Drug-Induced Hyperthermia and Rhabdomyolysis During the Perioperative Period : Report of Three Patients

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Abstract

Drug-induced hyperthermia is one condition that anesthesiologists may meet even though it is uncommon, it is life threatening. We report 3 cases of patients at Siriraj Hospital, Mahidol University who developed drug-induced hyperthermia and rhabdomyolysis from different mechanisms. In two of them, the diagnosis was suspected malignant hyperthermia. Rigidity, hyperthermia and tachyarrhythmia developed just after inhalation induction (halothane and sevoflurane) and intubation with succinylcholine. The other case was the result of amphetamine abuse. He also had received both succinylcholine and inhalation agent (isoflurane) but no obvious signs or symptoms were detected during anesthesia. He developed a gradual increase in fever over 13 hours post operation and complained of muscle pain (with leg muscle cramps). All of them showed a marked increase in muscle enzymes and had rhabdomyolysis. As a result of early detection and early manangement, these three patients survived without any permanent damage to vital organs. We conclude that Thai anesthesiologists should be more aware and alert to drug-induced hyperthermia especially as nowadays many teenagers abuse stimulant drugs and "triggering" drugs as antidepressant or serotonin reuptake inhibitors are prescribed more frequently. Early detection and management will decrease morbidity and mortality.

Key word : Drug Abuse, Malignant Hyperthermia, Amphetamine, Rhabdomyolysis

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Body temperature can be maintained at a nearly constant (36-37.5°C) despite fluctuations in the environmental temperature. This is the result of the special human ability of thermoregulation[1-3] that results from afferent thermal sensing, processing in the hypothalamus and efferent sympathetic activity that balances heat gain and loss. But some pathophysiological changes such as excessive heat production, decreased heat dissipation or loss of thermoregulation can cause hyperthermia. Severe hyperthermia (temperature over 41°C[3]) during the perioperative period may be related or unrelated to anesthesia. It is important to us because severe hyperthermia will injure many organs by both direct and indirect effects and will cause serious organ dysfunction such as liver and kidney impairment, rhabdomyolysis, DIC and fluid and electrolyte abnormalities. Hyponatremia, hypokalemia and hypomagnesemia caused by excessive loss from sweating. Hyperkalemia may be seen if there is skeletal muscle damage or metabolic acidosis. Calcium may be low in the early stages because of intracellular shift but becomes higher after that. Prevention, early detection and management may save the patients' life. We report 3 cases of patients at Siriraj Hospital who developed severe perioperative hyperthermia and rhabdomyolysis causes by different etiologies. Each patient received an inhalation agent (the 1st received halothane, the 2nd sevoflurane and the 3rd isoflurane) and succinylcholine that are potential triggering agents for malignant hyperthermia. Two of them were suspected malignant hyperthermia and the other was amphetamine abused. All of them survived and recovered well without any organ damage.

CASE REPORT

Case 1

A 2-year old girl, with a hemangioma of the left eye, needed anesthesia for skin graft surgery. Induction of anesthesia was performed with N_2O, O_2 and halothane. Because of severe masseter spasm she could not be intubated. Successful ventilation and intubation were done just after the nondepolarized muscle relaxant was given. At that time generalized skeletal muscles rigidity were detected. Her blood pressure and heart rate went up to 160/90 mmHg and 190 bpm. Anesthesiologist observed that there were peripheral vasodilatation and increased skin temperature but exact temperature was not measured. Blood gas analysis showed a severe metabolic and respiratory acidosis, pH = 6.9, $PaCO_2$ = 69 mmHg, PaO_2 = 342 mmHg, HCO_3 = 17 mEq/l. Malignant hyperthermia was suspected, so we gave her 100 per cent oxygen, gastric lavage with cool saline and vigorous sponging and then sent her to ICU. Her temperature when in ICU was 38°C (after aggressive cooling). Muscle enzyme CPK increased and peaked at 19,990 U/L in the 3rd day. There was a rise in SGOT, SGPT levels. Supportive treatment only by hydration with alkalinized fluid was given. She was extubated on the 2nd postoperative day and discharged from ICU on the 6th day.

