CASE REPORT

Case Report: Morphine withdrawal induced convulsions in an adult male patient [version 1; peer review: 1 approved with reservations]

Mahmoud M. Ali, Abdelrahman Hamad, Eman Nawash Alhamoud

1Hamad General Hospital, Hamad Medical Corporation, P.O. Box 3050, Doha, Qatar
2Clinical Medicine, Weill Cornell Medical College-Qatar, P.O. Box 24114, Doha, Qatar
3Pharmacy Department, Hamad Medical Corporation, P.O. Box 3050, Doha, Qatar

Abstract
This case report describes a possible unknown complication of morphine withdrawal in a patient with persistent back pain, treated with intrathecal morphine pump infusion. The patient presented with left lower extremity edema. After excluding deep vein thrombosis by Doppler ultrasound and worsening of the swelling despite oral antibiotics, peripheral edema caused by intrathecal morphine was suspected. Twelve hours following the termination of his intrathecal morphine pump and initiation of inequivalent doses of oral morphine and tramadol, he developed convulsions. After metabolic and structural causes of convulsion were ruled out by blood tests and head imaging, equivalent doses of morphine were given. Then the patient regained full consciousness, and no additional seizures occurred. After that, opioid withdrawal emerged as the most likely explanation. Seizure is a life-threatening condition; therefore, an awareness of this case is important and further studies are warranted to explore the potential association of opioid withdrawal and seizure.

Keywords
Morphine, Seizure, Withdrawal, Intrathecal morphine, Opioid, Convulsion

Corresponding author: Mahmoud M. Ali (dr.mahmoud.ali89@gmail.com)

Author roles: Ali MM: Writing – Original Draft Preparation, Writing – Review & Editing; Hamad A: Supervision; Alhamoud EN: Resources

Competing interests: No competing interests were disclosed.

Grant information: The author(s) declared that no grants were involved in supporting this work.

Copyright: © 2019 Ali MM et al. This is an open access article distributed under the terms of the Creative Commons Attribution Licence, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

How to cite this article: Ali MM, Hamad A and Alhamoud EN. Case Report: Morphine withdrawal induced convulsions in an adult male patient [version 1; peer review: 1 approved with reservations] F1000Research 2019, 8:1073 (https://doi.org/10.12688/f1000research.19819.1)

First published: 15 Jul 2019, 8:1073 (https://doi.org/10.12688/f1000research.19819.1)
Introduction

Morphine withdrawal is a common medical problem. Patients with morphine withdrawal can present with a variety of symptoms including runny nose, watery eyes, fever, vomiting, nausea, headaches, sweating, chills, muscle aches, diarrhea, high blood pressure, agitation, anxiety, irritability, depression, disorientation, insomnia. This case report describes a seizure as a clinical complication during an adult male patient’s withdrawal from morphine. The link between opioid withdrawal and seizures is not well studied in adult humans. To the best of our knowledge, only two case series of seven patients and three patients have been reported tying opioid withdrawal to seizures.

Case presentation

A 44-year-old Qatari man known to have persistent back pain admitted to our facility in 2017. He presented with left lower extremity edema that started approximately three to four weeks prior to admission. It was affecting his daily activities like showering and driving. The edema began in his foot and then gradually progressed to his abdomen. A physical examination found soft pitting edema in the left lower limb up to the sacrum posteriorly and to the umbilicus anteriorly. His lower limb showed some redness with no hotness, tenderness, or signs of chronic venous insufficiency. His past surgical history demonstrated multiple back surgeries, as follows; in 1986, he underwent surgical correction and fusion of lumbar scoliosis anteriorly and posteriorly. Additionally, in 1986, he had triple arthrodesis of his right foot. In 1992, he underwent lengthening of his atrophic flail right leg. In 1993, the Harrington rod from the dorsal and lumbar spine was removed. In 2004, he had anterior lumbar interbody fusion with cages at the levels of T10-T11 and T11-T12. In 2008, he underwent revision surgery to extend the anterior instrumentation from T2 to T12. In March of 2014, the patient had intrathecal morphine pump inserted with a morphine infusion rate of 5.75 mg/day.

Upon admission, a Doppler ultrasound scan of his left lower limb revealed no evidence of deep vein thrombosis (Figure 1). The patient was started empirically on amoxicillin-clavulanic acid (875 mg orally every 12 hours for five days), suspecting community-acquired cellulitis as one of the common causes of unilateral lower limb edema, but his edema did not improve. On the fifth day of admission, the patient started to develop new edema on the right leg. A pelvic and abdominal ultrasound scan showed no obvious mass (Figure 2). We then suspected that his intrathecal morphine infusion may be the cause of his peripheral edema, as other common causes were excluded, so the morphine pump was halted, and the pain management team initiated the patient on oral morphine (30 mg) twice daily and tramadol (50 mg) every six hours.

After twelve hours from pump termination, the patient started to convulse. He had three episodes of convulsion over two hours in the form of generalized tonic-clonic convulsion with rolled-up eyes; each episode was preceded by progressive muscle twitches. They were associated with continuous high blood pressure, ranging from 180/100 mmHg to 210/110 mmHg, and profuse sweating. All of the seizure episodes were aborted within a few seconds following the administration of 5mg intravenous diazepam, which was administered one to two minutes after the seizure started. Four hours later, another three seizure episodes occurred. The first was aborted by 5mg intravenous diazepam and the other two episodes required 10mg of intravenous diazepam.

