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Case Report

CASE REPORT

Delayed diagnosis of butyrylcholinesterase deficiency with insufficient neuromuscular monitoring and a confounding effect of SedLine® brain function monitoring: a case report

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Abstract

Intraoperative monitoring has always been a vital part of the care of an anaesthetised patient. Neuromuscular monitoring is important to use when patients have received neuromuscular blocking agents. Quantitative neuromuscular monitors are preferred over qualitative monitors and clinical judgement alone in reducing residual neuromuscular block and the associated respiratory complications. Additionally, brain function monitors can be utilised to assess the level of consciousness in anaesthetised patients. These monitors can be useful during surgical procedures and at the conclusion of a procedure to show the progress of a patient emerging from anaesthesia. We describe a case where a lack of neuromuscular monitoring after a single dose of succinylcholine coupled with an overemphasis on SedLine® brain function monitor values delayed the diagnosis of butyrylcholinesterase deficiency in a patient undergoing a mastectomy for breast cancer. This case shows the fundamental importance of using neuromuscular monitors in patients who receive neuromuscular blocking agents. It also stresses the necessity to utilise brain function monitors as clinical aids, but not allow them to hinder thinking about broader differential diagnoses when faced with challenging clinical scenarios.

Keywords: anaesthesia; BIS; breast cancer; butyrylcholinesterase deficiency; electroencephalogram; neuromuscular monitoring; SedLine; succinylcholine

Butyrylcholinesterase (BChE, also known as plasma cholinesterase) deficiency is a rare inherited or acquired defect in the BChE enzyme that consequently results in delayed recovery from certain neuromuscular blocking agents (NMBAs) used during general anaesthesia, specifically succinylcholine (succinylcholine apnoea) and mivacurium. BChE levels are not part of routine preoperative testing, and therefore, BChE deficiency is often diagnosed at the conclusion of surgery when a patient does not have sufficient muscle strength for their trachea to be safely extubated.

Neuromuscular monitoring is widely deployed in anaesthesia practice when NMBAs are administered. Quantitative, objective measurement of neuromuscular function is favoured over qualitative monitoring with a peripheral nerve stimulator when determining recovery from NMBAs.[1] Not using appropriate neuromuscular monitors can lead to increased rates of residual neuromuscular block and associated problems such as acute respiratory events (i.e. hypoxaemia and reintubation) and increased resource utilisation (i.e. increased hospital length of stay).[2]

Brain function monitors that use processed electroencephalogram (EEG) indices, such as SedLine® (Masimo Corporation, Irvine, CA, USA) or Bispectral Index™ (BIS™) monitors (Medtronic Inc., Minneapolis, MN, USA) are frequently used to characterise the depth of sedation or anaesthesia in patients undergoing various procedures.

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However, there is limited research studying the efficacy of processed EEG monitors such as SedLine or BIS in predicting adverse events.[3] To the best of our knowledge, this is the first report describing the confounding effect of a SedLine monitor in the absence of neuromuscular monitoring in diagnosing BChE deficiency. The patient has provided written consent for the publication of this report.

Case report

A 71-yr-old female with stage IIA invasive ductal carcinoma of the right breast presented to our institution for right mastectomy, targeted axillary node dissection, and sentinel node biopsy. She had recently completed six cycles of Taxotere–carboplatin–herceptin–pertuzumab (TCHP) chemotherapy with good clinical response and no complications. Her past medical history included moderately controlled hypertension and type 2 diabetes. Her past surgical history included a breast biopsy, cholecystectomy, and three Caesarean sections all performed at other institutions. She denied any prior complications with anaesthesia or any family history of complications.

The patient's preoperative vital signs were unremarkable except for a blood pressure of 175/89 mm Hg. She weighed 75 kg and had a BMI of 32 kg m^{-2}. Examination of the respiratory and cardiovascular systems was otherwise normal: examination of the airway showed good mouth opening and a Mallampati class III airway. Laboratory investigations revealed an elevated white blood cell count of 12.64 k μl^{-1} with a left shift. Her haemoglobin concentration was low at 9.8 g dl^{-1} and the platelet count was high at 538 k μl^{-1}. Additionally, her blood glucose concentration was elevated at 175 mg dl^{-1}, plasma potassium concentration low at 3.2 mmol l^{-1}, and plasma alkaline phosphatase concentration was high at 121 U L^{-1}. A recent electrocardiogram showed sinus tachycardia with possible left atrial enlargement. Her echocardiogram was normal with an ejection fraction of 55–60% and no valvular abnormalities.

