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Case Report

Suspected Malignant Hyperthermia in a Child with Post-Facial Burn Hypertrophic Scars and Ectropion: A Case Report at Kenyatta National Hospital

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Abstract: Malignant hyperthermia is a rare pharmacogenetic disorder of skeletal muscles. It occurs after subjection to potent volatile anaesthetics, succinylcholine and environmental agents like heat and strenuous exercise. Symptoms of malignant hyperthermia are variable based on age and the common symptoms being hyperthermia, tachycardia and hypercarbia. Dantrolene is the universal treatment of choice. The main aim of this case presentation was to highlight the successful management of malignant hyperthermia without the use of dantrolene. This was a case report of a one year and eleven months old baby who presented thirteen months post facial burn with hypertrophic scars, ectropion and contractures of the mouth. The patient was scheduled for contracture release of the mouth and ectropion repair. Intraoperatively, she had symptoms of suspected malignant hyperthermia such as hyperthermia (38.9°C), hypercarbia ($PETCO_2$> 55) and tachycardia (heart rate 202bpm). Dantrolene the drug of choice was available but had expired. Supportive care was initiated and patient managed successfully. The patient was extubated on the table uneventfully, taken to recovery and transferred to the wards afterwards. She recovered fully without any sequale of hyper metabolic crisis post operatively and was discharged home after two weeks. This case report illustrates that early recognition of malignant hyperthermia is the key to improved patient survival. Aggressive supportive care can lead to good outcomes even in the absence of the drug dantrolene.

Keywords: Malignant Hyperthermia, Hypercabia, Volatile Anaesthetics, Pharmacogenetic, Capnograph

1. Introduction

Malignant hyperthermia (MH) is a pharmacogenetic disorder of skeletal muscles. It occurs after subjection to halogenic volatile anaesthetics affecting calcium homeostasis in skeletal muscle [1, 2]. MH was first identified as a genetic disorder in the anaesthetic fraternity in 1960. Ten family members from one family in Australia had died after exposure to general anaethetics [3, 4]. The eleventh member, got malignant hyperthermia crisis intraoperatively after halothane exposure during surgery for compound fracture of the tibia and fibula. It started with cyanosis, hypotension, tachycardia followed by hyperthermia and unconsciousness. The gases were switched off and maintained on 100% oxygen. There was no response. Blood transfusion was started in view of the hypotension. He gradually recovered one and a half hours later after being immersed in ice which was being used in the nearby cardiac theatre. He recovered fully. It was after this incidence that the family was followed up and malignant hyperthermia discovered as a pharmacogenetic disorder. Years later, dantrolene was discovered as the drug of choice [3].

The major indicators of malignant hyperthermia include muscle rigidity after succinylcholine use, hyperthermia, tachycardia, hypercarbia and acidosis [1, 2, 5, 6].

Susceptibility to malignant hyperthermia is not associated with ethnic orientation. It occurs mostly among men compared to women (2:1). Its occurrence is more prevalent in children compared to adults with an incidence of 1:30,000 and

1:100,000, respectively [7, 8]. The mortality rates from malignant hyperthermia is estimated to be <5% in the United States when given dantrolene early [8]. The genetic risk can be assessed by testing the existence of the ryanodine receptor (RYR1) gene [9].

Malignant hyperthermia is diagnosed clinically by use of temperature measurement and capnography. The gold standard for diagnosis of MH currently is in vitro contracture test (IVCT), which is based on contracture of muscle fibres in the presence of halothane or caffeine [1]. IVCT is expensive, confined to specialized testing centers, it requires a surgical procedure and can yield equivocal as well as false positive and negative results [1]. DNA analysis, offers an alternative to the IVCT, requiring only a blood specimen to be sent to accredited diagnostic laboratory. It tests DNA mutation within the ryanodine receptor gene (*RYR1*) encoding the skeletal muscle calcium release channel [1, 10].

Dantrolene, the drug of choice is not readily available in most facilities due its pharmaco-economic model [7, 8]. This case shows successful management of suspected malignant hyperthermia without the use of dantrolene in a child.

