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CORRESPONDENCE

Recurrent non-epileptiform seizure-like phenomena secondary to propofol administration

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To the Editor,

Propofol is a short-acting, lipophilic anesthetic and has been used to treat refractory status epilepticus.[1] However, there have been reports of propofol-induced "seizure-like phenomena" (SLP).[1] Little is known regarding the underlying pathophysiology or electroencephalographic correlates of SLP,[1,2] and no reports of recurrent SLP exist.

We report a case of a 57-yr-old male, admitted for ulnar nerve transposition. Past medical history included mitral valve prolapse, gastro-esophageal reflux, dyslipidemia, and no known drug allergies. There was no history of seizures or alcohol/illicit drug abuse. Prior anesthetic history was unremarkable. Induction of anesthesia was achieved with midazolam (2 mg), fentanyl (200 μg), propofol (200 mg), and dexmedetomidine (44 μg). General anesthesia was maintained using sevoflurane and a dexmedetomidine infusion. Reversal of anesthesia, including awakening and extubation, were unremarkable. Total surgical time was 90 min. The patient was monitored in the postanesthesia care unit for ongoing nausea. Four hours postoperatively, the patient was witnessed to have a 15-min episode of what appeared to be uncontrollable shivering. Bilateral arm and leg movements were observed, with associated tachycardia (heart rate 204 beats·min^{-},[1] tachypnea (respiratory rate 24 beats·min^{-1}) and subsequent desaturation (SpO_2 85%). He was able to speak throughout. Oxygen saturation improved to 95% with supplemental oxygen, and temperature was 36.5°C at the time of the incident. The etiology of this unusual motor activity was not clearly established.

Eight months later, he returned for revision decompression. Induction of anesthesia was achieved with midazolam (3 mg), fentanyl (150 μg), propofol (150 mg), remifentanil (150 μg), and succinylcholine (60 mg). Anesthesia was maintained using desflurane (1.0 MAC) and hydromorphone boluses (1.6 mg total). Total surgical time was 100 min. Emergence was initially uneventful, with the patient extubated awake and following commands. Two minutes following extubation, he no longer followed commands. Subsequently, generalized movements of all four extremities appeared (SLP, video: available as Electronic Supplementary Material), and he was treated with intravenous midazolam (2 mg, followed by an additional 1 mg). The movements stopped after approximately one minute. Despite subsequent treatment with propofol and additional midazolam, intermittent episodes of movements with similar duration followed with increasing frequency throughout the patient's stay in

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the recovery room. He was eventually reintubated and admitted to the intensive care unit. Propofol infusion was initiated at 2.5 mg.kg.hr^{-1} and abnormal movements ceased. Neurology was consulted. Non-contrast computed tomography and magnetic resonance imaging of the brain were unremarkable. When the propofol infusion was decreased to 1 mg·kg^{-1}·hr^{-1}, SLP recurred. Concurrent electroencephalography demonstrated slow background activity, in addition to widespread frequency dispersion in wakeful rhythm (Figure), but no epileptiform activity. Seizure-like phenomena ceased with administration of a 20 µg bolus of dexmedetomidine, followed by a 0.8 µg·kg^{-1}·hr^{-1} infusion. He was successfully extubated, and discharged 24 hr later.

The unusual motor responses associated with propofol administration may be secondary to antagonism of glycine receptors located in subcortical structures.[3] Such antagonism may be more predominant at lower propofol doses, such as during emergence.[4] Higher doses result in suppression of movements. In our case, SLP appeared to cease during administration of higher propofol doses but re-emerged with decreasing doses. Other theories suggest that abnormal movements are secondary to the effect of toxic metabolites from altered propofol metabolism, or SLP may represent an allergic reaction to preservatives.[1] A psychogenic etiology has also been proposed.[1,2]

Given this behaviour following emergence from the second anesthetic, we re-evaluated the patient's unusual motor responses that followed the first surgical procedure, which led us to postulate that the SLP at that time may also have been associated with propofol administration. An important matter to consider is that the onset of symptoms occurred hours after propofol administration. A 200 mg propofol bolus would yield an expected effective site concentration of 0.06 mg·L^{-1} at 90 min, and 0.01 mg·L^{-1} at six hours.[5] Although these concentrations are sub-anesthetic, the relationship between the effect site concentration of propofol and SLP has not been elucidated. Propofol is lipophilic, with a large volume of distribution. Thus, despite its initial half-life of

