hemodynamic disadvantage, but is frequently associated with other congenital anomalies, especially atrial septal defect, and septal defect with anomalous connections of pulmonary veins.6-8 Electrical instability, dysrhythmia, and sudden death in patients with left superior vena cava have also been reported.6-8 The absence of the right superior vena cava is rare.

In summary, a relatively uncommon cardiac anomaly, a left superior vena cava, was discovered during Swan-Ganz catheterization. Although a left superior vena cava is not hemodynamically important, it is frequently associated with other anomalies. Electrical instability in association with left superior vena cava is also reported. Coblenz et al.9 have recently reported two cases where a left superior vena cava was entered from the left. In this case, the left superior vena cava was entered from the right, suggesting absence of the right superior vena cava, a rare event.

Those anesthesiologists utilizing pulmonary arterial catheter monitoring in the care of critically ill patients in the operating room or intensive care unit should be aware of this anatomic variant and its associated lesions.

REFERENCES


Orally Administered Dantrolene for Prophylaxis of Malignant Hyperthermia

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Malignant hyperthermia (MH), a condition characterized by a rapid increase in body temperature with or without muscle rigidity, is a rare but often fatal condition associated with anesthesia. There is no simple noninvasive test to identify the susceptible individuals. A history of hyperpyrexia and/or muscle rigidity during previous general anesthesia or a family history of such a condition provides the anesthesiologist with valuable information. Avoidance of potent inhaled anesthetic agents, succinylcholine, and amide-type local anesthetic drugs, and selective use of regional block techniques with ester local anesthetic agents, are the usual acceptable guidelines in the anesthetic management of susceptible individuals.

Dantrolene sodium (Dantrium, Eaton Laboratories), a hydantoin derivative and skeletal muscle relaxant, has been shown to be highly effective in the prevention and treatment of malignant hyperpyrexia in MH-susceptible swine.1,2 We have used orally administered dantrolene successfully as a part of the prophylaxis of malignant hyperpyrexia in a susceptible individual undergoing a major gynecologic operation.

REPORT OF A CASE

A 28-year-old white woman (57 kg) was referred to the gynecology service with a pelvic mass. Apart from the pelvic mass, she had been healthy, with no other systemic disorder. She had not had any condition necessitating surgical treatment in the past. Her father had died unexpectedly during a relatively minor operation with general anesthesia at the age of 44 years. It had been his second surgical operation with general anesthesia. Specific details were unavailable. The patient's 8-year-old son had received halothane and succinylcholine for tonsillectomy at the age of 7 years. He had become rigid and hot, cardiac dysrhythmias developed, and dark-colored urine was produced in the postoperative period. He survived the episode after being treated in the intensive care unit for several days. The anesthesiologist diagnosed the condition as malignant hyperpyrexia and issued him a Medic-Alert bracelet.

All available blood relatives of the patient were interrogated and investigated. More than half had elevated resting serum creatine phosphokinase (CPK) values (fig. 1). Many also had histories of unusual muscle cramps, especially in the calf muscles; however, the patient did not have this symptom, and her CPK value was normal. No member of the family except the two already described had ever been exposed to general anesthesia.

Since the patient had a significant risk of developing malignant hyperpyrexia during general anesthesia, it was decided to hos-
pitalize and pretreat her with orally administered dantrolene for three days before the operation, due to the operation is deemed necessary, and possibly continue oral administration of dantrolene in the postoperative period. It was planned to use lumbar epidural anesthesia with 2-chloroprocaine as the local anesthetic agent.

Results of liver function tests (serum glutamic oxaloacetic transaminase, serum glutamic pyruvic transaminase, lactate dehydrogenase, aldolase, protein, bilirubin and alkaline phosphatase) and serum CPK determinations done on the day of admission were normal, as was the CPK isoenzyme pattern. The patient was given dantrolene, 100 mg, orally, four times a day for three days before operation, and an additional dose of 100 mg as premedication on the day of operation. She underwent abdominal exploration with removal of a tubo-ovarian mass during continuous epidural anesthesia using 2-chloroprocaine (total dose 1,500 mg) supplemented with Innovar (2.5 mL iv). The procedure lasted two and a half hours. A cooling blanket, cool intravenous solutions, i.e. and other usual measures to treat hyperthermia were available. Body temperature and arterial blood gases were monitored. The course of anesthesia and operation and the immediate postoperative course were unremarkable. On the second postoperative day, the temperature was 38.5 °C and the serum CPK value was 165 mU/mL. The CPK isoenzyme pattern was normal. Oral dantrolene treatment was resumed, and the patient received 100 mg every six hours four times. Several serum CPK values were determined throughout the patient's hospital stay (fig. 2). The patient was discharged from the hospital a week after the operation without any problems.

