LETTER TO THE EDITOR

Severe Diabetic Ketoacidosis with Malignant Hyperthermia Like Syndrome and Rhabdomyolysis Treated with ECMO: Unusual Severity and a Rare Occurrence

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Dear Editor,

Malignant hyperthermia like syndrome (MHLS) in obese adolescents with hyperglycemic hyperosmolar syndrome (HHS) is a rare complication in diabetic children with very high mortality.[1–3] We report the case of an adolescent girl with severe diabetic ketoacidosis (DKA) with MHLS and rhabdomyolysis, renal failure, and refractory circulatory shock with ventricular tachycardia who survived with extracorporeal membrane oxygenation (ECMO) support. There are no previous reports of survival with ECMO support for this condition with high mortality, otherwise.

A 16-year-old adolescent girl with known type 1 diabetes, on insulin therapy, presented with fever and severe abdominal pain of 4 days duration with severe DKA [Blood glucose (BG) = 335 mg/dL, arterial bllod gas (ABG) = pH – 6.89, PCO_2 – 7.9 mm Hg, HCO_3 – 1.6 mmol/L, BE – 30 mmol/L, urine ketones 3]. She was started on controlled re-hydration and insulin infusion. She required intubation for progressive worsening of sensorium. Her computed tomography of brain was normal. She was treated with neuroprotective measures. She developed refractory circulatory shock, progressive acute kidney injury (AKI) with oligo-anuria and severe metabolic acidosis. Echocardiography showed normal cardiac functions.

At 21 hours she developed severe hyperthermia (105–106°F) refractory to paracetamol, surface cooling, and cold saline infusion. She was initiated on Continuous Renal Replacement Therapy for worsening AKI (BUN – 36 mg/dL, creatinine – 2.86 mg/dL), oliguria, persistent severe metabolic acidosis (venous blood gas (VBG): pH – 6.96, HCO_3 – 6.8 mmol/L) and extreme hyperthermia. She developed refractory ventricular tachycardia and was placed on peripheral VA-ECMO (Femoro-Femoral 16 Fr Edwards arterial and 22 Fr Biomedicus femoral venous with 8 Fr distal perfusion cannula) support emergently at 30 hours of admission (Fig. 1). Her serum creatinine phosphokinase (CPK) levels rose from initial value of 441 IU/L to peak values of 59,549 IU/L, next 6 days, suggesting rhabdomyolysis. She was successfully weaned off ECMO after 5 days. Post ECMO course, she developed pulmonary thrombus and critical illness-related myopathy necessitating tracheostomy and continued portable ventilator support. She could be discharged home on day 124 with normal renal and cardiac functions.

Extreme hyperthermia is known to cause disseminated intravascular coagulation, metabolic acidosis, cardiac dysfunction, and coma. Malignant hyperthermia like syndrome, an exceedingly rare complication of pediatric diabetes with HHS, is described in only eight other pediatric obese adolescent diabetics of black ethnicity in world literature, of whom only two survived.[1–3] The issue of note is the common incidence of extreme hyperthermia, refractory circulatory shock, and arrhythmias with high mortality (Table 1). Dantrolene is the treatment of choice for MH and has shown mortality benefits in other conditions with extreme hyperthermia.[4] Among the only two survivors so far of this fatal complication, in literature, dantrolene was used early. Kilbane et al. therefore proposed administration of dantrolene whenever any child with DKA develops features of rhabdomyolysis, until MHLS is ruled out.[3] Dantrolene is an expensive drug with short shelf life and may not be stocked in most hospitals, since its usage is infrequent, and was not available in our hospital too. The mechanism of MHLS in the setting of DKA or hyperosmolar syndrome is not clear. Hollander et al. propose that in susceptible individuals, acute physiological stress of hyperosmolarity coupled with usage of insulin preparations containing m-cresol could have led to the development of MHLS.[1] Absence of glucose for muscle metabolism and reliance on fatty acid in diabetics due to insulin deficiency/resistant state coupled with inborn error of lipid metabolism precipitating rhabdomyolysis

