

Cannabis Intoxication, a Neglected Cause of Altered Level of Consciousness in Children: A Case Series

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Abstract: Altered level of consciousness (ALC) represents a neurological emergency, which demands a methodical approach to evaluation and treatment. Emergency departments' Paediatricians dealing with children with ALC need a rapid and reliable diagnostic process to rule out life-threatening conditions. ALC can be caused by structural and non-structural conditions, and, among non-structural conditions, intoxications must always be investigated. Toddlers and young children exposed to cannabis may present ALC due to explorative ingestion of the substance.

We report three cases of toddlers who were admitted to our emergency department over a 12-month period with ALC due to cannabis intoxication. The three cases highlight how clinical presentation of cannabis intoxication can be variegated.

Therefore, in case of afebrile children presenting with ALC Cannabis intoxication must be suspected and a urine drug test should be performed.

Keywords: Altered level of consciousness, Cannabis, Intoxication, Infants.

INTRODUCTION

Altered level of consciousness (ALC) is a spectrum of disease whose clinical presentation varies from agitation or confusion up to lethargy, obtundation and coma, representing a diagnostic and therapeutic challenge to the paediatrician.

Many causes can be associated to an ALC and the mnemonic AEIOU TIPS can be helpful in listing the principal categories that should be remembered (Table 1) [1].

Table 1: AEIOU TIPS Mnemonic: Principal Categories to Consider as Etiology of ALC

A	Alcohol, Abuse of substances, Ammonia
E	Endocrine Disorders, Epilepsy, Encephalopathy, Electrolyte Abnormalities
I	Infection, Intussusception, Inborn errors of metabolism
O	Overdose, Oxygen Deficiency
U	Uremia
T	Trauma, Tumor, Toxins
I	Insulin
P	Psychiatric conditions
S	Shock, Stroke, Space-Occupying Lesions

To make the most appropriate treatment decisions, a fundamental differentiation must be done in the diagnostic process between structural and non-structural (medical) conditions [2, 3]. Therefore, a proper history taking must be always performed, ascertaining symptoms onset and duration, eventual trauma or ingestion of medications/alcohol/recreational drugs, associated symptoms (vomiting, headache, fever or convulsions) and relevant past medical or surgical history. A structured ABCDE approach with a simultaneous assessment and management of airway, breathing and circulation should be taken for children with decreased level of consciousness, including continuous cardio-respiratory monitoring, provision of supplemental oxygen and establishment of intravascular access. A complete neurologic examination must be performed focusing on brainstem examination, motor function and breathing pattern [4].

Usually, a history of trauma or of acute symptoms onset and focal neurological signs suggest a structural lesion, whereas a progressive symptom onset and lack of focality at neurological examination frequently indicate a medical cause.

As part of a careful general examination, core investigations should be performed to check any underlying medical cause of ALC (Table 2) [1, 5, 6].

An early cranial CT or MRI scan should be carried out when the child is stable and a lumbar puncture should be performed whereas no acute

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contraindications exist, in particular if signs of meningitis, encephalitis or sepsis are present.

Table 2: Core Investigations: Essential Diagnostic Workup in any ALC

Core Investigations
- Capillary and laboratory blood glucose, which must be obtained within 15 minutes
- Blood gas
- Full Blood Count + blood film
- Urea and electrolytes
- Liver function tests
- Plasma Ammonia and lactate
- Blood culture
- Urinalysis + 10 ml of urine for later analysis including urine toxicology

However, in the absence of a clear cause, particularly in an afebrile toddler, a toxic ingestion should be always suspected, and family members should be questioned about the availability of any medication or recreational drug. In fact, a toddler has the ability to explore the environment but does not yet have the cognitive ability to discriminate what can be harmful.

In particular, cannabis accidental exposure should be considered due to the fact that marijuana is the most cultivated and abused substance worldwide and is increasingly legalized in European and non-European countries [7].

Even though in paediatric population a drug intoxication diagnosis could be easily neglected, a urine drug screening should not be left out of the diagnostic workup of children with ALC.

