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An apathetic child with hallucinations

EDUCATIONAL CASE REPORT

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BACKGROUND

Lysergic acid diethylamide (LSD) is a potent, hallucinogenic substance that distorts the perception, state of consciousness and behaviour of the user. LSD poisonings are rare in children and may be difficult to recognise based on

clinical symptoms alone.

CASE PRESENTATION

A young boy was admitted to the hospital because of bizarre behaviour and reduced responsiveness towards his parents. At first, he was agitated. Later he fell silent and became apathetic. He suffered from ataxia and showed signs of visual hallucinations. A conclusive diagnosis of LSD poisoning was made possible through targeted and specific laboratory testing of blood and urine samples. The patient recovered completely without any specific treatment.

INTERPRETATION

We urge doctors who examine paediatric patients with acute and unexplained neuropsychiatric symptoms or abnormal behaviour to consider drug intoxication as a possible differential diagnosis. Blood and urine samples from such patients should be obtained as soon as possible and analysed for a broad spectrum of substances. No antidote exists for LSD. If sedation is required due to convulsions, tachycardia, agitation, or frightening hallucinations, treatment with a benzodiazepine, such as diazepam or midazolam, is recommended.

A child of late preschool age was brought to the hospital due to unexplained changes in his behaviour. The symptoms proved to be temporary, and several possible differential diagnoses were considered. A conclusive, validated diagnosis was obtained the day after admission based on additional laboratory tests.

A previously healthy boy of late preschool age was admitted to the hospital because he displayed bizarre behaviour. He had ceased talking and appeared disengaged and subdued. When he left the kindergarten, he had been hyperactive and agitated. The kindergarten had been on an excursion to town, followed by a pizza meal, and the boy's parents initially thought that he was just overexcited after a long and strenuous day. However, throughout the evening, he became increasingly apathetic. He fell silent and periodically laughed for no apparent reason. His parents could not make eye contact with him and felt as though he was 'looking straight through them'.
The boy was able to stand upright, but had an unsteady gait. His parents sought medical attention, and because his condition was so out of character from his usual behaviour, he was admitted to the hospital for further assessment.

The boy's parents were worried about his changed behaviour. However, there was still some uncertainty as to whether he had a medical condition or if he was merely tired after a long and eventful day. It can be difficult to distinguish patients who simply require rest from those who should be examined further. In this case, rapidly evolving neurological symptoms such as ataxia (unsteadiness), together with the absence of speech and eye contact, suggested a possible dysfunction of the central nervous system.

The admitting doctor suspected mushroom poisoning, as the boy had also been to the city forest. Other causes of acute neurological deficits in children include infections, such as meningitis or viral encephalitis, head injury, cerebrovascular events, electrolyte imbalance, and intoxication. In rare cases, partial epileptic seizures and autoimmune encephalitis should be considered among the differential diagnoses.

Upon arrival at the hospital, about 4–5 hours after his parents had noticed the first symptoms, the boy's behaviour was conspicuous. He was withdrawn and unresponsive, showing no visual contact with his surroundings. Despite being fully awake and in no apparent pain or discomfort, he would neither speak nor cooperate when addressed. He did not object to being examined and barely reacted when a blood sample was drawn. His pupils were markedly dilated, with a diameter of 9 mm. His pupillary light reflex was reduced and delayed, and the pupils' diameter was still at least 6 mm. He was unsteady and had a marked tendency to fall over.
All vital parameters were normal. His pulse was 104 beats per minute, blood pressure 105/62 mm Hg, respiratory rate 24 per minute, SpO_2 99 % in room air, and body temperature 36.6 °C. His general condition was considered satisfactory, and he had no photophobia or neck stiffness. Examination revealed slightly hypoactive bowel sounds but otherwise normal findings for the heart, lungs, abdomen, ears, neck, and throat. Preliminary blood tests were also normal. A urine collection bag was attached to obtain a sample of his first urine (he had not urinated since symptom onset before admission). He was admitted to the paediatric high dependency care unit for close monitoring.
Clinical and supplementary examinations provided no evidence of pathology beyond the nervous system. However, the boy's condition remained unexplained, and he was monitored closely in the period after admission to ensure that any clinical changes were recognised. He had no fever, photophobia, neck stiffness, or other signs of infection, and no increase in infection parameters. As such, a lumbar puncture was not considered to be indicated. Intoxication was among the differential diagnoses. However, if the child had ingested medicines or other toxic substances, it was likely too long ago for activated charcoal or gastric lavage to have an effect. Gastric lavage and especially induced vomiting are generally not recommended in cases of intoxication with an unknown substance because of the risk of aspiration pneumonia.

The most prominent symptom was his bizarre behaviour. Acute psychoses rarely occur in children and mainly affect individuals with delayed neurological development (1). The pupils' marked dilation was considered a possible sign of intoxication, for example with an anticholinergic or sympathomimetic substance. Head injury was not suspected, as he had not lost consciousness and had no symptoms of high intracranial pressure. Thus, there was not a strong indication for diagnostic imaging; this would also have been technically challenging, as the boy would probably have failed to cooperate throughout the procedure. Consequently, we decided to favour a strategy of close monitoring.