Case 2

A 17-month old girl had congenital adrenal hyperplasia and hyperplasia of the clitoris. She was to have elective clitoroplasty. Induction of anesthesia was started with N_2O, O_2 and sevoflurane. Succinylcholine was given for intubation but masseter spasm was seen. Intubation was performed successfully despite difficulties in opening her mouth. She then had generalized muscle rigidity, a progressive increase in heart rate to 190 bpm, the ECG showed tall peaked T waves which turned into a ventricular tachycardia of 200-220 bpm; her blood pressure was 150/90 mmHg. The nasopharyngeal temperature rose to 42-45°C. She was given 100 per cent oxygen and hyperventilated, blood gas analysis showed pH = 7.241, $PaCO_2$ = 43.5 mmHg, PaO_2 = 508.4 mmHg, HCO_3 = 18.7 mEq/l. Suspected malignant hyperthermia was diagnosed. At the same time she was paralyzed with atracurium and cooled by gastric lavage with cold saline, external sponging of the axillae and groin. She did not respond to 3 doses of lidocaine (total 3 mg/kg). So amiodarone and at the same time because of suspected hyperkalemia from the ECG appearance, $NaHCO_3$ and glucose together with insulin were given and ECG returned to sinus tachycardia. She was then sent to ICU and given supportive treatment with hydration and alkalinization of the urine. Her renal function was normal, but liver function SGOT/PT was highest on the 3rd day (1,053/392). Serum CPK was also highest on the 3rd day (33,620 U/L). She was extubated on the 1st day in ICU, and sent to the ward on the 7th day.

Case 3

A 23-year old man came to the emergency room because of bowel gangrene. He was very exited, restless and confused. His mother admitted that he

had just inhaled a stimulant drug (amphetamine) and had a 10 year history of abuse on a daily basis. Blood was later sent for analysis and found to be positive for amphetamine. He was markedly dehydrated with a mild fever (37.7°C) and his blood pressure was high normal (140/90 mmHg). After resuscitation to rehydrate him, he was anesthetized with IV thiopental for induction, succinylcholine for intubation, then maintained with atracurium, NO_2, O_2, isoflurane, and morphine. Hartman procedure, sigmoidectomy and colostomy were done. There were no serious concerns over the 2 $^1/_2$ operative hours, except he needed higher doses of anesthetic drugs than normal. So after operation he was sent to a normal postoperative ward. A few hour later, he became restless and confused again and his temperature gradually increased and peaked at about >42°C for 13 hours. The urine flow/hour was scant and dark brown in color and positive for myoglobin. Because of tachypnea and hypoxemia, he needed tracheal intubation and was admitted to ICU. Management in ICU was supportive treatment with aggressive cooling. To gain effective heat dissipation, we prevented shivering and reflex vasoconstriction by a nondepolarizing muscle relaxant (atracurium). He had a markedly abnormal CPK = 416,800 U/L (normal 20-195), SGOT/PT = 5, 718/1,246 U/L (normal 0-37/0-40) on the 5th postoperative day. We prevented renal failure from rhabdomyolysis by alkalinizing the urine and hydrating aggressively (1/2 NSS 1000 ml + $NaHCO_3$ 50 ml according to CVP and maintaining urine volume at 150-200 ml/h). Even though administration of sodium bicarbonate is controversial in amphetamine induced rhabdomyolysis because alkalinized urine might delay amphetamine excretion[4], we gave sodium bicarbonate mixed with the IV fluid to correct severe metabolic acidosis and also prevent renal failure from severe rhabdomyolysis (his blood gas was pH = 7.076, $PaCO_2$ = 29.9 mmHg, PaO_2 = 100.7 mmHg, HCO_3 = 10.1 mEq/L, BE = 21.5, CPK = 416,800 U/L). We believed that at the time the patient was admitted to ICU it was more than 33 hours after taking amphetamine so only a small amount of drug would be left in his body but the effect of muscle injury and rhabdomyolysis persisted and might continue to injure the renal tubular cells. The patient began to improve and could be extubated on the 5th day of ICU admission and sent to ward on the 9th day. Parameters compared between each patient are shown in Table 1.