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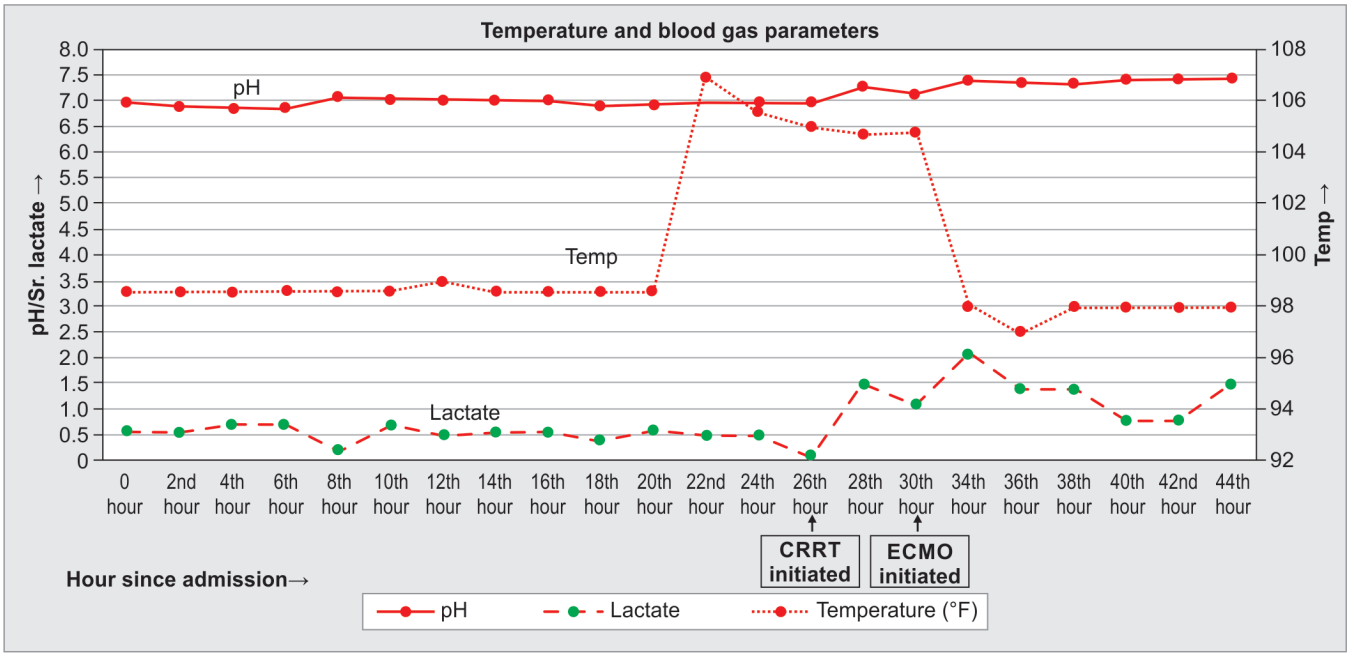

Fig. 1: Body temperature, pH, and their relation to ECMO initiation

Table 1: Common clinical features and outcomes in the reported cases of pediatric diabetics with malignant hyperthermia like syndrome and rhabdomyolysis[1–3]

Adolescent
Male
Obese
Hyperosmolar state with very high BG at presentation
Hyperthermia
Rhabdomyolysis with elevated CPK
Need for ventilator support due to obtundation
Refractory shock and need for multiple pressor support
Death due to refractory arrhythmias

is another proposed theory for MHLS with rhabdomyolysis.[3,5] This is the first case of severe DKA (without HHS) with this complication and also the first case of survival with ECMO in this clinical setting.

This case highlights the importance of early diagnosis of MHLS with rhabdomyolysis. Serial CPK monitoring, until recovery, should be undertaken in children hospitalized with DKA/hyperosmolar syndrome especially with risk factors (adolescent age, obesity, hyperosmolar state, persistent high-grade fever, pre-existent metabolic disorders). Pre-emptive dantrolene administration, if available, may avert fatal complications in DKA/HHS associated with rhabdomyolysis with evolving MHLS. Extracorporeal membrane oxygenation support should be considered in the setting of MHLS with refractory circulatory shock/arrhythmias and can be a bridge to recovery.

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