# POSTOPERATIVE MALIGNANT HYPERTHERMIA: A CASE REPORT

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THE FOLLOWING CASE differs somewhat from many reports of malignant hyperthermia recently published.[1–23] A sudden and certainly malignant hyperthermia associated with muscular rigidity occurred only after the operation was completed and the patient was on her way to the recovery room.

## CASE REPORT

A 22-year-old, slim, healthy female was admitted to hospital for removal of a right ovarian cyst. Her temperature and other vital signs were within normal limits. She did, however, complain of frequent spontaneous cramping of the leg muscles, unrelated to cold, sleep, or exercise.

Four years previously the patient had an uncomplicated general anaesthetic for a cystoscopy. The patient's father had had a spinal fusion following which he did not waken for four days. His sister, (aunt of the present patient) had had a minor general anaesthetic which had been followed by severe muscular aches and pains of two weeks' duration. Several months subsequent to recovery her CPK (creatine phosphokinase) was found to be 165 i.u. (normal 40 i.u.).

Pre-operative haemoglobin was 13.6 gm per cent, haematocrit 40 vol per cent, WBC 6,400, BUN 12 mg per cent, blood glucose 102 mg per cent and the urinalysis was normal.

Anaesthesia was induced at 0955 hours, 10 December 1969, with 400 mg of thiopentone and 60 mg of succinylcholine chloride intravenously. Some slight muscular fasciculation was observed prior to orotracheal intubation, which was carried out without difficulty. Anaesthesia was maintained with nitrous oxide and oxygen (2:2 L) plus halothane 1–1.5 per cent with controlled respiration in a semi-closed system. Succinylcholine chloride 300 mg in a 0.1 per cent solution was given intravenously during the operation, which provided excellent relaxation of the abdominal wall. Total anaesthetic time was ninety minutes – the operation ending at 1125 hours. During that period the blood pressure remained at 110/75 and the pulse rate varied between 70 and 80 per minute. Total blood loss was less than 150 ml (Table I).

At 1125 hours the patient seemed to be breathing adequately and was extubated. On transferring her to the stretcher she suddenly flexed her arms and rigidly maintained this position. No signs of consciousness were yet present. On arrival in the recovery room at 1126 hours respirations were jerky and the patient

