A Fatal Malignant Hyperthermia Syndrome in an Anxious Patient

Ülkü AYPAR
Meral SOYLU
Kemal ERDEM

Department of Anaesthesia, Faculty of Medicine, Hacettepe University Hospital, ANKARA

ANXİETELiHASTADA FATAL BİR MALİGN HİPERTERMİ VAKASI

Geliş Tarihi: 12 Aralık 1986

SUMMARY

A fatal case of malignant hyperthermia in a 30 year-old female was presented. The patient : was anaesthetized on 3 occasions previously and anesthesia was uneventful. Definite symptoms of Mil developed 5 minutes before the termination of the operation 12 ami a half hours after the be ginning of anaesthesia). The patient's oral temperature was over 43'C, serum K and creatine phosphokinase levels determined during the hypertermic episode ivere 6. 7 mmoi/L and 23 'WO iy/1, respectively. The same drugs were used for the first and third anaesthesia. They did not elicit the MH response. The patient's enxiely before the operation is believed to have played •iip role iWfdhe l^enWis of MR; The duration'of anaesthesia, known triggering agents and made quale anaesthesia might have been suspected as another triggering factors.

According to the patient's clinical picture, laboratory data and family history we consider that this case was a typical Mil synirome.

Key w -o! •. Malignant **hyperthermia,** anxiety

özet

30 yaşındaki kadın hastada Hallux Varus operasyonu sırasında göriden bir malign hipertermi vak •' sunuldu. Hastanın öyküsünden daha ome i kez anestezi aldığı ve anestezinin olaysız geçtiğiipğremldi.

Malign lıiperterminin hehrgın semptomları operasyonun biliminden 5 dakika önce ortaya çıktı {anestezinin başlangıcından 2.5 sual sonra). Has oral ısısı 13 (iun üzerinde ıdı ve hıpertermik dönemde serum K ' değeri s 7 mnud.lt ve kreatinın fosfokinaz seviyesi 2K0V0 irfit > la rak saptandı öyküsünden birinci ı e uçunca anestezisinde de aynı ilaçların uygulandığı ve malign h . ernıı cevabı oluşmadığı öğrenildi

Anestezi süresinin, bilinen tetik çekici ajanların ıhaiolhun. süksinilkolin) uygulanmış olması ve hastanın operasyondan önce mevcut anxietesinin malign lıiperterminin oluşmasında rot oynadığı düşünüldü

Hastanın klinik tablosu, laboratuar bulguları ve aile öyküsü birlikte değerlendirilen l; bu vaka nın tipik fatal bir malign hıpertermı sendromu olduğu kanısına varıldı.

Anahtar kelimeler: Malign hiperlrrmt, anxieh ,

T Kl Tıp Bil Araş Dergisi C.6, S.1, 1988 57-60;

TJ Research Med Sci V.6 N.1, 198857-60

Malignant hyperthermia is a potentially fatal condition and is characterized by an inherited susceptibility to certain drugs used in anaesthesia which cause a rapid increase in body temperature, muscle rigidity, severe metabolic and respiratory acidosis, hyperkalemia and myoglobinuria. Many patients known to have this condition have been exposed to the known inducing agent previously, sometimes on more than one occasion (Brit et al., 1970; Halshall et al., 1979; Fletcher et al., 1981). On the other hand, patients who have displayed MH reactions have been subsequently anaesthetized with contra-indicated drugs without any untoward effects (Halshall et al., 1979). The reason for the variable expression of the condition within on individual remains a mystery, although genetic variability has been implicated in this pattern of triggering, there is evidence suggesting that other factors could be involved, environmental factors or certain drugs can effect the response to MH triggers.

We wish to present a fatal case of MH in healthy young woman, who had 3 previous anaesthesia without hyperthermia.