2. Case Report

A one year eleven-month old female child, with a weight of 8kgs, presented with post facial burn hypertrophic scars, ectropion and contractures of the mouth thirteen months post injury. The patient was scheduled for contracture release mouth and ectropion repair under general anaesthesia. Preoperative evaluation done a day before surgery, she was classified as ASA11 (American Society of Anaesthesiologist classification) and also Mallampati 11 due to the post burn status with contracture of the mouth. Laboratory investigations for urea, creatinine, electrolytes and full haemogram were normal. The patient was not on any medications and had no previous anaesthetic exposure. The heart rate (HR) was 110 beats per minute, respiratory rate of 22 breaths per minute and the temperature was 36.7°C during the evaluation.

Intraoperatively, gaseous induction in oxygen with 8% sevoflurane was done, intravenous (iv) access was achieved and vital signs monitored. Fentanyl 15mcg, ketamine 10mg, propofol 5mg, were then administered intravenously. She was intubated uneventfully and put on mechanical ventilation. She was maintained on 50% oxygen and 1% isoflurane in nitrous oxide. Infraorbital block with 0.25% bupivacaine was done. She received iv ceftriaxone 375mg, iv dexamethasone 4mg and iv ondansetron 1mg. A few minutes later, a steady rise of end tidal carbon dioxide ($ETCO_2$) was noted and the minute ventilation was adjusted. This was to manage hypoventilation that may have occurred during induction. The soda lime canister had been replaced before surgery. There was no improvement even with manual ventilation. At the start of anaesthesia, the $ETCO_2$ was 63, heart rate 150bpm (HR was 110bpm a day before surgery) and temperature was 36.3°C. $EtCO_2$ continued to rise up to 81mmHg, there was rise in temperature to 38.9°C, with a tachycardia of 202 bpm. Morphine 0.4mg and paracetamol 120mg intravenously had been administered. Arterial blood gas (ABG) was done and it showed respiratory acidosis [figure 3]. Malignant hyperthermia was suspected and started on management for MH crisis. Volatile agents were switched off and patient put on 100% oxygen at 6L/min. Surgeons were alerted. Propofol 5mg was given every 5min as an intravenous bolus and hyperventilation done. There was only 1vial of dantrolene available but it had already expired. So dantrolene was not administered. Cooling was done with cold intravenous fluids from the fridge in the nearby cardiac theatre. Ice cold gauzes were placed on the forehead and feet which was being replaced frequently. 1 hour 30min later, temperature had come down to 37.9°C, $ETCO_2$ to 47mmHg and HR to 150bpm. Repeat ABG was done and the acidosis had improved (figure 4). Surgery was completed within three hours. Patient was extubated successfully, fully awake and taken to recovery area; being monitored for recrudescence of malignant hyperthermia. She was admitted to the ward post-operatively and discharged home after two weeks without any complication. There were no recrudescence signs of malignant hyperthermia like change in urine colour or evidence of rhabdomyolysis during the time the patient was admitted in the ward post operatively.

The mother was informed about the intraoperative incidence and the suspicion for malignant hyperthermia. The incidence was also recorded in the anaesthesia file for the patient.

3. Discussion

Malignant hyperthermia is an anaesthetic emergency and a rare occurrence in anaesthesia world. It is a hyper metabolic response in the genetically susceptible individuals after exposure to the triggering agents like volatile anaesthetics [1, 9]. It can also be caused by factors such as excess heat, emotional distress and exposure to depolarising muscle relaxants [9, 11].

Mutations in the ryanodine gene leads to altered calcium release [9, 12]. In the presence of triggering agents, mutated channels open more easily flooding the cytosol with calcium [9, 12]. This leads to sustained muscle contraction, accelerated metabolism, with production of CO_2 and cellular acidosis [1]. In children, sinus tachycardia and hypercapnia are the two most reliable early clinical signs [12]. Fever, hyperkalaemia and increased creatinine kinase are late signs and their absence does not exclude this diagnosis.

Rapid increase in temperature is marked by increase in core temperature at a rate of 1–2°C every five minutes. Severe hyperthermia (core temperature greater than 44°C) leads to a marked increase in oxygen consumption, carbon dioxide production, widespread vital organ dysfunction, and disseminated intravascular coagulation (DIC). DIC is a poor prognostic indicator. When body temperature exceeds 41°C, DIC is the usual cause of death [1].

Uncontrolled hyper metabolism leads to cellular hypoxia that is manifested by a progressive and worsening metabolic acidosis. If untreated, continuing myocyte death and rhabdomyolysis result in life-threatening hyperkalemia. Myoglobinuria may lead to acute renal failure. Other life-threatening complications include; congestive heart

failure, bowel ischemia, and compartment syndrome of the limbs due to profound muscle swelling, and renal failure from rhabdomyolysis [1].