About one hour after admission, the patient was re-examined. He was still not speaking but was beginning to show signs of understanding what was being said, and he cooperated to some degree during the examination. He also responded to simple questions by nodding or shaking his head. At this point, he appeared to be interacting more with his parents, and he started crying.
In the absence of any specific treatment, this spontaneous improvement strengthened the suspicion that the condition was caused by a substance that had been metabolised and/or excreted. The diagnosis was still unclear, but the child's condition was no longer considered dangerous due to the improvement.

About eight hours after symptom onset (three hours after admission), the patient improved further and started talking again. He still seemed lethargic but was able to recognise his parents and to name objects in the room. During this stage, he cried and seemed distressed and afraid. The following morning, his condition was still improving. His pupils remained dilated, but less than on admission (now 7–8 mm, 4–5 mm on illumination). Throughout the night, he showed signs of hallucinations, believing, for example, that smoke was coming from his hands. When asked, he could not explain what had happened to him earlier in the day, but during the night, he told his parents that he had eaten a gummy bear he had received from a male stranger while in town. However, he remembered nothing of this explanation when he woke up. The day after admission, his behaviour was normal again. He was discharged and has experienced no sequelae.
The symptoms, clinical development, and information provided by the boy all suggested that he had ingested a toxic substance. However, routine analyses failed to detect any such substances in his urine. Owing to continued suspicion of drug intoxication, a clinical pharmacologist was consulted, and it was decided to perform a high-resolution toxicology screen of the urine and blood samples. Lysergic acid diethylamide (LSD) and its metabolite, 2-oxo-3-hydroxy-LSD (OH-LSD), were detected in the urine via this method. The blood sample was initially considered negative. However, in light of the urine findings, a second targeted search was conducted using a more sensitive method, through which the presence of LSD and OH-LSD in the blood was confirmed. It was concluded that LSD poisoning was the most likely diagnosis, and the case was reported to the police.

The symptoms, including hallucinations and the absence of marked adrenergic stimulation, led us to suspect the ingestion of a hallucinogenic substance rather than a conventional stimulant or sedative. Typical symptoms (in adults) after ingestion of various recreational drugs are listed in Table 1 (2). The unusual drug formulation (a gummy bear) directed our suspicion towards low-dose substances, including synthetic cannabinoids and tryptamines. Such substances are not included in routine urine toxicology screens. Therefore, we decided to perform a high-resolution toxicology screen, which in principle, makes it possible to detect several thousand different substances. The method is not used routinely, as it is more labour-intensive and relatively expensive.

Table 1

Overview of typical symptoms upon poisoning with common substances of abuse (2).

Group	Drug family	Examples of substances of abuse/medications	Typical symptoms of intoxication
Stimulants	Phenethylamines	Amphetamine, methamphetamine, paramethoxymethamphetamine (PMMA), methylendioxymethamphetamine (MDMA)	Mydriasis, hypertension, tachycardia, hyperthermia, psychomotor hyperactivity, altered perception, hallucinations
		Cocaine	Mydriasis, hypertension, tachycardia, hyperthermia, psychomotor hyperactivity, agitation, arrhythmias, organ ischaemia, seizures

Group	Drug family	Examples of substances of abuse/medications	Typical symptoms of intoxication
Sedatives	Benzodiazepines and Z-hypnotics	Clonazepam, alprazolam, diazepam, oxazepam, zopiclone, zolpidem	Reduced consciousness, cognitive slowing, slurred speech, impaired coordination, confusion, amnesia
	Opioids	Morphine, heroin, codeine, oxycodone, buprenorphine, methadone, fentanyl	Reduced consciousness, reduced pain sensitivity, miosis, respiratory depression, reduced intestinal motility, hypothermia, hypotension, bradycardia
	Alcohols	Ethanol, methanol, isopropanol, ethylene glycol	Reduced consciousness, slurred speech, impaired coordination, uncritical behaviour, amnesia, confusion, hypotension, tachycardia. Methanol: visual disturbances, metabolic acidosis, hyperventilation. Ethylene glycol: metabolic acidosis, hyperventilation, kidney failure, hypocalcaemia. Isopropanol: acetone breath, elevated ketone levels without acidosis
	Gamma-hydroxybutyrate (GHB)	GHB, gamma-butyrolactone (GBL), butanediol	Reduced or fluctuating level of consciousness, hypotension, bradycardia, respiratory depression, hypothermia, agitation and hallucinations. Rapid recovery because of fast metabolism

Group	Drug family	Examples of substances of abuse/medications	Typical symptoms of intoxication
Hallucinogens	Cannabinoids	Cannabis, synthetic cannabinoids	Impaired attention, drowsiness, confusion, hallucinations, tachycardia, hypertension conjunctival injection, increased appetite
	Tryptamines	Lysergic acid diethylamide (LSD), psilocybin, dimethyltryptamine (DMT)	Perceptual disturbances, synaesthesia, hallucinations, panic or fear responses, gastrointestinal symptoms, mydriasis, hypertension, tachycardia

Discussion

Knowledge about LSD poisoning in children is limited to sporadic case reports. In connection with the preparation of this paper, we reviewed ten previous publications see appendix), which, in total, describe LSD poisoning in 21 children ((3–12). The most commonly observed symptoms in these children were dilated pupils, hallucinations/sensory illusions, erythema, and bizarre behaviour, including unusual movements and a lack of interest in their surroundings – not unlike our patient's symptoms. Further, most of the children were perceived as anxious or distressed, while only a few were considered to be euphoric.

