“Is There a Link Between Exercise Heat Exhaustion and Malignant Hyperthermia”

By: Lynne McDonald

Summary:

This report discusses the management of a 37 year old male who presented to Palmerston North Hospital’s Emergency Department, with a near fatal temperature of 41.4C [106.52F], following collapse during an exercise session in hot humid conditions.

He presented with an altered mental state, excessive perspiration and respiratory distress.

These features were typical of severe exertional heat illness.

Alternative diagnoses to be considered were heat stroke, rhabdomyolysis, or malignant hyperthermia.[MH]

The patient had no known history of any adverse reaction, and initially was treated with Dantrolene.

Patient had recovered fully 4 weeks after the episode.

An in-vitro contracture test [muscle biopsy] was carried out, 3 months later. There was no reaction to both Halothane and caffeine, supported by a negative sevoflurane test.

A screen of 26 ryanodine receptor gene mutations was undertaken, no mutations were identified.

Key Words:

Fever, heat stroke, heat exhaustion, malignant hyperthermia, rhabdomyolysis and dantrolene.
Introduction:

A brief description of each of the conditions considered.

1. **Fever:**
   An abnormally high body temperature often accompanied quickened pulse, and delirium.
   This can cause dehydration or depletion of electrolytes.
   [That is why fever occurs with diarrhoea].

2. **Heat Exhaustion:**
   This is considered less severe than heat stroke and usually occurs after several days of electrolyte and water depletion due to heat exposure.

3. **Heat Stroke:**
   This condition is life threatening. The person’s cooling system becomes dysfunctional and the internal body temperature rises to the point where brain damage and damage to other internal organs may result.
   Heat stoke takes one of two forms:
   - The classic form occurs in people whose cooling mechanisms are impaired and combined with high ambient temperatures.
   - The exertional form occurs in healthy people who over exert themselves in high ambient temperatures or in hot environments to which they are not acclimatised.

4. **Malignant Hyperthermia:**
   Malignant hyperthermia [MH] is an inherited disorder which occurs in response to specific anaesthetic agents.
   It is a pharmacogenetic disorder inherited in an autosomal dominant fashion, and is caused by a defect in the skeletal muscle calcium haemostasis.
   It is usually triggered in otherwise healthy susceptible individuals exposed to potent inhalational anaesthetic agents and the muscle relaxant, Suxamethonium.
   On rare occasions stress may trigger an MH reaction.
   MH-like symptoms unrelated to anaesthesia has been associated with strenuous exercise, excitement or environmental heat. More recently, the connection between MH and exercise has been sustained by the demonstration of both positive In-vitro Contracture test [IVCT] and the presence of ryanodine receptor [RYR] mutations in patients with a history of exercise-induced rhabdomyolysis [EIR].
5. **Rhabdomyolysis:**

A condition in which skeletal muscle breaks down, releasing myoglobin [the oxygen carrying pigment in muscle] together with enzymes and electrolytes from inside the muscle cells.

Rhabdomyolysis can cause kidney failure since myoglobin is toxic to the kidneys. Exercise-induced rhabdomyolysis can occur in patients with normal tissue, particularly if they are physically untrained, their perspiration mechanism is impaired, and/or their physical exertion occurs in extremely hot conditions.

During exercise, potassium plays an important role in the vasodilatation necessary to maintain skeletal muscle blood flow, and potassium depletion can result in muscle weakness. In the absence of other risk factors, physical exertion alone usually does not cause severe rhabdomyolysis. This condition is rare and must be recognised quickly and treated early.

Intracellular muscle components – potassium, phosphate, myoglobin, creatine kinase, and urate - are released into the circulation.

6. **Exertional Heat Illness:**

Exertional Heat Illness can affect athletes during high intensity or long duration of exercise, and can result in withdrawal from the sporting endeavour or collapse during or soon after activity is completed.

This spectrum includes exercise associated muscle cramping, heat exhaustion, or exertional heat stroke. While certain individuals are more prone to collapse from exhaustion in the heat [ie; not acclimatised, using certain medications, dehydrated, or recently ill], exertional heat stroke [EHS] can affect seemingly healthy athletes even when the environment is relatively cool.

