Delayed awakening from anesthesia may be a difficult diagnostic problem, particularly in a previously healthy patient undergoing non-life-threatening surgery. The following case report should illustrate how this problem may be both a public health and medical-legal issue which affects all personnel who participate in patient care.

**REPORT OF A CASE**

An eight-year-old girl was scheduled for elective meatoplasty to correct a scarred external auditory canal caused by a chronically draining right middle ear. She had received no premedications prior to arriving in the preoperative playroom directly from the admitting office. Past medical history obtained from the patient's mother just prior to surgery revealed psychomotor retardation, good general health, and no history of previous surgery, anesthesia, or drug ingestion. Preoperatively, the child was playful and alert. Physical examination was unremarkable except for psychomotor retardation. The complete blood count and urinalysis obtained preoperatively were normal.

Anesthesia was induced and maintained with nitrous oxide and halothane. Two doses of morphine (0.1 mg/kg) were given iv 60 min and 30 min prior to awakening to treat persistent tachycardia perceived secondary to light anesthesia, and also to facilitate a smooth emergence from anesthesia. Otherwise, surgery (confined to the external auditory canal) and anesthesia were uneventful. The trachea was extubated while the child was well-anesthetized so that coughing could be avoided.

In the recovery room, continuous humidified oxygen was given and constantly attended by a nurse. After one hour, she remained responsive only to deep pain. Naloxone, 0.15 mg, was given iv two times to reverse depression presumed secondary to the narcotic but only brief arousal occurred; otherwise, she remained somnolent. The rest of her neurologic examination revealed good motor strength in all extremities, brisk and symmetric deep tendon reflexes, plantar flexor responses bilaterally, and intact cranial nerves with 1-mm equal and round pupils. No other signs or symptoms were noted that could account for her somnolence. After four hours, she was transferred to the intensive care unit (ICU) because of delayed awakening.

On admission to the ICU, her vital signs were normal. Physical examination was unremarkable except for coma responsive only to deep pain; the neurologic examination was unchanged. Blood urea nitrogen, serum sodium, potassium, chloride, bicarbonate, blood glucose, liver enzymes, and analysis of arterial blood gases were within normal limits. Throughout the next 24 hours, she demonstrated a pattern of intermittent arousal and somnolence. When aroused, she could follow commands (hand squeezes), stand, and recognize her mother. The mother also was noticed to be administering clear fluids to the child even after requests by the ICU nurses not to do so. When not actively aroused, the patient again became somnolent. Her aunt also reported at this time that the patient frequently had trouble awakening at home. Neurologic and psychiatric consultants were puzzled by her condition.

During the second 24 hours in the ICU, her mental status improved. She was able to sit or stand for several minutes without becoming somnolent. A drug screen was obtained empirically and she was transferred to a hospital room. During the first four hours in a hospital room, the mother was constantly with the patient. On several occasions, nurses observed the mother to be forcing fluids into the child, even when the patient was not fully alert. While being examined by a physician, the patient suddenly sustained a cardiac arrest. Cardiopulmonary resuscitation was begun immediately, but efforts were unsuccessful. During the resuscitation, the previously obtained drug screen was reported as positive for phenothiazines.

As soon as the resuscitative efforts were discontinued, all physicians', nurses', and pharmacy records were reviewed. No nurse or physician had recorded any clues of phenothiazine overdose such as orthostatic hypotension, dry mouth, or nasal stuffiness. There was no record of any phenothiazines being ordered, obtained, or administered. No phenothiazines were available in the nursing stations. Since the pharmacy utilizes a unit-dose system, any phenothiazines released would have been recorded by the pharmacy. The Medical Examiner's office and hospital attorney were alerted.
Gross autopsy findings by the Office of the Medical Examiner (L.R.) were consistent only with prolonged resuscitation. Toxicologic examination was performed by a modification of the method of Goldbaum and Dominguez. Free chlorpromazine was determined by gas chromatography using a flame ionization detector; combined levels of chlorpromazine and its metabolites were done by ultraviolet spectrophotometry.

