Case Report

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Clinical Course and Management of Drug-Induced Catatonia and Paranoid Behavior in an Adolescent

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ABSTRACT:

Clinical course and management of drug-induced catatonia and paranoid behavior in an adolescent

A 19-year-old Hispanic male with past psychiatric history of illicit drug use was brought by his mother to the emergency room of a tertiary care hospital with altered mental status. According to patient's mother his paranoid symptoms consisted of increased suspiciousness towards his friends and other family members, but were not to the extent for him to seek out any medical help. Clinical course and management of this patient, who later progressed to full blown catatonia, is described in this report. Patient had paradoxical disinhibition when treated with benzodiazepine, limiting treatment options. Patient's mother would not consent for ECT treatment after which Olanzapine was selected to manage his catatonic symptoms. This patient's preexisting paranoid ideations and catatonia were stabilized successfully with a few days of olanzapine with significant decrease in Bush-Francis Catatonia Score. Initial catatonia score of 14 points at baseline decreased to 3 points after 20 days of inpatient management. Historically, when risperidone (strong 5HT2A antagonist) was combined with sertraline (serotonin reuptake inhibitor), it potentiated action of 5HT1A receptors and was implicated in development of catatonia. Olanzapine does not bind to 5HT1A receptors; hence it does not possess this risk. On the contrary, it has strong potency for 5HT2A receptors, inhibition of which increases dopamine concentration in striatum via glutamate-GABA pathway. At his 10 months follow-up, patient reported sustained improvement in his symptoms after 6 months of treatment. Rationale of selecting Olanzapine as medication alternative based on pathophysiological basis of catatonia is described and follow-up information after 10 months is presented in this report. Patient's vital parameters, results of investigation modalities, catatonia rating scores and serial description of the events are documented in the report.

Despite limited evidence of the use of second-generation antipsychotics for catatonia, this can be a viable treatment option, especially in adolescent patients who are more prone to paradoxical disinhibition.

Conclusion: The LOI-CV and OBQ-CV had promising psychometric properties in a community sample of Turkish children and adolescents.

Keywords: Catatonia, LSD, olanzapine, paranoid delusions

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INTRODUCTION

The term 'Catatonia' (Greek: cata= destructively increased; tonia=muscle tone) was coined by Karl Kahlbaum (1874) and described it in his paper Die Katatonie oder das Spannungsirresein (Tension Insanity or Catatonia)[1]. Catatonia is a clinical syndrome characterized by varied behavioral abnormalities which may include psychomotor and autonomic disturbances, and other striking

abnormalities induced or triggered by any insult to the brain. Although mood disorders account for most of the cases of catatonia of psychiatric origin, it can be due to other psychiatric disorders as well like schizophrenia, post-traumatic stress disorder, etc. Catatonia can be due to drug/ toxin-induced, medication-induced or from withdrawal of any recreational drug/ medication.

Generally seen in advanced psychiatric illness, it is a rare diagnosis and not frequently encountered in non-psychiatric setting. Among the patients diagnosed with catatonia, 20-25% are related to mood disorders and 10% are related to schizophrenia. The exact number of patient suffering from drug addiction developing catatonia is unknown; however, the number is increasing gradually.

Several theories have been proposed in development of catatonic syndrome; namely dopamine hypoactivity, γ-aminobutyric acid (GABA) hypoactivity, glutamate hyperactivity, serotonin hyperactivity, and cholinergic hyperactivity[2]. Since field or clinical trials on mechanisms leading to catatonia are extremely difficult to conduct, the proposed theories are more or less product of pharmacological responses to the administered treatment modality. Here we present a case which was successfully treated with low dose second generation antipsychotic and discuss about possible mechanisms responsible for the outcome.

CASE REPORT

A 19 year-old Hispanic male with no past medical and psychiatric history was brought by mother to the emergency department (ED) of a tertiary care hospital with altered mental status. Patient was at home when his mother noticed him not responding to her commands, sitting in one posture for prolonged duration with staring spells, visual hallucinations, confusion and periodic hyperarousals with seemingly unimportant activities and with significant slowing of his movements and speech. Patient admitted to using "acid" (Lysergic acid diethylamide) two days prior to the initial presentation to the emergency room. Patient was not able to provide good history and was also not able to fully cooperate during physical examination.

