Malignant Hyperthermia Associated with Atypical Central Core Disease

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Management of a patient with malignant hyperthermia (MH) continues to challenge the anesthesiologist. The following case is that of a patient who has central core disease (CCD) and few clinical features associated with CCD.

Report of a Case

A healthy 14-year-old, 45 kg girl who had a diagnosis of internal derangement of the left knee was scheduled for arthroscopic examination. Medical history was negative except for an uneventful appendectomy at 12 years of age under spinal anesthesia. Family history was also negative. Physical examination revealed a mild degree of thoracic scoliosis without evidence of muscle weakness or other neurologic abnormalities. ECG and other laboratory data revealed no abnormalities. The serum CK level was not examined.

After premedication with pentazocine, 15 mg, and hydroxyzine, 50 mg, im, she received epidural anesthesia with 10 ml of 2 percent mepivacaine via an epidural catheter at the L_{3-4} interspace, which resulted in not satisfactory analgesia and extreme anxiety.

Then, general anesthesia was induced with thiopental, 250 mg. Jaw muscle rigidity followed the administration of succinylcholine, 50 mg, and prevented laryngoscopy. Effective ventilation was easily maintained by mask with 100 percent oxygen during this period. Immediately after the administration of 2 percent halothane, however, the heart rate increased from 84 to 126 beats/min and polypnea was noted. The soda-lime cannister was found to be markedly heated. Halothane administration was immediately discotinued and rectal temperature monitoring was initiated. Her temperature rose from 37.5 to 38.8°C in the next 15 minutes and a diagnosis of MH was made. Fresh soda lime and a new anesthetic circuit were used. The patient was treated with 100 percent oxygen, surface cooling with ice and alcohol, and intravenous infusion of 2500 ml of iced Ringer's lactated solution. The inital arterial blood-gas values showed pH 7.06, $Paco_2$ 90 mmHg, Pao_2 55 mmHg, HCO_3^- 26 mEq/l and base excess −7 mEq/l, when the patient was spontaneously breathing room air. Laboratory data as follows; serum CK 582 IU/l (normal 20–70 IU/l), serum K^+ 3.1 mEq/l and serum total Ca 7.1 mg/dl. After fentanyl, 0.1 mg, was given iv, the trachea was intubated and ventilation was assisted with 100 percent oxygen. Sodium bicarbonate, 33 mEq, methylprednisolone, 1000 mg, and furosemide, 20 mg, were administered intravenously. Despite the vigorous cooling procedure, temperature rose to 39.6°C within 45 minutes. Over the next 45 minutes, it decreased to 37.7°C, when cooling was discontinued.

Although temperature gradually rose to 38°C within the next 30 minutes, it decreased to 37.6°C in 30 minutes after successful treatment

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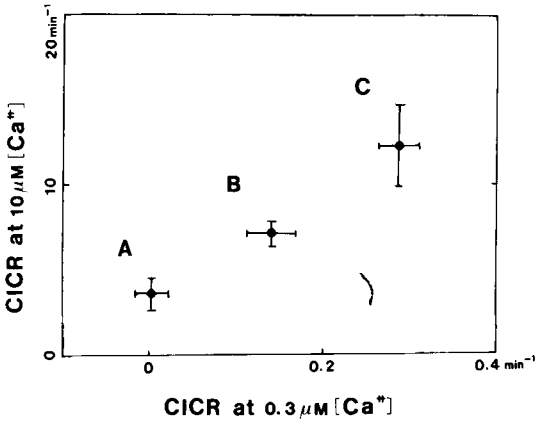

Fig. 1. Results in the study of the rate of Ca-induced Ca release (CICR) measured by Dr. Makoto Endo

This shows the rate of Ca release induced by Ca ion at 0.3 μM [Ca^{++}] (horizontal axis) and at 10 μM [Ca^{++}] (vertical axis). Mean ± SE are plotted against each Ca ion. A right and upward position of each plot indicates an increase in the rate of CICR.

A: a case with no increase in CICR

B: this case with an increase in CICR

C: a case with more increase in CICR as compared with this case

with cooling procedures and the intravenous administration of dantrolene sodium, 60 mg. Her heart rate also decreased from 118 to 88 beats/min 20 minutes after the administration of dantrolene had been started. Arterial blood-gas values showed pH 7.33, $Paco_2$ 48 mmHg, Pao_2 317 mmHg, HCO_3^- 26 mEq/l and base excess 0 mEq/l. She was alert and her respiratory rate was 18/min. Temperature remained unchanged. The trachea was then extubated and she was transfered to the intensive care unit, where she continued an uneventful course. On the following day, laboratory data showed CK value of 4985 IU/l and normal value of serum total Ca of 9.1 mg/dl.

On the 7th day, her calf muscle was biopsied under local anesthesia. Skinned fibers prepared from the biopsied muscle were examined on the rate of Ca-induced Ca release from the sarcoplasmic reticulum under various concentration of Ca ion and on the contracture sensitivity to caffeine. The result revealed an increase in the rate of Ca-induced Ca release (fig. 1), while the contracture sensitivity to caffeine showed a small increase with no significant difference from that in normal muscles.