Table 1. Parameters compared between each patient.

	Highest temp °C	Onset of ↑ temp.	Pathognomonic signs	Highest total CPK	Highest SGOT/PT	Organs failure	Result
Case 1 MH	>38	Sudden after succinylcholine	Masseter spasm generalized rigidity, CO_2 retention	19,990 on 3rd day	774/174 on 2nd day	Liver	Improved
Case 2 MH	44	Sudden after succinylcholine	Masseter spasm generalized rigidity, CO_2 retention	33,620 on 3rd day	1,053/392 on 3rd day	Liver	Improved
Case 3 Amphetamine	42	Gradually	Hypertension, tachycardia metabolic acidosis	416,800 on 5th day	5,718/1,246 on 5th day	Kidney, liver	Improved

DISCUSSION

The causes of an increase in body temperature are many:- A combination of an increase in heat production over heat loss, and/or an abnormality of the thermoregulating center. These conditions can be found during the perioperative period[1] as follows:-

Iatrogenic:- overwarming or too much covering.

Secondary to disease:- as in pheochromocytoma, thyroid storm, familial dysautonomia/Riley-Day syndrome, osteogenesis imperfecta, CNS dysfunction (seizure, autonomic imbalance, abnormal posture), and muscular dystrophies.

Drugs induced hyperthermia:- as in malignant hyperthermia, neuroleptic malignant syndrome, central anticholinergic syndrome, serotonin syndrome, or others.

Injury to the thermoregulating center:- at the brain stem/hypothalamic level or because of excessive heat production after seizures.

Infection

Transfusion reaction

Drug induced hyperthermia is an important cause that is found with increasing frequency in Thailand. Stimulant drugs are used by teenagers and antidepressants, serotonin reuptake inhibitors and dysautonomia drugs in the elderly. These drugs can interfere with the body's catecholamine reserve so we have to deal with patients with cardiovascular instability and an abnormal response to vasoactive drugs. Another major problem is metabolic effect. Mechanisms of drug-induced hyperthermia are the effects of hypermetabolism, impairment of heat loss and/or thermoregulating center[5]. The beta stimulation with increasing metabolism causes an increase heat production. The alpha adrenergic vasoconstriction and anticholinergic drugs cause an impairment of heat loss and sweating. Some drugs affect hypothalamic thermoregulating center by imbalance of dopamine and serotonin (decreased activity of dopamine and/or increased serotonin). In the normal process of anesthesia and surgery these patients will have nothing by mouth for a period of time and also a high risk of drug, interactions such as with droperidol, and narcotic e.g., pethidine. Effect of hyperthermia and hypermetabolism may involve many organs. The patient can develop seizures, myocardial failure, arrhythmia, acute respiratory distress syndrome, DIC, rhabdomyolysis, and kidney and/or liver failure. The exact mechanism of hyperthermia-induced cell injury is still unclear but may cause denaturation of enzymes, liquefaction of membrane lipids, damage mitochondria and affect phospholipids and the stability of lipoproteins[6]. Prevention, early detection and early management can attenuate the severity of the insult.

Malignant hyperthermia is a condition that may result from a genetic mutation with autosomal dominant inheritence[6]. 50 per cent of the patients [3,7,8] show an abnormality at RYR1gene on chromosome 19. With triggering agents (Table 2), there is an abnormal release of calcium ions from the sarcoplasmic reticulum in skeletal muscle[3] and this causes skeletal muscle spasm and rigidity. These actions are prolong because of a decrease in reuptake calcium ions back to sarcoplasmic reticulum that allow prolonged and tensed interaction between the contractile proteins, actin and myosin. The clinical picture is most often seen after administration of succinylcho-

Table 2. Anesthetic drugs and MH[7,13,19].

