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CASE REPORTS

Sufentanil-Associated Seizure-Like Tonic–Clonic Activity in a Patient with Pituitary Macroadenoma and Hypopituitarism: A Case Report

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ABSTRACT

BACKGROUND:

Opioid-associated convulsive episodes are exceedingly rare during anesthesia induction. When they occur, they typically manifest within seconds of intravenous opioid administration as generalized tonic–clonic movements without epileptiform EEG activity, suggesting a pharmacodynamic origin.

CASE:

We present a 67-year-old male with a pituitary macroadenoma and panhypopituitarism who developed generalized tonic–clonic seizure-like activity immediately after receiving 20 µg of sufentanil during anesthesia induction. The episode lasted approximately 30 seconds, accompanied by a blood pressure spike to 220/110 mmHg and oxygen desaturation to 65%. It resolved spontaneously with supportive care. Surgery was postponed, and the patient was monitored in the intensive care unit; later that day, neurological examination and EEG results showed no acute abnormalities.

CONCLUSIONS:

Even small doses of sufentanil may rarely be associated with seizure-like motor phenomena during anesthesia induction. Because EEG was not recorded during the event, definitive differentiation between an epileptic seizure and opioid-induced nonepileptic motor activity was not possible. Underlying endocrine dysfunction may have represented an additional vulnerability, although this association remains speculative.

Keywords: Sufentanil; Seizure-like activity; Hypopituitarism; Pituitary macroadenoma; Adrenal insufficiency; Anesthesia induction

Introduction

Opioids used during anesthesia induction are rarely associated with seizure-like activity, but such cases have been reported since the early 1980s (1). Subsequent reports described similar generalized tonic–clonic movements after alfentanil, sufentanil, and remifentanil (2). These episodes typically develop within seconds of intravenous opioid administration and may present as generalized tonic–clonic movements without epileptiform activity on electroencephalography (EEG), raising the possibility of opioid-associated excitatory motor phenomena rather than definite epilepsy (1–3).

Proposed mechanisms include acute disinhibition of GABAergic interneurons, opioid-induced muscle rigidity manifesting as convulsions, or activation of subcortical motor pathways (1–3, 5). Notably, fentanyl and sufentanil have no known convulsant metabolites, supporting the possibility of a direct pharmacodynamic contribution to these events (1–3).

Patient-specific factors such as metabolic or endocrine disorders may contribute to a lowered seizure threshold (4–7). In particular, adrenal insufficiency may reduce the production of neurosteroids that enhance GABA-mediated inhibition and is often associated with hyponatremia; both of these consequences of cortisol deficiency may predispose patients to seizure-like phenomena (4–7). Because intra-event EEG monitoring is rarely available during anesthesia induction, distinguishing epileptic seizures from opioid-associated nonepileptic motor phenomena may be challenging.

Case Presentation

A 67-year-old male (94 kg) with a 2.5 cm pituitary macroadenoma extending to the suprasellar area and compressing the optic chiasm was admitted for an elective transsphenoidal resection. The patient had no personal history of seizures or epilepsy. Informed consent was obtained from the patient prior to the preparation of this report.

Preoperative endocrine evaluation revealed secondary adrenal insufficiency and central hypothyroidism consistent with hypopituitarism. He was stabilized with hormone replacement therapy. As part of perioperative management, 100 mg of hydrocortisone was administered intravenously one hour before induction. No sedative premedication was administered. Standard monitors were applied (ECG, noninvasive blood pressure, pulse oximetry, and bispectral index). Initial vital signs were stable: oxygen saturation 99%, heart rate 78/min, and blood pressure 135/80 mmHg.

Following preoxygenation, induction began with an intravenous dose of 20 µg sufentanil administered over 20 seconds. No hypnotic or neuromuscular blocking agent had been administered before the event. Within seconds of injection, the patient developed generalized tonic–clonic seizure-like activity characterized by generalized rigidity, tonic extension, clonic limb movements, upward gaze deviation, and loss of consciousness. The episode lasted approximately 20–30 seconds. During the event, arterial pressure increased to 220/110 mmHg, and oxygen saturation decreased to 65%. Assisted mask ventilation with 100% oxygen was initiated, and 5 mg of intravenous midazolam was administered. The episode resolved spontaneously and transient nonsustained arrhythmias were observed on ECG monitoring. After stabilization, anesthesia was deepened with propofol and rocuronium, and the trachea was intubated uneventfully.