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TABLE I

CLINICAL AND LABORATORY FEATURES

| Time | | T °F | HR | BP | RR | CVP cm$H_2O$ | $Paco_2$ | pH | BE mEq | Na mEq/L | K mEq/L | Ca mg% | Pi mg% | Gluc mg% | BUN mg% | Hb | Hct | WBC | CPK | SGOT | LDH | Alk Phos | Urine Vol | Urine Color | Urine Sugar |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 10 Dec. | Pre-op | 98 r | | | | | | | | | | | | 102 | 12 | 13.6 | 40 | 6,400 | | | | | | Yell. | Neg. |
| Op. | 0955–1125 | | OPERATION | | | | | | | | | | | | | | | | | | | | | | |
| Post-op | 1135 | 105 r | 120 | 60/? | | <1 | | | | | | | | | | | | | | | | | | | |
| | 1145 | 109 r | 160 | | | | | | | | | | | | | | | | | | | | | | |
| | 1150 | | >200 | | | | | | | | | | | | | | | | | | | | | | |
| | 1155 | 112 np | >200 | | | | 62 | 7.04 | −15 | 146 | 6.0 | | | | | | | | | | | | | | |
| | 1210 | | | | | | 70 | 7.09 | −11 | 154 | 6.8 | | | | | | | | | | | | | | |
| | 1230 | | | | | | 40 | 7.49 | +6 | 153 | 5.4 | | | | | | | | | | | | | | |
| | 1245 | 98 np | | | | | | | | | | | | | | | | | | | | | | Red | |
| | 1300 | 96 np 95 r | 112 | 90/50 | | | | | | | | | | | | | | | | | | | 700 | | |
| | 1355 | 94 r | 104 | 110/60 | | 14 | | | | | | | | | | | | | | | | | | | |
| | 1600 | | 124 | 110/60 | 24 | | 46 | 7.33 | −2 | 136 | 2.1 | | | 585 | 22 | 9.8 | 29 | 2,800 | | | | | 1710 | | |
| | 1630 | 93.2 r | 124 | 110/60 | | | | | | | | | | | | | | | | | | | | Red | 3+ |
| | 1800 | | 122 | 99/40 | 24 | | | | | | | | | | | 8.4 | 24 | | | | | | | | 2+ |
| | 2200 | 93.2 r | 128 | 100/60 | 24 | 6 | | | | | | | | | | | | 3,100 | | | | | | Red | 3+ |
| | 2400 | 95 r | 104 | 104/80 | 18 | 4 | | | | | | | | | | | | | | | | | 1645 | Red | |
| 11 Dec. | 0500 | 92.8 r | 110 | 104/80 | 16 | 10.5 | | | | | | | | | | | | | | | | | | Red | 1+ |
| | 0800 | 91 r | 80 | 110/70 | 8 | 8 | 35 | 7.43 | −1 | 142 | 2.7 | 7.6 | 0.6 | | | 10.4 | 31 | 5,500 | >20,000 | 500 | 8,500 | | | | 3+ |
| | 1200 | 92.8 r | 92 | 95/70 | 8 | 7 | | | | | | | | | | | | | | | | | | | |
| | 1600 | 94.1 r | 112 | 94/70 | 12 | 5 | 37 | 7.33 | −5 | 146 | 2.8 | | | 226 | 21 | 12.0 | 34 | | | | | | | Red | 1+ |
| | 2400 | 98.3 r | 110 | 104/70 | 20 | 4 | | | | | | | | | | | | | | | | | | | 1+ |
| 12 Dec. | 0800 | 100 r | 140 | 110/65 | 20 | 5 | 38 | 7.41 | 0 | 146 | 3.3 | 7.5 | 2.2 | 184 | 15 | | | | | | | 0.8 | | Yell. | Neg. |
| | 1600 | 98.7 r | 132 | 98/60 | 20 | 8.5 | 36 | 7.39 | −2 | 149.5 | 3.4 | 7.8 | 3.5 | 124 | 17 | 11.8 | 35 | 11,400 | | | | | | | Neg. |
| 13 Dec. | 0800 | 98.9 r | 116 | 122/80 | 20 | 4 | 37 | 7.42 | +2 | 142 | 3.1 | | | 174 | 17 | | | | | | | | | Yell. | Neg. |
| 14 Dec. | 0800 | 98.7 r | 94 | 120/80 | | | 37 | 7.42 | 0 | 137 | 4.1 | | | 124 | 16 | 11.5 | 33 | 7,100 | | | | | | Yell. | Neg. |
| 15 Dec. | 0800 | 98.1 | 92 | 120/80 | 20 | | 37 | 7.40 | 0 | | | | | 116 | 21 | 11.8 | | | | | | | | Yell. | Neg. |
| 16 Dec. | 0800 | 98.1 | | 124/84 | | | | | | | | | | | | 13.0 | 40 | | | | | | | | |

was cyanotic (Table II). She was therefore oxygenated by mask, reintubated and placed on a Bird ventilator. During the interruption of ventilation for intubation she became cyanotic within an unusually short time. Generalized muscle rigidity, a hot skin and a rectal temperature of 105° F were first detected at 1135 hours. At this time the blood pressure was 60 mm Hg systolic, and the pulse was weak and thready and 120 per minute. Within a few minutes the pulse rate rose to 160 per minute and then shortly became uncountable.

At 1135 hours 10 mg of methoxamine was given intravenously but without effect on the blood pressure. A diagnosis of malignant hyperthermia was then assumed and the respirator was set at 100 per cent oxygen.

By 1145 hours the temperature was 109° F (rectal). Alcohol sponging and rectal cooling were begun. The patient was packed in crushed ice and placed on a hypothermia blanket over which a fan was blown. Seventy-five mg of chlorpromazine was injected. As an initial central venous pressure reading was less than 1.0 cm of water, a litre of lactated Ringer's solution was rapidly infused.

