MALIGNANT HYPERPYREXIA AND ISOFLURANE

A Case Report

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Malignant hyperpyrexia is an inherited condition which may present during general anaesthesia as a progressive increase in body temperature associated with hypercapnia, metabolic acidosis and muscle rigidity. Halothane and succinylcholine are the most commonly suspected triggering agents.

CASE REPORT

A 50-yr-old man was admitted for pyelolithotomy. He was noted to be in good general health, although with a plethoric appearance, on the preoperative visit. His haemoglobin concentration was 17 g dl⁻¹; he was a smoker. He had received a dental anaesthetic in the 1950s. Temazepam 30 mg was prescribed as premedication.

Anaesthesia

Following the insertion of an appropriate cannula to a vein, anaesthesia was induced with sodium methohexitone 160 mg and maintained with nitrous oxide and isoflurane in oxygen. Tracheal intubation was facilitated with vecuronium 8 mg; muscle relaxation was adequate for this purpose. Fentanyl 100 µg was given at this stage and an extradural catheter inserted at T7. The patient was transferred to the operating table and positioned for surgery.

Monitoring consisted of an ECG, measurement of arterial pressure (Dinamap), end-tidal carbon dioxide concentration (Datex) and neuromuscular transmission. The patient’s lungs were ventilated using a Manley ventilator, and the tidal volume monitored (Wright's respirometer).

Following the positioning of the patient, 10 ml of 0.5 % bupivacaine plain solution was injected to the extradural space. Figure 1 summarizes the subsequent course of the anaesthetic.

One hour following the induction of anaesthesia the patient was observed to be hypercapnic, the end-tidal carbon dioxide concentration having increased from its original value of 4.8 % to 6.0 %. It was thought at this stage to be a result of underventilation and, after extensive examination of the ventilator and the ventilator tubing, the minute volume was increased to 8 litre min⁻¹ and, subsequently, to 12 litre min⁻¹. Calibration of the end-tidal carbon dioxide monitor was carried out and the carbon dioxide cylinder removed from the back of the anaesthetic machine to rule out inadvertent leakage into the fresh gas supply. The patient was noted to be sweating profusely and an axillary temperature was recorded as 37.5 °C.

At the same time fentanyl 100 µg was given in case the sweating was caused by inadequate depth of anaesthesia. Additionally, vecuronium 2 mg was given. The end-tidal carbon dioxide concentration continued to increase; the temperature had now increased to 38 °C. A provisional diagnosis of malignant hyperpyrexia was made and the patient was given dantrolene 100 mg i.v. At the same time arterial blood-gas tensions and serum electrolyte concentrations were measured.

SUMMARY

Malignant hyperpyrexia developed, and was successfully treated, in a 50-year-old man undergoing pyelolithotomy. Early diagnosis with the assistance of end-tidal carbon dioxide monitoring facilitated prompt treatment with i.v. dantrolene. A positive muscle biopsy subsequently confirmed the diagnosis. The only likely triggering agent used was isoflurane.


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Active cooling was undertaken with ice packs and the patient received sodium bicarbonate 50 mmol. Ventilation was continued with 100% oxygen and surgery was completed rapidly. The patient's temperature was now 38.5 °C and his end-tidal carbon dioxide concentration was over 10%. Initial blood-gas analysis showed a mild acidosis with a base deficit of -3 mmol litre$^{-1}$ with a $P_{a\text{CO}_2}$ of 8.6 kPa. Repeat blood-gas analysis following the administration of bicarbonate and the dantrolene showed an improvement in arterial carbon dioxide concentration which had decreased to 6.2 kPa; the base deficit remained at -3 mmol litre$^{-1}$. By this time the patient was awake and, as he was distressed by the presence of the tracheal tube, the trachea was extubated and he breathed 40% oxygen via an anaesthetic face mask.

