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Case Report

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Transdermal Fentanyl–Induced Seizures: Case Report and Literature Review

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Fentanyl is a well-known opioid used in general anesthesia and pain management.[1] Although opioids have anticonvulsant properties, they might have proconvulsant effects. Seizures caused by fentanyl are rare. As of this writing, only a few cases have been reported in humans (Table 1[2–10]), namely in the setting of general anesthesia.[2,8,11] Seizures after the administration of fentanyl in association with other drugs (such as lidocaine) have been reported in the literature.[11]

Case Report

Here, we report a case of seizure that occurred in a 46-year-old man treated in an ambulatory setting for chronic neuropathic back pain related to previous lumbar surgery. The patient's medications included oral acetaminophen 1,000 mg and diazepam 5 mg, both if needed. A few hours after the first application of a fentanyl transdermal patch (50 μg), the patient was brought to the emergency department (ED) due to involuntary facial and limb movements. Upon his arrival, besides the Glasgow Coma Scale[12] score of 11, his physical examination, laboratory workup, and neuroimaging results were within normal limits (Supplementary Material Topic 1). The neurologic examination revealed erratic involuntary movements of the 4 limbs, not rhythmic, uncoordinated, without tongue biting or sphincter incontinence. The movements lasted a few seconds with impaired awareness. Seizure onset and frequency were unknown.

After regaining consciousness, he had spasmodic speech without aphasia, with preserved oral comprehension and writing and reading abilities. The differential diagnoses included (1) epileptic seizures, (2) psychogenic nonepileptic seizures, (3) stroke, and (4) syncope. Stroke was ruled out due to the absence of focal or cortical signs as well as the normal computed tomography scan. Syncope was ruled out since the patient had no hemodynamic changes and his electrocardiogram was within normal limits. A psychiatric assessment was required due to the hypothesis of psychogenic nonepileptic seizures/conversion disorder (functional neurologic symptom disorder), with attacks or seizures (F44.5 according to *DSM-5* criteria). The patient recalled a similar episode after treatment with tramadol. Moreover, there was no significant psychiatric symptom, psychosocial context suggesting psychological stress, or history of psychiatric medication. A final hypothesis of seizure induced by a substance or medication was considered. A literature search retrieved a few case reports of fentanyl-induced seizures, including 1 published in 2003 describing such a phenomenon after a 7-day fentanyl treatment in small doses with phenytoin.[8]

The definitive diagnosis was motor epileptic seizures with unknown onset (Supplementary Material Topic 2 provides the updated International League Against Epilepsy 2017 classification of epilepsy) induced by fentanyl. Hence, the psychiatrist decided to treat the patient with intravenous valproic acid (15 mg/kg in 30 minutes). The patient improved suddenly after approximately 20 minutes, with no specific symptom improvement pattern as seen in other conditions,[13] and was discharged with oral valproic acid 1,000 mg once a day. One week later, in the outpatient clinic, he was asymptomatic. Three months later, he was reexamined and discharged since he remained symptom free.

Discussion

This is the first report, to our knowledge, to describe fentanyl-induced seizures in ambulatory care, rather than in the context of preoperative general anesthesia (as previously described in the literature). The exact mechanisms underlying seizures caused by fentanyl are not understood. However, these types of seizures are more likely to originate in the subcortical areas, which would not be detectable by surface electrodes. No electroencephalography was performed at the ED, which would reveal a pattern of drug-induced seizures.[14] Scott and Sarnquist[4] proposed that seizures can result from myoclonic movements due to the depression of inhibitory neurons or possibly that the abnormal movements might exacerbate muscular rigidity caused by even small doses of fentanyl. This report reminds psychiatrists and physicians to be aware of drug-induced seizures (namely related to opioids such as fentanyl, as in the current case).

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Table 1. Summary of Case Reports of Seizures Induced by Fentanyl

Authors	Year of Publication	Fentanyl Dose	Rate of Administration	Age and Weight
Safwat and Daniel[2]	1983	200 µg IV	NA	Age: 79 y Weight: 79 kg (174 lb)
Hoien[3]	1984	100 µg IV	NA	Age: 17 y Weight: 54 kg (119 lb)
Scott and Sarnquist[4]	1985	600 µg IV	4-minute interval	Age: 73 y Weight: 81 kg (179 lb)
Rosenberg and Lisman[5]	1986	100 µg IV	2-minute interval	Patient 1 Age: 20 y Weight: 80 kg (176 lb) Patient 2 Age: 56 y Weight: 60 kg (132 lb)
Goroszeniuk et al[6]	1986	150 µg IV	NA	Age: 45 y Weight: 59 kg (130 lb)
Webb[7]	1990	250 µg IV	NA	Age: 20 y Weight: 54 kg (119 lb)
Sprung and Schedewie[8]	1992	350 µg IV	5-minute interval	Age: 67 y Weight: 88 kg (194 lb)
Fujimoto et al[9]	2003	100 µg IV	NA	Age: 79 y Weight: 54 kg (119 lb)
El-Karamany[10]	2017	50 µg IV	NA	Age: 71 y Weight: 80 kg (176 lb)

Abbreviations: IV = intravenous, NA = not applicable.

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Supplementary material: See accompanying pages.

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Supplementary Material

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List of Supplementary Material for the article

1. Supplementary Material Topic 1
2. Supplementary Material Topic 2

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Supplementary Material Topic 1. Summary of the patient´s physical examination, laboratory workup and neuroimaging upon arrival at the emergency department

Glasgow Coma Scale[1] score was 11 (spontaneous opening of the eyes, no verbal response, obeying motor commands). The blood pressure was 125/73 mm Hg, the electrocardiogram was normal with cardiac frequency of 79 beats per minute, O2 saturation was 100%, and glycemia was 140 mg/dL. The respiratory and cardiac auscultations were normal, and he had no peripheral edema. The blood tests as well as the CT scan were unremarkable.

Reference

1. Sternbach GL. The Glasgow Coma Scale. *J Emerg Med*. 2000;19(1):67–71.

Supplementary Material Topic 2. Updated ILAE (2017) Classification of Epilepsy

For an updated Classification of Epilepsy, please visit the website of The International League Against Epilepsy (ILAE), 2017: https://www.ilae.org/guidelines/definition-and-classification/operational-classification-2017.

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