Cannabis-Induced Bipolar Disorder with Psychotic Features: A Case Report

by MASOOD A. KHAN, MD, and SAILAJA AKELLA, OMS-IV

Staff Psychiatrist at the Greater Binghamton Health Center, Binghamton, New York; fourth year student, New York College of Osteopathic Medicine, New York, New York

Psychiatry (Edgemont) 2009;6(12):44–48

ABSTRACT

There has been considerable debate regarding the causal relationship between chronic cannabis abuse and psychiatric disorders. Clinicians agree that cannabis use can cause acute adverse mental effects that mimic psychiatric disorders, such as schizophrenia and bipolar disorder. Although there is good evidence to support this, the connections are complex and not fully understood.

As the research in the endocannabinoid system is emerging, the neurobiological effects of cannabis are being evaluated in the development of psychiatric illness for those individuals who may be genetically vulnerable. Here we present a case of a college student who initially suffered from an acute psychotic breakdown secondary to cannabis abuse that manifested into bipolar disorder with psychosis.

FUNDING: There was no funding for the development and writing of this article.

FINANCIAL DISCLOSURE: The authors have no conflicts of interest relevant to the content of this article.

ADDRESS CORRESPONDENCE TO: Masood Khan, MD, 425 Robinson St., Binghamton, NY 13904; E-mail: bimdmak@omh.state.ny.us; Sailaja Akella, E-mail: sakella@nyit.edu

KEY WORDS: Cannabis, psychosis, schizophrenia, bipolar disorder, substance-induced psychotic disorder

INTRODUCTION

The role of cannabis in psychiatric illnesses has been an area of interest. Epidemiological studies have shown that as the frequency of cannabis abuse increases, so does the risk for a psychotic disorder such as schizophrenia.[1] Studies have also shown that cannabis is the most commonly abused drug among those diagnosed with bipolar disorder.[1] Looking at the pharmacokinetics of the psychoactive agent Δ9-tetrahydrocannabinol (Δ9-THC), its effects are perceptible within minutes. Δ9-THC is extremely lipid soluble and can accumulate in fatty tissues reaching peak concentrations in 4 to 5 days. It is then slowly released back into the body, including the brain, reaching high concentrations in the neocortical, limbic, sensory, and motor areas.[2] The tissue elimination half-life of Δ9-THC is about seven days, and absolute elimination of a single dose may take up to 30 days. Interestingly enough, the plasma levels of Δ9-THC poorly correlate with urine levels,

making the urine toxicology screen a wholly unspecific test.[2]

Cannabis intoxication can lead to acute psychosis in many individuals and can produce short-term exacerbations of pre-existing psychotic diseases.[3–6] Cannabis use also causes symptoms of depersonalization, fear of dying, irrational panic, and paranoid ideas, which coincide with acute intoxication and remitted quickly.[7] In one survey, it was reported that 15 percent of cannabis users identified psychotic-like symptoms, the most common being hearing voices or having unwarranted feelings of persecution.[8] What research has failed to show is if cannabis use is a consequence or cause of psychiatric disorders.[9] Based on research reviews, looking at the connection between cannabis and psychosis, two hypotheses have been developed.[10] The first hypothesis is that cannabis use causes psychotic symptoms in an otherwise healthy individual that would not have occurred with abstinence. The second hypothesis is that cannabis use may precipitate psychosis in individuals who are predisposed to acquiring a psychotic disorder.[10,11] Only two case studies have reported prolonged depersonalization after cessation of cannabis use.[12,13] Symptoms experienced during drug-free periods are rarely reported.[7]

The role of cannabis in causing bipolar disorder is not well documented. Epidemiological studies have shown that bipolar disorder has the highest rate of substance abuse comorbidity of any axis I disorder.[1,15,16] The Epidemiologic Catchment Area (ECA) study found that 41 percent of patients with bipolar disorder had a comorbid substance use with cannabis being the most frequently abused.[16] Cannabis abuse prior to development of bipolar disorder has a significant effect on first-episode mania and on the course of the disease. Another study reported that using cannabis at baseline can significantly increase the risk for manic symptoms during follow up.[17]

Recent advances in cannabinoid receptors and endogenous ligands have renewed interest in the mechanisms by which cannabis can cause major psychiatric disorders.[1,5] It is now recognized that the endocannabinoid system represents a new signaling process in the nervous system that regulates neurotransmitter systems, energy metabolism, and immune function.[1,18] Researchers now believe that cannabis consumption during critical phases of brain development can lead to a strong disturbance of the endocannabinoid system and ultimately cause an inappropriate hardwiring of the brain. Cannabis may play a role in the complex interactions involving dopamine, gamma aminobutyric acid (GABA), and glutamate transmission or other factors that cause psychotic disorders. However, the question remains as to why, in a general population of cannabis abusers, do only a small population exposed develop a psychiatric illness.[5]

We present a unique case of a young college student, with no family history of any psychiatric illness, who presents with psychosis secondary to cannabis abuse. His psychosis persisted long after he stopped abusing cannabis, and he needed to be treated medically for new onset bipolar disorder with psychotic features. In the face of no known genetic predisposition, it is interesting that cannabis was his only trigger for psychosis, which warrants further study into understanding the exact mechanism that cannabis affects the neurotransmission at various receptors.