We hereby report three cases of acute cannabinoid intoxication caused by unintentional exposure admitted to our paediatric Emergency Department during the past 12 months.

CASE SERIES

Case 1

A previously healthy 14-month-old female was referred to our Emergency Department for acute onset of ALC and lethargy, in absence of other symptoms. Her caregivers denied a recent history of head injury as well as toxic exposure.

On admission, she was afebrile, hypotonic, soporose, responsive to pain stimulus (Glasgow Coma

Scale 11). Vital signs and glycaemia were within normal range. Apart from myotic pupils, no other anomalies were found at physical examination. Initial core investigations resulted to be normal.

An electrocardiogram (ECG) and a chest X-ray did not present any alteration. A head computed tomography (CT) scan ruled out a structural cause of the clinical presentation.

Finally, a quantitative urine toxicology test resulted positive for THC (tetrahydrocannabinol), leading to the diagnosis of cannabis intoxication.

A nasogastric (NG) tube was placed and gastric lavage with aspiration of any residual was carried out. Afterwards, activated charcoal was administered via NG tube, together with IV fluids. Vital signs were monitored up to complete recovery, obtained in 12 hours.

Case 2

A 12-month-old female was admitted to our Emergency Department with complaints of acute onset of lethargy and paleness. Her parents stated that she was at home when she started presenting cough and spasms of vomiting, followed by a short episode of hypertonia and apparent loss of consciousness. The father denied any trauma or history of toxic exposure.

On admission, she was afebrile, extremely lethargic, and responsive to pain stimulus (Glasgow Coma Scale 8). She presented inconstant nystagmus and mydriatic pupils, without any other significant features at physical examination. Blood glucose levels and vital signs were normal but, during observation, she presented a brief episode of apnoea and desaturation (SpO₂ 65%), resolved with stimulation and oxygen supplementation. Initial core investigation resulted to be within normal range.

Head CT scan, ECG, chest X-ray and electroencephalography were all unremarkable.

Eventually, a urine quantitative toxicology exam tested positive for THC and once again diagnosis of cannabis intoxication was made.

Treatment was only supportive, with administration of IV fluids and observation until complete recovery, obtained in 8 hours.

Case 3

An 18-month-old female with no prior medical history, presented a seizure-like episode characterized

by loss of consciousness, increased muscular tone with arm flexion and blank stare.

For this reason, she was conducted to our Emergency Department. At first evaluation, she was afebrile, lethargic, and responsive to pain stimulus (Glasgow Coma Scale 11). She was tachycardic, with elevated systolic blood pressure. At physical examination, increased muscular tone and mydriatic pupils, unreactive to bright stimulus, were found.

Her mother reported no family history of seizures or other neurological diseases and denied any possible ingestion of toxic substances.

During observation a new episode of loss of consciousness and increased muscular tone occurred and the consciousness level remained fluctuating, with Glasgow Coma Scale ranging from 9 and 15. Initial core investigations were normal. ECG and chest X-ray did not show any abnormality. A urine drug test was performed and found positive for THC. An NG tube was placed with subsequent administration of activated charcoal, with a prompt resolution of the symptomatology within 4 hours.

DISCUSSION

Cannabis is the most commonly used illicit drug throughout the world, with over 183 millions of users [7]. As its recreational use has been legalized in different countries in the last two decades, a consequent increase in unintentional paediatric intoxications has been reported [8, 9]. Unintentional paediatric exposure can derive from passive smoke inhalation or from exploratory ingestion of cannabis itself or its derived resins. Toddlers tend to explore the environment with their mouth, so those who have access to toxic substances are at higher risk of ingestion. Moreover, older children may be attracted by the colourful packaging of commercial cannabis-infused products, particularly in countries where they are sold legally, or by home-baked cannabis edibles.

Ingestion of cannabis leads to a wide range of symptoms, most frequently involving an ALC [10, 11]. Symptoms usually have a delayed onset that ranges from 30 minutes to 3 hours, with clinical effects lasting up to 12 hours [12].