Malignant hyperthermia is diagnosed by clinical and laboratory testing and is confirmed by caffeine-halothane contracture test [9, 12]. This test requires approximately 2g of muscles excised from vastus lateralis or vastus medialis muscle [11]. Because of the large amount of muscles needed for this test, it is not recommended for children less than 5years of age or weighing less than 20kg. In vitro measurement of contracture response of the biopsied muscle to graded concentrations of caffeine and 3% halothane is diagnostic [9, 11]. This diagnostic test is done three months after suspected MH crisis to avoid false positive results, usually as an outpatient [11, 13]. Therefore, clinical grading scale to diagnose the likelihood of occurrence of malignant hyperthermia during a hyper metabolic crisis is important.

There is a clinical criterion for diagnosing malignant hyperthermia susceptibility intraoperatively. It was described by Larach et al in 1994 and is used to diagnose MH during hyper-metabolic crisis in patients [14]. The grading system has 6 ranks, 6 being almost certain for the likelihood of MH occurring [14] as indicated on Figure 1. Our patient was rank 5 with a score of 38 [Table 1], which indicated a likelihood for MH. We did not do any test regarding confirmation of muscle breakdown like blood creatinine phosphokinase, serum myoglobin or urine myoglobin as the patient improved with no evidence of myonecrosis.

Other conditions with hyper metabolic crisis include sepsis, thyroid storm, pheochromocytoma, patient being on vigorous exercises, heat stress or use of antipsychotic drugs [12, 15]. These were ruled out from preoperative patient assessment for our patient. In addition, heating devices (like bair hugger) were not used intraoperatively so there was no iatrogenic overheating for our patient.

Could the presence of post burn hypertrophic scars been a trigger to the hyper metabolic crisis in this child? Currently, there are no published studies showing relationship between post burn scars and occurrence of malignant hyperthermia. However, with burn injury there is both local and systemic pathophysiologic responses in terms of metabolic, hemodynamics, cardiac, renal, hepatic, gastro-intestinal and immunologic responses [16]. The hyper metabolic response leads to muscle wasting and injury [16]. The structure and function of essential organs (heart, liver, skeletal muscle, skin), the immune system and the cellular membrane transport system are compromised [16]. We speculate that the pathophysiological responses to burn injury may interfere with muscles' physiology and calcium homeostasis and trigger malignant hyperthermia crisis.

Table 1. *Malignant hyperthermia score in our patient.*

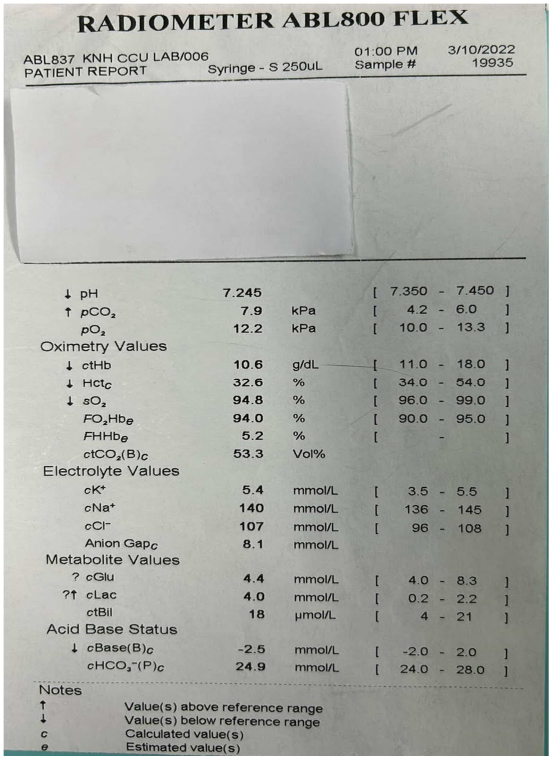
CLINICAL INDICATOR	POINTS
$PETCO_2$ > 55 with controlled ventilation	15
Rise in temperature > 38.8°C in Peri-operative period.	10
Arterial Blood PH <7.25	10
Inappropriate Tachycardia	3
Total Score	38

Raw Score	MH Rank	Description of MH Likelihood
0	1	Almost never
3 to 9	2	Unlikely
10 to 19	3	Somewhat less than likely
20 to 34	4	Somewhat greater than likely
35 to 49	5	Very likely
50 and Above	6	Almost certain