$Paco_2$ was 62 mm Hg, pH 7.04, $CO_2$ content 18 mEq/L, and base deficit 11.5 mEq at 1150 hours. An infusion of 178.4 mEq of sodium bicarbonate was commenced.

At 1155 hours the nasopharyngeal temperature registered 112° F – the highest level reached. Gastric cooling was started at this time.

At 1210 hours the serum sodium was 154 mEq/L, serum potassium 6.8 mEq/L, and serum chloride was 102 mEq/L. The $Paco_2$ had risen to 70 mm Hg, while the pH was 7.09, the $CO_2$ content 22.5 mEq/L, and the base deficit was —11 mEq.

One litre of 10 per cent glucose containing 20 units of regular insulin was started at 1215 hours.

Propranalol 1 mg was injected at 1218 hours in an unsuccessful attempt to stop the tachycardia. Solucortef 1 gm was infused one minute later.

Between 1226 and 1234 hours procaine amide 700 mg was slowly infused under EKG control.

The $Paco_2$ had fallen to 40 mm Hg by 1230 hours, while the pH had risen to 7.49, $CO_2$ content to 31.5 mEq/L, and base excess to +6 mEq. Serum potassium was now 5.4 mEq/L.

By 1245 hours, i.e. 19 minutes after the commencement of the procaine amide, the heart rate had slowed to 112 per minute, the blood pressure had risen to 90/50, and the nasopharyngeal temperature had fallen to 98° F.

At 1300 hours the temperature was 96° F (nasopharyngeal) and 95° F (rectal). Active cooling was therefore discontinued. Because of the passage of 700 ml of red urine since the termination of the operation, 500 ml of 20 per cent mannitol was commenced.

The patient remained comatose at 1310 hours. Oxygen concentration was lowered to 40 per cent and artificial hyperventilation was continued. Five units of regular insulin in 50 ml of 50 per cent glucose were given at this time and again at 1327 hours. Solucortef 1 gm was infused again at 1335 hours.

By 1355 hours the CVP had risen to 14 cm $H_2O$, the blood pressure was 110/60 and the pulse was stronger and 104 per minute.