EHS is defined as a rectal temperature greater than 40 degre Celsius accompanied by symptoms or signs of organ system failure, most frequently central nervous dysfunction.

Early recognition and rapid cooling can reduce both the morbidity and mortality associated with EHS.

The clinical changes associated with exertional heat illness can be subtle and easy to miss if coaches, medical personnel, and athletes do not maintain a high level of awareness and monitor at risk athletes closely.

When athletes collapse from exhaustion in the hot conditions, the term heat exhaustion is often applied.
Case Report:

A 37 year old, non smoker, physically fit male who weighed 80kg presented to the emergency department via ambulance. He had collapsed while strenuously exercising [running with a pack for over 90 minutes] in extreme heat [31C].
He had lost consciousness on collapse, with subsequent agitation and profuse sweating, and he had a temperature of 41.4C,
Heart rate 160 beats per minute,
Blood Pressure 90 systolic/70 diastolic mmHg,
Hot skin and flushed.
Midazolam was prescribed to settle the patient.
Active cooling with ice packs was administered and cool IV fluids commenced.
He was initially managed by ambulance paramedics who transported him to hospital.
On examination in the Emergency Department [ED], he was found to be agitated and delirious with a Glasgow Coma Score of 10/15. [E+V+M]

<table>
<thead>
<tr>
<th>Glasgow Coma Score</th>
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<tbody>
<tr>
<td>Eye Opening (E)</td>
</tr>
<tr>
<td>4=Spontaneous</td>
</tr>
<tr>
<td>3=To voice</td>
</tr>
<tr>
<td>2=To pain</td>
</tr>
<tr>
<td>1=None</td>
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Total = E+V+M

Temperature was >41C,
Heart rate 120beats per minute and regular,
Systolic blood pressure was 105mmhg.
He was hyperventilating with oxygen saturations of 94% on high oxygen flow via a Hudson mask.
Chest sounds were clear, abdomen unremarkable.
He was sedated, then intubated [rapid sequence technique] and ventilated to facilitate CT scanning and subsequent management.

Computerised Tomography [CT] of head:
Showed there were no abnormalities detected [NAD]

Patient was then transferred to Intensive Care Unit [ICU].

Active cooling measures were continued and he was treated with two doses of IV dantrolene and started on sodium bicarbonate infusion.
**Blood results were:**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Normal Range</th>
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<tbody>
<tr>
<td>Creatinine</td>
<td>162 umol/L</td>
<td>50 – 120</td>
</tr>
<tr>
<td>Sodium [Na]</td>
<td>139 mmol/L</td>
<td>135 – 147</td>
</tr>
<tr>
<td>Potassium</td>
<td>4.1 mmol/ L</td>
<td>3.4 – 5.0</td>
</tr>
<tr>
<td>Haemoglobin</td>
<td>148 g/l</td>
<td>125 – 170</td>
</tr>
<tr>
<td>Platelets</td>
<td>144 x 10Eq/l</td>
<td>150 – 400</td>
</tr>
<tr>
<td>White cell count</td>
<td>3.6 x 10Eq/l</td>
<td>4.0 – 10.0</td>
</tr>
<tr>
<td>International Normalized Ratio Blood Test [INR]</td>
<td>1.6 [ratio of]</td>
<td>0.8 – 1.1</td>
</tr>
<tr>
<td>Troponin T</td>
<td>less than 0.01</td>
<td>0.00 – 0.03</td>
</tr>
<tr>
<td>Creatine Kinase</td>
<td>626 U/L</td>
<td>20 – 215</td>
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**Arterial Blood Gas [Patient was Ventilated],**

- pH 7.21,
- pCO2 41,
- pO2 170,
- HCO3 16,
- Base deficit 11

**Echocardiogram:**
The result demonstrated mild enlargement of atria, normal contractility, with no significant valve disease.

**Initial Management**
Cooled IV fluids + general cooling cares + chlorpromazine + dantrolene + urinary alkalinisation.
Central Venous Line [CVP] was inserted.
Arterial line was inserted into R] femoral artery, and an indwelling urinary catheter was cited in the bladder.

**Progress:**
Metabolic acidosis settled.
Creatine kinase [CK] peaked at 6137 U/L [normal range is 20 - 215].
Initially after extubation, patient was mildly confused.

