Case Report

UNVEILING THE COMPLEXITIES: A CASE REPORT ON COMPLICATIONS OF PROPIONIC ACIDEMIA

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ABSTRACT:

Propionic acidemia is a rare inherited metabolic disorder caused by a defect in propionyl-coenzyme A (CoA) carboxylase, resulting in the accumulation of propionic acid. We present a case involving a 5-year-old male with a known history of propionic acidemia who presented to the emergency department with decreased oral intake, vomiting, and diarrhea. Despite initial interventions, the patient developed severe metabolic acidosis, respiratory distress, and gastrointestinal symptoms. The case highlights the varied complications of propionic acidemia, including cardiac complications, intellectual difficulties, and recurrent respiratory distress. The patient's course involved intensive care management, including mechanical ventilation and cardiac support. This report contributes to the understanding of the multifaceted challenges posed by propionic acidemia and emphasizes the importance of a multidisciplinary approach in the management of this rare metabolic disorder.

Keywords: Propionic Acidemia, Metabolic Disorder, Respiratory Distress, Cardiac Complications, Intellectual Disabilities, Multidisciplinary Management

INTRODUCTION

Propionic Acidemia (PA) is a rare inherited metabolic disorder characterized by a defect in propionyl-coenzyme A (CoA) carboxylase, preventing the proper processing of certain proteins and amino acids. This defect leads to the accumulation of propionic acid. The overall incidence rate of propionic acidemia ranges from 1:100,000 to 1:150,000 (1). The disorder results from a defect in the mitochondrial enzyme propionyl CoA carboxylase, responsible for converting propionyl-CoA to methylmalonyl-CoA. Consequently, genetic mutations in the subunits (PCCA and PCCB) of propionyl-CoA carboxylase cause an elevated level of propionyl-CoA. Moreover, the enzyme propionyl CoA carboxylase plays a crucial role in the catabolism of amino acids, the building blocks of proteins. As a result, a defect in this enzyme disrupts the metabolism of certain amino acids, leading to metabolic acidosis and various complications(1).

Patients with propionic acidemia may present with symptoms such as diminished muscle tone (hypotonia), poor feeding, vomiting, dehydration, lethargy, and seizures in the early days of life. In later stages, patients may experience metabolic acidosis and may manifest multi-organ problems, including failure to thrive, hypotonia, vomiting, sensitivity to protein, mobility difficulties, developmental delays, and cardiomyopathy (2).

Case Presentation

A 5-year-old male child presented to the emergency department (ED) of a tertiary care hospital with a complaint of decreased oral intake for 5 to 6 days, along with diarrhea and vomiting for 2 days. According to the father, the child had multiple admissions due to these complaints in local hospitals. Additionally, the child has some intellectual difficulties and has a known case of propionic acidemia, which was diagnosed in the first month of his birth.

On physical examination, the child appeared pale, lethargic, and dull with increased breathing efforts. Additionally, on initial assessment, the child was awake and alert, with a Glasgow Coma Scale (GCS) 15/15. The cardiovascular system showed normal S1 and S2 sounds, and the chest examination revealed tachypnea with an

increased workload of breathing and bilateral crepitation. The abdomen was soft and not tender on physical examination. The vital signs on the first arrival to the Emergency Room (ER) were as follows: heart rate 140 beats/minute, respiratory rate 45/minute, blood oxygen saturation 98%, and body temperature 36.5 °C.

The laboratory investigations indicated that the child had 3+ ketones in urine, and arterial blood gas report showed a bicarbonate level of 10mEq/L. The patient received bicarbonate, and his L-carnitine dose was doubled.

Intravenous ceftriaxone and oral metronidazole were administered in the emergency department. However, his respiratory distress worsened, and he was subsequently shifted to the Pediatric ICU (PICU). On arrival at the PICU, he exhibited cold peripheries, delayed capillary refill time, and acidotic breathing. Non-invasive mechanical ventilation was initiated, and intravenous fluids were continued at 1.5 times maintenance with 5mEq bicarb/100ml. His urinary ketones, blood gases, and vital signs were monitored. His GCS dropped, and his respiratory rate increased. Epinephrine infusion was initiated, a central venous catheter was placed, and due to respiratory distress, the child was subsequently intubated. The chest X-ray report showed interval development of inhomogeneous areas of airspace opacification in the right lower lung zone, suggesting atelectatic changes with possible infiltrates (Figure 1). The patient's condition improved, and he was successfully extubated. Plans were made for discharge, but he afterwards developed fever spikes, and tachypnea, along with poor pulses and perfusion. Consequently, the decision was made to transfer the patient to the Cardiac Intensive Care Unit (CICU). The echocardiogram report showed a mild reduction in heart function. Milrinone was added to the treatment plan, which is a medication that improves cardiac contractility. The infectious disease and metabolic teams were also consulted. The patient's condition became a little bit stable, but the patient's father expressed a desire to go home. He was counselled in detail regarding the need for a hospital stay and further management, but the father refused to stay and left against medical advice.