TABLE II

TREATMENT OPERATIVE DAY

| 10 Dec. Time | $NaHCO_3$ mEq | KCl mEq | Ca Gluconate mg | Solucortef mg | Meperidine mg | Chlorpromazine mg | Promethazine mg | Methoxamine mg | Propranolol mg | Procaine Amide mg | Regular Insulin Units | 50% Glucose in DW ml | 10% Glucose in DW ml | 5% Glucose in DW ml | 5% Glucose in NS ml | Normal Saline ml | Lactated Ringer's ml | Blood ml | Rheomacrodex ml | Mannitol Gm | % $O_2$ | Bird Ventilator | Endotracheal Tube | Ice Packs | Hypothermia Blanket | Internal Cooling |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Pre Op | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Op 0955–1125 | | | | | | | | | | | | | | | | | | | | | | | In | | | |
| Post Op 1125 | | | | | | | | | | | | | | | | | | | | | | | Out | | | |
| 1135 | | | | | | | | 10 | | | | | | | | | | | | | 100 | On | In | | | |
| 1140 | | | | | | 75 | | | | | | | | | | | 1000 | | | | | | | | | |
| 1145 | | | | | | | | | | | | | | | | | | | | | | | | Yes | Yes | Yes |
| 1150 | 44.6 | | | | | | | | | | | | | | | | | | | | | | | | | |
| 1215 | | | | | | | | | | | 20 | | 1000 | | | | | | | | | | | | | |
| 1219 | | | | | | | | | 1 | | | | | | | | | | | | | | | | | |
| 1220 | | | | 1000 | | | | | | | | | | | | | | | | | | | | | | |
| 1225 | 44.6 | | | | | | | | | | | | | | | | | | | | | | | | | |
| 1226 | | | | | | | | | | 100 | | | | | | | | | | | | | | | | |
| 1227 | | | | | | | | | | 100 | | | | | | | | | | | | | | | | |
| 1228 | | | | | | | | | | 100 | | | | | | | | | | | | | | | | |
| 1229 | | | | | | | | | | 100 | | | | | | | | | | | | | | | | |
| 1230 | 44.6 | | | | | | | | | | | | | | | | | | | | | | | | | |
| 1231 | | | | | | | | | | 100 | | | | | | | | | | | | | | | | |
| 1233 | | | | | | | | | | 100 | | | | | | | | | | | | | | | | |
| 1234 | | | | | | | | | | 100 | | | | | | | | | | | | | | | | |
| 1235 | 44.6 | | | | | | | | | | | | | | | | | | | | | | | | | |
| 1245 | | | | | | | | | | | | | | | | | | | | 100 | | | | Off | Off | Off |
| 1310 | | | | | | | | | | | 5 | 50 | | | | | | | | | 40 | | | | | |
| 1327 | | | | | | | | | | | 5 | 50 | | | | | | | | | | | | | | |
| 1335 | | | | 1000 | | | | | | | | | | | | | | | | | | | | | | |
| 1430 | | | | | | | | | | | 15 | | | | | | | 500 | 500 | | | | | | | |
| 1630 | 89.2 | 80 | 1000 | | | | | | | 100 | | | | | | | | | 500 | | | | | | | |
| 1800 | | | | | | | | | | | | | | | | 250 | | | | 20 | | | | | | |
| 1830 | 89.2 | 80 | | | 20 | 20 | 20 | | | | 15 | 50 | | | | | | 500 | 500 | | | | | | On | |
| 2015 | | | | | 10 | 10 | 10 | | | | | | | | | | | | | | | | | | | |
| 2100 | | | | | 10 | 10 | 10 | | | | | | | | | | | | | | | | | | Off | |
| 2400 | 44.6 | 40 | | | 10 | 10 | 10 | | | | | | | | | | | 500 | 500 | | | | | | On | |

The rectal temperature had fallen to 93.2° F at 1430 hours. As the urine was 3+ for sugar, 15 units of regular insulin were administered subcutaneously. Because the blood pressure had fallen again to 70/40, 500 ml of rheomacrodex and 500 ml of blood were started.

By 1600 hours the blood pressure had risen to 110/60 and the pulse rate to 124 per minute. A diuresis of 1710 ml of red urine had occurred since 1230. The BUN was moderately elevated at 22 mg per cent, while the blood glucose was up to 585 mg per cent. Serum sodium was 136 mEq/L, serum chloride 90 mEq/L, and serum potassium only 2.1 mEq/L. $Paco_2$ was 46 mm Hg, pH 7.33, $CO_2$ content 22.5 mEq/L, and base deficit −2 mEq.

Eighty mEq of potassium chloride, 89.2 mEq of sodium bicarbonate, 1.0 gram of calcium gluconate, 500 ml of rheomacrodex, and 100 mg of procaine amide were infused at 1630 hours.

By 1800 hours the Hb had fallen to 8.4 Gm per cent, the Hct to 24 vol per cent and the WBC to 2,800. The infusion of 20 grams of mannitol and 250 ml of normal saline was begun.

The cooling blanket was switched on at 1830 hours since the rectal temperature had gone up to 96.8° F. By now the patient was responding to commands but because of restlessness a lytic cocktail consisting of 100 mg of chlorpromazine, 100 mg of meperidine, and 100 mg of promethazine in 500 ml of 5 per cent glucose in DW was commenced. This was administered as required in variable increments during the remainder of the day. Fifteen units of regular insulin in 50 ml of 50 per cent glucose, 89. 2 mEq of sodium bicarbonate, 80 mEq of KCl, 500 ml of blood, and 500 ml of rheomacrodex were also given intravenously.

The cooling blanket was turned off at 2100 hours when the rectal temperature had gone down to 95° F.

