Malignant hyperthermia in a patient with King syndrome

LYNNE K. PIPPIN, MB, FFARCS
JEFFREY ARMSTRONG, MD
TERRY SCHREIBER, CRNA, BSN
Kansas City, Kansas

A case of malignant hyperthermia is reported in a child who subsequently is diagnosed as having King syndrome, a rare genetic disorder first described in 1960. Several unique features associated with this case make it clinically noteworthy. It is important to recognize the patient with King syndrome preoperatively, as King syndrome is a disorder universally linked with the development of malignant hyperthermia during volatile anesthesia.

The syndrome of malignant hyperthermia (MH) under general anesthesia was described initially by Denborough and Lovell in 1960. Although much is known about the characteristics of the syndrome, the exact pattern of inheritance still is elusive, making preanesthesia identification of susceptible individuals extremely difficult.

This report deals with a case of MH under halothane anesthesia in a child who subsequently is identified as having King syndrome, a disease known to include MH susceptibility.

Case report

A 30-month old, 10.1 kg black male, the product of an uncomplicated pregnancy, presented for repair of a congenital cleft palate. There was no family history of anesthetic complications, but it was positive for hospitalizations at 12 and 22 months of age for respiratory infections.

A previous attempt to repair the cleft palate at age 23 months was aborted, because of what were described as tonic-clonic seizures following the induction of anesthesia with halothane. The management of the difficult airway was complicated by mucus plugging the endotracheal tube. The possibility of MH was considered, but dismissed, based on arterial blood gases (ABGs) demonstrating a pure respiratory acidosis, lack of tachycardia, absence of temperature elevation, normal creatine phosphokinase (CPK) values and bilateral basilar pneumonia on postoperative chest x-ray. An uneventful recovery followed this episode, and palate repair was rescheduled.

On admission, the patient was observed to have markedly delayed intellectual and psychomotor development and was below the fifth percentile in height and weight. He was noted to have the following abnormal characteristics: generalized hypotonia, downslanting palpebral fissures, bilateral ptosis, crowding/irregular dentition, cleft palate, micrognathia, low-set ears, marked pectus carinatum, winged scapulae, lumbar lordosis and thoracic kyphosis (Figure 1). His wrist and elbow extension was limited and his hands and feet were narrow and unusual in appearance, with bilateral flexion contractures of the interphalangeal joints. His gait was unusually wide-based and his testes undescended (Figure 1). His lungs were clear to auscultation and his heart sounds were regular and without murmur. Hemoglobin and hematocrit were 10.5 g/dl and 34.4%, respectively. A chest x-ray revealed...
bilateral fibrotic scarring. His vital signs were: temperature 36.8°C, heart rate (HR) 120, blood pressure (BP) 110/60 and respiratory rate (RR) 32.

An inhalation induction was performed using halothane, and an intravenous line was started. Endotracheal intubation was attempted under inhalation anesthesia, but was hampered by a generalized increase in muscle tone which was attributed to inadequate anesthesia. Ventilation was facilitated using a nasal airway. Vital signs were consistent with those obtained prior to induction. Anesthesia was supplemented with lidocaine 20 mg, atropine 0.12 mg and succinylcholine 10 mg intravenously. Tracheal intubation then was accomplished.

Marked whole-body rigidity was observed immediately. The patient’s vital signs were: temperature 37.1°C, HR 170, BP 130/70 and RR controlled at 30. His temperature rapidly increased to 37.8°C. Anesthesia was discontinued immediately.

Ten minutes after the initial administration of dantrolene, the patient’s vital signs were: temperature 37.4°C, HR 150, BP 120/70, RR controlled at 35. ABGs revealed pH 7.23, PaO₂ 331, PaCO₂ 53, BE -6. The patient was transferred to the recovery room and an additional 10 mg of dantrolene was administered. Diazepam 3 mg total and pancuronium 1 mg facilitated mechanical ventilation. A chest x-ray revealed a left lower lobe atelectasis.

Several hours later, the patient’s ABGs and vital signs were within normal limits, except for a mild fever which was attributed to atelectasis. Serum CPK was 292 IU/1, with normal isoenzymes, the next day. In the intensive care unit, the patient developed recurrent atelectasis, pneumonia and oliguria without evidence of myoglobinuria. Urine output gradually improved over the first seven days. Attempts at ventilator weaning and extubation were complicated by atelectasis secondary to copious secretions and ineffective coughing. Extubation was accomplished on his 17th ICU day, and three days later the patient was transferred to the ward.

