CLINICAL VIGNETTE

Propofol Infusion Syndrome

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Case Presentation

A 37-year-old male with no prior medical history presented to the emergency room with total body swelling and shortness of breath for the past 2 weeks. He had significant weight gain and progressively worsening of shortness of breath and dyspnea on exertion. He had no fever or chills. He denied any sick contact. Patient was not taking any medication. He did not smoke cigarettes, but drank up to 12 beers a day.

Physical examination was remarkable for a morbidly obese male. Temp 99.2, P122, BP 126/93, RR 25, BMI 50. His lungs were clear, cardiac examination was unremarkable except for tachycardia. His abdomen was obese and protuberant. He had anasarca on his abdominal wall, and his lower extremities were markedly edematous. His chest x ray revealed cardiomegaly and interstitial edema. His initial arterial blood gas (ABG) was PH 7.18, PCO2 105, PO2 99. His electrolytes were Na 137, K 4.6, Cl 95, HCO3 30.

He was initially treated for congestive heart failure (CHF), and acute respiratory failure. He was intubated and a propofol drip was started for sedation. His intensive care unit(ICU) stay was complicated by atrial flutter with fast ventricular response. Weaning him from the ventilator was difficult, due to the tachycardia. He was placed on amiodarone for his atrial flutter.

On hospital day 10, he remained intubated and sedated with propofol. He was found to have low-grade fever 101.4, and his creatinine (CR) was elevated to 1.5 mg/dl. He was pan cultured and empirically started on intravenous piperacillin/tazobactam and vancomycin.

On Day 11, he spiked a temperature to 106.6, other vital signs were: HR 140, systolic BP 70, and the PO2 dropped to 60. His CR had risen to 3.7 mg/dl, AST 60, creatine kinase(CK) 1238, lactic acid 1.2., and triglyceride 445.

On Day 12, his AST was 500, CK >22000, CR 4.5, pH 7.19. He was thought to have developed propofol infusion syndrome. His propofol infusion was discontinued, and his sedation was changed to midazolam and fentanyl. He was treated with hemodialysis, pressors, and antibiotics.

After a prolonged ICU stay, he was able to be extubated. He developed aspiration due to vocal cord injury and required percutaneous endoscopic tube placement for feeding. He survived to leave the hospital after a prolonged hospitalization.

Discussion

Since 1993, Propofol has been approved by the Food and Drug administration for sedation of patients receiving mechanical ventilation. It is widely used due to its favorable pharmacokinetic profile. However, numerous cases of adverse effects and deaths have been reported in pediatric and adult patients.[1] Bray was first to described propofol infusion syndrome (PRIS) in 1998.[2] He reported 13 deaths in children associated with propofol use. The syndrome was defined as sudden bradycardia, metabolic acidosis, rhabdomyolysis, lipemic plasma, and enlarged liver. In 2009, Roberts et al, reported PRIS in critically ill adults who were receiving propofol infusion greater than 24 hours.[3] They reported an incidence of 1.1%.

The pathogenesis of PRIS is not known, but likely due to the interference of propofol with fatty acid metabolism. Under stressful conditions, there is a shift of the body's usage of glucose as its major energy source to the usage of fatty acids.[4] Propofol inhibits the transfer of fatty acid into the mitochondrial membrane and affects mitochondrial electron transport chain, thereby disrupting the mitochondrial energy production.[5] Inhibition of the mitochondrial respiratory chain leads to impaired ATP production. Cellular necrosis may occur when metabolic demands exceed ATP production, leading to metabolic acidosis and rhabdomyolysis. Increased free fatty acids have been associated with cardiac arrhythmias. This combines with acidosis, and creates an arrhythmogenic environment.[5] Cardiovascular collapse is the common final pathway of PRIS. Rhabdomyolysis and hypotension can lead to acute renal failure and worsening of metabolic acidosis.

There is no specific reversal therapy for PRIS. Treatment is primarily supportive in nature and discontinuation of the propofol infusion. Risk factors for the development of PRIS are critical illness, use of vasopressors, carbohydrate depletion (liver disease, starvation, or malnutrition), carnitine deficiency, and subclinical mitochondrial disease.[4] PRIS is associated with higher dose and prolonged propofol use. Key to prevention is to avoid using it more than 48 hours and less than 4mh/kg/hr.[6] During propofol infusion, it is recommended that ABG, electrolytes, lactate level, creatinine kinase, creatinine, and serum triglyceride be monitored.[7]

Conclusion

This patient was found to develop a rare but potentially fatal propofol infusion syndrome. Once the possibility of PRIS was

considered, his propofol infusion was discontinued. He was treated with hemodialysis and supportive care.

While there is no predictive test to identify patients who are at risk of developing PRIS, avoiding high dose of propofol infusion of ≥4 mg/kg/hr and avoiding prolonged use of propofol for more than 48 hours may help reduce the incidence of PRIS. Our patient was on 3 mg/kg/hr of propofol but received it for a period of 12 days. Perhaps requiring a renewal order for propofol infusion greater than 48 hours, on a daily basis, may reduce the incidence of PRIS. We must keep a high index of suspicion for the development of PRIS when a patient deteriorates while on propofol infusion. Unexplained metabolic acidosis, cardiac dysfunction, elevated liver, and pancreatic enzymes, hypertriglyceridemia, rhabdomyolysis, hyperkalemia, and acute kidney injury warrant consideration of PRIS.[4]

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