By 2200 hours the temperature was 93.2° F. The urine was still 3+ for sugar, 2+ for albumin, and showed 0–2 red blood cells although remaining red.

At midnight the CVP was only 4 cm $H_2O$. Consequently 500 ml of blood and 500 ml of rheomacrodex were begun. A further 44.6 mEq of sodium bicarbonate and 40 mEq of KCl were also injected. Since the rectal temperature had gone back up to 95° F, the cooling blanket was again turned on.

Twenty-five units of insulin in 500 ml of 5 per cent glucose in DW was given at 0200 hours on 11 December 1969 (Table III).

At 0300 hours 44.6 mEq of sodium bicarbonate, 40 mEq of KCl, 50 mg of solucortef, and 450 ml of 5 per cent glucose in DW were infused.

By 0500 hours the blood pressure was 104/80, the heart rate was 110 per minute, the CVP was 10.5 cm $H_2O$, and the rectal temperature was 92.8° F. The cooling blanket was switched off. One litre of 10 per cent glucose in DW containing 15 units of regular insulin was started and 89.2 mEq of sodium bicarbonate was infused.

By 0800 hours the serum potassium was still only 2.7 mEq/L. The serum calcium was 7.6 mg per cent, serum phosphorus 0.6 per cent, serum bilirubin 0.7 mg per cent (indirect), and 0.6 mg per cent (direct). The Hb had risen to 10.4 Gm per cent, Hct to 31 vol per cent, and WBC to 5,500. The CPK was greater than 20,000 i.u. and the LDH was 8,500 i.u. The urine was red, 2+ for albumin and 3+

## TABLE III

### Treatment Postoperative Days

| | $NaHCO_3$ mEq | KCl mEq | Ca Gluconate mg | Solucortef mg | Meperidine mg | Chlorpromazine mg | Promethazine mg | Regular Insulin Units | 50% Glucose in DW ml | 10% Glucose in DW ml | 5% Glucose in DW ml | 5% Glucose in NS ml | Normal Saline ml | Lactated Ringer's ml | Blood ml | Mannitol Gm | % $O_2$ | Bird Ventilator | Endotracheal Tube | Hypothermia Blanket |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 11 Dec. 0200 | | | | | 30 | 30 | 30 | 25 | | | | 500 | | | | | | | | |
| 0300 | 44.6 | 40 | | 50 | 20 | 20 | 20 | | | | 450 | | | | | | 40 | | | |
| 0500 | 89.2 | | | | | | | 15 | | 1000 | | | | | | | | | | Off |
| 0600 | | | | | 30 | 30 | 30 | | | | | | | | | | | | | |
| 0800 | 22.3 | | | 63.5 | | | | 15 | | 250 | | | | | | | | | | |
| 1200 | | | | 60 | | | | 15 | | 400 | | | | | | 20 | 20 | Off | | |
| 1335 | | | | | | | | | | | | | | | | | | | Out | |
| 1445 | | | | 40 | | | | | | | | | | 400 | 500 | | 40 | On | In | |
| 1530 | | 36 | | | | | | | | | 200 | | 100 | 600 | 100 | | | | | |
| 1600 | | | | | | | | | | | | | | | 400 | | | | | |
| 2100 | 89.2 | 20 | | 350 | 75 | 75 | 75 | 10 | | | 1200 | | | 600 | | | | | | |
| 2400 | | | | 100 | | | | | | | | | 100 | | 500 | 80 | | | | |
| 12 Dec. 0200 | | | | | | | | 10 | | | | | 130 | | 450 | | | | | |
| 0800 | 89.2 | 40 | | 100 | 75 | 75 | 75 | 10 | 1100 | | | | | | | | | Off | | |
| 1600 | | 40 | | | | | | | 1050 | | | | | | | | | | | |
| 2100 | 62.4 | 28 | 1400 | 140 | | | | 7 | 700 | | | | | | | | | | | |
| 13 Dec. 0800 | 89.2 | 50 | 600 | 180 | | | | 13 | | | 1300 | | | | | | | | Out | |
| 1600 | 89.2 | 40 | | 100 | | | | 10 | | | 1000 | 450 | | | | | | | | |
| 2400 | 89.2 | 40 | | 100 | | | | 10 | | | 1000 | | | | | | | | | |
| 14 Dec. 0100 | 27.4 | 12 | | 30 | | | | 3.6 | | | 300 | | | | | | | | | |
| 0800 | 71.4 | 32 | | 80 | | | | 9.6 | | | 800 | | | | | | | | | |
| 1600 | 89.2 | 40 | | 100 | | | | 10 | | | 1000 | | | | | | | | | |