The patient's surgery was completed under general endotracheal anaesthesia. She received premedication with intravenous (i.v.) midazolam 2 mg, and then anaesthesia was induced i.v. with lidocaine 60 mg, propofol 150 mg, and fentanyl 50 μg. Succinylcholine 100 mg was administered to facilitate tracheal intubation. The anaesthetic was maintained with inspired desflurane (range 6–8%) and an additional dose of i.v. fentanyl 50 μg given upon incision. She was ventilated using a volume-controlled mode with tidal volumes of 400 ml, ventilatory frequency of 10 bpm, positive end-expiratory pressure of 5 cm H_2O, and fraction of inspired oxygen (FiO_2) of 50%. The surgery proceeded smoothly, and the patient's condition remained stable throughout.

At the conclusion of surgery, and after 1.5 h of operating time, the patient experienced a delayed awakening from anaesthesia. The SedLine monitor, which we routinely use during all anaesthetics at our institution, had shown a patient state index (PSI) that ranged from 25 to 36 during the majority of the operation. PSI values between 25 and 50 indicate an optimally anaesthetised patient, and our patient's values remained 30–40 even after the desflurane had been turned off for more than 30 min. Additionally, the patient was not initiating any spontaneous breaths on the ventilator. Both i.v. naloxone 0.4 mg in divided doses and flumazenil 0.2 mg were administered out of concern for delayed metabolism of fentanyl and midazolam, respectively, yet the patient's status remained unchanged.

Even with the low SedLine PSI readings, our focus now turned to residual neuromuscular block and specifically BChE deficiency. Our patient did not receive non-depolarising NMBAs and only received succinylcholine on induction. When we checked the response to train-of-four peripheral nerve stimulation at the ulnar nerve, only two weak twitches of the adductor pollicis muscle were detected. Around this time, the SedLine PSI finally started to increase, and the patient even briefly opened her eyes to command. With a high suspicion for BChE deficiency, we immediately started an i.v. propofol infusion 70 μg kg^{-1} min^{-1} to prevent awareness in the setting of prolonged muscle paralysis.

The patient remained sedated on the ventilator and was transferred to the post-anaesthesia care unit (PACU). In the PACU, the patient started to follow some commands to voice and was initiating spontaneous breaths on a pressure-assist mode of ventilation. Her grip strength remained weak, and she required more ventilatory support than would be needed to safely extubate her trachea. We then transferred her to the intensive care unit (ICU) with a working diagnosis of BChE deficiency.

Several hours later in the ICU, the patient had four strong twitches at the adductor pollicis muscle in response to ulnar nerve stimulation. An arterial blood gas was obtained and showed a normal pH and satisfactory oxygenation and ventilation on minimal ventilatory support with a low FiO_2. Her sedation was completely weaned off, and she was easy to arouse, following verbal commands, and with little to no pain at the surgical site. The trachea was successfully extubated ~8 h after the administration of i.v. succinylcholine. The patient was observed in the ICU overnight and discharged home the following day.

Just before the patient was discharged from the hospital, we asked her if she remembered anything from her time in the operating room, PACU, or ICU. She had no recollection of being in the operating room. She did remember being in the PACU and ICU, but stated she had remained comfortable with the sedation and ventilatory support. Before the patient left the hospital, we sent a sample of her blood to an outside laboratory to check a BChE level and dibucaine number. Her BChE level was low at 797 U L^{-1} (normal 2900–7100) and dibucaine number was low at 29% (normal >80%), strongly suggesting that she has the homozygous atypical variant of BChE deficiency. She was counselled on the disease process of BChE deficiency and understood the implications for future anaesthetics and surgical procedures.

Discussion

Neuromuscular monitoring for patients who have received NMBAs has been advocated globally as a result of the increased recognition of the adverse effects of impaired muscle function on clinical outcomes.[4] Many anaesthesiology societies have national guidelines stating that the depth of neuromuscular block must be monitored in patients receiving NMBAs, ideally with quantitative monitors at a peripheral nerve.[5] The American Society of Anesthesiologists does not currently provide guidelines for monitoring neuromuscular block, although development is reportedly underway.[6] In our case, we did not place a peripheral twitch monitor on the patient after she was administered succinylcholine. Admittedly, had we placed a twitch monitor (our institution does not have quantitative monitors) early in the anaesthetic care, we would have likely recognised the unusually long duration of deep

paralysis from a single dose of succinylcholine much sooner. This may have led us to more quickly diagnose BChE deficiency.