This contrasts with results from clinical trials with healthy adults, where LSD primarily is reported to induce a pleasant sensation (13, 14). However, adverse effects are more common with increasing doses (15, 16). Children inadvertently subjected to LSD are probably more likely to receive higher doses per kilogram of body weight than adults. This may, in part, explain why a majority of these children experienced negative effects.

The pharmacokinetics of LSD have been relatively well studied in adults at doses of 100–200 µg, which corresponds to typical drug doses for recreational use (14). LSD is rapidly and completely absorbed after oral administration. Symptoms of intoxication will generally develop within 30–45 minutes, reaching a peak after 1.5–2.5 hours. The acute, subjective effects usually subside after 9–12 hours (17), as observed in our patient. The half-life is approximately three hours, and the drug can usually be detected in blood

samples up to 12 hours after a single dose (14, 15, 17). LSD is mainly metabolised to OH-LSD, which usually is present at lower concentrations than the parent drug in the blood. However, OH-LSD is concentrated in the urine, where it also has a longer detection window than LSD (up to four days), making it a good marker for LSD use (17, 18).

In the urine sample from our patient, which was collected approximately eight hours after symptom occurrence, we detected LSD, OH-LSD, and iso-LSD. Iso-LSD is not a metabolite of LSD, but it may be formed during LSD production under poorly controlled conditions. Accordingly, it can be used as an additional marker for illegally manufactured LSD. We could not detect LSD or OH-LSD in serum using our laboratory's routine method for a high-resolution toxicology screen. However, by using a more sensitive instrument LSD could be identified. The serum concentration was not quantifiable with this analytical method but was presumably low. A weak correlation between serum concentrations and symptoms has been observed in clinical trials in adults, although the results are ambiguous (15, 18).

LSD is a low-toxic substance, but serious complications, including seizures, coma, respiratory disorders, and death, have been reported in the literature (19, 20). In the historical material we reviewed, the largest reported dosage was 2 000 µg LSD, which corresponds to 10–20 standard user doses. The child in question recovered without sequelae after the poisoning. However, LSD was not detected in blood or urine samples, which leaves open the possibility that the poisoning resulted from the ingestion of another drug or that the actual dose was significantly lower than the one stated by the author (11).

There is no known antidote against LSD. Observation in hospital is recommended, along with symptomatic supportive care if required (20). Reassuring and shielding the child (and parents) is usually sufficient. Activated charcoal and gastric lavage will rarely be indicated, owing to the rapid absorption of LSD. If sedation of the child is necessary because of seizures, tachycardia, agitation, anxiety, or frightening hallucinations, a benzodiazepine, such as diazepam or midazolam, may be prescribed. Phenothiazines, including chlorpromazine, which has been suggested as a treatment option in previous reports, are no longer recommended as they may lower the seizure threshold (21).

Sweets, such as gummy bears, laced with recreational drugs have become increasingly common. This is particularly the case in the USA and Canada, partly due to the legalisation of cannabis products (22). Cannabis and synthetic cannabinoids are more often associated with this 'formulation' than LSD, but LSD products packaged as sweets are also readily available on the internet. Several cases of children ingesting toxic substances they thought were ordinary sweets have been reported (23).

Intoxication with LSD and other hallucinogenic drugs is rare in children and can be challenging to identify clinically. This is especially true for young children with limited opportunities for verbal communication, as the symptoms are mainly non-specific. Confirmatory laboratory tests may therefore be crucial diagnostic tools. We would advise clinicians who encounter paediatric patients with unexplained physical and neuropsychiatric symptoms to consider

intoxication as a possible differential diagnosis. Where possible, both blood and urine samples should be obtained on admission. Many recreational drugs, including LSD, have a short half-life, and the interval between ingestion and sampling will have an impact on whether or not the substance can be detected. In addition to an initial toxicology screen, several of the larger hospitals in Norway have access to high-resolution instruments that can detect more uncommon substances that are not part of routine screening. Contacting the Norwegian Poison Information Centre can also be helpful if poisoning with an unknown substance is suspected. They can offer advice on obtaining samples and on follow-up and treatment. If mushroom poisoning is suspected, they can also arrange contact with a laboratory that offers gastric contents/vomit analysis.

The patient's guardians have consented to the publication of this article.

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