The side effects of oral dantrolene treatment were extreme weakness of all the muscles, incoordination of skeletal muscles, drowsiness, dizziness, and diarrhoea. These were especially marked on the first day of treatment but became much less incapacitating later. Appetite remained good throughout the treatment period. Long-term treatment with dantrolene may be associated with hepatic dysfunction (FDA Drug Bulletin, July–August 1975); however, no change in liver function was observed after brief exposure to dantrolene in this case.

**DISCUSSION**

The positive family history made this patient at risk for development of MH during general anesthesia.

![MH family pedigree](image)

<table>
<thead>
<tr>
<th>Female - Normal Serum CPK</th>
<th>Male - Normal Serum CPK</th>
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</thead>
<tbody>
<tr>
<td>Elevated Serum CPK</td>
<td></td>
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<tr>
<td>The Patient</td>
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Serum CPK values in parenthesis (normal range 0-35 mU/mL).

- **Fig. 1.** MH family pedigree.

- **Fig. 2.** Pre- and postoperative serum creatine phosphokinase values.

This was true although her preoperative serum CPK and isoenzyme pattern were normal. The presence of high resting serum CPK levels in more than half of her family identifies the family as being susceptible to MH. With this background, it was thought that potential risk of development of MH during anesthesia in this case (even though not extremely likely) far outweighed the potential risks and discomforts of dantrolene treatment.

Dantrolene is not a new drug. It is generally used for chronic spastic conditions of the skeletal muscles. Its site of action is neither the central nervous system nor the neuromuscular junction, but skeletal muscle itself. It acts by uncoupling the excitation-contraction mechanism possibly by decreasing release of Ca²⁺ from the sarcoplasmic reticulum. Van Winkle, in a recently published article, stated: "... In the intact skeletal muscle, dantrolene sodium acts at a site on the sarcoplasmic reticulum which suppresses but does not completely inhibit the release of Ca²⁺ necessary for the activation of the contractile apparatus." It does not affect smooth muscle. Although it has been successfully used in experimental animals for the prevention and treatment of malignant hyperpyrexia, its use in man for this purpose had not been described previously.

Presumably dantrolene treatment in this case lowered the CPK values both pre- and postoperatively. However, this effect might have been due partly to bed rest. The rise in temperature and moderate elevation of the CPK values on the second postopera-
tive day were probably secondary to the trauma of the operation.

The purpose of this report is not to claim that dantrolene pretreatment was solely or primarily responsible for the prevention of MH in this case, since one cannot be sure it would have developed had this precaution not been taken. Since stress (e.g., porcine stress syndrome) may be an etiologic factor in the animal variant, and since successful regional anesthesia cannot be guaranteed, it seemed worthwhile to use dantrolene pretreatment. This paper does call attention to the fact that dantrolene, a highly effective drug to prevent MH in susceptible individuals, is available for oral use, and we suggest an effective dose schedule. The dose of dantrolene used in this case was 1.7 mg/kg, q.i.d., for three days, or 7.02 mg/kg/day for three days. This dose schedule is recommended by Brit$ (personal communication), who considers at least three or four days of treatment with 100 mg, every six hours, necessary for an average adult to build an adequate dantrolene level in sarcoplasm. Kerr et al., in a recently published report, have suggested that protection by dantrolene-induced block following oral administration is dose-related. They found that complete blockade of MH syndrome in susceptible pigs occurred only with a dose of 5.5 mg/kg/12 hours, four times (11 mg/kg/24 hours, two days). Lietman et al. suggested that orally administered dantrolene has a half-life of about seven hours and that it is safe to use the drug in divided doses of 4–12 mg/kg/day for at least two weeks (the maximum period in the study). Since dizziness, drowsiness and weakness are the side effects observed, especially during the first day of treatment, it is recommended that the patient be hospitalized during the treatment period (three days preoperatively).

After we managed this case we came to know that in a recent meeting of the FDA Advisory Committee on anesthetic agents (Brown, personal communication) it was recommended that a dose of 2–3 mg/kg of dantrolene sodium three times a day for at least one day is necessary for protection from malignant hyperthermia.

Addendum

Since we wrote this paper we have successfully managed five other MH-susceptible patients, including a sister and a nephew of the present patient (resting CPK levels, 51 and 52 mU/ml; see figure 1). Each of these patients was pretreated by oral administration of dantrolene, 2–3 mg/kg, for one to two days. Two of these patients received spinal anesthesia (tetracaine); two, local infiltration (procaine); the other, general anesthesia (nitrous oxide, narcotic, d-tubocurarine).

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