Unexpected prolonged coma after general anesthesia in a patient with history of type II diabetes mellitus

Sir,

Delayed emergence from general anesthesia (GA) is a relatively common occurrence in the operating room. It is often caused by the effect of drugs administered during the surgery. It can also be caused by other etiologies such as metabolic and electrolyte disturbances. However, prolonged coma after GA has not been reported in the literature.

A 43-year-old female patient (height 175 cm and weight 100 kg), presented for bilateral breast reduction under GA for symptomatic macromastia. Her medical history was significant for nonischemic cardiomyopathy with an ejection fraction of 55%, hypertension, chronic kidney disease, obesity, and noninsulin-dependent diabetes mellitus (DM). The patient had undergone a successful gastric bypass 4 years prior to this admission and stopped her diabetic medications 1-year ago as instructed by her primary care physician.

Her current medications included metoprolol, hydralazine, furosemide, simvastatin, amlodipine, aspirin, and isosorbide. She did not visit our preanesthesia clinic as requested. At the time of preoperative evaluation, the patient denied taking any medications in the morning of surgery. Her preoperative lab results were: Hb 10.6 g/dL; platelets 243 k/μL, Na 137 mmol/L; K 4.3 mmol/L; Cl 109 mmol/L; CO_2 21 mmol/L; blood urea nitrogen 27 mg/dL; Cr 1.6 mg/dL; fasting blood sugar 106 mg/dL on the day of surgery. Echocardiogram: Normal sinus rhythm with heart rate 65 bpm.

In total, 2 mg of midazolam was administered preoperatively for anxiolysis. GA was induced with propofol and fentanyl and maintained with sevoflurane. Rocuronium was administered for muscle paralysis. The patient remained hemodynamically stable throughout the intra-operative course. Bispectral index monitoring numbers were maintained in high 30 s to low 50 s range. The total operative time was a little over 5 h. For entire surgery, she received 250 μg of fentanyl and 2 mg of hydromorphone (dilaudid) for pain control and 4 L of lactated Ringer's solution. Toward the end of the procedure, sevoflurane was switched off, and paralysis was fully reversed. Her respiratory rate was 15-18/min, and end-tidal CO_2 was between 35 and 45 on pressure support ventilation. However, the patient did not emerge from GA despite zero end-tidal sevoflurane concentration. Physical examination revealed a pin-point pupil on the left side (her right pupil was obscured by corneal opacification). Naloxone (total 200 μg) was administered, and miosis was reversed; however, the patient remained unconscious.

Venous blood gas (VBG) was drawn, which showed normal electrolyte and hematocrit levels. However, the patient's blood glucose was found to be 40 mg/dL, which improved to 174 mg/dL with immediate treatment. She was still unresponsive to verbal and painful stimuli.

The patient remained intubated and was immediately subjected to a head computed tomography scan, which was negative for any acute changes. The patient was then transferred to the Surgical Intensive Care Unit (SICU) for a neurological consultation. Her laboratory results on admission to SICU showed Na 138 mmol/L; K 4.4 mmol/L; Cl 113 mmol/L; calcium 8.6 mg/dL; magnesium 1.4 mg/dL and phosphorus 3.5 mg/dL. Detailed inquiry with her family after surgery led to the finding that she self-administered 10 units of neutral protamine hagedorn insulin the night before surgery, the fact which she either forgot or chose not to share with the medical team.

In SICU, she remained unresponsive to sternal rub or nail bed pressure. Her left pupil was unresponsive/minimally responsive to light. Spontaneous dorsiflexion of the left foot followed by extension and inward rotation of the right arm was consistent with decorticate posturing. There were some episodes of rhythmic movements without clonus in SICU that raised the question of seizure activity. On the postoperative day (POD) 1, 24-h continuous video electroencephalography (EEG) was performed, which showed a burst-suppression-like pattern with prominent voltage attenuation and occasional θ and δ waves. However, there was no seizure activity. A detailed neurological assessment was performed, including EEG, magnetic resonance imaging, diffusion-weighted imaging of the head, and magnetic resonance angiography of the head and neck, all of which were negative for any diagnostic findings.

On POD 2, a physostigmine trial and more naloxone were administered, and the patient remained comatose with sporadic movement of extremities. Our inability to wean her off from the ventilator necessitated a tracheostomy on POD 9.

