International Journal of Community Medicine and Public Health
Sharma SJ et al. Int J Community Med Public Health. 2024 Oct;11(10):4071-4073
http://www.ijcmph.com
pISSN 2394-6032 | eISSN 2394-6040

DOI: https://dx.doi.org/10.18203/2394-6040.ijcmph20242896

Case Report

Fatal outcome of suspected delayed-onset malignant hyperthermia in an infant with phocomelia: challenges in diagnosis and management

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Received: 27 July 2024
Revised: 17 September 2024
Accepted: 19 September 2024

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ABSTRACT

Malignant hyperthermia (MH) is a rare, life-threatening condition triggered by certain anesthetic agents, characterized by rapid onset of hypermetabolism, muscle rigidity, hyperthermia, and metabolic acidosis. Timely identification and the administration of dantrolene are pivotal in preventing fatal outcomes. We report the case of a 10-month-old male infant with phocomelia who developed delayed-onset MH following an otherwise uneventful herniotomy. The infant presented with seizures and an acute rise in body temperature (106°F) three hours post-surgery, suggesting a diagnosis of MH. Despite immediate administration of anticonvulsants and the initiation of aggressive cooling protocols, the seizures persisted, necessitating intubation, paralysis, and thiopentone infusion. Laboratory investigations showed severe metabolic acidosis and signs of rhabdomyolysis, such as reddish urine. A CT scan later revealed brain edema. Management was further complicated by the unavailability of dantrolene, the definitive treatment for MH, leading to a progressive decline in the patient's condition and, eventually, multi-organ dysfunction and death. This case highlights the atypical presentation of delayed-onset MH in a pediatric patient with congenital anomalies and underscores the critical need for prompt recognition, effective management strategies, and the availability of essential treatments like dantrolene. It also emphasizes the importance of preparedness and adaptability among clinicians to manage rare, life-threatening conditions effectively and improve patient outcomes.

Keywords: Malignant hyperthermia, Infant, Phocomelia, Dantrolene, Brain edema

INTRODUCTION

Malignant hyperthermia (MH) is a rare, life-threatening pharmacogenetic disorder triggered by exposure to certain anesthetic agents, such as halothane and succinylcholine, which induce a hypermetabolic state characterized by rapid onset of muscle rigidity, hyperthermia, tachycardia, hypercapnia, and acidosis due to increased carbon dioxide production and oxygen consumption. If not promptly recognized and managed, MH can lead to severe complications such as rhabdomyolysis, disseminated intravascular coagulation, multi-organ failure, and death. The estimated incidence of MH varies from 1 in 10,000 to 1 in 150,000 anesthetic administrations, predominantly affecting young males and often presenting during or immediately after anesthesia induction, although delayed onset has been documented in rare cases.[1,2] The pathophysiology

involves uncontrolled calcium release from the sarcoplasmic reticulum due to mutations in the ryanodine receptor (RYR1) gene, which are implicated in most cases.[3] Early diagnosis, discontinuation of triggering agents, aggressive supportive care, and administration of dantrolene-the only specific antidote-are crucial to mitigate morbidity and mortality in MH episodes.

CASE REPORT

We report a rare and challenging case of a 10-month-old male infant who underwent herniotomy for bilateral congenital inguinal hernia. Notably, the baby also suffered from phocomelia, a condition characterized by malformed or absent limbs. The infant had an unremarkable medical history apart from this congenital abnormality, with appropriate developmental milestones for age. The laboratory tests yielded normal results, and the 2D echocardiogram revealed no signs of cardiac abnormalities. The 7 kg infant received anesthesia with sevoflurane, 10 µg fentanyl, and 4 mg atracurium for muscle relaxation. Airway was secured with an i-gel and anesthesia was maintained with O2, N2O, and sevoflurane. Post-induction, 0.25% bupivacaine (6 ml) was administered caudally. Surgery lasted 60 minutes without issues. Muscle relaxation reversal with neostigmine and glycopyrrolate preceded i-gel removal, leading to a smooth recovery and conscious transfer to the PICU.

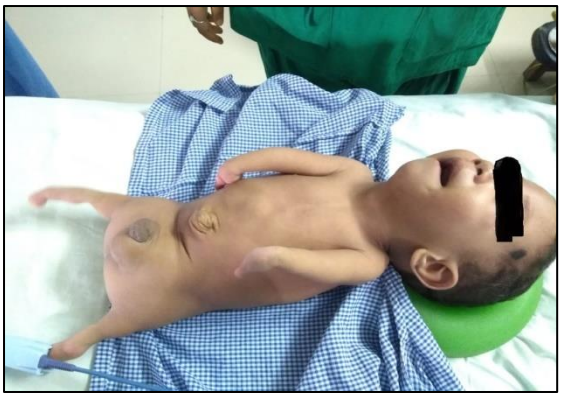

Figure 1: Patient prior to induction.

Figure 2: Patient in lateral position for caudal block.