Table - I

Results of Laboratory Tests

Creatinine Phosphokinase	**28.000**	**U/l**
Lactic dehydrogenase	**1.680**	**U/l**
Serum Na	**113**	**m mol/1**
Serum K	**7.80-8.70**	**m mol/1**
Clorur	**81**	**m mol/1**
Carbondioxide	**9**	**mEq/1**
Triiodothyronine (T3)	**.25**	**n mol/1**
Thyroxine (T,)	**20.08**	**n mol/1**
Cortisol	**9828**	**n mol/1**
ACTH	**200**	**pqr/ml**
Ionized calcium (Ca)	**.50**	**m mol/1**

CASE REPORT

A 30 year-old female was admitted to the hospital for the surgical treatment of hallux varus. She had been in good health and physical and neurologic examination were within normal limits. She had minimal bilateral exophtalmus but serum triiodothyronine and thyroxine levels and thyroid scanning were within normal limits. She was anaesthetized on 3 occasions previously. 5 years ago she had undergone surgery for acute appendicitis under general anaesthesia. The anaesthesia and recovery was uneventful and the drugs used were thiopentone, 0_2, N_2O, halothane and succinylcholine. 2 years previously second surgical intervention was for D-C, and the same anaesthetic drugs were administered, except succinylcholine. At the same year, she had undergone a surgery for hallux varus. The same anaesthetic technique was used that time. The anaesthesia and recovery were also uneventful.

She was very anxious before last intervention. She was premedicated with atropine 0.5 mgr and haloperidol 5 mgr i.m. before the operation. Anaesthesia was induced with thiopentone sodium 5 mg/kg i.v. Endotracheal intubation was performed with 1 mg/kg i.v. succinylcholine without difficulty. Anaesthesia was maintained with 0.5-1% halothane and 70% N_2O in O_2 in a semi-closed system. Two more doses of succinylcholine (50 and 50 mg) were given during the anaesthesia. After spontaneous respiration had returned, her respiration was assisted till the end of the anaesthesia. The course was uneventful for the 2 and a half hours. The arterial blood pressure was 120-130 mrnHg and heart rate was 80-90/min during the anaesthesia. About 5 min before the end of the operation (2 and a half hours after the beginning of the anaesthesia) a severe tachycardia (150/ beats per min) and tachypnea was observed. The body temperature started to increase very rapidly. The anaesthetics were immediately discontinued. Ventilation was controlled with 100% 0_2. The operation was rapidly terminated. Ectopic beats became evident followed by bradycardia. The patient was very hot, sweating and cyanosed in spite of breathing 100% O_2. Malignant hyperthermia was suspected. Because the patient's oral temperature was over 43 C and an energetic surface cooling was initiated with cooling blanket and ice. The anaesthetic tubing and soda-lime were replaced with new units. Blood samples were withdrawn for the determination of K^+, Ca**, creatinine phosphokinase, lactic dehydrogenase, ACTH, $C0_2$, Ca^, T_3, T_4. Arterial blood samples were taken for pH, $pC0_2$ and $p0_2$. The muscular rigidity and cardiac arrest occurred. Sodium bicarbonate 700 m mol and two litre of ice-cold ringer lactate solution were infused. A urinary catheter was inserted. Methylprednisolone 2 gr, prilocaine 400 mg and frusemide 80 mg and glucose 17.5% with soluble insulin 24 units were given.

Dopamine 200 /ig/min was infused to increase cardiac out-put. The patient responded to the resusitation and blood pressure was 50 mmHg, oral temperature was over 43 C and her pulse rate 160 beats per minute. In spite of active cooling and vigorous treatment, urinary output was 20 ml during resusitation. Cardiac arrest occurred again and the pupils were dilated and were not reacting to light. Pulmonary oedema was realized and the patient did not response to resusitation. Arterial gas analysis during hyperthermia episode reveoled severe acidosis (pH 6.94, $pC0_2$ 56 mmHg, $p0_2$ 91 mmHg). Serum creatine phosphokinase and lactic dehydrogenase were 28.000 u/1 and 1680 I/L, respectively during hyperthermia. The laboratory data obtained during hyperthermia were as follows; serum Na 113 mmol/litre, serum K 8.7 mmol/litre, serum chloride 81 mmol/litre, glucose 81 mol/litre, Cortisol 9828 m mol/litre, ACTH 200 pqr/ml, T_3 25 n mol/1, T_4 20.08 n mol/1. The results of laboratory tests is shown in Table-I.

