Complicated opioid withdrawal- A case report

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Abstract
Although, anecdotal case reports are being published describing complicated opioid withdrawal e.g. seizure and delirium, various international classification system and standard textbooks do not mention about the complicated withdrawal like with alcohol. Interestingly, these complications reported from specific form of the opioid and specific geographical region. The case in this report presented with complicated opioid withdrawal like picture which later found to be due to medical condition. Hence, we report this case here to discuss various possibilities to be explored while dealing with the case of complicated opioid withdrawal.

Keywords: Opioid, Complicated withdrawal, Seizure, Delirium.

Introduction
Opioid withdrawal is usually characterized by craving for an opioid drug, rhinorrhea or sneezing, lacrimation, muscle aches or cramps, abdominal cramps, nausea or vomiting, diarrhoea, pupillary dilatation, piloerection or recurrent chills, tachycardia or hypertension, yawning and restless sleep as per ICD-10 DCR¹ and similarly, DSM-IV-TR² and DSM-V³ describes it without quoting complications such as seizure and delirium. Recently, anecdotal reports are emerging with the conditions such as withdrawal seizure and delirium due to opioid withdrawal after ruling out all the possibilities.⁴,⁵ However, authors also do not deny the possibility of such complications could be due to impurities present in the street opioids. Present report describes a case of opioid dependence presented with unusual withdrawal (delirium) and later diagnosed to be due to infectious cause. Hence, in the view of secondary causes, the presentation raised the query on such complicated withdrawal due to opioids per se and we have discussed the possibilities which should be looked into for exploring the causative factors of the complicated withdrawal.

Case History
A 45-year-old male presented to psychiatry OPD with chief complaints of hostile behavior, decreased sleep, poor oral intake, poor self care, seeing vivid images, commanding type auditory hallucination, suicidal ideation and withdrawn behavior for 10 days. He had history of smack (street drug) consumption for 1½ years with last intake reported 10 days back prior to hospitalization and cannabis abuse for 10 years with last intake 6 months back. He had experienced opioid withdrawal for initial 4-7 days after the substance was stopped while having continued withdrawal behavior, agitation and restlessness, lack of spontaneity in speech and disturbed sleep and appetite. No history of other substance abuse, fever, head injury, seizure and psychiatric/ neurological illness were present currently and in the past.

On initial Mental State Examination (MSE), at the time of hospitalization, the patient was found to be conscious and well oriented to time, place and person. He was having decreased psychomotor activity, lack of spontaneity in speech, poverty of speech, visual hallucination and commanding type auditory hallucinations. His vitals were within normal limits and no abnormality was found in systemic examination. Routine investigations revealed: Hemoglobin-15.1 mg%, Total Leukocyte Count- 19,200/cumm, Differential Leukocyte Count-Neutrophil - 83, Leukocyte –15, Eosinophil - 2, Blood Urea-15.60 mg%, Serum creatinine-0.90 mg%. However, on the same day of hospitalization in the night, he became severely agitated, restless, disoriented to time, place & person with fluctuating level of consciousness. Keeping in mind the published reports of complicated withdrawal due to opioid, this delirious picture was suspected to be due to complicated opioid withdrawal. However, the possibility of complicated opioid withdrawal remained doubtful as the delirious picture appeared after 10 days of last intake of smack and after remission of usual withdrawal due to opioid. Further, after reviewing basic investigations the suspicion of medical cause was aroused. Opinion of medical specialist was sought and as per his examination patient was found not to be following simple commands, tone increased in both lower limbs, plantar was withdrawal bilaterally, knee and ankle jerks were exaggerated and no sign of meningeal irritation was present, however. Non Contrast Computed Tomography-Brain revealed – two old calcified granulomatus lesion on right parietal region. Cerebrospinal Fluid examination revealed hazy appearance, Total Leukocyte Count -70 cells/c, polymorphs-70% and mononuclear cells-30% (sample was grossly hemorrhagic). Electrolytes were as follows: S. Sodium- 137.0meq/L, S. Potassium- 3.50meq/L and
S. Calcium- 9.10meq/L. Fundus examination of both eyes were within normal limits. The patient was shifted to ICU where the diagnosis of meningoencephalitis was kept and treated accordingly. He was managed accordingly and discharged after 10 days in satisfactory condition. The patient was turned up for follow-up after 2 weeks. He was found to be abstinent from drugs and overt psychopathology could not be elicited. He was better physically as well.

