POSTOPERATIVE PROLONGED APNEA IN WEILL MARCHESANI SYNDROME

WEILL MARCHESANI SENDROMUNDA UZAMIŞ POSTOPERATİF APNE

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SUMMARY: Weill Marchesani Syndrome (WMS) is an unusual systemic connective tissue disorder: This case report describes two sisters, 17 and 18 years old. wirh WMS. Both patients underwent glaucoma surgery and had prolonged postoperative recovery times because of apnea and on apparent residual neuromuscular block. Additional anesthetic exposures with different anesthetic drugs in both patients were uneventful. In this report, the possible interactions among the applied drugs, rho hereditary syndrome and prolonged apnea were discussed.

Key Words: Weill Marchesani Syndrome, Complications, Anesthesia, Postoperative Apnea.

ÖZET: Weill Marchesani Sendromu (WMS), nadir görülen bir sistemik konnektif doku hastalığıdır. Sendrom karakteristik olarak mikroseferofaki, ektopik lens, glokom, brakiodaktili ve brakiomorfi içermektedir. Bu olgu sunumunda, glokom cerrahisi geçiren, belirgin rezidüel blok ve postoperatif apne gelişen 17 ve 18 yaşlarında ikt kız kardeş bildirilmektedir. Her iki hastanında bir sonraki anestezi uygulamaları farklı anestezik ajanlar kullanılarak sorunsuz tamamlanmıştır. Bu yazıda, uygulanan ilaçlar arasındaki muhtemel reaksiyonlar, konjenital sendrom ve uzamış apne nedenleri araştırılarak, tartışılmıştır.

***Anahtar** Kelimeler: Weill Marchesani Sendromu, Komplikasyon, Anestezi, Postoperatif Apne.*

INTRODUCTION

Weill Marchesani syndrome (WMS) was first reported by Weill in 1932 (1). It is an inherited, unusual systemic connective tissue disorder characterized by microspheraphakia, ectopia lentis, glaucoma, brachydactyly and brachymorphy (2.3). In this report, we describe two sisters, 17 and 18 years old, with WMS, who underwent glaucoma surgery and had prolonged postoperative recovery times because of apnea and an apparent residual neuromuscular block. Additional anesthetic exposures in both patients with different anesthetic drugs was uneventful. The possible interactions between the applied drugs, the hereditary syndrome and the etiology of pmlonged apnea are discussed.

CASE REPORTS

Case I: An 18-year-old female (155 cm, 58 kg) received an urgent operation for acute glaucoma. She was healthy. and there was nothing remarkable in her history before the operation. Her neck and metacarpals were short. Except for limited joint mobility, physical examination and laboratory investigations showed normal results. Premedication was not carried out. Anesthesia was induced with i.v. thiopental 6 mg/kg, and intubation was facilitated with succinylcholine i.v. (1 mg/kg). After

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returning respiratory effort, further muscle relaxation was provided with pancuronium 0.06 mg/kg. Anesthesia was maintained with 0.5-1% end-tidal halothane and 50% nitrous oxide in oxygen. The patient did not need additional muscle relaxant, and no opioids were given. Ventilation was performed manually, the respiratoly rate was 14-17 per minute and end-tidal CO_2 partial pressure ($ETCO_2$) was 35-40 mmHg. She received mitomycin 0.50 mg for trabeculotomy. No complications occurred during the 90 minutes of the operation. Five minutes before the end of the surgery halothane was discontinued. At the end of surgery, there was no respiration effort. Miotic pupillary positive light reflex and negative corneal reflex were obsewed, and $ETCO_2$ was 45 mmHg. Body temperature measured in the axilla was 36.6°C. While vital parameters (arterial pressure, pulse) were in normal ranges and stable, she was unconscious and apneic. Manual ventilation with 100% oxygen was maintained. At this time, neummuscular monitoring (Fisher & Paykel innervator NS 252 constant current peripheral newe stimulator, New Zealand) was initiated, and the trains of four stimuli (TOF) were applied. A twitch response was the only visible response to the first stimulus of TOF. When TOF testing was repeated at maximal currents, the patient did not show any discomfort. The TOF rate (T4 I T1) was found to be 60% at the 30th minute following the discontinuation of halothane, and neuromuscular blockage was reversed with neostigmine (1.5 mg) and atropine (0.5 mg). Respiration improved at the postoperative 40th minute. The patient was extubated when she responded to verbal commands and spontaneous respiratory rate exceeded 16 breaths/min (postoperative 60th min.). After the application of oxygen (3 L /min) for I hour, she was transferred to the ward without complications.