In the pediatric intensive care unit (PICU), standard monitoring was initiated, showing stable conditions initially, allowing the infant to breastfeed after two hours. However, three hours post-operation, seizures commenced. Immediate administration of 0.5 mg midazolam briefly halted the seizure, but it quickly resumed, prompting the initiation of fosphenytoin. The seizures persisted despite various anti-epileptic drugs (midazolam, fosphenytoin, levetiracetam). Consequently, the infant underwent urgent intubation, paralysis, and thiopentone infusion. The axillary temperature was recorded 106°F. Active cooling measures like cold saline infusions, gastric lavage, surface cooling, and paracetamol infusion were swiftly initiated. A preliminary diagnosis of malignant hyperthermia was established; however, dantrolene, the necessary medication, was unavailable. The pediatric case presented challenges due to the rare occurrence and delayed onset of malignant hyperthermia symptoms, complicating prompt diagnosis and treatment. The absence of crucial medication intensified the complexity of managing this life-threatening situation.

Blood gas analysis indicated severe metabolic acidosis, while investigations ruled out other potential causes of seizure and fever like hypoglycemia, hyperthyroidism, and infection. Urine output, although sufficient, exhibited a reddish color, prompting forced alkaline diuresis as per rhabdomyolysis protocol. CT scan performed the next day revealed brain edema. Despite stopping thiopentone infusion after 20 hours and cessation of seizures, the infant remained unresponsive, progressing to a comatose state. Unfortunately, the infant developed multi-organ dysfunction and passed away after three days.

DISCUSSION

Malignant hyperthermia (MH) is a rare, life-threatening reaction to specific anesthetic drugs, inducing an excessive metabolic response triggered by inhalation agents like halothane, sevoflurane, desflurane, and succinylcholine. It can also be induced by intense physical activity and heat exposure.[4,5] Predisposing factors include various muscle disorders like muscular dystrophies and myotonia-related conditions.[6,7] MH occurs in 1 in 10,000 to 1 in 150,000 anesthesia cases, primarily in young males, and follows an autosomal dominant pattern genetically, potentially emerging during or after anesthesia.[1,2] Initial signs include increased heart rate, high CO2 levels, and post-succinylcholine muscle stiffness. Complications may lead to severe acidosis, rapid breathing, high blood potassium, muscle cell death, rhabdomyolysis, kidney failure, and fatal issues like DIC, heart failure, and bowel ischemia. The main diagnostic tool, the in vitro contracture test (IVCT), specifically the caffeine halothane contracture test (CHCT) by the European malignant hyperthermia group (EMHG) and the North American malignant hyperthermia group (NAMHG) is costly, facility-restricted, invasive, and inconclusive.[8] Alternatively, DNA analysis from blood

offers a less invasive diagnosis,8. Advanced methods like nuclear magnetic resonance spectroscopy for ATP depletion assessment during activity and microanalysis combined with caffeine injection for carbon dioxide measurement via capnography are newly explored.[9] During an acute MH crisis, immediate steps are vital: stop triggers, enhance ventilation, administer dantrolene, and initiate cooling methods like ice packs, lavage, saline infusion, and, if needed, hemodialysis. Avoid combining dantrolene with calcium channel blockers to prevent hyperkalemia.[6]

Dantrolene starts at 2.5 mg/kg, adjusted to manage symptoms, up to 10 mg/kg initially and continued at 1 mg/kg every 4-8 hours for 24-48 hours. Cooling strategies involve ice, lavage, saline, and potential hemodialysis. Manage arrhythmias, seizures, prevent kidney failure from myoglobin, ensure urine output using mannitol, furosemide, and fluids. Close ICU monitoring for 48-72 hours is crucial. Preventive measures include thorough anesthesia history to spot MH susceptibility, avoiding triggering agents in myotonia or muscular dystrophy cases, temperature monitoring in anesthesia, caution with succinylcholine in younger patients, and educating at-risk individuals about heat stroke risks in high temperatures. This case illustrates a rare instance of malignant hyperthermia co-occurring with phocomelia in a 10-month-old, presenting immense challenges due to its rarity and complexity.

Delayed symptom onset complicated swift diagnosis and treatment, aggravated by dantrolene unavailability. Managing this critical condition became more daunting. Severe metabolic acidosis and subsequent brain edema were evident despite efforts, accentuating the urgency and intricacy of care. This underscores the need for heightened vigilance among practitioners, emphasizing preparedness for atypical MH presentations and the urgency of securing critical medications. Adaptable approaches for congenital anomalies reinforce the need for proactive and nuanced management, emphasizing the vital role of prompt recognition and effective intervention strategies in such rare and critical cases.

CONCLUSION

This case presents a rare occurrence of malignant hyperthermia (MH) in a 10-month-old with phocomelia, complicated by delayed symptoms and lack of dantrolene. The outcome highlights the need for vigilance and preparedness in managing atypical MH cases and ensuring access to critical treatments. This case report advances understanding by highlighting the complexities of managing malignant hyperthermia (MH) with delayed onset in an infant with congenital anomalies, such as phocomelia. It underscores the critical importance of early recognition of atypical MH presentations, swift intervention, and access to essential treatments like dantrolene to prevent fatal outcomes. The findings emphasize the need for enhanced awareness, preparedness, and proactive management strategies among healthcare professionals when dealing with rare and life-threatening conditions. This case contributes to the limited literature on MH in paediatric patients with congenital disorders and guides future clinical practice in similar scenarios.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Sharma SK, Deori P, Bora BB, Khound M, Pao M. Fatal outcome of suspected delayed-onset malignant hyperthermia in an infant with phocomelia: challenges in diagnosis and management. Int J Community Med Public Health 2024;11:4071-3.