for sugar. Fifteen units of regular insulin in 250 ml of 10 per cent glucose in DW, 400 ml of 5 per cent glucose in DW, 22.3 mEq of sodium bicarbonate, and 63.5 mg of solucortef were infused.

An EKG taken at 0930 hours showed non-specific myocardial damage.

Solucortef 60 mg, 400 ml of 10 per cent glucose containing 15 units of regular insulin, and 20 grams of mannitol were infused at 1200 hours. The Bird ventilator was disconnected as the patient seemed able to breathe normally without assistance.

She was extubated at 1335 hours but by 1415 hours the respirations were again shallow and she was reintubated with a nasotracheal tube and put back on the Bird ventilator.

The patient was conscious but with poor muscle power by 1600 hours. The CVP was down to 5 cm $H_2O$, the heart rate was 112 per minute and the blood pressure 94/70. The rectal temperature was up to 94.1° F. $Paco_2$ was 37 mm Hg, pH 7.33, $CO_2$ content 20.5 mEq/L, base deficit −5 mEq, serum sodium 146 mEq/L, serum chloride 104 mEq/L, serum potassium 2.8 mEq/L, BUN 21 mg per cent, blood glucose 226 mg per cent, Hb 12 Gm per cent, and Hct 30 vol per cent. Since noon one litre of lactated Ringer's solution, 200 ml of 5 per cent glucose in DW, 100 ml of normal saline, 1000 ml of blood, solucortef 40 mg, and KCl 36 mEq had been infused.

By 2100 hours a further 1200 ml of 5 per cent glucose in DW, 600 ml of lactated Ringer's Solution, regular insulin 10 units, solucortef, sodium bicarbonate 89.2 mEq, and KCl 20 mEq had been administered.

At midnight the rectal temperature was 98.3° F. The urine was less red than previously. Since 2100 hours solucortef 100 mg, mannitol 80 mg, 500 ml of blood, and 100 ml of normal saline had been given. Throughout this day a total dosage of 155 mg each of chlorpromazine, promethazine and meperidine had been infused.

On the second post-operative day the temperature ranged between 98.7 and 100.0° F, the CVP between 8.5 and 4 cm $H_2O$, the heart rate from 90 to 140 per minute and the blood pressure between 110/70 and 98/60. The urine became straw coloured.

An EKG showed a sinus tachycardia and electrolyte abnormalities. A chest X-ray revealed a normal cardiac silhouette and a pneumonic infiltration of both bases which was more marked on the right side. Laboratory results were $Paco_2$ 36 mm Hg, pH 7.39, $CO_2$ content 23 mEq/L, base deficit −2 mEq, serum sodium 149.5 mEq/L, serum chloride 114 mEq/L, serum potassium 3.4 mEq/L, serum calcium 7.5 mg per cent, serum phosphorus 2.2 mg per cent, BUN 15 mg per cent, blood glucose 184 mg per cent, Hb 11.8 Gm per cent, Hct 35 vol per cent, WBC 11,400, and urine negative for sugar. The hypothermia blanket was removed. Intravenous drug and fluid therapy consisted of solucortef 240 mg, sodium bicarbonate 151.6 mEq, KCl 108 mEq, regular insulin 27 units, calcium gluconate 1.4 gm, chlorpromazine 75 mg, promethazine 75 mg, meperidine 75 mg, 5 per cent glucose in DW 2850 ml, blood 450 ml, and normal saline 130 ml.