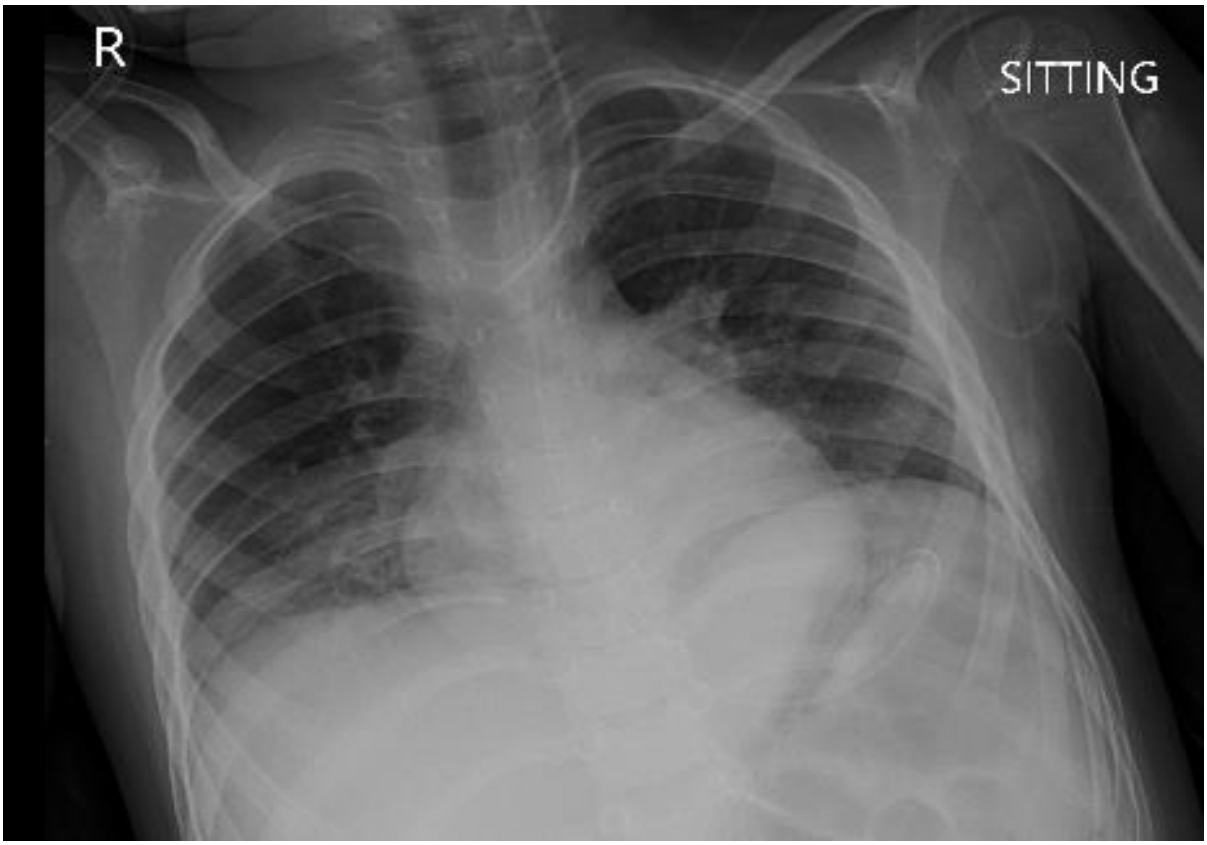

Figure 1. Chest X-ray (PA View) shows atelectatic changes with possible infiltrates

Table 1. Summary of laboratory investigations.