It is not unusual for patients at our institution undergoing breast surgery to receive a single dose of succinylcholine to facilitate tracheal intubation without any further need for non-depolarising NMBAs. We find that ventilating the lungs of such patients after the succinylcholine has been metabolised is not typically a problem. We rarely see significant changes in airway pressures when an adequate depth of anaesthesia with inhalation agents and opioids is maintained. Our patient's lungs did remain easy to ventilate throughout, yet this is typically the case with these types of procedures at our institution, so it did not alert us to anything unusual happening with her pulmonary compliance.

It is certainly prudent to check that a patient has recovered completely from succinylcholine utilising a quantitative neuromuscular monitor or at least a qualitative twitch monitor. It is difficult to know how many practitioners throughout the world quantify the depth of neuromuscular block after a single dose of succinylcholine, and there is likely significant variance between nations and even hospitals within each nation. In fact, a Danish study looking at >30 000 patients found the use of neuromuscular monitors in patients only receiving succinylcholine to be as low as 3%.[7] Other physicians have published case reports on the necessity of neuromuscular monitoring in order to establish a diagnosis of BChE deficiency in those patients receiving succinylcholine.[8 9]

The SedLine monitor can be a valuable tool to help clinicians assess the depth of anaesthesia in patients undergoing various surgical procedures.[10] Whether this equates to less intraoperative awareness or better patient outcomes remains largely unknown.[11] In our case, the low SedLine PSI values and our failure to deploy a neuromuscular monitor early on, led us to think that our patient was a slow metaboliser of the volatile anaesthetic, opioids, or benzodiazepines. This led to a delay in considering other possibilities for the prolonged emergence from anaesthesia that our patient experienced.

Our institution utilises the SedLine monitor in the majority of operations requiring general anaesthesia. The regular use of this monitor at our institution stems from a few cases of patient awareness under general anaesthesia that occurred over several years. Although the SedLine PSI values correlate with the depth of anaesthesia, the monitor itself may not aid in predicting adverse events or even awareness under anaesthesia, and therefore is not advised for routine use.[3 11 12] We have become accustomed to following PSI values on most patients, and in our case the continued low PSI values caused us to focus on ways to reverse the patient's depth of anaesthesia. Had we not used the SedLine monitor, yet also applied a twitch monitor after the administration of succinylcholine, we may have broadened our differential diagnosis more rapidly to include conditions such as BChE deficiency.

Delayed emergence after anaesthesia is typically related to the lingering effects of anaesthetic agents or analgesic medications. Other causes of delayed emergence include drug interactions, serotonin syndrome, postoperative delirium, central anticholinergic syndrome, psychiatric disorders, narcolepsy, surgical complications, and regional anaesthesia complications.[13] These rare causes of delayed emergence are mostly limited to case reports. In our case it is possible that our patient had another reason for delayed emergence such as residual anaesthetic agents in addition to having BChE deficiency. Our patient did not display major signs of being awake yet paralysed, such as extreme hypertension and tachycardia. Furthermore, there is no guidance in the literature on whether BChE deficiency itself can lead to a delayed wakeful state of consciousness. Fortunately, our patient had no recollection of the delayed emergence giving some merit to the low PSI values that we continued to observe.

It is imperative to use neuromuscular monitors after the administration of all NMBAs, including succinylcholine, in order to avoid the effects of residual neuromuscular block, and in our case, aid in the diagnosis of BChE deficiency. The use of neuromuscular monitors (ideally quantitative monitoring of the abductor pollicis muscle) is supported by a solid body of evidence and guidelines from many national anaesthesiology societies. Additionally, EEG brain function monitors, such as SedLine, have allowed clinicians to objectively assess a patient's depth of consciousness under anaesthesia. However, our case shows that these monitors have the ability to be a confounding factor and can even delay the diagnosis of BChE deficiency. This case highlights the importance of always using neuromuscular monitors when NMBAs are administered, maintaining a broad differential diagnosis when confronted with delayed emergence, and using brain function monitors such as the SedLine as clinical aids while acknowledging their limitations.

Authors' contributions

Wrote the manuscript and performed the literature search: AL.
Helped review and edit the manuscript: VR.
Conceptualised, designed, edited, and reviewed the manuscript: DN.

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Declaration of interest

The authors declare that they have no conflicts of interest.

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