Figure 1. *MH raw score and Rank [14].*

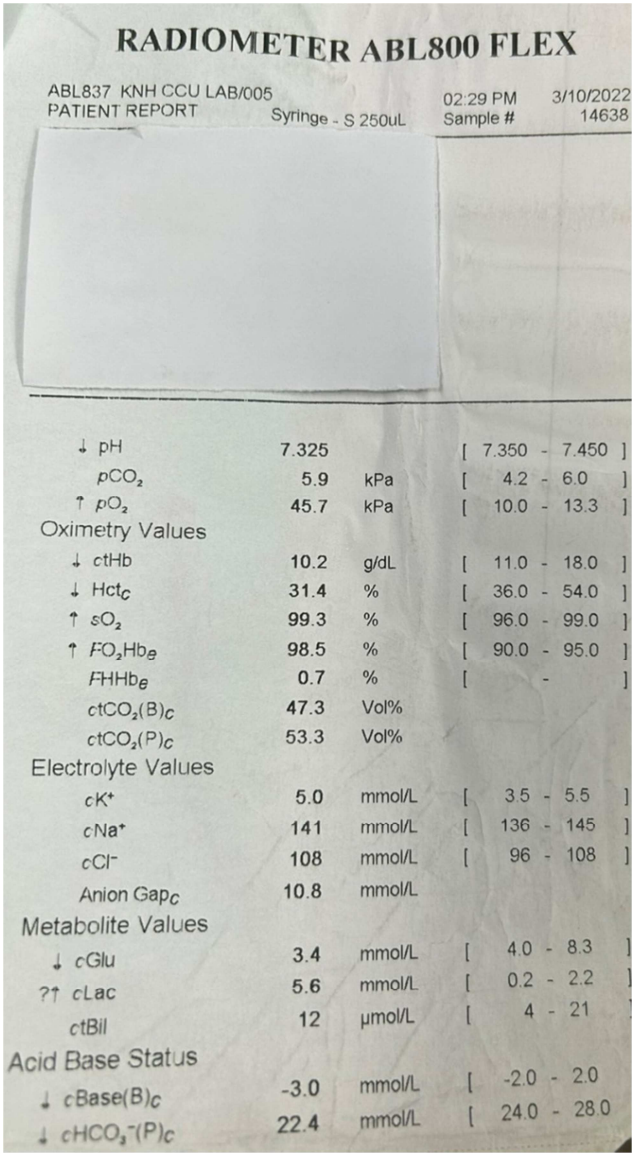
Clinical Indicators	Points
Muscle rigidity	
Generalized rigidity	15
Masseter rigidity	15
Process II: Myonecrosis	
Elevated CK> 20,000 (after succinylcholine administration)	15
Elevated CK> 10,000 (without exposure to succinylcholine)	15
Cola- colored urine	10
Myoglobin in urine> 60 mg/L	5
Blood/plasma/serum K^+> 6 mEq/L	3
Process III: Respiratory acidosis	
$PETCO_2$ >55 with controlled ventilation	15
$PACO_2$ >60 with controlled ventilation	15
$PETCO_2$ >60 with spontaneous ventilation	15
Inappropriate hypercarbia	15
Inappropriate tachypnea	10
Process IV: Temperature increase	
Rapid increase in temperature	15
Inappropriate temperature > 38.8 °C in perioperative period	10
Process V: Cardiac involvement	
Inappropriate tachycardia	3
Ventricular tachycardia or fibrillation	3
Others:	
Arterial base excess more negative than -8 mEq/L	10
Arterial PH < 7.25	10
Rapid reversal of malignant hyperthermia signs of metabolic and/ or respiratory acidosis with intravenous dantrolene	5
CK: Creatine Kinase	

Figure 2. *Clinical Indicators [11].*



Arterial blood gas done on suspicion of malignant hyperthermia.