Contraindication	Safe	Controversy
Halothane	Nitrous oxide	Anticholine esterase
Enflurane	Barbiturates	Ketamine
Isoflurane	Propofol	Digoxin
Desflurane	Etomidate	Potassium
Sevoflurane	Ketamine	Calcium
Succinylcholine	Opiates	Theophylline
Combination of calcium antagonist and dantrolene*	Amide/ester local anesthetics	Atropine
	Noradrenaline	Glycopyrrolate
	Adrenaline	
	Dopamine	
	Dobutamine	

* combination of calcium antagonists and dantrolene are dangerous because they promote hyperkalemia and calcium should be use with cautiusly.

line and inhalation agents. This abnormal muscle contraction also increase in a breakdown of glucose and glycogen as well as generate heat[1,3]. So signs of MH include an increased metabolism (CO_2 retention, increased O_2 consumption, metabolic acidosis), skeletal muscle spasm and rigidity, increased sympathetic tone, and hyperthermia. An increased temperature is caused by an increase in metabolism. Imbalance of oxygen between supply and demand will induce metabolic acidosis and muscle cell damage. Cells injury can be detected when moderate to severe hyperthermia (body temperature >40°C[9]). If there is severe damage of skeletal muscle cells, risk of acute renal failure will increase (from rhabdomyolysis induces myoglobinurea). Six clinical criteria[10] of suspicious MH are *1) Family history, 2) Generalized masseter rigidity* (spasm, stiff jaw in about 50% of cases[11] but 50% of masseter spasm is a normal response to succinylcholine[12]), *3) Muscle break down* as evidenced by an increase in creatine phosphokinase (CPK) from sustained muscle contraction and sustained muscle glycolytic metabolic anerobic metabolism resulting in rhabdomyolysis (skeletal muscle breakdown), *4) Respiratory acidosis* and hypercapnea as a result of increased production by metabolism and an increase in oxygen consumption, *5) Increased temperature, 6) Cardiac involvement.* Others abnormality include metabolic acidosis (pH<7.25), hyperkalemia and rapid depletion of energy stores[12]. Another suggestive sign is rapid reversal of these signs by dantrolene[8], a hydantoin derivative which is directly inhibited releasing of calcium ions from sarcoplasmic reticulum. The two most significant signs after induction of anesthesia that should alert the anesthesiologist are an unexplained increase in end-tidal CO_2 plus a tachycardia[12,13]. These signs occur before the temperature rises. In most cases, the onset of MH is from a few minutes to a few hours after an exposure to a triggering agent, mostly seen in operating room, rare cases occur later[14]. Hyperthermia in MH is caused by increased sympathetic tone and by muscle hyperactivity but in some cases it may absent[7,15]. The onset and clinical outcome of MH depend on how fast, how much and how effective particular drugs accumulate in muscles and stimulate a rise in the intracellular ionized calcium concentration[12] and also by any physiological variables that help or maintain the rise in the intracellular ionized calcium concentration. In case 1 and 2 abnormal muscle spasm, tachycardia and increased metabolism occurred just after administration of succinylcholine but in case 3 the fever increased gradually and the insults took too long to be caused by MH (nearly 13 hours). So it was less likely to be caused by MH. Anyhow in MH, the symptoms and signs in the patient varies with different triggerring drugs which have a different potency at different doses and different species responsiveness. Signs of MH in the patient who received sevoflurane may showed later that is shortly after reversed using a nondepolarized muscle relaxant[6]. The Ca^{2+} induced Ca^{2+} release mechanism stimulates generalized severe skeletal muscle contraction and rigidity. Sarcolemma integrity is broken down so potassium and CPK leak from CPK containing cells (skeletal muscle) and myoglobinuria is detectable[16]. These also cause an increase in oxygen consumption and excess carbon dioxide production. Tachycardia, carbon dioxide retention (may be the earliest sign[1]) and fever are not specific just to MH. An increase in CK may be caused by many factors such as trauma, ischemia, inflammation, drugs, and genetic disorders.

There is a score for grading the severity of malignant hyperthermia that uses the severity of generalized rigidity or just masseter spasm, muscle break down, respiratory acidosis, fever, cardiac arrhythmia, family history and other signs related to MH to rank the likelihood of the diagnosis of MH. Our first 2 cases had score of 53 or MH rank of 5 that means the diagnosis is very likely. The 3rd case had a score of 28 that means it is only a little bit likely to be MH. Muscle biopsy and the halothane, caffeine, ryanodine, 4-chloro-m-cresol contracture tests[17] are widely accepted as helping to make the diagnosis of MH. There are many new tests for diagnosis of MH such as molecular genetic tests, nuclear magnetic resonance spectroscopy, lymphocyte tests and muscle cell culture. Anyhow, we have no facilities to perform these tests in Thailand.

