Clinical Case Report

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Prolonged neuromuscular block associated with cholinesterase deficiency

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Abstract

Rationale: Hereditary genetic mutations may cause congenital cholinesterase deficiency. When succinylcholine and mivacurium are applied on cholinesterase-deficient patients during general anesthesia, prolonged postoperative asphyxia occurs, which is an uncommon but very serious complication.

Patient concerns: A previously healthy 30-year-old female presented prolonged spontaneous breathing recovery after general anesthesia.

Diagnoses: After the patient's postoperative spontaneous breathing recovery delayed, the plasma cholinesterase was found to be 27 U/L, which was far below the normal level (4000 U/L to 13500 U/L). This patient had no disease that can cause plasma cholinesterase deficiency and was therefore diagnosed as congenital cholinesterase deficiency.

Interventions and outcomes: The patient was sent to the intensive care unit (ICU) intubated for mechanical ventilator support, and on the next day the tracheal tube was removed without any complications when her spontaneous respiration resumed.

Lessons: Cholinesterase is an enzyme secreted by the liver involved in many physiological processes in human body. Plasma cholinesterase commonly contains acetylcholinesterase (AChE) and butyrylcholinesterase (BChE). When succinylcholine and mivacurium are applied on patients with cholinesterase-deficiency during general anesthesia, prolonged postoperative asphyxia occurs, which is an uncommon but very serious complication. Lately, new evidences have suggested that hereditary genetic mutations may be responsible for congenital cholinesterase deficiency.

Abbreviations: AChE = acetylcholinesterase, BChE = butyrylcholinesterase, BCHE = butyrylcholinesterase gene, COLQ = acetylcholinesterase associated collagen gene, ICU = intensive care unit.

Keywords: gene mutation, plasma cholinesterase deficiency, prolonged neuromuscular block, succinylcholine

1. Introduction

Plasma cholinesterase refers to an enzyme with a tetrahedral structure called pseudocholinesterase produced in the liver. It generally contains acetylcholinesterase (AChE) and butyrylcholinesterase (BChE). It has significant relationship with clinical anesthesia for its influence on the metabolism of muscle relaxants such as succinylcholine and mivacurium.[1–3]

Succinylcholine is a depolarizing muscle relaxants which has been used in clinical for decades for its ability to create the ideal intubation condition in 60 seconds.[4–6] However, due to its side effects including myalgia, massive hyperkalemia, malignant hyperthermia, and apnea observed in individuals with plasma cholinesterase deficiency, there were scholars thought it had been out of date and should be eliminated.[7] As administrated, succinylcholine is metabolized by pseudocholinesterase and turns to the succinylmonocoline, only a small amount of which can reach the neuromuscular junction.[8] It explains why patients will experience prolonged spontaneous breathing recovery when they suffered from plasma cholinesterase deficiency.

So far, few cases of delayed anesthesia caused by cholinesterase deficiency have been found. While this study is about a patient we have recently encountered that has a cholinesterase deficiency and prolonged postoperative recovery.

We have obtained written consent from the patient for publication and the image of it has been attached. There is no ethical approval because this study is a retrospective case report.

2. Case report

A-30-year-old, 50-kg, 160-cm woman, ASA I, was prepared to undergo resection of her vocal cord polyps, before which she had undergone no other surgery. During our preoperative assessment, no significant family history or personal history was found and no special laboratory or radiographic examination concerned to us. We used 10 mg propofol, 0.2 mg fentanyl for the anesthesia induction. Succinylcholine 100 mg was administered to facilitate endotracheal intubation, after which we used cisatracurium 4 mg for the intraoperative muscle relaxation. Without any complications, the whole surgery lasted for 30 minutes approximately with propofol and remifentanil for anesthesia maintenance. Unexpectedly, the patient had not been breathing spontaneously for