Figure 3. *ABG done during the crisis.*



RADIOMETER ABL800 FLEX

ABL837 KNH CCU LAB/005
PATIENT REPORT Syringe - S 250uL
02:29 PM 3/10/2022
Sample # 14638

↓ pH	7.325		[7.350 - 7.450]
pCO_2	5.9	kPa	[4.2 - 6.0]
↑ pO_2	45.7	kPa	[10.0 - 13.3]
Oximetry Values			
↓ ctHb	10.2	g/dL	[11.0 - 18.0]
↓ Hct_C	31.4	%	[36.0 - 54.0]
↑ sO_2	99.3	%	[96.0 - 99.0]
↑ FO_2Hb_B	98.5	%	[90.0 - 95.0]
$FHHb_B$	0.7	%	[-]
$ctCO_2(B)_C$	47.3	Vol%	
$ctCO_2(P)_C$	53.3	Vol%	
Electrolyte Values			
cK^+	5.0	mmol/L	[3.5 - 5.5]
cNa^+	141	mmol/L	[136 - 145]
cCl^-	108	mmol/L	[96 - 108]
$Anion\ Gap_C$	10.8	mmol/L	
Metabolite Values			
↓ cGlu	3.4	mmol/L	[4.0 - 8.3]
?↑ cLac	5.6	mmol/L	[0.2 - 2.2]
ctBil	12	µmol/L	[4 - 21]
Acid Base Status			
↓ $cBase(B)_C$	-3.0	mmol/L	[-2.0 - 2.0]
↓ $cHCO_3^-(P)_C$	22.4	mmol/L	[24.0 - 28.0]

Arterial Blood Gas done 1hour 30min Later

Figure 4. *ABG done during the supportive care.*

The clinical indicators of malignant hyperthermia observed in our patient were $PETCO_2$ > 55 with controlled ventilation, temperature > 38.8°C, arterial blood PH <7.25, and inappropriate tachycardia. These signs have also been observed in different MH cases from different regions [15, 17, 18]. Rapid temperature increase is marked by increase in core temperature at a rate of 1–2°C every five minutes [1]. This was not the case with our patient.

Dantrolene is the drug of choice, and it reduces mortality rate from 80% if untreated, to less than 10% if given early [7, 11, 17, 18]. However, it is not readily available in many institutions due to its pharmaco- economic model. It is relatively expensive, its shelf life is limited and it might expire before being used as malignant hyperthermia occurs rarely. The only vial available at our facility had already expired.

There are case reports of successful management of malignant hyperthermia in children without the use of dantrolene [7, 17]. Aggressive supportive management can improve survival as evidenced in this case. This involves [1, 9]:

1) Discontinuing the triggering agent.
2) Use of activated charcoal filter to reduce the concentration of volatile agents in the breathing circuit.
3) Starting oxygen on maximum flow rates.
4) Hyperventilation to reduce the $ETCO_2$ levels.
5) Temperature management with active cooling.
6) Managing the sequel of hyper metabolic crisis: treat arrhythmia, hyperkalaemia, rhabdomyolysis and dialysis for acute kidney injury.
7) Do blood gases, electrolytes, creatine kinase, blood and urine for myoglobin; coagulation profile, check values every 6–12 hours.
8) Ensure urine output of 2 ml/kg/hour with mannitol, furosemide, and fluids as needed.
9) Evaluate need for invasive monitoring and continued mechanical ventilation.
10) Admission to the critical care unit for mechanical ventilation and use of vasopressors.
11) Tests for disseminated intravascular coagulation (DIC). DIC is most frequent when body temperature exceeds 41°C and it is a poor prognostic indicator.
12) Monitor urine for myoglobinuric renal failure.
13) However, patients experiencing malignant hyperthermia should receive dantrolene to increase their survival chances. They should be monitored closely for 48–72 hours, as 25% of patients will experience a recrudescence of the syndrome despite dantrolene administration.

We did not recommend genetic testing for our patient due to financial constraints. In addition, muscle biopsy is not recommended for our patient as she was less than 5 years of age and weighing less than 20kgs.

The mother was informed about the suspected incident and it was also recorded in the patient's file for anaesthesia record.

4. Conclusion

The presented case highlights that careful monitoring is the key to early detection of malignant hyperthermia. Routine use of capnograph and temperature probes during anaesthesia is vital for early awareness. The use of clinical grading scale developed by Larach et al is the criteria for diagnosing malignant hyperthermia during a hyper metabolic crisis. Aggressive supportive management in suspected cases can improve survival even in the absence of dantrolene; but dantrolene should be made available for best chance of patient survival.

In addition, activated charcoal should be readily available to reduce the concentration of volatile agent from the breathing circuit. There is hardly a diagnostic center for confirmation of malignant hyperthermia in Kenya, making malignant hyperthermia a clinical diagnosis in our set up.

Further research studies in Kenya and other African countries is needed to determine if there exists a possible

association between burn injuries and malignant hyperthermia in children.

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