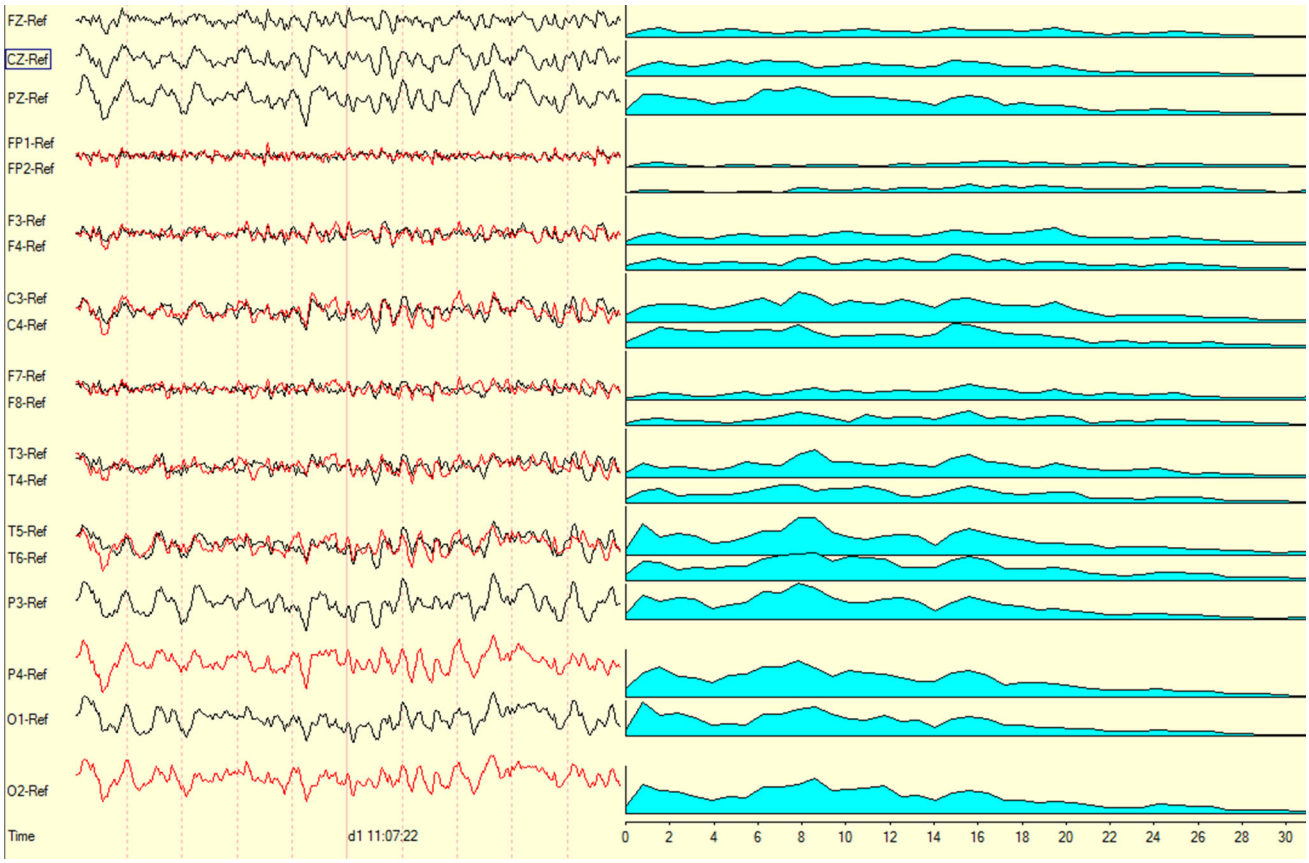

Figure Non-epileptic abnormalities noted on electroencephalogram (EEG) recorded from surface scalp electrodes during seizure-like phenomena that may be propofol related. *Left panel*: black trace: left hemisphere; red trace: right hemisphere. *Right panel*: wide-spread frequency dispersions (depicted by frequency distributions in a pattern of multiple peaks) of the corresponding EEG signal shown on right. Sensitivity 5 mcV/mm. Time scale in seconds

approximately 40 min, it has a terminal half-life that ranges from 60 min to as much as three days, thereby persisting in the body for hours.[1,2] About 25% of cases of SLP attributed to propofol administration occur following emergence.[1] Of course, we cannot rule out other anesthetic drugs' contribution to the appearance of the observed episodes of SLP. With our patient, the abnormal movements appeared to cease following administration of dexmedetomidine, suggesting that it may be an effective treatment for propofol-induced SLP, possibly by increasing central GABAergic transmission.[6]

Conflicts of interest None declared.

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