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10 minutes since the end of the surgery. Then we used neostigmine 1 mg and atropine 0.5 mg to reverse the neuromuscular blockade. However, the patient showed no reaction for the next 30 minutes. In order to exclude the effect of residual fentanyl, we added naloxone 0.2 mg. Without knowing the reasons for the patient's spontaneous breathing failure to recover, we immediately gave her a blood biochemical test and found the plasma cholinesterase was measured and was low at 27 U/L, far below the normal level (4000 U/L to 13500 U/L). Then with stable vital signs, the patient was left intubated and transferred to the intensive care unit (ICU) for further treatment, provided with mechanical ventilatory support. Without any complications, she was extubated when she had been breathing spontaneously the next morning, when was about 10 hours after the operation. Since this patient had no diseases that would cause cholinesterase deficiency previously, we highly suspect her cholinesterase deficiency is congenital. Although after she was discharged from the hospital, we would like to conduct further examinations for her, which includes genetic test, but failed to obtain patient consent.

3. Discussion

Generally, human body mainly contains 2 cholinesterases: acetylcholinesterase (AChE) and butyrylcholinesterase (BChE). Plasma cholinesterase deficiency could be caused by a variety of factors including genetic causes, kidney or liver disease, malnutrition, major burns, cancer, pregnancy, certain drugs or after cardiopulmonary bypass.[9–12] These may be associated with amino acid mutations at the active site of the enzyme, which reduces the cholinesterase of charged compounds, thus reducing the affinity of the charged substrate such as acetylcholine.[13] Under normal circumstances, the degradation of acetylcholine mainly depends on the connection of cholinesterase and AChE associated collagen gene (COLQ) collagen chains, 1 end of which is linked to an enzyme-active cholinesterase, and the other is linked to an anchor protein in the cell membrane. The AChE subunit, together with the anchor protein, regulates the activity and function of the enzyme. The reduction of AChE will eventually lead to the prolonged action of muscle relaxants (such as succinylcholine) and delayed recovery.[14,15] The latest study found that patients with cholinesterase deficiency have a large number of inserts and multiple mutations in the COLQ gene, which leads to the change of No. 430 or No. 432 amino acid and cause structural and functional abnormalities in collagen Q. Eventually, collagen Q may cause an abnormal release of cholinesterase, resulting in a decrease in serum AChE content.[16] On the other hand, as an autosomal recessive trait, mutations in the gene of different efficacies may also caused BChE deficiency.[17–21] Butyrylcholinesterase gene (BCHE) is a small gene located at chromosome 3, 3q26.1- 26.2.[22–24] According to previous studies, some significant variants related to decreased enzyme activity have been discovered such as the atypical (A-variant),[25] the Kalow (K-variant),[26] the fluoride (F-variants)[27] and the silent variant (S-variants). Evidence has suggested that seven new variants of the BCHE which might cause the BChE deficiency and led to the prolonged effect of succinylcholine and mavacurium finally.[21]

In this case, the patient was a young woman who was admitted to our hospital for vocal cord polyps. Not suffering from any kidney or liver disease or taking any special medicine, she was considered most likely to be congenital cholinesterase deficiency. However, due to limited conditions, we did not have the opportunity to give her a genetic test or check the plasma cholinesterase levels of her family members.

4. Conclusion

In conclusion, patients with cholinesterase deficiency may be encountered in our work. Once a patient highly skeptical, comprehensive laboratory tests are essential preoperatively and succinylcholine should be avoided during anesthesia. So far, no optimal management has been established for prolonged neuromuscular blockade following succinylcholine. Continuous mechanical ventilation until the function of the neuromuscular recovers is one feasible option as we did in this case. As 1 option to supplement the plasma cholinesterase, fresh frozen plasma may be administered to facilitate the recovery of muscle relaxation.[28] In this case, if we had a neuromuscular stimulator to measure the neuromuscular blockade, we would deal with the situation of this patient faster and better. Better equipment support and better genetic testing for special patients may be the direction of our efforts in future anesthesia work.

Author contributions

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