DISCUSSION

The patient exhibited the typical features of MH with the characteristic signs of high temperature, tachycardia, hyperventilation, cyanosis at the end of anaesthesia. The same anaesthetic drugs were used (thiopentone, N_2O, 0_2 and halothane) for the first, third and fourth anaesthesia. Succinylcholine was used with halothane for the first, third and fourth anaesthesia. It was not used for the second time, because it was for D-C and was performed without endotracheal intubation. The previous anaesthetics didn't elicit the MH response. At once, the case suggested the similarity of the signs and symptoms of a thyroid storm. Because thyroid storm or decompensated thyrotoxicosis can occur if the hyperthroid patient is stressed. The severity of a thyroid storm varies from a febril reaction to hypotension, coma, cardiac decompensation and ultimately death (Mackin et al., 1974). The patient has had bilateral

exophtalmus. However, serum triiodotyronine and thyroxine levels and also thyroid scan were within normal limits before the operation. These levels were 20.08 nmol/1 and .25 nmol/1 during MH episode, respectively, excluding the possibility of thyrotoxicosis. Many of clinical manifestations of both disorders (thyrotoxicosis and malignant hyperthermia) are compensatory mechanism for dissipation of excessive heat and both disorders appear to be associated with stress and sudden death. The similarity of these two disorders has been suggested by Peters, Nance and Wingard, 1981. They reported 2 children in whom thyrotoxicosis was mistaken for MHS, We didn't suggest the present case as thyrotoxicosis after the determination of creatinine phosphokinase. Because it was reported hyperthroidism had decreased the level of creatinine phosphokinase, to the half of normal (Nevins, et al., 1973). Serum creatine phosphokinase level was 28.000 ti/1 and serum trirodothyronine and thyroxine levels were very low. So the present case was considered to be MH. But we believe that thyrotoxicosis should be considered in the differential diagnosis of MHS at any age.

The patient had general anaesthesia previously without any complication. Many patients known to be MH. susceptible have had previous anaesthetics without untoward effects (Brit and Kalow, 1979; Halshall et al., 1979; Kolb et al., 1982). The previous anaesthetics didn't elicit the MH response in our patient. The MH response at the fourth anaesthesia may be explained by the anxiety of the patient. She was afraid of death before the fourth anaesthesia and triggering agents (halothane and succinylcholine) were used together for this time. Anxiety is believed to play an important role in the genesis of MH (Mogenson, Misfeldt, 1974) and this may explain why some MH patients may previously not have reacted to known triggening agents. Wingard (1977), described intolerance of MH patients to stresses such as heat, emotions and trauma. Anxiety, inadequate anaesthesia (light anaesthesia) and known triggering agents (halothane, succinylcholine) all of together could be responsible for this fatal case. Screening of the patient's family history revealed that her symptoms were hereditary. Her father and her sister had a history of muscle cramping. Her father had a history of recurrent dislocations of the shoulders.

He underwent total hip prothesis 15 years ago. He died in the operation theatre. The cause of death was obscure (unknown, but it could be related to anaesthesia).

The striking feature of this case was the onset of MH at the end of the operation. Beldaws et al. (1971) have argued that the delay in onset of symptomps indicate low grade susceptibility of the patient due to a relative mild genetic defect that therefore fairly large and prolonged concentration of anaesthetic agents are required to trigger a MH episode. The fact the patient had been previously anaesthetized using contraindicated drugs without developing MH raises serious doubt as to the role of incomplete penetrance of MH gene(s-)< as an important reason why susceptibility infrenqurently expresses itself (Halshall et al., 1979; Kolb et al., 1982).