There are two groups of susceptible patients with overt or without myopathy, and Denborough suggest that the myopathies that associated with MH susceptibility are Evans myopathy, King-Denborough and central core disease[18].

Dantrolene, a hydantoin derivative that is a direct skeletal muscle relaxant which acts by blocking calcium release from the sarcoplasmic reticulum and is the drug of choice in the treatment of MH[13]. The recommended dose is 2 mg/kg IV which should be repeated as necessary every 5-10 minutes and continued at a dose 1-2 mg/kg every 4-8 hour for 24-48 hour[1] not exceeding 10 mg/kg. A MH prophylaxis with dantrolene in the patients who have only

history of MH is no longer recommended. Only prophylactic use of dantrolene is recommended to patient who has experienced of life-threatening episode of MH[1] with a dose of 2-2.5 mg/kg IV before surgery. Bromocriptine, amantadine, levodopa and carbidopa can be used to manipulate the thermoregulating center.

Amphetamine, a racemic beta phenylisopropylamine (Fig. 1) is a CNS stimulant with peripheral alpha and beta adrenergic actions[20-22]. Its effect is also indirect sympathomimetic action[21]. This will result in acute releasing and chronic depletion of norepinephrine, dopamine and serotonin[23,24]. Mechanism of action of an acute or chronic use is different. It depends on catecholamines in the storage sites at a nerve terminal. It has many effects that cause an addictive euphoria, decreased need to sleep, mental alertness, decreased appetite and increased sexual pleasure. The addition of a methyl group to amphetamine will enhance lipophilicity which increases absorption by the brain and a more potent, rapid onset and longer duration of action[20]. Because all amphetamines are weak bases pK = 8.0-10.5, so renal elimination is increased with acidic urine[24] but decreased with a prolonged effect in alkalinized urine[20,21]. This may enhance renal damage by myoglobinurea[22]. Other amphetamine analogs are synthesized by attaching substituents (methoxy, halogen, sulfur) to different positions on the phenyl ring of amphetamine or methamphetamine (ice, crystal, tweak, speed)[25]; 3, 4 methylenedioxymethamphetamine (MDMA, ecstasy), 3, 4 methylenedioxyethamphetamine (MDEA, eve) 3, 4 methylenedioxyamphetamine (MDA, Adam) methylenedioxyethmethamphetamine (Eve, MDEA), paramethoxyamphetamine (PMA). Because these drugs are used in dance clubs then has named the cause of death as the "dance of death". Routes of administration are by ingestion, intravenous injection, inhalation or smoking[23].

The acute stimulant effect is caused by an increase in the catecholamines, dopamine and serotonin in the brain[24] and an increase in the level of norepinephrine at the presynaptic nerve terminal and the synaptic cleft. These are a combination of the effects of blocking reuptake of norepinephrine into the presynaptic nerve terminal, inhibition of active uptake of norepinephrine to storage vesicles, and inhibition of the enzyme monoamine oxidase that degrades norepinephrine. As the result of this, norepinephrine accumulation leads to increased action on many organs : -

Neurological effects:- seizures, cerebral hemorrhage, inappropriate ADH secretion[26], urinary retention, serotonin syndrome (hypertonicity, hyperthermia, autonomic instability), nystagmus, hyperreflexia, hallucinogenic action[27]. They are directly neurotoxic to brain serotonin and dopamine axonal markers[23] that cause cognitive and memory defects[25], hyperthermia, and inncreased anesthetic requirement[21].

Cardiovascular system:- causes tachyarrhythmias, ventricular ectopy, ventricular fibrillation, myocardial ischemia/infarction, left ventricular dysfunction, and cardiomyopathy.

Respiratory system:- pulmonary hypertension and noncardiogenic pulmonary edema[27].