After she was discharged on the 11th day, she often suffered from hyperthermic episodes with headache. Her temperature was found to rise to approximately 39°C from 36.6°C within 30 minutes after a mild degree of exercise, such as walking, climbing stairs and sweeping, but decreased to baseline level by taking a rest. This bothered her in daily life. Oral administration of dantrolene sodium was planned, which failed to be continued because of the side effect such as severe nausea and vomiting.

One month later, she admitted to the pediatrics for evaluation of development of fever following exercise and for arthroscopy of internal derangement of the knee. Physical findings on admission revealed a mild degree of ptosis, thoracic scoliosis of 30°, decreased grasping power (18 kg right, 16 kg left), atrophy of bilateral thenar muscles and distal portions involving lower limbs, which suggested a possible correlation with underlying muscle disease. The electromyography showed mild changes of a myopathic character. Muscle biopsy and arthroscopic procedure were uneventfully performed under spinal anesthesia with tetracaine, 8 mg. Biopsied muscle showed evidence of central core disease (fig. 2).

Discussion

A new congenital non-progressive myopathy, initially described in 1956 by Shy and Magee was given the term "central core disease" (CCD) in 1958 for the histological appearance of cores in the muscle fiber[1,2]. The association of CCD and MH, however, was not made until Denborough et al later demonstrated CCD in the aunt of the proband in their original family in 1973[8]. Although the occurrence of MH and CCD in the same individual or family has seldom been reported, CCD has been well known to be most susceptible to MH[4-6].

The patients with CCD have certain clinical features as follows[1]. The onset is probably congenital or within the first months of life. Hypotonia is evident in the children but not in the adults. Muscle weakness is proximal and most severe in the lower extremities. This dis-

order results in delayed walking. They may also have some physical abnormalities such as ptosis, scoliosis, pes cavus, congenital dislocating hips and high-arched palate[4-6]. However, our patient showed no evidence of hypotonia and her motor development was almost normal. She started to sit at 8 months and to walk at 15 months of age. Although the clinical features of our patient resembles those of cases of CCD with normal development described by Bethlem et al.[4], whether their patients developed MH or not is unknown. In this case, the development of MH gave a clue to a diagnosis of CCD, which was confirmed by physical abnormalities on admission which suggested myopathy, and by histological appearance in the biopsied muscle.

Because CCD can be associated with susceptibility to MH, the clinical importance of this association must be emphasized. In the patient with weakness and hypotonia in his infancy, a detailed history of MH reactions in pedigree members, musculoskeletal abnormalities, CK values and especially, muscle histochemistry should be investigated for making a diagnosis of CCD. In cases of surgical emergency, in which there may be no detailed informations described above, the patients with physical abnormalities such as ptosis, kyphoscoliosis and congenital dislocating hips (floppy patients) should always receive anesthetic regimen for MH.

The diagnosis of MH subsequently is confirmed by means of a muscle biopsy. At present, the most reliable tests performed on the biopsied muscle are the measurement of the rate of Ca-induced Ca release and the contracture sensitivity to caffeine in the skinned fibers[7,8]. Our patient showed an increase in the rate of Ca-induced Ca release but almost normal sensitivity to caffeine. This discrepancy between the two results may be contributed to the difference in methodology.

In summary, we described a case of malignant hyperthermia associated with atypical central core disease (CCD) manifesting practically subclinical involvement which may parallel histochemical findings. In this case, an increase in the rate of Ca-induced Ca release and almost normal sensitivity to caffeine were observed in the studies using skinned fibers.

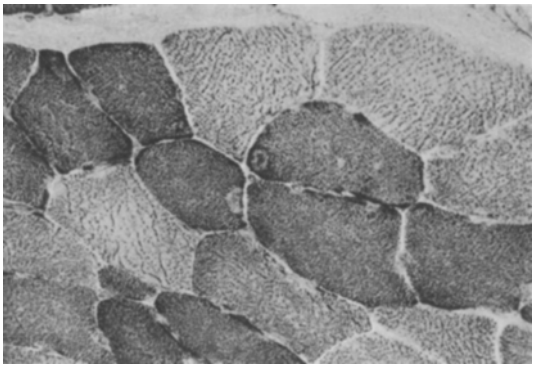

Fig. 2. Histochemical appearance of quadriceps femoris muscle in transverse section
Dark staining fibers are type 1 and light staining fibers are type 2. A small proportion of the type 1 fibers (about 3.5%) has single well-defined cores devoid of NADH-TR, most of which are eccentrically placed. No cores are present in the type 2 fibers. (NADH-TR ×360)

This patient has been suffering from hyperthermic episodes following a mild degree of daily exercise after she recovered from an episode of malignant hyperthermia under general anesthesia.

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