complications, Severe COVID-19 pneumonia

INTRODUCTION

Patient with symptoms of viral pneumonia which was unexplained by any other known etiology was first identified in Wuhan, China in December 2019.[1] The pandemic COVID-19 is a medical condition caused by a novel virus with mild to severe respiratory distress.[2] As of 4 December 2021, Nepal reports eight hundred twenty-two thousand and three hundred and ninety-two (822,392) COVID-19 cases and eleven thousand and five hundred forty (11,540) death cases due to the pandemic.[3] The comorbidity of diabetes ketoacidosis (DKA) among the cases with severe COVID-19 pneumonia demonstrates more medical complications.[4]

DKA being a metabolic complication can also be precipitated by infections.[4] The cases with COVID-19 infection also triggers DKA.[1] However, very few studies have been conducted in this regard globally. Here, we report a 48 year female who suffered from severe COVID-19 pneumonia with ARDS and DKA, with no history of prior diabetes mellitus.

CASE REPORT

A 48 years' female with no history of diabetes mellitus presented in the emergency department (ED) of Dhulikhel Hospital, Kathmandu University Hospital (DH, KUH). She had complaints of fever, cough, myalgia, and increased thirst for 3 days. On examination, she was identified to be tachycardic, tachypneic and dehydrated. During admission, her saturation was 83 percent in room air, blood pressure was 130/80 mmHg, temperature was 37.9 degree Celsius and heart rate was 120 beats per minute. Her polymerase chain reaction (PCR) test for SARS COVID-19 was positive. The arterial blood gas (ABG) reported PH: 7.25, HCO3: 15, PCO2: 32, PO2: 58 and AG: 22 (High Anion gap metabolic acidosis with type I respiratory failure). The chest imaging (fig. 1) reported patchy opacities in bilateral lung fields. The laboratory findings (table 1) showed 376 mg/dl of random blood sugar, positive urine ketone, 12.9 percent of HBA1c, escalated inflammatory markers (CRP, D-dimer, LDH) and ketonuria, glycosuria, and proteinuria. She was admitted with the diagnosis of severe COVID-19 pneumonia with

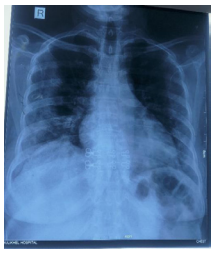

Figure 1. Chest X-ray during admission

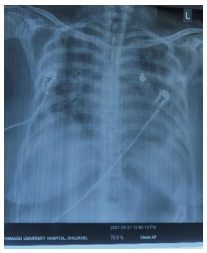

Figure 2. Chest X-ray during severe COVID ARDS

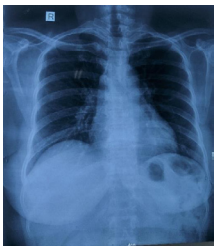

Figure 3. Chest X-ray during follow up (after 3 months)

Table 1. Laboratory investigation findings of the indexed case

Parameters	Findings		Normal Value Range
	Admission	Follow up	
Total Count (uL) (x103/uL)	*14.4*	*6.8*	*4.0-11.0*
Differential Count (%) N=Neutrophil, L=Leukocytes	N 67	N 67	N 45-75
	L 22	L 29	L 20-45
Hemoglobin (g/dl)	11.5	12.1	12-16
Platelets (x103/uL)	403	248	150-450
Prothrombin Time/ International Normalization Ratio (second)	13/1.0		12 (ISI-1.0)
Random blood Sugar (mg/dL)	376		60-100
Fasting blood sugar (mg/dL)	154	126	60-100
Post prandial (PP)	424	174	60-100
HbA1C (%)	12.9	8.2	4.5-5.6
Sodium (mEq/L)	141	140	135.0-148.0
Potassium (mEq/L)	4.6	4.3	3.5-5.3
Urea (mg/dL)	8	26	10.0-45.0
Creatinine (mg/dL)	0.4	0.5	0.4-1.1
Urine-sugar	2+	Nil	
Urine-albumin	1+	Nil	
Urine-ketone	3+	Negative	
C-Reactive Protein (mg/L)	>150	<5	<5.0
Lactate Dehydrogenase (LDH) U/L	850	120	132-248
d-Dimer	2.25	0.36	

acute respiratory distress syndrome (ARDS) along with moderate-severe DKA. DKA is defined as plasma blood glucose level > 250 mg/dl, a positive test for urine ketones and arterial pH < 7.35 and/or serum bicarbonate < 18 mmol/L.[5] Severe pneumonia for an adult has been defined as a condition with fever or suspected respiratory infection, plus one of the following: respiratory rate > 30 breaths/min; or severe respiratory distress; or SpO_2 ≤ 93 percent in room air.[4]

Due to unavailability of the ICU, she was managed in high dependency unit (HDU) with intravenous fluid and insulin infusion. Oxygenation was done via reservoir (non-rebreather) mask, while intermittently with noninvasive ventilation (NIV) i.e., continuous positive air pressure (CPAP) at 8 mmHg pressure support. Other management strategies included antiviral (Remdesivir), antibiotics and low molecular weight heparin- LMWH (Enoxaparin). After 48 hours, her culture report for blood, urine and sputum specimen were negative.