Neuromuscular effects:- amphetamines are potent neurotoxins; they increase muscle contraction, trismus, jaw clenching, rhabdomyolysis, increase creatinine phosphokinase and transminase.

Psychiatric effects:- anxiety, paranoia, delirium, aggression, suicidal ideation during the withdrawal period[20].

Metabolic disorder:- hypoglycemia, hyperthermia and metabolic acidosis[28].

Electrolytes disturbance:- hyper-or hyponatremia (acute overdose of MDMA hyponatremia [25]), hypokalemia as a result of cathecolamine effects but if there is rhabdomyolysis, there will be hyperkalemia and early hypocalcemia.

Liver function:- toxic hepatitis, especially in single overdoses and after chronic usage. Damage to liver is also associated with hyperthermia.

Striated muscle:- rigidity, injury and rhabdomyolysis[29].

Renal function:- renal ischemia and infarction from vasculitis. Effect of rhabdomyolysis which causes renal vasoconstriction, radical formation and tubular obstruction from cast production[29-31].

Blood gas analysis:- respiratory alkalosis, and metabolic acidosis.

Others:- DIC, and leukocytosis.

Chronic abuse causes depletion of catecholamines stored in the body, and interferes with dopamine and serotonin in the brain[22,23]. Tachyphylaxis can be explained by the depletion of catecholamines. Catecholamines depletion causes autonomic instability and sensitivity to drugs that depress the cardiovascular system and depletion of serotonin may cause personality change, cognitive and memory effects, paranoid psychosis[22] and suicidal feelings (as in case 3). Because of chronic depletion of these

chemical agents and also direct irriversible neurotoxic activity, chronic abuses also develop cross-tolerance to other sympathomimetic drugs. Typical signs of cocaine and amphetamine intoxication are anxiety, paranoia, tremor, mydriasis, tachycardia, diaphoresis, hypertension, hyperthermia and seizures followed by hypotension and coma. Onset of action is about 10 or 40 minutes after inhalation or ingestion respectively[23]. Duration of action is around 8-30 hours and the effect of alkalinizing the urine can prolong the effect for up to one week[23].

Acutely, they increase a minimal alveolar concentration (MAC) of inhalation agent, so these patients require a small dose of anesthetic drugs[21]. But after long-term use, they cause depletion of catecholamines and this will decrease the MAC of inhalation agents and cause cardiovascular instability.

Treatment is symptomatic and supportive. If within 2 hours of digestion, activated charcoal should be given *via* nasogastric tube with awareness of the risk of aspiration because of seizures. Agitation should be controlled with benzodiazepine[27]. Phenytoin or barbiturate should be used as anticonvulsant. Persistent hypertension should be treated with nitroprusside or calcium channel blocker. Beta adrenergic blocker should not be used because it does not cover alpha so it can increase vasospasm[27]. With clinical hyperthermia, the patient should be given nondepolarizing muscle relaxant (e.g., atracurium) and dantrolene if the temperature is over 39°C. Good hydration is needed to prevent myoglobin precipitation in renal tubules and to facilitate elimination. Mannitol is good in this situation[28] because 1) it produces an osmotic diuresis that can prevent obstructive myoglobin casts that can prevent obstructive myoglobin cast, 2) it increases renal blood flow and glomerular filtration rate, 3) and decreases cell edema 4) it is a free radical scavenger. Acidification of the urine may enhance amphetamine elimination but it will potentiate the effect of myoglobinuria on the renal tubules and causes renal failure[4,27,31,32]. Alkalinization of the urine is not reccommended because it will decrease a rate of renal elimination of amphetamine. Loop diuretics (furosemide, bumetanide, torsemide) can be used with advantages of acidify urine and increase tubular flow[27]. Electrolytes imbalance should be corrected, but even though ionized calcium is low, care should be taken with calcium administration because dystrophic calcification may occur. Diazepam is a drug of choice in management of agitated, aggressive and hyperactive patients. Neuroleptic drugs should be avoided because they cause hypotension and decrease a threshold of seizures [31]. When there is rhabdomyolysis the patient should be well hydrated to facilitate an elimination and to prevent renal shunt down from myoglobin precipitation in renal tubules.