Case II: A 17-year-old female (157 cm, 65 kg) patient, the sister of Case I, was operated on with the same anesthesia protocol for the same disorder. A trabeculotomy was performed with mitomycin. During the 100 minutes of the operation, opioid or additional muscle relaxant were unnecessary. Halothane was decreased from 1% to 0.5% in the last 20 minutes and discontinued in the last 10 minutes of the operation to avoid postoperative prolonged apnea, which developed in Case I. The patient was unconscious and showed no respiration effort at the end of surgery. At this time, $ETCO_2$ was 40 mmHg, and the TOF rate was 50%. While ventilation was maintained with 100% oxygen, the respiration effort started spontaneously in the postoperative 25th minute. Neuromnscular blockage was reversed with neostigmine (1.5 mg) and atropine (0.5 mg). The patient improved approximately in the postoperative 45th minute and was extubated. Twenty minutes later, she was alen and all vital signs were normal. She was transferred to recovery without complications.

Case I was operated on again for secondary glaucoma 1 week after her first operation. and Case II was operated on for chomidal detachment 10 days after the first operation. In both patients, endotracheal intubation was performed using atracurium (0.6 mg/kg) following induction with thiopental (6 mg/kg). Anesthesia was maintained with 0.8-1.5% end-tidal isoflurane and 50% N_2O in O_2 and a repeated dose of atracurium (0.4 mg/kg). Ventilation was performed manually during the operation and the respiratory rate was 14-17/min and $ETCO_2$ was 35-45 mmHg. The patients did not receive mitomycin during their second surgeries. At the end of surgery. spontaneous breathing and swallowing started. Meanwhile the TOF rates were 70-80%. No complications occurred dnring the operations, which lasted 145 and 170 minutes, nor dnring the postoperative period.

DISCUSSION

Postoperative prolonged apnea is one of the most important complications of general anaesthesia. Frequent causes are relative overdoses of the administered hypnotic agent, the opioid or the muscle relaxant (4). Furthermore, abnormal pseudocholinesterase (PCE) can prolong recovery with the usual doses of succinylcholine (5). Antibiotics, especially aminoglycosides, in clinical doses can augment depolarizing and nondepolarizing neuromuscular block (6). WMS is a connective tissue disorder associated with skeletal brachymorphism. Hypertrophy of connective tissue may impair nerve function, but no primarily neuromuscular dysfunction has been related to WMS. To our knowledge, there is no article about postoperative apnea in WMS although many patients with

WMS have been operated under general anesthesia. (7). There were three factors which may have caused prolonged apnea in our patients: 1) the prolonged central effects of halothane, 2) the use of mitomycin and 3) the use of succinylcholine (the presence of an atypical PCE enzyme).

Volatile anesthetics can substantially increase the effect of neuromuscular blocking drugs (8). Halothane, at subanesthetic concentrations, is known to decrease the acute hypoxic response. The 0.11% concentration of halothane on the ventilatory response can cause hypoxia. The initial depression of the TOF responses in these cases indicates residual neuromuscular block. However, these are more than sub-MAC concentrations of halothane.

Mitomycin is an antineoplastic agent. Systemic toxicity and respiratory depression was not reported, although very high concentrations of mitomycin are widely used in surgical procedures (9,10). Mitomycin 1-2 ml out of. 0.25 mg/ml solutions was administered by the surgeon performing the operations on our patients. We do not think that such a small dose of mitomycin has systemic effects and causes prolonged apnea.

The prevalence of homozygotes for an abnormal PCE in the general population is about 1 in 2500 (5). Although the patients' PCE levels were in normal limits (Case-1= 5260 U/L, Case-2= 6870 U/L; 4000-10.000 U/L), the patients may have suffered from an inherited, homozygous defect of the PCE, and thus showed a prolonged neuromuscular block after succinylcholine. The time for sufficient recovery of neuromuscular function following the usual doses of succinylcholine (1-1.5mg/kg) was of 3-6 hours in patients homozygous for the atypical gene (11). We were unable to detect whether the PCE enzyme was abnormal due to technical limitations. Nevertheless, the postoperative apnea that we encountered was not as protracted. Therefore, we thought that it was not due to an abnormal PCE enzyme. However, Ostergaard and co-workers reported that a prolonged effect of non-depolarising drugs is seen following succinylcholine (12). With the findings discussed above, we thought the reason for the prolonged apnea in our patients was the prolonged effect of pancuronium following succinylcholine.

In conclusion, it is a problem for many anesthetists to correctly diagnose prolonged apnea in patients, especially patients with an inherited disorder. We therefore urge the anesthetist to use neuromuscular monitoring.

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