A computed tomography review of the patient’s head was grossly normal and revealed no acute intracranial event (Figure 3). A complete metabolic panel was done and revealed no acute metabolic process or hypoglycemia. The patient’s morphine regimen changed to 5 mg administered intravenously every four hours with oral tramadol (50 mg) every six hours. In the evening, the patient regained full consciousness and no additional seizures occurred.

Upon patient request, the intrathecal morphine pump was restarted. One day after, the patient’s swelling in left lower limb started to increase so the intrathecal morphine pump was stopped, and the patient was started on patient-controlled analgesia fentanyl (50 mcg/hour) and oral methadone (10 mg every six hours). His left- and right-side edema disappeared gradually over seven days and after he regained his baseline functional capacity, he was discharged.

Discussion

Central nervous system irritability is a known opioid withdrawal sign in neonates and is accompanied by seizures in 2% to 11% of cases. While a high degree of cerebral activity and seizure has been reported in rodent model opioid withdrawal studies, the link between opioid withdrawal and seizures is not well studied in adult humans. To the best of our knowledge, only two case series of seven patients and three patients have been reported tying opioid withdrawal to seizures.

Our patient was not known to be an opioid addict from their history and their opioid risk tool score of one, so the concurrent use of another known seizure-inducing substance was unlikely. He was receiving an intrathecal dose of morphine which changed to an unequal oral dose of morphine, in addition to tramadol. Seizures are not mentioned in the literature as a known complication of morphine withdrawal, and the patient’s complication may have been caused by severe pain accompanied by inadequate doses of analgesics.

Conclusions

This case illustrates a possible connection between opioid withdrawal and seizure in an adult male patient. Seizure is a
Figure 1. Doppler ultrasound scan for the left lower limb. A and B) left common femoral vein; C, D and E) left superficial femoral vein; F) left popliteal.
Figure 2. Ultrasound scan of abdomen. A) urinary bladder; B) urinary bladder postvoid; C) mid abdomen; D) gallbladder; E) right kidney; F) left kidney; G) spleen.
Figure 3. A–E) Computed tomography of the patient's head.
life-threatening condition; therefore, an awareness of this case is important and further studies are warranted to explore the potential association of opioid withdrawal and seizure.

Data availability
All data underlying the results are available as part of the article and no additional source data are required.

References

1. Sadock BJ, Sadock VA, Ruiz P: Kaplan and Sadock’s Synopsis of Psychiatry. 11th ed. New Delhi: Wolter Kluwer; 2015. Reference Source
2. Parkar S, Seethalakshmi R, Adarkar S, et al.: Is this ‘complicated’ opioid withdrawal? Indian J Psychiatry. 2006; 48(2): 121–2. PubMed Abstract | Publisher Full Text | Free Full Text
3. Jain S, Singhai K, Swami M: Seizure as a primary presentation in opioid withdrawal. Psychiatry Clin Neurosci. 2018; 72(10): 802–803. PubMed Abstract | Publisher Full Text
4. Herzlinger RA, Kandall SR, Vaughan HG Jr: Neonatal seizures associated with narcotic withdrawal. J Pediatr. 1977; 91(4): 638–641. PubMed Abstract | Publisher Full Text
5. Zelson C, Rubio E, Wasserman E: Neonatal narcotic addiction: 10 year observation. Pediatrics. 1971; 48(2): 178–189. PubMed Abstract
6. Kandall SR, Gartner LM: Late presentation of drug withdrawal symptoms in newborns. Am J Dis Child. 1974; 127(1): 58–61. PubMed Abstract | Publisher Full Text
7. Pinsky C, Dua AK, Labella FS: Peptidase inhibitors reduce opiate narcotic withdrawal signs, including seizure activity, in the rat. Brain Res. 1982; 243(2): 301–7. PubMed Abstract | Publisher Full Text
8. Webster LR, Webster RM: Predicting aberrant behaviors in Opioid-treated patients: preliminary validation of the Opioid risk tool. Pain Med. 2005; 6(6): 432–442. PubMed Abstract | Publisher Full Text

Consent
Written informed consent for publication of their clinical details and/or clinical images was obtained from the patient.

Grant information
The author(s) declared that no grants were involved in supporting this work.
Open Peer Review

Current Peer Review Status: ?

Version 1

Reviewer Report 09 September 2019
https://doi.org/10.5256/f1000research.21742.r52978

© 2019 Ruben J. This is an open access peer review report distributed under the terms of the Creative Commons Attribution Licence, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Johnson Pradeep Ruben
Department of Psychiatry, St. John's Medical College and Hospital, Karnataka, India

The Case report is interesting and very useful. There are few suggestions.
1. There needs to be more details about the use of opioids in the past surgeries, whether the patient was dependent to Opioids in the past?
2. Did the patient have status epilepticus?
3. More information about what blood investigations were done and details about the same.
4. Discussion is very superficial and the pathophysiology of seizures in a opioid withdrawal needs to be discussed.
Kindly answer the above questions.

Is the background of the case's history and progression described in sufficient detail?
Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?
Partly

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?
Partly

Is the case presented with sufficient detail to be useful for other practitioners?
Partly

Competing Interests: No competing interests were disclosed.
Reviewer Expertise: Addiction Psychiatry, Child Psychiatry, Resilience in wives of alcoholism,

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

The benefits of publishing with F1000Research:

- Your article is published within days, with no editorial bias
- You can publish traditional articles, null/negative results, case reports, data notes and more
- The peer review process is transparent and collaborative
- Your article is indexed in PubMed after passing peer review
- Dedicated customer support at every stage

For pre-submission enquiries, contact research@f1000.com