In conclusion, amphetamine abuse is growing. The effect of these drugs and their derivatives differs according to dose and duration of usage and also clinical management. So it is important to identify and manage according to the clinical picture and the likely pathological changes that may occur.

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ไข้จากผลของยาในระยะ perioperative : รายงานผู้ป่วย 3 ราย

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หนึ่งในภาวะแทรกซ้อนซึ่งมีอันตรายร้ายแรงถึงชีวิตที่อาจพบได้ในระยะ perioperative คือตัวร้อนจัด/ไข้สูง (hyperthermia) และ rhabdomyolysis จากยา ภาวะนี้จะพบได้มากขึ้นเรื่อยๆในประเทศไทยดังเช่น ผู้ป่วยรายที่สามซึ่งเป็นผลจากยาม้า อันตรายต่อผู้ป่วยจะลดลงถ้าได้รับการช่วยเหลือที่ถูกต้องและรวดเร็ว ฉบับนี้เป็นรายงานผู้ป่วย 3 รายที่เกิดภาวะตัวร้อนจัดและมี rhabdomyolysis ในระยะ perioperative ซึ่งมีสาเหตุจากยาทั้งสิ้นแต่มีกลไกการตอบสนองที่ต่างกัน 2 รายแรกเป็นเด็กหญิง แพทย์สังเกตเห็นความผิดปกติของเด็กทั้งสองได้อย่างชัดเจนและรวดเร็วหลังจากได้รับยาดมสลบไอระเหยและ succinylcholine กล่าวคือมีกล้ามเนื้อเกร็ง (rigidity) โดยเริ่มที่กล้ามเนื้อ masseter และต่อไปยังกล้ามเนื้อลายทั่วไป ชีพจรเร็วขึ้นมาก หายใจเร็ว ต่อมาความร้อนในร่างกายสูงขึ้นอย่างรวดเร็ว ตรวจพบหลักฐานว่ามีการทำลายกล้ามเนื้อลายอย่างรุนแรง กล่าวคือพบภาวะ rhabdomyolysis นอกจากนี้หน้าที่ของตับและไตผิดปกติร่วมด้วย ที่เวลา 1-2 วันหลังจากนั้นได้รับการวินิจฉัยเป็น suspected malignant hyperthermia สำหรับผู้ป่วยรายที่สามมีประวัติติดยาม้านานว่าสิบปี และเพิ่งได้รับยาก่อนมาโรงพยาบาล มีปัญหาของลำไส้เน่า (grangrene) มารับการดมยาสลบเพื่อผ่าตัดลำไส้ส่วนที่เน่าออก ผู้ป่วยได้ยาดมสลบชนิดไอระเหยและ succinylcholine ไม่พบ masseter spasm และ/หรือความผิดปกติอื่นในระหว่างการดมยาผ่าตัด ยกเว้นผู้ป่วยต้องการยาสลบขนาดสูงมากกว่าปกติ ภายหลังผ่าตัด 13 ชั่วโมงที่หอผู้ป่วย พบว่าผู้ป่วยมีไข้สูง มี rhabdomyolysis หน้าที่ของตับและไตผิดปกติ ผู้ป่วยทั้ง 3 รายได้รับการรักษาแบบประคับประคองอย่างใกล้ชิด ได้ผลลัพท์ที่น่าพอใจ คือผู้ป่วยฟื้นตัวดีและสามารถกลับบ้านอย่างปลอดภัยทุกคน วิสัญญีแพทย์และพยาบาลไทยควรระลึกถึงภาวะ drug-induced hyperthermia ให้มากขึ้น เพื่อที่จะวินิจฉัยภาวะนี้ได้รวดเร็วและรีบให้การดูแลอย่างถูกต้องรวดเร็วด้วย ปัจจุบันมีรายงานเกี่ยวกับ suspected malignant hyperthermia มากขึ้น รวมทั้งมีวัยรุ่นจำนวนมากใช้ amphetamine เพิ่มขึ้น

คำสำคัญ : การติดยา, ไข้สูง, ยาบ้า, การสลายของกล้ามเนื้อลาย

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