On 13 December 1969 (third post-operative day), the patient's ventilatory capacity was considerably improved and she was extubated without difficulty.

Except for the persistent tachycardia ranging between 116 and 134 per minute all vital signs were within normal limits. While skeletal muscle power was objectively improved the patient complained of extreme muscle weakness, especially of the leg muscles, as well as muscle pain and tenderness. The left leg was found to be swollen. Serum potassium was 3.1 mEq/L, blood glucose was 174 mg per cent. All other laboratory values were within normal limits. Solucortef 380 mg, regular insulin 33 units, sodium bicarbonate 267.6 mEq, potassium chloride 130 mEq, erythromycin 3.0 grams, 5 per cent glucose in normal saline 450 ml, and 5 per cent glucose in DW 3300 ml were infused. The patient had begun to take fluids orally.

By 14 December both legs had become swollen and painful. The heart rate had slowed to between 92 and 112 per minute. Other vital signs were normal. The blood sugar was 124 mg per cent. The BUN, serum electrolytes and blood gases were all normal. Sodium bicarbonate 188 mEq, KCl 84 mEq, and 5 per cent glucose in DW 2100 ml, were given intravenously.

Vital signs continued normal on 15 December except for the moderate tachycardia. The Hb had risen to 13 Gm per cent and the Hct to 40 per cent. The urine while normal in output and colour and negative for sugar continued to show a trace of albumin. A persisting pneumonic infiltration of the RLL could still be seen on the chest X-ray. Although still very weak and requiring considerable assistance, the patient was got up in a chair. As she was taking fluids well, all intravenous fluid therapy was discontinued.

The remainder of the post-operative course was uneventful. The patient was discharged on the 21st post-operative day, 31 December 1969. For several months she continued to complain of easy fatigue and generalized muscular weakness. However, eight months later she appeared to be fully recovered. At that time the CPK was 60 i.u., LDH 120 i.u., SGOT 26 i.u., serum calcium 9.0 mg per cent, serum phosphate 3.6 mg per cent, serum potassium 4.0 mEq/L, serum magnesium 1.7 mg per cent, serum lactate 1.63 $\mu$M/L, and serum pyruvate 0.2 $\mu$M/L. The serum $T_3$, PBI, radioactive iodine uptake, BMR and urine catecholamines were all within normal limits. Electromyography was also normal. The results of muscle biopsy studies carried out at the University of Toronto have been partially detailed by Kalow *et al.*[24] The remainder will be detailed in a future publication.

## Discussion

A number of points important in the diagnosis and management of malignant hyperthermia are raised by this case.

A prior normal anaesthetic does not rule out the development of malignant hyperthermia during a subsequent anaesthetic. This patient had a previous uneventful general anaesthetic. In other recorded cases the hyperthermic anaesthetic was preceded by as many as three apparently normothermic anaesthetics.[25]

Malignant hyperthermia may develop late during the course of the anaesthetic so vigilance must be maintained throughout the entire procedure. The relatively modest elevation of the CPK after recovery (60 i.u.) may indicate that this patient's inherent defect was relatively mild and that therefore fairly large and

prolonged concentrations of anaesthetic agents were required to trigger an acute episode.

The time of therapy is of critical importance especially for temperature control and potassium replacement therapy. It has been previously observed[25] that although vigorous cooling is essential to effect a temperature reduction and so to prevent irreversible cellular damage, too prolonged cooling must be avoided, otherwise an equally dangerous hypothermia with an apparent loss of central temperature control may develop. Active cooling of this patient had to be discontinued and then restarted several times in order to maintain her temperature in the moderate hypothermic range. This necessitated continuous temperature monitoring.

The early transient rise of serum potassium due to leakage across damaged cell membranes was shortly replaced by a prolonged potassium depletion, probably because of renal loss. Therefore frequent serum potassium measurements were made to determine the requirement for potassium chloride infusions and for judging their amount and timing.