In a recent systematic review, Richards *et al.* described the most common signs of cannabis intoxication in young children to be lethargy, ataxia, hypotonia, mydriasis, tachycardia and hypoventilation

[9] emphasizing that, as seen in our small series of patients, clinical presentation can be polyhedral, without any pathognomonic signs and symptoms. In fact, although all infants at the moment of hospital arrival presented with an ALC many differences characterize the three presented cases. The most common signs of cannabis intoxication are summed up in Table 3, but we would like to emphasize that clinical presentation can be atypical.

Table 3: Principal Symptoms of Cannabis Intoxication

Central Nervous System	Dizziness/Lethargy Hypotonia Coma Agitation/Irritation Euphoria Ataxia Convulsions Nystagmus
Gastrointestinal System	Nausea/Vomiting Abdominal pain
Respiratory System	Bradypnea Apnea
Cardiovascular System	Bradycardia Tachycardia Hypotension Hypertension
Autonomic Nervous System	Mydriasis Myosis Hypersalivation Hypothermia

The infant on the Case 2 presented with cough and spasm of vomiting as initial signs, and, during hospital observation, a short episode of apnoea and desaturation occurred. Case 3 began with a seizure. This is an uncommon finding among those associated to cannabis intoxication; nevertheless, it has been already anecdotally described in literature [11, 13, 14]. Considering vital signs, usually sympathomimetic effects are observed, as confirmed in Case 3, but they can also be within normal range such as in Case 1 and Case 2.

Also, ocular findings are not pathognomonic. Two out of three infants from our case series presented with mydriasis and one with myosis, confirming that mydriasis is far more common than myosis, as reported in literature [9, 14-16]. Furthermore, in Case 2 inconstant nystagmus was described, which to our knowledge, has been previously reported in acute cannabis intoxication only occasionally [17].

Such a diverse clinical presentation of cannabis intoxication may be challenging when it comes to diagnosing this condition, especially if no suspicion is raised during history recollection.

Recreational use of cannabis is indeed illegal in Italy, and parents can therefore be reluctant to admit possible access of their children to this illicit substance. In fact, in none of the three cases described above, cannabis ingestion came up as a possible diagnosis during the initial caregivers' interview at hospital arrival.

Nevertheless, in cases of nonspecific symptomatology involving ALC, even if a clear history of toxic exposure is lacking, cannabis intoxication should not be ruled out without performing a urine test. Diagnosis of acute cannabis intoxication is extremely simple indeed, as it only requires a urine sample on which immunoassay semiquantitative or quantitative test are performed [18, 19].

Acute cannabis intoxication management in young children involves only supportive measures: it is crucial to assess airways, breathing, and circulation and to provide oxygen support to patients with lethargy or coma. In case of seizures or dysphoria, which are rarely described, and more frequently observed when a history of co-ingestion (e.g., cocaine) is reported, initial treatment consists of benzodiazepines. Gastrointestinal decontamination with activated charcoal is scarcely effective due to the delayed onset of psychoactive symptoms after marijuana ingestion.

In addition to medical management, clinicians facing with cases of cannabis intoxication in children need to address the topic of child safety. Child Protective Services should always be noticed to identify at-risk families, potential situation of neglect, and, to rule out any form of child abuse [20].

Nevertheless, the consumption of marijuana is quite common among young people even after they became parents [21, 22], and due to the progressive legalization of its medical and recreational use its consumption is meant to grow. For these reasons we also believe it might be useful to educate marijuana users to take preventive measures to safeguard children's health, such as keeping it in not accessible places and not using it in presence of minors.

In conclusion, our three cases suggest the importance of always considering illicit drug ingestion as causative for ALC, even when no suspicion comes from parents' interview, above all in those countries

where marijuana is not legalized. Urine toxicology test is a cost-effective and non-invasive procedure. It allows a quick and specific diagnosis, it is useful for avoiding unnecessary tests and procedures and should be performed in every case of altered state of consciousness in afebrile infants.

Further studies are needed to better characterize and tightly monitor cannabis intoxication in paediatric population, which is still under-reported but expected to dramatically increase, and to raise awareness of the potential dangers of unintentional cannabis poisonings amongst not only health care workers but also general public.

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