Postanesthetic Malignant Hyperthermia with Convulsions

Tatsuru ARAI, Kentaro DOTE, Kenji NITTA
and Isao TSUKAHARA

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We experienced a case of malignant hyperthermia (MH) which became apparent 140 min after anesthesia. The notable feature in it was that it began with convulsions.

Report of a Case

A 50-year old, 65 kg man was scheduled for elective lumbar laminectomy for disc herniation at L_{4-5} interspace. He had no history of previous anesthesia, CNS disorders, head trauma, epilepsy, or family history indicative of susceptibility to MH. Anesthesia was induced at 1500 hours, with 200 mg of sodium thiopental iv. Succinylcholine 40 mg iv was administered to facilitate tracheal intubation. Muscle regidity was not noted and the intubation was done with ease. Anesthesia was maintained with nitrous oxide 3 l/min, oxygen 2 l/min and halothane 0.5–1.0%. Pancuronium bromide 7 mg iv was used for muscle relaxation during the 4 h operation. Surgical and anesthesia courses were uneventful. Arterial blood pressure (AP) and heart rate (HR) rose from 130/90 mmHg to 210/120 mmHg and 65/min to 90/min, respectively, as the anesthetic concentrations were reduced at the end of the operation. Rectal temperature was 36.5°C. Thiopental 75 mg was given iv followed by propranolol 1.5 mg in divided dosage, resulting in an AP decrease to 160/120 mmHg. Neuromuscular bolckade was reversed by neostigmine 2 mg and atropine 1 mg with restoration of good spontaneous respiration. Trachea was extubated and the patient was transferred to a recovery room at 1955 hours. Patient was not fully conscious and could not follow any verbal commands. His legs occasionally jerked at the knee joint, and the patient groaned and grimaced as if he was feeling severe leg pain. AP was 200/90 mmHg, HR 114/min and axillary temperature 37.0°C. No dysrhythmia was observed. Serum Na was 139 mEq/l, K 3.9 mEq/l, Cl 100 mEq/l, Ca 5.0 mEq/l and blood glucose was 180 mg/dl. Pentazocine 30 mg and diazepam 15 mg in divided dosage during next 1 h, had no effect on patient's movement, groaning or state of consciousness. At 2040 hours the axillary temperature was 37.2°C. At 2100 hours the patient developed weak tonic convulsions, evidenced by holding of his breath for 3–5 sec every 1–3 min. Respiration between the convulsions was deepened. AP was 200/100 mmHg and HR 120/min. Premature ventricular beats, 4–5/min, were observed. Arterial blood gases (ABG) while breathing oxygen enriched air via Ventimask® were pH 6.96, P_{CO_2} 75 mmHg, P_{O_2} 97 mmHg and BE −18. At 2115 hours the patient developed a generalized clonic convulsion of short duration. Systolic pressure dropped to 50 mmHg. HR was 125/min. He was reintubated and ventilated manually with

Department of Anesthesiology, Ehime University School of Medicine, Ehime-ken, Japan

Address reprint requests to Dr. Arai: Department of Anesthesiology, Ehime University School of Medicine, Shigenobu-cho, Onsen-gun, Ehime-ken, 791-02 Japan

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an Ambu-bag®. Resuscitative medications were started immediately, etilefrine (Efortil®) 10 mg in divided dosage, dopamine 5–15 μg/kg/min, sodium bicarbonate 200 mEq, hydrocortisone 500 mg and rapid infusion of 800 ml Hartmann's solution containing 5% dextrose. A hundred mg of phenobarbital was given im for convulsion. By 2145 hours AP rose to 90/40 mmHg, and under forced ventilation by Ambu-bag with oxygen enriched air ABG were pH 7.23, P_{CO_2} 62 mmHg, P_{O_2} 115 mmHg and BE −4.5. Weak convulsive movement of the body and/or the face were observed occasionally for 2 h.

At 2215 hours the high temperature of the patient's skin was first noticed. Axillary temperature was 40.5°C. ABG were pH 6.94, P_{CO_2} 62 mmHg, P_{O_2} 197.7 mmHg and BE −21 under manual hyperventilation with oxygen enriched air. AP was 108/40 mmHg and HR was 100/min. Diagnosis of MH was assumed. Surface cooling with ice pack and stomach lavage with cooled saline were started. Sodium bicarbonate 400 mg and hydrocortisone 500 mg were infused during next 3 h.