Discussion

To the date, various forms of opioids are being abused in India which varies from raw to impure street drugs. Also, pharmaceutically formulated opioids drugs are abused like Capsule/Injection Fortwin (Pentazocine) and Capsule Spasmo-proxyvon (Acetaminophen, Dicyclomine and Dextropropoxyphene) which are supposedly devoid of impurities. The impurity varies widely depending upon the various factors and from country to country. In a sample of seized street drugs in Cairo, Egypt concentration of heroin ranged from 0.27 mg % to 34.56 mg % with an average concentration of 9.59 mg %. Most common impurities found in this sample were alkaloid impurities including: 6- mono acetyl morphine, acetyl codeine, morphine, papaverine and meconin. Other major adulterants were paracetamol, caffeine and ephedrine. To the lesser extent chlorpheniramime, phenobarbitone, methylene-dioxymeth- amphetamine (MDMA), carbamazepine and theophylline were found. The impurities which are clearly implicated for withdrawal complications which have been found in this study are phenobarbitone and carbamazepine. Unpublished data on impurities in street drugs implicate that mannitol, quinine, benzodiazapines and dextromethorphan are also being used.

When emerging published data on complicated opioid withdrawal were examined it was found that all the cases with complicated opioid withdrawal were street drug abuser. A study reported that 43% of brown sugar (street drug) abusers in his study had seizure, 26% developed confusion after seizure and 17% experienced psychotic symptoms. However, this incidence is unexpectedly higher in comparison to data available. Hence, the possibility of contents of impurities which has definitive causation in complicated withdrawal is higher in this group of subjects who are supposed to hail from same geographical area, subjecting to abuse of street drugs with similar impurities hence having higher incidence. Other case in a report was also a smack abuser, i.e. a street drug. Further, a study reported that seven cases were used to inhale the heated drug which reflects the high possibility of street drug abuse and only one case had history of benzodiazepine abuse among them. Again, the seizure ( complication)-substance association was found to be present in impure form of heroin and poppy husk while pentazocine and buprenorphine abuse were not associated with seizure (complication) while association with complication was found with dextropropoxyphene in intoxicated phase instead of withdrawal phase depicting that complication is associated with street drug only. To the best of knowledge of authors, data on complicated withdrawal due to prescription opioid drugs is not available. Hence, it may be speculated that the complication is resultant of impurities in street drugs rather than opioid itself.

Additionally, two reports are available which depicts that naloxone and naltrexone when introduced to reverse opioid toxicity and detoxification, respectively resulted into delirium. In first report, where naloxone was used to reverse respiratory depression due to toxicity the impurity of scopolamine is documented which may be the cause of delirium. The second case in which naltrexone was used patient was abusing alcohol as well and status of which was uncertain due to unreliable informant, may be the cause of alcohol withdrawal delirium. Another possibility in both these cases is that the introduction of antagonists compelled the rapid dissociation of agonist and rapidity of switching from agonist maintenance to antagonistic status in the receptor cascade system itself resulted into delirium. Thus, gives rise to a great possibility of complicated withdrawal attributed to other factors rather than opioid per se.

Conclusion

The published data reveals that complicated withdrawal due to opioids occurs in the subjects who are abusing impure form of opioids only. The impurities known to cause complicated withdrawal are being clearly reported in street drugs in a study. The scientific data emerging with complicated opioid withdrawal (seizure/delirium) pertains to India only which may be due to particular impurity mixed in this geographical area which causes withdrawal complications. Standard textbooks are also silent on such complication due to opioid withdrawal. Conditions like CNS infections, as the case above, may be another possibility for such presentation. Hence, the likeliness of complicated opioid withdrawal due to opioid per se seems very less and other causative factors must be ruled out. In the view of unavailability of research regarding impurities in street drugs in India researches are required to explore the types of impurities mixed in street drugs in India.

References