Following the event, surgery was aborted, and the patient was transferred to the intensive care unit for observation. On admission, his neurological examination was normal with no focal deficits. Serum sodium, glucose, calcium, and magnesium levels were within normal ranges before and after the event. An EEG performed later that day showed no epileptiform activity, although this did not exclude a transient peri-induction epileptic event. A postoperative head CT scan showed no acute intracranial abnormalities, and neurological examination remained normal without focal deficits. In light of these findings, the procedure was postponed for one week.

One week later, anesthesia induction was modified, given the prior adverse event: no sufentanil bolus was used, and anesthesia was maintained with target-controlled infusions of propofol and remifentanil. The second induction and surgery were uneventful, and the patient made a full recovery.

Discussion

The close temporal relationship between sufentanil administration and symptom onset strongly suggests an association between sufentanil exposure and the observed event. However, because no intra-event EEG was available, definitive differentiation between epileptic seizure activity and opioid-induced nonepileptic motor phenomena was not possible. Similar episodes have been documented with fentanyl and sufentanil during induction; these episodes were usually brief and self-limited (1–3).

The differential diagnosis includes transient epileptic seizure, opioid-induced rigidity, opioid-induced myoclonus, hypoxia-related convulsive activity, metabolic disturbances, and psychogenic nonepileptic activity. Metabolic causes were considered unlikely given normal glucose and electrolyte values before and after the episode. Hypoxia-related motor activity was also considered less likely because oxygen desaturation occurred after the onset of abnormal movements. Opioid-induced rigidity remains a plausible alternative explanation, particularly given the temporal relationship with opioid administration and the presence of generalized tonic posturing.

Underlying endocrine dysfunction may have represented an additional vulnerability in this patient. Adrenal insufficiency has been associated with altered neurosteroid-mediated GABAergic inhibition and lowered seizure threshold in experimental and clinical settings. However, the patient had received perioperative hydrocortisone replacement and had normal electrolyte and glucose values at the time of the event. Therefore, any contribution of hypothalamic–pituitary–adrenal axis dysfunction remains speculative. Structural epilepsy related to the pituitary macroadenoma could not be definitively excluded, although the patient had no previous seizure history, postoperative neurological examination was normal, and head CT imaging showed no acute intracranial abnormalities. A psychogenic nonepileptic event was considered unlikely in the context of abrupt onset immediately following intravenous opioid administration during anesthesia induction.

In comparison with previously reported cases of opioid-associated seizure-like activity, the present case shares several key features. Across published reports, including the review by El-Karamany (1) and the case described by Silva-dos-Santos et al. (2), the characteristic pattern consists of generalized tonic–clonic movements beginning within seconds of intravenous opioid administration at low or standard doses, resolving spontaneously within 30–60 seconds, and—when EEG was simultaneously available—showing no concurrent epileptiform activity. Tonic–clonic activity specifically following sufentanil administration has been documented since at least 1987 (1), and comparable events have been reported with fentanyl, alfentanil, and remifentanil. The present case is consistent with this established pattern in all major respects: onset within seconds of a 20 µg sufentanil bolus, generalized tonic–clonic semiology with rigidity and upward gaze deviation, and spontaneous resolution within approximately 30 seconds. A distinguishing feature of the current case, not uniformly reported in the literature, is the severity of hemodynamic compromise (arterial pressure 220/110 mmHg, oxygen desaturation to 65%) and the concurrent endocrine vulnerability. The absence of prior seizure history and the unremarkable post-event neurological evaluation and neuroimaging further align with the nonepileptic pattern characteristic of most reported opioid-associated motor events (1, 2).

The marked hypertension, oxygen desaturation, and transient arrhythmias observed during the episode emphasize the importance of prompt airway and hemodynamic support when unusual motor phenomena occur during anesthesia induction. Although EEG monitoring is not routinely used during anesthesia induction, additional neurophysiological monitoring may help characterize similar events in selected high-risk patients.