Lab	Value	Lab	Value
HGB	8.3	Lymphocytes	51.8
Haematocrit	23.9	Platelets	484
R.B.C.	3.38	Glucose random	102
WBC	5.1	Sodium	142
M.C.V.	70.7	Potassium	2.6
M.C.H.	24.6	Chloride	100
R.D.W.	21.3	PH	7.40
Neutrophils	41.7	PCO2	28.10
Bicarbonate	10	Ketones in urine	3+

DISCUSSION

This case highlights the complications associated with propionic acidemia, a rare metabolic disorder. Previous studies also show that PA is associated with numerous complications, including metabolic acidosis, respiratory distress, developmental and cognitive disabilities, seizures, cardiac complications, gastrointestinal issues, and various other complications (3). The current case also presented with some gastrointestinal symptoms, such as vomiting, diarrhea, and decreased oral intake. Propionic acidemia patients may exhibit nonspecific symptoms, including vomiting, weight loss, unstable body temperature, irritability, lethargy progressing to coma, and seizures(4). In addition, both in neonatal and late-onset disease, prevalent initial symptoms include inadequate oral intake and vomiting. Subsequently, late-onset cases often manifest failure to thrive and growth impairment. Pancreatitis-induced abdominal pain may serve as a presenting symptom, attributed to complications arising from propionic acidemia. Furthermore, the presence of gastrointestinal symptoms might be complicated by concurrent viral illness, as acute illnesses frequently act as triggers for metabolic crises Henning and Glasser (5).

In the present case, the child was suffering from metabolic acidosis because his bicarbonate level was 10 mEq/L, which is low. Additionally, there were also +3 ketones in his urine, indicating acidosis. Individuals suffering from propionic acidemia might encounter repeated incidences of metabolic acidosis characterized by ketosis and hyperlactatemia. These episodes are typically triggered by either excessive protein intake or infections (6). The primary components of managing propionic acidemia involve implementing dietary adjustments, specifically adopting a low-protein diet. Additionally, the approach includes the use of metronidazole to decrease gut species that produce propionic acid and L-carnitine to enhance the renal clearance of propionic acid. In cases of acute acidosis and hyperammonemia, prompt initiation of intravenous fluid administration containing dextrose and bicarbonate is essential, together with immediate treatment of underlying precipitating factors, such as infection (6). In the present case, the patient was also receiving metronidazole, L-carnitine, intravenous rehydration fluids with bicarbonate, and antibiotics.

The other complication to which the patient was prone to develop was a cardiac complication. As, the patient developed cardiac symptoms such as fever spikes, and tachypnea, along with poor pulses and perfusion. Consequently, he was transferred to the Cardiac Intensive Care Unit (CICU). His echocardiogram report showed a mild reduction in heart function. Marchukq, Wang (7) have also reported that PA is commonly associated with cardiac complications particularly QT prolongation. Approximately 25% of PA patients have cardiac issues. Although protein restriction and liver transplant can improve outcomes, some still experience persistent heart problems. The likelihood of cardiac issues increases with age in PA patients. Similarly, Henning and Glasser (5)

have also mentioned that PA frequently results in complications such as ventricular dysfunction, cardiomyopathy, QT prolongation, and sudden cardiac death, usually presenting before the age of 10 years. In instances of metabolic crises, individuals may experience either acute or chronic heart failure. Consistent findings have not been identified through cardiac imaging in such situations.

The other complication reported by the patient's father in the present case was intellectual difficulties. The father reported that the child has difficulty in learning and also experiences developmental delays in some milestones. Marchukq et al. (7) also state that patients diagnosed with PA display various neurological symptoms, such as cognitive impairment, developmental delays, intellectual disabilities, structural abnormalities, disruptions in neuro-psychomotor development, and metabolic decompensations. Additionally, patients with PA may exhibit typical neurological manifestations, including lethargy, inadequate feeding, coma, and intermittent seizures (8).

In the present case, the patient has experienced various episodes of respiratory distress. His respiratory rate was periodically elevated, accompanied by an increased workload of acidotic breathing. Additionally, signs of respiratory distress, such as an increased respiratory rate, occurred after the extubation. Marchukq et al. (7), also stated that patients with propionic acidemia might experience respiratory distress following surgery due to fatigue or upper airway blockage. It is recommended to delay tracheal extubation until the patient has sufficiently regained strength in order to minimize potential complications. These patients are also sensitive to opiates, so a combination of local and general anesthesia should be used without opiates to prevent respiratory distress. Additionally, postoperative humidified oxygen is recommended as a preventive measure against respiratory complications.

CONCLUSION

In conclusion, patients with propionic acidemia experience various challenges and complications throughout their lives, such as feeding difficulties, lethargy, respiratory problems, metabolic acidosis, cardiac issues, intellectual challenges, and developmental delays. To address and manage these issues more effectively, diagnosing and treating them promptly is crucial. Therefore, a multidisciplinary approach should be employed, involving specialists such as dieticians, infectious diseases specialists, metabolic diseases specialists, cardiologists, pulmonologists, gastroenterologists, and others to manage these patients effectively.

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