Table 1 lists the concentrations of free chlorpromazine and chlorpromazine and its metabolites in a 5 A.M. blood sample on the day of death, in blood obtained during autopsy and various postmortem tissue concentrations. The presence of chlorpromazine in the 5 A.M. blood sample established that the child had been receiving chlorpromazine in the past, and the large increase in concentrations between the 5 A.M. and blood sample from the autopsy strongly indicates that she had received a large dose of chlorpromazine after 5 A.M. on the day of her death.

Since the mother was the only person other than hospital personnel who had access to the child, the case was referred to the United State's Attorney's office. Their investigation revealed that the mother had severe psychiatric problems, had received psychiatric assistance, and had filled prescriptions for large doses of chlorpromazine. We also discovered that the mother was known to the child abuse clinic at our hospital and that official records were in conflict with the history given by the mother. Records of previous hospital care described the mother's refusal to follow physician advice and documentation of abnormal drowsiness in the patient also were uncovered. The findings were presented at a hearing before a grand jury which returned an indictment of first degree murder against the mother.

A few weeks later, prior to the case going to jury trial, the mother was found dead at home.

**DISCUSSION**

For medical-legal reasons, it was necessary to establish that the tissue levels were in a toxic range; that is, that the cardiac arrest was not an idiosyncratic reaction. We also had established that the drug had not been administered therapeutically or inadvertently by hospital personnel. The latter was excluded by the investigation of hospital records. Documenting the levels to be in a toxic range is difficult because chlorpromazine has a complex metabolism with multiple metabolites of varying half-lives. No absolute level in humans has been found that all toxicologists would agree is the minimal amount needed to produce a fatal reaction. Many fatalities have occurred in patients taking chlorpromazine in therapeutic dosages, and until recently, only a few cases had postmortem toxicologic analysis. Curry states that any blood level greater than 0.1 mg/dl is significant. LeCstma and Koenig reported eight fatal cases in adults with blood levels of 0.2–4.4 mg/dl. The levels in this case are within lower levels of that range, and when considered in terms of drug weight/kg of body weight, are higher. Cardiac toxicity from chlorpromazine may be more severe in young patients, and, thus, significant cardiovascular effects may occur at lower blood levels.

No fatal case of chlorpromazine poisoning in a child undergoing anesthesia for surgery has been reported. Rivera-Calimlin et al. studied psychotic children receiving high doses of chlorpromazine and found blood levels greater than 0.01 mg/dl to be associated with hypotension and seizures, while most children with levels over 0.001 mg/dl were drowsy. The upper level recommended for children was 0.008 mg/dl. The blood level during autopsy in this case was 0.15 mg/dl, which is much higher than any previously reported in children, and probably high enough to precipitate cardiac arrest.

Therefore, the 5 A.M. blood toxicologic analysis confirmed that the patient was under the influence of chlorpromazine in the postoperative period, and her mental status alteration during that time could be best explained by the drug effect. However, since the first phenothiazine level was more than 24 hours after the surgery, we can only speculate that the altered mental status in the first 24 hours was secondary to phenothiazine given in the perioperative period. The seven-fold increase of free chlorpromazine in the autopsy blood, the fact that peak plasma levels of chlorpromazine usually occur within two hours of an oral ingestion, and other information concerning the mother's behavior and history indicate that the cardiac arrest occurred following a large dose of chlorpromazine probably administered by the mother within several hours preceding the cardiac arrest.