When the surgery was rescheduled, the anesthetic plan was adjusted—notably avoiding a rapid sufentanil bolus. Anesthesia was maintained with titrated infusions of propofol and remifentanil, and the second surgery proceeded without incident. The uneventful second procedure after modification of the anesthetic plan supports the practical value of avoiding rapid sufentanil bolus administration following a suspected opioid-associated neuroexcitatory event, although it does not establish definitive causality.

Conclusion

Sufentanil may rarely be associated with seizure-like tonic–clonic activity during anesthesia induction. In the absence of intra-event EEG monitoring, distinction between true epileptic seizure and opioid-induced nonepileptic motor activity may be impossible. Careful opioid titration, avoidance of rapid bolus administration, optimization of endocrine status, and readiness for immediate airway and hemodynamic support may improve perioperative safety in vulnerable patients.

Table 1. Timeline of peri-induction events

Time/Event	Clinical findings and interventions
Preoperative evaluation	Pituitary macroadenoma with secondary adrenal insufficiency and central hypothyroidism diagnosed; patient stabilized with hormone replacement therapy
1 h before induction	100 mg intravenous hydrocortisone administered
Baseline monitoring	Blood pressure 135/80 mmHg; heart rate 78/min; oxygen saturation 99%
Induction initiated	20 µg intravenous sufentanil administered over 20 seconds; no hypnotic or neuromuscular blocking agent given prior to event
Seconds after sufentanil administration	Generalized tonic–clonic seizure-like activity: generalized rigidity, tonic extension, clonic limb movements, upward gaze deviation, and loss of consciousness
During the episode	Blood pressure increased to 220/110 mmHg; oxygen saturation decreased to 65%; transient nonsustained arrhythmias observed
Immediate management	Assisted mask ventilation with 100% oxygen; 5 mg intravenous midazolam administered
After resolution of the episode	Anesthesia deepened with propofol and rocuronium; tracheal intubation performed uneventfully
Post-event management	Surgery aborted; patient transferred to intensive care unit for observation
Same-day evaluation	Neurological examination normal; laboratory findings unremarkable; EEG showed no epileptiform activity; head CT showed no acute intracranial abnormalities
One week later	Repeat anesthesia without sufentanil bolus using target-controlled infusions of propofol and remifentanil
Final outcome	Second surgery uneventful; patient recovered without neurological sequelae

REFERENCES

1. El-Karamany M. Epilepsy-like movements induced by fentanyl analgesia: case study and review. Egypt J Intern Med. 2017;29(2):86–90.
2. Silva-dos-Santos A, Costa S, Moitinho M. Transdermal fentanyl–induced seizures: case report and literature review. Prim Care Companion CNS Disord. 2022;24(3):20cr02885.
3. Vanmarcke A, Lormans P, Vandewaeter C. Status epilepticus following intrathecal bupivacaine and sufentanil: a case report. J Investig Med High Impact Case Rep. 2022;10:23247096221090841.
4. Nardone R, Brigo F, Trinka E. Acute symptomatic seizures caused by electrolyte disturbances. J Clin Neurol. 2016;12(1):21–33.
5. Reddy DS, Rogawski MA. Neurosteroids – endogenous regulators of seizure susceptibility. In: Noebels JL, Avoli M, Rogawski MA, Olsen RW, Delgado-Escueta AV, editors. Jasper's Basic Mechanisms of the Epilepsies. 4th ed. Bethesda: National Center for Biotechnology Information; 2012.
6. Villegas K, Eason B, Janiec K, et al. A case of adrenal insufficiency presenting with seizures, complicated by developmental cerebral venous anomaly and Takotsubo cardiomyopathy: a case report. J Med Case Rep. 2025;19:424.

7. Choudhary S, Alam A, Dewan V, et al. An unusual presentation of Addison's disease – a case report. Clin Pediatr Endocrinol. 2011;20(3):57–60.

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Ethics approval. For every elective and urgent procedure in our Hospital, it is required to obtain an informed consent form. The patient had signed the informed consent form and therefore gave the Hospital permission to perform procedures as well as use the data for scientific purposes with strong protection of personal information. Written informed consent for publication was obtained as part of the institutional consent procedure.

Conflict of interest. The authors declare that they have no conflicts of interest.

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