Progressively, with the improvement in her symptoms, her DKA resolved on the 3rd day of her admission. However, the case desaturated abruptly on the 5th day despite of the noninvasive ventilation. She was immediately transferred to the ICU and was managed with high flow nasal canula and proning. In ICU, chest x-ray (fig. 2) was done which showed bilateral diffuse patchy opacities. High resolution computed tomography (HRCT) chest (fig. 4) showed multifocal, peripheral, patchy consolidations and ground glass opacities in bilateral lung fields with CORADS VI, CT severity score 21/25. These findings along with ABG suggested it as severe ARDS. Endotracheal intubation was not required as she was tolerating CPAP and after 10 days of admission in ICU, her saturation improved dramatically with marked clinical improvement and then she was shifted to the general ward. She got discharged on 25th day of admission with domiciliary O_2 at 4 l/min and premix Insulin This study followed the patient for about 3 weeks after the discharge, which was limited in other studies. At home, her O_2 requirement tapered and in around 3 weeks her SpO_2 was maintained in room air. On follow up after 3 weeks, her blood sugar was under control, and she had shortness of breath (SOB) during exertion only. The HRCT chest (fig. 5) showed diffuse ground glass opacities in bilateral lung fields with few fibrotic strands, more in the peripheral parts, likely due to sequel of COVID-19 infection. After 3 months (her recent follow up), her entire residual symptoms resolved, her chest x-ray was grossly normal (fig. 3) and was under oral hypoglycemic agents (HbA1C:8.2) for diabetes. The critical case of severe COVID-19 pneumonia with DKA improved dramatically within 3 months. Spirometry finding after the complete recovery was normal.

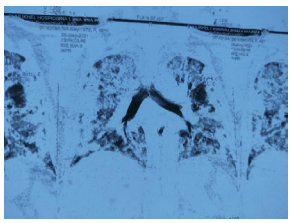

Figure 4. HRCT on 5th day of admission

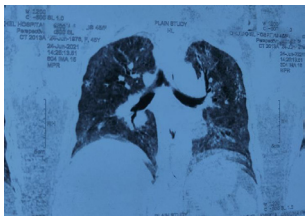

Figure 5. HRCT on 1st follow up (after 45 days)

The author had obtained informed consent from the case to present this case study, assured voluntary participation and maintained confidentiality and privacy throughout the study.

Both figure 4 and 5 are the coronal images of HRCT chest. The figure 4 shows the diffuse bilateral consolidation and ground glass opacities. The findings were resolving in the follow up HRCT chest (fig. 5).

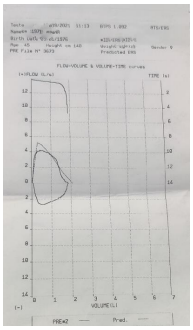

Figure 6. Spirometry of the case

DISCUSSION

This case study presents a 45 year female case with no known comorbidities with DKA aggravated by COVID-19 pneumonia. Other study showed precipitation of DKA by COVID-19 infection without any respiratory symptoms and this did not hinder the management of acidosis with IV fluids. The case in this study had moderate ARDS at the time of admission, which was different from other cases, which made the fluid management quite complicated. Fluid management was done meticulously with respect to the ARDS.

Diabetes mellitus (DM) has been linked to significant rate of morbidity and mortality among COVID-19 cases.[6] A meta-analysis study reported that DM is associated with a two-fold increase in mortality and severe disease in COVID-19 cases.[6] The COVID-19 cases with DM also have greater levels of proinflammatory indicators such as interleukin 6, C-reactive protein, ferritin, and D-dimer in their blood.[7] A previous study in among 174 cases, observed that diabetic patients have a higher risk of severe pneumonia, uncontrolled inflammatory responses, and hypercoagulable state.[7]

COVID-19 causing SARS-CoV-2 enters cells through angiotensin-converting enzyme 2 receptors.[8] This was similar to the SARS-CoV infection in 2002-03. Pancreatic islet cells contain angiotensin-converting enzyme 2 receptors. During an acute SARS-CoV infection, hyperglycemia has been observed, which could be linked to the virus's transitory damage to the pancreatic islets.[7] DKA is a common complication in type 1 DM cases, and it has also been well documented in type 2 DM cases.[8] Acute infections can cause insulin resistance, which can lead to the relative insulin insufficiency and diabetic ketoacidosis. The incubation period can last up to 14 days, and the most common symptoms are those associated with a lower respiratory tract infection, such as fever, cough, and shortness of breath, which can develop to acute respiratory distress syndrome and, in extreme cases, multiorgan failure.[9]

The index case having both DKA and severe COVID pneumonia had an issue of fluid management during treatment. Other study also demonstrated fluid management as an issue in the case with both COVID-19 and DKA.[10] The American Diabetes Association currently recommends an insulin infusion and intensive IV fluid replacement for DKA. Patients with COVID-19 who have respiratory symptoms, on the other hand, are being treated with fluids with caution due to the danger of developing ARDS. Following the standard treatment protocol, treating DKA by providing IV fluids can be problematic with a case of DKA and COVID-19 ARDS.[11]

This case study concluded that despite the complication in the case management due to the dreadful combination of COVID-19, ARDS and DKA, the case recovered with the positive outcome. Pneumonia with severe ARDS with DKA is troublesome but timely intervention and adequate fluid management with close monitoring in ICU setting lead to appropriate prognosis. Meticulous IV fluid management and timely oxygenation are two cornerstone management of the DKA with COVID-9 ARDS.

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