The patient was transferred to the Intensive Care Unit (ICU) for further management. His subsequent treatment involved ensuring a large volume urine output and careful monitoring of temperature. His serum creatinine phosphokinase (CPK) and urinary myoglobin concentrations were monitored for 3 days after operation (table I). The highest recorded CPK concentration was 1360 iu litre$^{-1}$; no myoglobin was detected in the urine.

He was discharged from the ICU on the 3rd day after operation, without any further hyperpyrexic episodes. The following day his temperature

### Table I. Concentrations of serum electrolytes, and myoglobin in the urine

<table>
<thead>
<tr>
<th></th>
<th>Before op.</th>
<th>After op.</th>
<th>Days after operation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Serum potassium (mmol litre$^{-1}$)</td>
<td>4.3</td>
<td>5.3</td>
<td>4.6</td>
</tr>
<tr>
<td>CPK (iu litre$^{-1}$)</td>
<td>—</td>
<td>147</td>
<td>1360</td>
</tr>
<tr>
<td>Urinary myoglobin</td>
<td>—</td>
<td>nil</td>
<td>nil</td>
</tr>
</tbody>
</table>
began to increase once more. However, this was secondary to a wound infection. This infection resolved slowly; in other respects the patient made an uneventful recovery. Referral for follow-up muscle biopsy and related in vitro tests was made to the Malignant Hyperpyrexia Investigation Unit at St James’s University Hospital, Leeds. These tests confirmed the patient’s susceptibility to malignant hyperpyrexia. All investigations at this unit were carried out in accordance with the procedure accepted by the European Malignant Hyperpyrexia Group (Ellis et al., 1984).

**DISCUSSION**

The report describes the successful management of an episode of malignant hyperpyrexia. Several factors make it worth reporting.

The measurement of end tidal carbon dioxide concentration is a non-invasive method of detecting malignant hyperpyrexia in its early stages (Baudendistel et al., 1984). For some years capnographs have been available on every anaesthetic machine at this hospital. This case shows that in a hyperpyrexial episode it was a much more sensitive warning device than temperature.

The steady increase in end-tidal carbon dioxide concentration in the face of increasing minute volume was responsible for the prompt diagnosis and the treatment with dantrolene. As a result, the patient developed only a mild acidosis and a peak axillary temperature of 38.5 °C. Moreover, he exhibited only a minor increase in serum CPK concentration, and this may in part have been the result of prompt treatment.

Although the patient had received a previous dental anaesthetic, the details were unavailable. If malignant hyperpyrexia triggering agents were used at that time the duration of exposure may have been short and any mild metabolic disturbance could have passed undetected. Even in this case, if a capnograph had not been used, the diagnosis might have been delayed.

On this occasion isoflurane would appear to be the most likely trigger agent. Vecuronium was the only neuromuscular blocking drug used and there have been no reports of its implication as a triggering agent. Bupivacaine and nitrous oxide are probably safe to use, and are used in patients already known to be susceptible to malignant hyperpyrexia without complication. Although there have been two previous reports of malignant hyperpyrexia occurring in association with isoflurane, both patients had received suxamethonium and in neither patient was the diagnosis confirmed by muscle biopsy (Boheler et al., 1982; Joseph, Shah and Viljoen, 1982). In this case, the patient received a trigger-free anaesthetic, apart from the isoflurane. As the patient had a thoracic extradural catheter in situ, the inspired concentrations of isoflurane were low, perhaps explaining the slow development of the hyperpyrexia, and again illustrating the sensitivity of the monitoring of end-tidal carbon dioxide concentration in diagnosis.

Initial studies on isoflurane have shown that it can produce a three-fold increase in caffeine-induced contraction of the frog sartorius muscle at clinical concentrations (this compares with a four-fold increase for enfurane and an 11-fold increase with halothane (Wade and Wendell, 1981)). It is, therefore, not surprising that it can cause malignant hyperpyrexia in man.

This would appear to be the most convincing report of isoflurane-induced malignant hyperpyrexia. The fortuitous use of a technique in which isoflurane was the only likely triggering agent enables this conclusion to be reached.

**REFERENCES**