Genetic consultation confirmed a diagnosis of King syndrome. After three uneventful days on the ward, the patient was transferred to a hospital near his home, where he died two days later following a cardiopulmonary arrest. Postmortem examination recorded the cause of death as severe bronchopneumonia and pulmonary edema with congestion of the liver, spleen and kidneys.

Discussion

MH can be triggered by a variety of anesthetic agents, with the onset occurring most abruptly when succinylcholine is employed. Symptomatic treatment results in a 60-70% mortality, while aggressive therapy including dantrolene sodium reduces mortality to 10%.

The genetics of MH are controversial and complex, and some are arguing that it may be autosomal dominant with reduced penetrance and variable expressivity. Others refute reduced penetrance, while still others feel that the pattern of inheritance fits no known genetic model.

In 1973, King and Denborough described the occurrence of MH in four white male patients.
who exhibited anomalies which included small stature, delayed motor development, thoracic kyphosis, lumbar lordosis, pectus carinatum, hypognathia, low-set ears, webbed necks, antimongoloid slant of palpebral fissures and cryptorchidism.King’s original description stressed the susceptibility of these patients to MH. It also suggested that CPK normality precludes susceptibility. However, it now is appreciated that CPK is elevated in only 70% of susceptibles and therefore serves as an unreliable predictor. Gronert described the King syndrome as “the only disorder that apparently always involves malignant hyperthermia.” In contrast to the initial description, females may similarly manifest the disorder. Table I summarizes eight previously reported cases of the syndrome, including the patient discussed here, for comparison. This patient was unique in that he was considerably younger than the patients described previously and was black.

### Table I

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td># Patients</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Sex</td>
<td>mmmmm</td>
<td>m</td>
<td>m</td>
<td>m</td>
<td>f</td>
<td>m</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>10-13</td>
<td>10</td>
<td>6</td>
<td>7</td>
<td>12</td>
<td>2.5</td>
</tr>
<tr>
<td>Race</td>
<td>Cauc</td>
<td>Cauc</td>
<td>Cauc</td>
<td>Hisp</td>
<td>Cauc</td>
<td>black</td>
</tr>
<tr>
<td>Stature &lt;10%</td>
<td>+ + + +</td>
<td>?</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Delayed motor</td>
<td>+ + + +</td>
<td>+</td>
<td>?</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>development</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal intelligence</td>
<td>+ + + +</td>
<td>?</td>
<td>?</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Hypotonia</td>
<td>+ + + +</td>
<td>?</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Winged scapulae</td>
<td>+ - - +</td>
<td>?</td>
<td>?</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Kyphoscoliosis</td>
<td>+ + + +</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Pectus carinatum</td>
<td>+ + + +</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Malar hypoplasia</td>
<td>+ + + +</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Downslanted palpebral fissures</td>
<td>+ + - +</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Hypoplastic jaw</td>
<td>+ + + +</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Ptosis</td>
<td>- + + +</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Low-set ears</td>
<td>+ + + +</td>
<td>?</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Undescended testicles</td>
<td>+ + + +</td>
<td>?</td>
<td>+</td>
<td>+</td>
<td>na</td>
<td>+</td>
</tr>
</tbody>
</table>

+ indicates characteristic present in patient
- indicates characteristic not present in patient
? indicates status of characteristic not known in patient
Hisp = Hispanic
Cauc = Caucasian
na = not applicable

*Journal of the American Association of Nurse Anesthetists*
The induction of anesthesia in this case included agents known to trigger MH, with the patient experiencing a rapid temperature elevation concomitant with other manifestations of MH. The immediate initiation of definitive therapy apparently aborted a continued temperature rise and progression of the syndrome.

Although making a diagnosis of King syndrome prior to giving an anesthetic obviously is important, most cases have been noted after an episode of MH has occurred. The case discussed here illustrates the susceptibility of patients with King syndrome to MH and the need to identify patients with this syndrome prior to the induction of anesthesia.

REFERENCES


AUTHORS

Lynne K. Pippin, MB, FFARCS, is a staff anesthesiologist at Bethany Medical Center, Kansas City, Missouri. She obtained her MB at Guy's Hospital, London, England, and completed her Senior Registrar in Anaesthetics at the Bristol Royal Infirmary, Bristol, England.

Jeffrey Armstrong, MD, is an assistant professor of anesthesiology at the University of Kansas Medical Center, Kansas City, where he also completed his medical degree and anesthesia residency.

Terry Schreiber, CRNA, BSN, is a nurse anesthetist in Jacksonville, Florida. His nursing and anesthesia education were obtained at the University of Kansas in Kansas City.