The duration of anaesthesia for this time was longest compared with the previous anaesthesias. Halothane and succinylcholine were used for this anaesthesia. The patient's anxiety before the operation is believed to have played an important role in the genesis of MH. Fletcher et al., 1981 reported a 30 year old female who was anaesthetized on three occasions. The safe anaesthetic drugs were used for the first anaesthesia and anaesthesia was uneventful. Addition of suxamethonium on the second occasion and use of the original drugs plus nitrous oxide for the third anaesthesia produced symptoms of MH. Frinberg et al., (1983) reported three cases of postoperative malignant hyperthermia in whom safe anaesthetics was used. The considered stress in the postoperative period may have been triggering factor responsible for these reactions. A case of another postoperative malignant hyperthermia was presented by Schulte, et al. (1983). Definite symptoms of MH developed in a 3 year old girl who had six previous anaesthesia 30 min after the termination of anaesthesia. The unusual occurrence of MH in the postoperative period was discussed with the regard to the human stress syndrome.

In the preoperative period, it is important to avoid subjecting the patient to anxiety and stress. We were not aware from the patient's susceptibility of MH before the operation. We consider the maximum body temperature and serum K levels were important in the prognosis of this fatal case. If serum K levels exceeds 7 mEq/per liter the mortality sharply increased and mortality was directly related to the severity of the fever (Brit, et al., 1977). The patient's K level was 7.3, 7.7 mEq/liter and 8.8 mEq/liter during MH and body temperature was over 43 C creases the armamentarum of the anaesthetist in treating patient's with MH. We have no dantrolone in our clinic. We believe the drug is specific for the treatment of MH. Despite absence of a muscle biopsy (due to the legal problems) we can consider that the present case was very typical fatal MH syndrome.

Acknowledgements

We would like to thank Dr. Mümtaz Alpaslan, Associate Professor, Department of Orthopaedic Surgery, Hacettepe University Hospital, for their help.

REFERENCE

1. Mackin JF, JJ Canary, CS Pittman: Thyroid and its management. N.Eng.J.Med. 291:1396-1398, 1974.
2. Peters RK, P Nance, DW Wingard: Malignant hyperthyroidism or malignant hyperthermia. Anaest.Analg. 60, 613-615, 1981.
3. Nevins MA, S Madhukar, M Bright, LJ Lyon: Pit falls in interpreting serum creatinine phosphokinase activity. J.A.M.A. 224, 1382-1386, 1973.
4. Brit BA, W Kalow: Malignant hyperthermia: A statistical review. Can.Anaesth.SocJ. 293-315, 1970.
5. Halshall PJ, PA Cain, R Ellis: Retrospective analysis of anaesthetics received by patients before susceptibility to malignant hyperpyrexia was recognized. Br.J.Anaesth. 51, 949-954, 1979.
6. Kolb ME, ML Home, R Martz: Dantrolone in human malignant hyperthermia. A multicenter study. Anesthesiology 56, 254-262, 1982.
7. Mogenson JV, BB Misfeldt, HK Hanel: Preoperative excitement and malignant hyperthermia. Lancet 1, 461, 1974.
8. Wingard DW: Malignant hyperthermia acute stress syndrome of man; in Malignant Hyperthermia Current Concepts (ed. ED Henschel), p. 79, New York, Appleton-Century-Crofts, 1977.
9. Beldavs J, V Small, DA Cooper, BA Britt: Postoperative malignant hyperthermia: A case report. Can.Anaesth. Soc.J. 18, 202-212, 1971.
10. Fletcher R, E Ranklev, K Olsson, S Leander: Malignant hyperthermia syndrome in an anxious patient. Brit.J. Anaesth. 53, 993-995, 1983.
11. Frinberg R, G Edelist, A Gordon: Postoperative malignant hyperthermia episodes in patients who received "safe" anaesthetics. Can.Anaesth.Soc J. 30, 273-276, 1983.
12. Schulte US, W Hess, HJ FJberlein: Postoperative malignant hyperthermia and dantrolone therapy. Can.Anaest. Soc.J. 30, 635-640, 1983.
13. Brit BA, FF Kwong, and Endrenyl Laszlo: The clinical and laboratory features of malignant hyperthermia: Current Concepts, pp. 9-45, EO Henschel (ed.), New York, Appleton-Century-Crofts, 1977.