**Discharge from ICU on 3rd day.**
Patient was transferred to High Dependency Unit [HDU].
Once in HDU, patient began mobilising, eating and drinking well.
Observations were:
Blood Pressure 128/75mmHg,
Heart rate 80 beats per minute,
Temperature 37.5°C,
Oxygen saturation 96% on room air,
Respiratory rate 35 breaths per minute,
Bowel motion was loose, and patient had no recollection of events on admission, still slightly disorientated.
Intravenous fluids were continued, patient was very tired and in sinus rhythm.
Developed localised, deep pink papular rash symmetrical on medial aspects of the elbows, cleared but similar area developed on medial thigh. This was not typical of a drug reaction. Unknown cause of “heat rash” [may have been a reaction to soap powder used in the hospital laundry].
Not itchy and no other rash, no wheeze, and feeling systemically well.
Patient was prescribed Loratidine as necessary for itch.

**Transferred to ward:**
Confusion became less after patient was transferred to the general ward.
Developed a productive cough and purulent nasal discharge, went on to become febrile and Chest X-ray consistent with right middle lobe pneumonia.
Patient responded well to IV antibiotic Cefotaxime and then oral Augmentin for 5/7 days.
Bowel motions were loose, and were resolved with no obvious treatment.
Sputum, urine and blood cultures non contributory.
Patient had initial muscle weakness, especially in his arms, but this improved over time, once he was more alert, active and out of bed.
Ultra sound of upper abdomen, liver and billary tree, with no abnormalities detected.
Platelets also reduced, presumably part of the septic / heat-stressed picture and also subsequently on improve.

**Discharge Home Plan:**
Patient was to have three weeks off work, and to complete five days of prescribed Augmentin, and use the script for Loratidine should it be needed for the rash.
Anaesthetists planned for an outpatient muscle biopsy for malignant hyperthermia screen.
There was to be no exercise for at least 2 weeks, then gentle re-introduction only.

**Discharge bloods and Observations:**
Creatinine 75umol/L,
Sodium 137mmol/L,
Potassium 3.6mmol/L,
Haemoglobin 115g/l,
Platelets 411 x 10^11 Eq/l,
White Cell Count 5.9 x 10^9 Eq/l,
Blood Pressure 132/72mmHg,
Heart rate 48 beats per minute,
Oxygen saturation 97%,
Temperature 36.7°C, the patient was alert, eating and drinking well.

Advice to GP:
He was to take things easy during his break from work, no exercise for at least two weeks.
Avoid alcohol. It would be wise not to return to driving for several weeks and is to see GP with any concerns.
He was discharged from hospital nine days after initial episode.

Discharge problem list:
Heat stroke
Ventilator – associated pneumonia [right middle lobe]
Rhabdomyolysis
IVCT – Muscle Biopsy
Discussion:

The initial diagnosis was always going to be difficult as the symptoms, presented to the medical staff, suggested clinically exertional heat illness with a remote possibility of MH.

Aggressive cooling, intravenous resuscitation and Dantrolene administration avoided a fatal outcome.

Exercise induced rhabdomyolysis and heat stroke were discussed, as these can occur in the untrained athlete undertaking vigorous exercise in hot humid weather.

With a negative DNA and IVCT for MH, exercise induced rhabdomyolysis or exertional heat illness were the most likely diagnosis for this patient.

After eliminating the conditions considered with the initial symptoms presented exertional heat illness was considered to be the most likely diagnosis, because this condition characteristically fitted the patient’s symptoms and response to the treatment given by medical staff at Palmerston North Hospital.
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Acknowledgements:

I wish to thank Dr. Neil Pollock [Consultant Anaesthetist – Palmerston North Hospital] for his assistance, advice and expertise in the compiling of this case report.

Also Bruce McDonald for reviewing this manuscript.
A CASE STUDY

“IS THERE A LINK BETWEEN EXERCISE HEAT EXHAUSTION AND MALIGNANT HYPERTHERMIA”

By Lynne McDonald
Senior Anaesthetic Technician
Palmerston North Hospital
New Zealand
To Karen Bennett and the Executive Panel:

Please find attached my completed Case Study for the Covidien Award.

Yours sincerely,

L.D. McDonald