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Death Caused by Malignant Hyperthermia: Two Case Reports+

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In this paper, we present two cases of death caused by malignant hyperthermia and discuss their properties according to the literature data.
First case: a 24-year-old-male was taken to the operating room for lombar disc hernia operation. At the 30th minute of the operation, tachycardia (120/min) was observed followed by bradycardia and cardiac arrest occurred at the 45th minute of the operation. After resuscitation, his fever was 39.5°C (103.1°F), then the fever rised to 40°C (104°F). CPK-MB level was high. The patient died on the seventh day after the operation.
Second case: a 27 year-old male was taken to the operating room for rhinoplasty. After few minutes, his pulse decreased to 50/min, thus atropine was injected. Then his pulse and blood pressure rose up to high levels. SpO_2 decreased from 96% to 90%. Fever rose up to 41°C (105.8°F) and CPK-MB was high. The case died in seven hours after the beginning of anesthesia.
All of the medical-forensic documents of these cases were analyzed at the First and Third Specialization Board of Council of Forensic Medicine, Turkey and it was evaluated that death was due to malignant hyperthermia in both of them.
Key Words: Malignant Hyperthermia; Anesthesia; Death.

Ölümle Sonuçlanan Malign Hipertermi: İki Olgu Sunumu

Bu yazıda, malign hipertermi nedeniyle gelişen iki ölüm olgusu sunuldu ve olguların nitelikleri literatür verileri ışığında tartışıldı.
Olgu 1: 24 yaşında erkek hasta lomber disk hernisi nedeniyle ameliyat salonuna alınmıştı. Operasyonun 30. dakikasında taşikardi (120/dk), takiben bradikardi ve ameliyatın 45. dakikasında kardiak arrest gelişmişti. Resusitasyon sonrasında 39.5°C (103.1°F) ölçülen ateş, kısa sürede 40°C (104°F)'ye yükselmiş, CPK-MB yüksek bulunmuştu. Olgu operasyonun yedinci günü kaybedilmişti.
Olgu 2: 27 yaşında erkek hasta rinoplasti uygulanmak üzere ameliyata alınmıştı. Birkaç dakika sonra, nabzın 50/dk'ya düşmesi nedeniyle yapılan atropini takiben nabız ve kan basıncı yükselen, SpO_2 değeri %96'dan %90'a düşen olgunun ateşi 41°C (105.8°F) ölçülmüş, CPK-MB değeri yüksek bulunmuştu. Olgu anestezinin başlangıcından yedi saat sonra kaybedilmişti. Olguların tıbbi ve adli belgeleri Adli Tıp Kurumu Birinci ve Üçüncü Adli Tıp İhtisas Kurulu'nda incelendi. Her iki olguda da ölümün malign hipertermiye bağlı olarak meydana geldiği kararına varıldı.
Anahtar Kelimeler: Malign Hipertermi; Anestezi; Ölüm.

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Introduction

Malignant hyperthermia (MH, malignant hyperpyrexia) susceptibility (MHS) is a rare pharmacogenetic muscular disorder and may lead to potentially fatal complications during and/or after general anesthesia. MH is triggered by volatile anesthetics and depolarizing muscle relaxants.[1,2]

In this paper, we present two death cases caused by MH which had developed during general anesthesia, and we discuss their properties according to related data.

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Case Reports

Cases' medical-forensic documents were evaluated retrospectively in the First and Third Specialization Board of the Council of Forensic Medicine (F-TSBCFM), Turkey, and the cases' progresses were as follows:

Case 1

The case, a 24-year-old-male, was taken to the operating room for lombar disc hernia operation in a state hospital. Preoperative anesthetic examination findings and laboratory analyses were found normal and the case was evaluated as an ASA-1 patient. When anesthesia was begun, the pulse was 85/min, systolic blood pressure (BP) was 125 mmHg, SpO_2 was 96%. Induction was realized by 300 mg propofol + 100 mg succinylcholine + 45 mg atracurium besilate**.** Anesthesia maintenance was provided by 50% O_2/N_2O, 1.5-2% halothane, 25 mg atracurium besilate**.** After 30 minutes, tachycardia (120/min) was observed, which was followed by bradycardia at the 35th minute and cardiac arrest at the 45th minute of the operation. Anesthetic gases were immediately turned off and 100% O_2 was given. The patient was taken to the supine position and cardiopulmonary resuscitation (CPR) was applied. Since his cardiac beats came back on the 15th minute of CPR, intubated patient's treatment was continued in the intensive care unit. Mechanical ventilation support had been provided (SIMV Mod, SpO2: %80, RR: 10/dk TV: 650 ml). Antiedema theraphy was started for hypoxic encephalopathy. He was unconscious. His fever was 39.5°C (103.1°F) and convulsions were observed. BP: 130/90 mmHg, pulse: 130/min. The patient was transported to another hospital's intensive care unit, with the diagnosis of "cardiac arrest + malignant hyperthermia + hypoxic encephalopathy", on the same day. Upon admission to the other hospital, he was unconscious, babinsky +/+, BP: 160/100 mmHg, pulse: 186/min and the fever was measured as 40°C (104°F). The doctors continued to the antipyretic theraphy and cooling application. Creatine kinase (CK) was 2838 U/L and CK-MB was 102,3 U/L. Spontaneous respiration was present but insufficient, so mechanical ventilation support was continued. After antipyretic and cooling application, the fever declined to 36°C. Slight brain edema was determined at the cranial tomography. Forty eight hours later, widespread brain edema and spontaneous subarachnoidal hemorrhage were observed. At the seventh day of the operation, Glasgow coma scale was 3. Despite inotropic therapy, BP was low (70/40 mmHg). The patient died at the same day (after seven days from the operation).