AP dropped to 50–60 mmHg in systole at 2330 hours in the midst of high fever. Eight hundred ml of blood and 2,500 ml of balanced salt solution were given over 3 h with improvement of AP. High fever, 40–40.5°C, continued till 0045 hours, falling below 37.0°C by 0410. Active cooling of the patient was stopped at 0150 hours when temperature was 38.0°C. At 0025 hours patient had voided dark red urine, which later revealed a myoglobinurine. Thirty mg of furosemide in divided dosage was given iv to enhance urinary outflow. Also at 0025 hours patient was placed on respirator (Aika-R120 PPA) with aid of pancuronium bromide, 4 mg iv. The ABG normalized by 0345 hours.

Patient was transferred to the ICU of the University Hospital 19 h after operation. He was comatose responding only to strong pain stimuli and tracheal suctioning. Pupils were anisocoric and reaction to light was slow. AP was 130/60 mmHg, HR 70/min and rectal temperature was 38.4°C, falling below 37°C within 3 h aided by cooling blanket. Laboratory data were Na 143, K 3.0, Cl 112 (mEq/l), urea N 14, creatinine 1.5, Ca 7.6, total bilirubin 0.6, glucose 322 (mg/dl), GOT 224, CPK 8057 (IU/l) and ammonia 24 (μg/l). CT scanning of the brain revealed no edema, hemorrhages, or other abnormalities. On EEG 5 to 7 hz slow waves were dominant. Patient was placed on a ventilator (Servo-900C). Mild tonic convulsions of short duration were seen occasionally for the first 2 days in ICU. Urine and blood were positive for myoglobin for 3 days and 7 days, respectively, and peak values wer 50,000 and 43,000 ng/ml, on the second day, respectively. CPK value fell gradually to 416 IU/l at 2 weeks. Patient was tracheostomised and vastus medialis muscle was biopsied on the 7th day. The calcium induced calcium release in the skinned fiber was comparably low (examined at Department of Pharmacology, Tokyo University School of Medicine), however control value was not obtainable. He was weaned from ventilator 9 days after admission to ICU. His consciousness improved slowly. He opened his eyes by verbal commands on 7th day after admission but was in a state of somnolence or stupor for about 1 month. Repeated neurological examinations and CT scannings did not indicate any abnormalities in the brain. Ten months later his state of consciousness was clear but he suffered from irritability, emotional disturbance, slight dysarthria and decreased activity. Two years later he was still slightly disoriented.

Discussion

The first question in this case is whether it was an MH episode or some sort of acute CNS disorder resulting in fever and convulsions with accompanying rhabdomyolysis. We diagnosed it as an MH episode because of the following:

(1) The degree and rapidity of body temperature increase[1,2], from 37.2°C to

40.5°C within 95 min during immediate postoperative period, normalizing within 6 h.

(2) Markedly elevated serum myoglobin and CPK value with an overt myoglobinuria indicative of rhabdomyolsis[1,2].

(3) No evidenc of CNS disorders in medical history, physical examinations or laboratory data to explain the temperature elevation and convulsions.

The next question then is what mechanism caused the convulsions, high temperature resultant of MH, direct effects of MH on the brain cells, or other unknown pathology? Febrile convulsions are confined to young children[3] and are unusual for an adult who completely lacked any evidence of CNS disorders in his medical history, physical examination and laboratory data. The ABG at the beginning of tonic convulsions showed severe metabolic and respiratory acidosis. The acidosis per se has deleterious effects on the brain function, usually general depression[4], but convulsion is unlikely. Imbalance in serum electrolytes may cause convulsions, but they were within normal limits in the blood drawn at the end of operation. Also hypoxic or hypotensive episode which might cause brain cell injury was not experienced in either the operating or recovery room.

Thus we assume that the convulsions might have been caused by MH affected brain cells. No animal or human study has proved that brain cells are affected primarily by MH as are skeletal and cardiac muscles[2]. But the evidence suggests that MH is a widespread membrane defect[1] and may involve a generalized disorder of permeability affecting calcium movement[5]. Brain cells need highly active calcium metabolism for normal functioning and its impairment results in a dysfunction as is shown in cerebral ischemia[6]. In our case the calcium metabolism of the brain along with skeletal and cardiac muscles might have been affected from the beginning, causing the convulsions before the MH became full blown as evidenced by temperature. This is partly supported by the neurological dysfunctions after anesthesia, i.e. obtunded consciousness, unusual jerking movement of the knees, and groaning. The longstanding neurological sequelae of the patient also supports it, since AP and P_{O_2} never became so low as to cause brain cell damage of such extent. Murphy et al.[7] reported an MH case in which the patient complained severely of pain, unexplainable by physical examination, long before MH became apparent. We assume that the same mechanism might be at work in their case as in ours.

In conclusion we assumed that the convulsions noted in our case were caused by the direct effect of MH on the brain cells and thus post-anesthetic convulsion could be a sign of MH.

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