Past, Social, and Family History

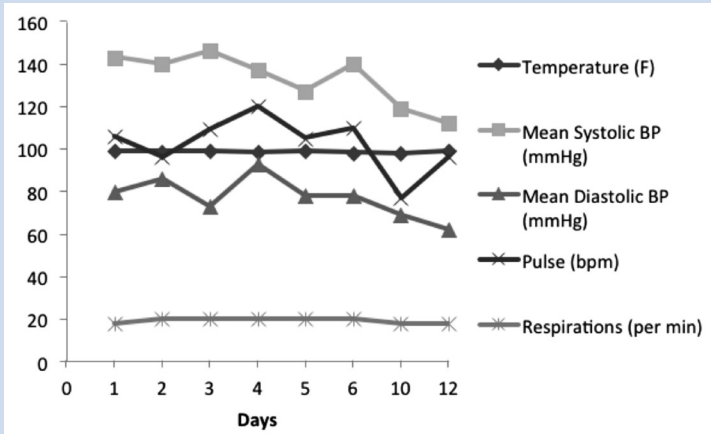
Patient's past psychiatric history was significant for illicit drug use which started 5 months ago with recent onset of paranoia which started 3 weeks prior to this presentation. According to patient's mother, his paranoid symptoms consisted of increased suspiciousness towards his friends and other family members but were not to the extent for him to seek out for any medical help. There was no past history of prior safety compromising behaviors, no symptoms of depression, mania, anxiety, or trauma prior to this incident. Patient did not have any prior hospitalization, without any subacute or chronic medical condition, no known allergies, and was not on any medications. Two of his friends reported weekly cannabis use and experimentation with Lysergic acid diethylamide (LSD) use three times total. Patient and his friends denied any other drug use including stimulants which were also found in his belongings. Patient admitted to using drugs intermittently since summer of the same year. He initially started with smoking cannabis daily and tried LSD total three times with his friends. Patient admitted to using LSD two days prior to his arrival in the ER and denied any other drug use, however, medications used to treat ADHD (atomoxetine and dextroamphetamine) were found in his bag. Urine drug screen showed only cannabis and special test for newer hallucinogen NBOMe (N-methoxybenzyl) was requested which later came back negative. From patient's journal which mother provided, it was evident that he was highly functional prior to the incident. Family psychiatric history of drug addiction was reported in his paternal uncle and his paternal grandmother suffered from unknown, undiagnosed psychiatric condition. Family medical history comprises of hypertension, diabetes and breast cancer. Patient

is the older of two siblings, and reportedly had no significant dysfunctions during his early development period. According to mother, he was a very smart and all-As student at school who received scholarship to complete his college education. Patient's education history was significant for multiple changes in his major field of education in past 2 years, however, no reports of poor academic performance was reported. Patient's social history was significant for parental divorce 8 years ago which, according to mother, did not have adverse impact on patient's life.

Clinical Course

A complete outline of the clinical course is illustrated in Figure 1. Patient was brought to the ED by mother with altered mental status. He was admitted to medical floor for further work-up and management. After two days into hospital admission patient was agitated, not redirectable, and was demanding to leave the hospital, not oriented and confused; haloperidol was administered intravenously by the primary team considering underlying questionable diagnosis of

Table 1: Outline of clinical course with Mental Status Examination (MSE), Investigations, Vital signs, & Treatment received (Rx).

	Beginning of first week	End of second week
Patient information	-Patient presented to ED with mother-starring looks, decrease in voluntary movements, decreased volition, non-fluent. -Patient was agitated twice, with minimal reaction to environmental stimuli, and continued high BFCS score.	-Patient started to show slow but stable improvement in his responsiveness to the environment -Patient gradually involved in daily activities on the psychiatric unit with normalizing of his appetite and sleep.
Mental Status Examination (MSE)	Appearance-reduction in blinking, behavior-unable to comprehend or cooperate, speech-non-fluent, vocabulary limited to few words, affect-flat, decreased range and intensity, sensorium & orientation - awake & alert, orientation intact	Appearance-smiling and talking to staff, engaging with mother during family meeting, behavior-very cooperative, clearly following commands, speech-no abnormality noted, full vocabulary, affect-full range and intensity, sensorium & orientation-intact
Investigations	Blood: elevated anion gap, normal CK; Urine: drug screen + cannabis, Urinalysis - trace of protein, 3+ ketones	Special laboratory test (NBOME) came back negative
Imaging	CT-head negative	None obtained
Vitals & other parameters		
Rx	Day-1: Intravenous fluids infusions Day-3: Intravenous Haloperidol 2 mg administered twice 9 hours apart Day-4: Intravenous fluid infusion and trial of 1 mg intravenous Lorazepam Day-6: Oral Olanzapine 2.5 mg started	By Day-10 received total of 40 mg Olanzapine with maximum daily dose of 10 mg