Clinically, this case impacts on three major areas: the "family unit" concept of care of the hospitalized child; the need for available integrated, unified, interdepartmental system of medical records, and the problem of delayed awakening from anesthesia. The "family unit" concept of care attempts to involve the family as much as possible in the child's care, especially in situations of intensive care and surgical experiences. The rapid emergence of short stay units in pediatric surgery programs is based on the integration of the family into the child's care. The "family unit" concept of care works extremely well in nearly all cases. However, in the presence of severe disturbance of one or both parents, as demonstrated in this case, the concept may not work well. Unified integrated records should be available and

**Table 1. Results of Toxicologic Analysis**

<table>
<thead>
<tr>
<th></th>
<th>Chlorpromazine and Chlorpromazine Metabolites (mg/dl)</th>
<th>Free Chlorpromazine (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 A.M. blood</td>
<td>0.12</td>
<td>0.02</td>
</tr>
<tr>
<td>Autopsy blood</td>
<td>0.24</td>
<td>0.15</td>
</tr>
<tr>
<td>Bile</td>
<td>3.0</td>
<td>—</td>
</tr>
<tr>
<td>Liver</td>
<td>3.2</td>
<td>7.6</td>
</tr>
<tr>
<td>Lung</td>
<td>1.9</td>
<td>0.5</td>
</tr>
<tr>
<td>Kidney</td>
<td>1.1</td>
<td>0.2</td>
</tr>
</tbody>
</table>

* 12 hours prior to death.
reviewed by anesthesiologists to alert them to potential child abuse by parents.

This case is the only report of delayed awakening from anesthesia due to probable child abuse, although child abuse masquerading as other illness has been reported. Other causes of delayed awakening include the anesthetic agent, hypoxia, hypercarbia, hypoglycemia, electrolyte derangements, hyperthermia, other drugs, and surgical complications. Of the numerous factors that may account for delayed awakening, the anesthesiologist should be aware that preoperative or postoperative undocumented or unauthorized drug administration are possible etiologic factors.

In summary, the goal of the "family unit" concept of care is to involve the family as much as possible in the care of the hospitalized child. Our case demonstrates that the family cannot universally be relied on to provide care and accurate information. Because of this observation, we recommend: 1) screening the parents for child abuse before utilizing the "family unit" concept of pediatric hospital care; 2) monitoring parents when administering any substance to their hospitalized child; and 3) obtaining a drug screen on patients who exhibit unexplained or unusual patterns of awakening from anesthesia.

The authors acknowledge the help of Barry Salzman, Esq., former assistant U. S. Attorney for the District of Columbia, and Homicide Detective, William G. Steakley, of the District of Columbia Metropolitan Police Department.

REFERENCES

2. Curry AS: Advances in Forensic and Clinical Toxicology. Cleveland, CRC Press, 1972, pp 120-126

Anesthesiology
58:180-182, 1983

Malignant Hyperthermia in Duchenne Muscular Dystrophy


Duchenne muscular dystrophy (DMD) is the most severe and rapidly progressive form of the common muscular dystrophies. Muscle biopsy is an essential part of the laboratory evaluation and usually must be obtained during general anesthesia because the patients are usually pediatric patients.

Anesthesia-related cardiac arrest and rhabdomyolysis have been described in patients with DMD. Rowland recently suggested that these cases may also have malignant hyperthermia (MH), although this interpretation has been questioned by Rosenberg. Willner et al. also suggested that MH may occur in patients

Received from the Departments of Clinical Neurosciences, Anesthesiology, and Surgery and Pediatrics, University of Calgary, the Department of Pathology, Foothills Provincial General Hospital, and the Alberta Children's Hospital, Calgary, Alberta. Accepted for publication August 4, 1982. Supported in part by a research grant from the Medical Services Research Foundation.

Address reprint requests to Dr. Brownell: Department of Clinical Neurosciences, University of Calgary, 3330 Hospital Drive, N. W., Calgary, Alberta, Canada T2N 4N1.

Key words: Anesthesia: pediatrics. Hyperthermia: malignant hyperpyrexia. Muscle, skeletal: Duchenne muscular dystrophy.

0005-3022/83/0200/0180 $00.95 © The American Society of Anesthesiologists, Inc.