At the autopsy, there was no specific finding macroscopically. Edema in the lungs and in the brain was determined histopathologically. The results of the systematical toxicologic analyses were negative.

Case 2

The case, a 27-year-old-male, was taken to the operating room for rhinoplasty operation in a private hospital. A rhinoplasty operation to the patient's sister was performed without any problem by the same operation team last year. Before the anesthesia application, his pulse was 85/min, BP was 130/70 mmHg and intramuscular 50 mg pethidine HCl was injected. Induction was realized by 400 mg thiopental sodium + 80 mg succinylcholine and vecuronium bromide 4+2 mg + isoflurane 1-2% were used for anaesthesia maintenance. After a few minutes, the pulse decreased to 50/min. 0.5 mg atropine was injected and the pulse increased to 120-130/min/arrhytmic. This pulse rate was evaluated as due to the atropine injection and 5 vials local anaesthetic injection with ephynephrine to the operation area for hemostasis. Despite the antiarrhythmic drug application, his pulse and BP progressed at high levels. SpO_2 decreased from 96% to 90% Then, the operation was terminated. Anesthetic gases were turned off and 100% O_2 was used. When the operation clothes were removed away from the patient, it had been observed that his skin color was rather reddish and his fever was 41°C (105.8°F). Fever decreased to 37-38°C by cooling application. It was thought that the patient might be an MH case. Since his spontaneous respiration was insufficient, extubation couldn't be performed. Hypotension developed (6-7 mmHg max), and dopamine infusion was started. In the blood analysis, CK-MB was 105 U/L. After 5-6 hours from the beginning of the operation, hemorrhage increased in the operation area. Thus two units of fresh blood were perfused to the patient. Since respiratory insufficiency was continuing, the patient was transported to another hospital's intensive care unit. Although resusitation was applied twice (during the transportation and on the entrance to the intensive care unit), the case died after seven hours from the beginning of anesthesia.

At the autopsy, the left lung, binding the main bronchus region, was taken out for analysis of pethidine, ceftriaxone, prostigmine, lidocaine, metoprolol and active ingredients of dopamine, ketamine and atropine There was no a specific finding macroscopically. The histopathological results revealed edema and diffused intraalveolar fresh hemorrhage in the lungs; and, vascular congestion in the brain, liver, kidneys, surrenals and pancreas. Toxicologic analyses' results were as follows: active ingredients of pethidine and lidocaine were determined in the internal organ samples; a subtance of barbituric acid derivation (95 ng/ml), 0,432 microgram/ml lidocaine, 0,447 microgram/ml pethidin

were determined in the blood sample; isoflurane was determined in the lung. Halothane and other substances (ceftriaxone, prostigmine, metoprolol and active ingredients of dopamine, ketamine and atropine) were negative in the blood. Other systematical toxicologic analyses' results were negative as well.

After all of the medical-forensic documents of both cases' were investigated at the F-TSBCFM, Turkey, they were evaluated as MH cases.

Discussion

MH is a dominantly-inherited skeletal muscle disorder. MH can make a fatal uncontrolled skeletal muscle hypermetabolic reaction with general anaesthetics. This is caused by the increased release of Ca^{2+} from the sarcoplasmic reticulum to the cytoplasm by the ryanodine receptor 1 (RyR1). Most of the persons who have MHS have a parent with MHS. However, the parent may not have experienced an episode of MH.[3-5] Only few diagnostic tests are available for screen the patients. The most accurate test is a skeletal muscle biopsy.[6] Clinical signs of MH involve hyperthermia to high degrees, tachycardia, tachypnea, acidosis, unexplained elevation of end-tidal CO2, increased oxygen consumption, hypoxemia, muscle rigidity, evidence of rhabdomyolysis and renal failure.[2,6]

Larach et al analyzed the cases of MH reported to the North American MH Registry.[7] They found out that 74.8% of the cases were young males with 286 episodes. MH family history was determined in 6.5% of all cases. Hypercarbia, sinus tachycardia or masseter spasm were the most frequent initial MH signs.[7] Similarly, both of our cases were young males and there was not a family history in any of them.

There is no data about the incidence of MH in Turkey. Both of our cases were, 24 and 27 years old, males. Propofol + succinylcholine + atracurium besilate + halothane were used in the first case whilst thiopental sodium + succinylcholine + vecuronium bromide + isoflurane were used in the second case for anaesthesia. Therefore, both succinylcholine and volatile anaesthetics, which may trigger MH, were used for the anaesthesia of both cases. First case died seven days after the operation and his general situation was bad during this period. Similarly, second case died after seven hours from the starting of anesthesia. Tachycardia (120/min), followed by bradycardia, and cardiac arrest at the 45th minute of the operation and 39.5°C (103.1°F) - 40°C (104°F) fever, and hypoxemia were the first symptoms of the first case. On the other hand, bradycardia (50/min), followed by tachycardia and arrhytmia (130-140/min), decreased SpO_2 (from 96% to 90%), and 41°C (105.8°F) fever were the first symptoms of the second case. CPK-MB was high in both cases but muscle rigidity was not observed in any of them. Operations were planned and MH courses were lethal in both cases.

If a patient doesn't have a related family history, MH is often discovered after the patient is given anesthesia during surgery and the course carries fatal risk. Although its incidence is seldom at the present time, patients given general anesthesia still carry risks for developing MH.

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