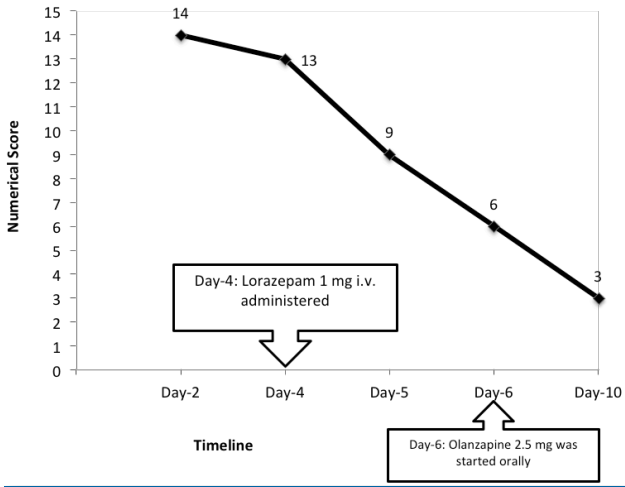


Figure 1: BFCRS (Bush-Francis Catatonia Rating Scale) Score

delirium. The next day patient's condition showed only transient improvement and his psychomotor retardation worsened later that day, pointing to another etiology of patient's signs and symptoms. After initial workup, history, and clinical course in first three days, diagnosis of substance-induced catatonic syndrome was made which was corroborated with increased Bush-Francis Catatonia Rating Score (Figure 1). Patient exhibited abnormally still posture, mutism, staring gaze held longer than 20 seconds, catalepsy, moderate rigidity, and waxy flexibility. Electroconvulsive therapy (ECT) is considered one of the most effective treatments for catatonia (simple or malignant) regardless of the etiology; however, patient's mother did not consent to this invasive modality of treatment. Since the alternative treatment option for this patient's catatonia was a trial of benzodiazepine, Lorazepam 1 mg was administered intravenously on day-4 of hospitalization, however, patient showed features of paradoxical disinhibition in which he started pulling intravenous lines and was agitated requiring physical restraints, all of which corroborated to the onset of medication action. After this incident patient's mother was reluctant to try any new medication, however, after multiple family meetings and psychoeducation sessions, she agreed for the trial of another medication. He was started on very low oral dose of Olanzapine: starting with 2.5 mg and gradually increased over 2 days to 7.5 mg a day total dose. In addition, regular psychoeducation sessions were undertaken with mother and the primary team and behavioral measures were implemented to ensure adequate support to his already compromised cognitive and emotional status. Considering the serotonergic effects of LSD any serotonergic agents including the SSRIs, Mirtazapine, Trazodone, etc. were avoided. Over the period of next 2 days patient's condition improved remarkably and he started engaging in his daily activities and his mental status examination improved dramatically. After discharge, patient continued his Olanzapine treatment and was provided with outpatient follow-up. At 10 months follow-up phone call, patient did not report any active symptoms, was not using any illicit drugs, and started his first year of college education. He continued Olanzapine treatment for 6 months after his discharge from the hospital and reported being at his baseline functioning level.

DISCUSSION

Catatonia is a medical and psychiatric emergency. Rapid detection and timely management prevents future complications and is crucial to prevent fatality. Etiology of catatonia ranges from primary psychiatric (mood disorders, schizophrenia, conversion disorder, personality disorders) to any secondary medical (cerebrovascular, metabolic derangements, neoplasms, infections) or due to drug intoxication or withdrawal. Catatonia secondary to psychiatric conditions can be categorized into retarded-stuporous or excited-delirious type with common signs of mutism, negativism, posturing, staring, catalepsy, echolalia, or echopraxia. Absence of tonic clonic activity and absence of inter-episodic recovery of orientation differentiates catatonia from epilepsy and delirium respectively. Catatonia secondary to non-psychiatric conditions tend to have severe rigidity, autonomic nervous system instability, and altered mental status[3]. Few hallmark features such as fever (malignant catatonia & NMS), hyperreflexia and myoclonus (serotonin syndrome), or prior history

of drug use (drug intoxication or withdrawal) are helpful in narrowing down the differential diagnoses in non-psychiatric etiologies of catatonia.