The patient gradually became more responsive over the next 2 weeks. She started mouthing words on POD 26. Two days later, when a speech valve was implemented, she started talking, following commands, but was still not oriented with respect to time, place, and the person. With the help of physical therapy, she regained muscle strength and was able to ambulate. Her cognitive function recovered slowly as well.

She was discharged to a rehabilitation facility 9 weeks from the day of her initial surgery.

On finding pin-point pupil, we considered opioid overdose was the reason of delayed emergence. However, naloxone reversed miosis, but did not awaken the patient. Hypoglycemia was also considered a possible culprit, but again she remained unresponsive even after we corrected hypoglycemia. She continued to have 2 months of coma after GA. Although hypoglycemia was the only abnormal finding throughout her hospital course, she did not show signs of "typical" hypoglycemic coma.

First, the duration of coma was extremely long. It was unusual for a patient to take 4 weeks to regain consciousness after hypoglycemia coma. Most patients with hypoglycemic coma become awake shortly after treatment.[1] The reason of prolonged coma after hypoglycemia in our patient is unclear. Hypothyroidism has caused delayed emergence from GA.[2] Although the symptoms of hypothyroidism can be subtle, our patient did not have fatigue, weight gain, mood changes, etc. Her single thyroid - stimulating hormone level after discharge was normal. Patients with mitochondrial disease are sensitive to anesthesia[3] and hypoglycemic coma can be the presenting sign in Addison's disease.[4] However, we did not think these were possible etiologies based on medical history of our patient.

Second, the reversibility of the long period of coma after hypoglycemia was surprising. The desired duration of insulin-induced coma is 30 min because the "reversible coma" would become "irreversible coma" if the patient remained comatose for longer than 30 min. Severe and persistent hypoglycemia can cause irreversible neuronal damage. Widespread decortication occurs after 60 min of hypoglycemic coma.[5] Our patient did wake up after 4 weeks of unconsciousness and did not have "irreversible" coma although she lost her short-term memory. Studies have shown sevoflurane attenuated ischemic brain damage.[6] Whether sevoflurane provides cerebral protection during a hypoglycemic insult is intriguing. Our case is in agreement with the previous statement that "coma of substantial depth and duration is less dangerous when caused by hypoglycemia than by anoxia-ischemia.[7]"

Third, during hypoglycemia, the brain cells catabolize protein and deaminate amino acids, resulting in increased ammonia production. Decreased glycolytic flux during hypoglycemia also causes decreased production of lactate. Therefore, one of the biochemical changes in hypoglycemic brain damage is metabolic alkalosis, which results from increased ammonia production and lactate deficiency. We did not check arterial blood gas intra-operatively; however, VBG of our patient at the end of surgery showed pH 7.28, PCO_2 47.3, and lactate 0.7. The patient did not have metabolic alkalosis, and her lactate level was at the lower end of the normal range.

Blood glucose levels widely overlap in different clinical pictures. In a prospective study of 125 patients admitted in the emergency department, the glucose levels at which a patient became comatose ranged between 2 and 18 mg/dL, whereas a patient may not enter coma at glucose levels between 5 and 25 mg/dL.[7] Because the blood glucose level does not predict symptoms. Investigators disagree as to what the blood glucose level should be before the symptoms can be attributed to hypoglycemia.[7] However, compared with diet-controlled diabetic patients, those who take insulin and oral hypoglycemic drugs are at greater risk for hypoglycemia.[1,7] These patients need more attention during the peri-operative period. Detailed preoperative evaluation should be performed for each patient, ideally in preanesthesia clinic. Had this patient been consulted in our preanesthesia clinic, she would have been inquired in more details and educated in terms of appropriate insulin use before surgery and would probably not have had hypoglycemia. A huge medical cost would have been saved by avoiding a potential complication. This case emphasizes the important role of anesthesiologists as peri-operative physicians in patient care and patient safety.

Currently, American Society of Anesthesiologists guidelines are silent about intra-operative rechecking of blood glucose levels in either healthy patients or those with well-controlled diabetes who had normal preoperative glucose values. There are no consensuses or other guidelines for monitoring such patients. However, patients with a history of DM, even currently off diabetic medications need more attention during peri-operative period. We suggest frequent intra-operative monitoring of glucose levels in patients with risk factors for hypoglycemia, particularly for prolonged cases.

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