Many agents used had several interrelated actions – some desirable and some undesirable. Examples are sodium bicarbonate, mannitol, insulin, and solucortef. These were all useful in moderating the initial hyperkalaemia and so in ameliorating its arrhythmic effects on the heart. Each had other significant actions. The continued use of insulin even after the onset of hypokalaemia may have been useful not only in shifting potassium back into the cells but also in improving glucose uptake into the cells and thereby in restoring depleted ATP stores.[26] Although the large doses of sodium bicarbonate necessary to correct the metabolic acidosis and to control the early hyperkalaemia did cause some mild elevation of serum sodium, this undesirable state of affairs was prevented from getting out of hand by the concomitant use of mannitol. Mannitol was also of value in dislodging myoglobin from the renal tubules and so in forestalling an acute renal failure. The large doses of solucortef may have assisted in restoring the integrity of the cell membranes.

Although this patient was young and healthy with normal pulmonary function prior to anaesthesia, a high concentration of oxygen and hyperventilation were required to prevent clinical cyanosis, and respiratory acidosis developed in spite of the hyperventilation. Increased oxygen consumption and carbon dioxide production by the hypermetabolic cells could account for these changes. There would be an accelerated extraction of oxygen from and an increased addition of carbon dioxide to the capillary blood. Therefore if laboratory facilities permit, venous as well as arterial oxygen tension measurements would probably be of assistance in determining the availability of oxygen to the tissues.

This patient received a large dose of procaine amide (700 mg) at the height of her fever. Its administration was followed not only by the cessation of the previously refractory arrhythmia but also by relief of the skeletal muscle rigidity and by a rapid fall in the temperature – from 112° F to 95° F within a period of 19 minutes. Such a precipitous temperature reduction is most remarkable because in other reported malignant hyperthermia patients, even the most extreme cooling efforts have been followed by a continued temperature rise for some time or by a

very slow rate of temperature fall.[25] Procaine amide is known to accelerate calcium uptake into the sarcoplasmic reticulum and to prevent calcium loss from the sarcoplasmic reticulum.[27] It has been suggested that the rigid form of malignant hyperthermia is associated with an elevated intracytoplasmic calcium due to an inability of some membrane (e.g. sarcoplasmic reticulum, plasmic, transverse tubular, or mitochondrial) to store calcium during the relaxation phase.[24,28] Such an elevation would lead to prolonged rigidity of both skeletal and cardiac muscle due to activation of myosin ATPase and to accelerated heat production secondary to the associated accelerated hydrolysis of ATP and of the various reactions which replenish ATP.[28] The use of procaine amide would reverse this cytoplasmic calcium elevation and so would relieve both the rigidity and the fever.


## Summary

We have reported a case of delayed malignant hyperthermia occurring in a young healthy female. The temperature rose to 112° F, skeletal muscle rigidity, ventricular tachycardia and hypotension, respiratory and metabolic acidosis, hyperkalaemia followed by hypokalaemia, serum enzyme elevations, and a moderate hypocalcaemia were all observed. Successful treatment consisted of vigorous cooling, hyperventilation, 100 per cent oxygen, procaine amide, sodium bicarbonate, insulin with glucose, mannitol, solucortef, calcium gluconate, potassium chloride, meperidine, promethazine, and chlorpromazine.

## Résumé

Nous rapportons un cas d'hyperthermie maligne a retardement; il s'agissait d'une jeune femme en santé. La température s'est élevée jusqu'à 112° F; elle a présenté de la rigidité des muscles squelettiques, de la tachycardie ventriculaire et de l'hypotension, de l'acidose respiratoire et métabolique, de l'hyperkaliémie suivie d'hypokaliémie, de l'élévation des enzymes sériques et une légère hypocalcémie. Le traitement a été un succès; il a consisté en un vigoureux refroidissement, de l'hyperventilation, de l'oxygène à 100 pour cent, de la procaïne amine, du bicarbonate de sodium, de l'insulin et du glucose, du mannitol, du solucortef, du gluconate de calcium, du chlorure de potassium, de la mépéridine, de la promethazine, et de la chlorpromazine.


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