Current case report presents LSD and possible cannabis induced etiologies of catatonia. Drug-induced catatonia likely subsides past the clearance of substance from the body; however, this patient had persistence of signs and symptoms beyond likely clearance of the illicit substances which was possibly complicated secondary to his pre-existing paranoid ideations. Patient had improvement in his BFCS score; however, clinically he was further away from his baseline functioning abilities as noted by his mother. Since benzodiazepines are the drug of choice for catatonia owing to their pharmacological mechanism on GABA-A receptor, a trial of Lorazepam was conducted. However, this 19 year-old patient got paradoxical disinhibition from Lorazepam requiring physical restraints and other environmental measures to ensure safety. After this episode of disinhibition, patient's family member was reluctant to try any new treatment modality and refused to proceed with ECT. Subsequently, owing to the facts of decrease in number of catatonic schizophrenic patients after the introduction of second generation antipsychotics[4], successful use of Olanzapine in few catatonic patients in the past, patient's undiagnosed and unaddressed pre-existing paranoid ideations, and limited treatment choices available for this patient, Olanzapine was considered as the next medication. The mechanisms of action specifically for Olanzapine to be potentially considered effective in catatonia are: potent D2 blockade with 'loose receptor attachment' but relative rapid dissociation, blocking 5-HT2A receptor (reducing potential for EPS effects from D2 blockade), anxiolytic and cognitive enhancing properties from 5-HT2C blockade, and also providing sedation through potent H1 blockade[5]. Olanzapine was also used to provide smoother control of agitation and potentially served as a platform for brain to recover preventing the occasional spurts of fluctuations in cognition and alertness in this patient.

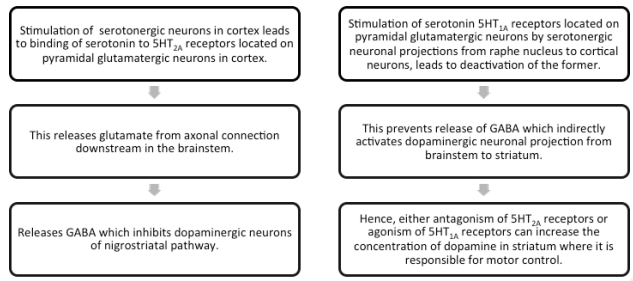


Figure 2: Effects of receptor stimulation on GABA and dopamine pathways

The difference between typical and atypical antipsychotics is the ability of the later to modulate serotonin-dopamine pathways in brain. As stated above, second generation (atypical) antipsychotics are antagonists to 5HT2A receptors and possess agonistic actions to 5HT1A, both properties potentially increasing concentration of dopamine in striatum (Figure 2). Historically, when risperidone (strong 5HT2A antagonist) was combined with Sertraline (serotonin reuptake inhibitor), potentiated action of 5HT1A receptors and was implicated in development of catatonia.

Olanzapine do not bind to 5HT1A receptors, hence it does not possess this risk. On the contrary, it has strong potency for 5HT2A receptors, inhibition of which increases dopamine concentration in striatum via glutamate-GABA pathway[6]. Hence, in striatum D2 receptor agonism by increasing local concentration of dopamine in the area, prevents not only EPS but also other motor catatonic symptoms and possibly cognitive symptoms. Furthermore, Hallucinogens like D-lysergic acid diethylamide (LSD), psilocybin, and dimethyltryptamine (DMT) are strong serotonergic stimulants acting via 5HT2A receptors. A highly serotonergic compound which could potentially lead to dopamine depletion in nigrostrial pathway, likely instigated catatonic symptoms in this patient. GABAB agonism by baclofen has shown to produce catatonia whereas GABAA agonism by lorazepam tends to alleviate it[7]. As documented in literature, about 70% of the afferents to substantia niagra dopaminergic neurons are GABAergic[8], possessing both GABAA

and GABAB receptors. Stimulating GABAA receptors by lorazepam can alleviate catatonic symptoms as it serves as the first line of agent to be considered.

Substance withdrawals have been known to reveal underlying psychiatric symptoms such as anxiety, depression, inattention, etc.[9] and association of cannabis and psychosis is very well documented in literature. This case report highlights how patient's underlying psychotic symptoms were uncovered by drug intoxication and/or withdrawal and the potential of antipsychotics in augmentation of patient's recovery in drug induced catatonic syndrome. Historically, antipsychotics are considered one of the culprits for catatonia or worsening a catatonic conundrum or even leading to Neuroleptic Malignant Syndrome (NMS)[10]; however, this case provides prospect of second generation antipsychotics to be used as a treatment choice.

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