PRESENTATION

Mr. X was a 21-year-old, African-American man who presented to our facility for his second psychiatric hospitalization. He was discharged one week prior after a 30-day stay with a diagnosis of cannabis-induced psychotic disorder. He started using cannabis shortly afterward and became symptomatic with more pronounced delusions and psychotic behavior. He was brought to the Greater Binghamton Health Center (GBHC), Binghamton, New York, for exhibiting hostile and grandiose behavior at a local deli where he refused to pay for his meal because he had "nine billion dollars" in his bank account. He had pressured speech, racing thoughts, flight of ideas, insomnia, and delusions of grandeur that he "owns this hospital" and worked as a "successful rap artist." His physical exam was unremarkable except for his urine toxicology, which tested positive for cannabis. He rejected all his medications, including isoniazid (INH) for a positive purified protein derivative (PPD) with negative chest x-ray, and was taken to court to obtain an order of "treatment over objection" (TOO). Mr. X was not treated for two months and continued to exhibit the above symptomatology in contrast to his first admission where his psychosis had remitted rather quickly.

Past psychiatric history. During his first psychotic break, he was brought to the Comprehensive Psychiatric Emergency Program (CPEP) by the police one week prior to his second admission. His girlfriend notified the police that he had been hearing voices lately and was fearful that he may be a threat to others. She reported that he was acting increasingly delusional and suspicious since his trip from Africa—making statements that people were out to get him and had planted a microphone in his stomach to broadcast his thoughts. The physical exam was unremarkable except for a positive urine toxicology for cannabis, which he did admit to using while abroad and in the recent past. At CPEP, he needed to be restrained several times, which prompted his transfer to GBHC.

During his stay at GBHC, the patient did not display the same aggressive and disorganized symptoms. He did not endorse any affective symptoms. He denied any anxiety spectrum of symptoms but did acknowledge that he had symptoms of paranoia prior to his

arrival to CPEP. He admitted to being paranoid that people had "bugged" his room with microphones. He reported hearing voices from these microphones that were running a commentary on his life telling him repeatedly "you're over." These auditory hallucinations, which he referred to as "reverb," had only occurred when he smoked cannabis. He denied hearing any "reverb" during his stay at GBHC or having any visual hallucinations. He was diagnosed with cannabis-induced psychotic disorder since his symptoms occurred during the time he was smoking cannabis. Also, his initial psychotic behavior quickly subsided upon his arrival to this hospital and during his subsequent stay at GBHC. The patient was observed for any changes in mental status; none were noted, and therefore he was not treated with any medications.

Mr. X underwent a Minnesota Multiphasic Personality Inventory (MMPI) Second Edition with the psychologist to gain insight into his personality and diagnosis. The report showed that he displayed persecutory beliefs, had a risk of developing an addictive disorder, a grandiose personality, and a dismissive view of authority. Based on the assessment, he was diagnosed with cluster B traits with predominant antisocial traits on Axis-II. The patient was consequently discharged with recommendation to follow up with the university psychiatrist.

Substance use/abuse history. Mr. X started using cannabis when he was 16-years old. He only used it rarely in the past, but started using it on a daily basis in the past few months and in greater quantities. He began using alcohol when he was 14-years old. He typically drank ("a few beers") on the weekends. He did not report passing out or withdrawal seizures. He denied any other illicit drug use.

Family history. There was no reported psychiatric illness in his family.

Researchers now believe that cannabis consumption during critical phases of brain development can lead to a strong disturbance of the endocannabinoid system and ultimately cause an inappropriate hardwiring of the brain.

Mental status exam. Mr. X appeared stated age. He was in healthy condition with a muscular build and tall height. He was well groomed and dressed appropriately for the weather. Throughout the interview he made fair eye contact. He remained guarded and needed to be further prompted to elicit information. He often laughed inappropriately but quickly adjusted his demeanor when questioned. Mild psychomotor agitation was noted. He reported his mood to be "fine." Although no affective symptoms were endorsed during the interview, he did show extreme lability on the unit: He would laugh at himself one moment and become tearful the next. He spoke at normal rate but in low tones. His thought process was linear but limited to only few-word answers. His thought content included several delusions, such as being a billionaire because of his successful music career. He stated that he owned the hospital and all the staff. He reported that his father wanted him dead because of his successful career. No auditory or visual hallucinations were endorsed; however, he seemed to be internally preoccupied with staring at himself in the mirror and talking to unseen others for hours at a time. His insight and judgment were poor: He refused to take any medications, including INH for a positive PPD. No suicidal and homicidal ideations were reported at that time.

Summary formulation and differential diagnosis. Mr. X was readmitted to GBHC one week after discharge after being nonadherent with his follow-up recommendations. This time he displayed delusional ideations, extreme grandiosity, and mood lability. He was hospitalized for a duration of four months. During the first two months, he refused to take any medications and continued to display this same bizarre behavior. In addition, he appeared to be internally preoccupied and would stare at himself and talk to himself for hours at a time. His diagnosis was soon changed to bipolar disorder with psychotic features. After obtaining the TOO, he was administered and responded quickly to olanzapine orally disintegrating tablets (Zyprexa® Zydis®, Eli Lilly and Company, Indianapolis, Indiana) and valproic acid liquid (Depakene®, Abbott Laboratories, Abbott Park, Illinois), which was later changed to olanzapine 15mg orally, twice daily and divalproex sodium 750mg orally, at bedtime. Upon discharge, Mr. X was asymptomatic with no residual signs of psychotic or affective symptoms.

DISCUSSION

Several case studies and longitudinal studies have illustrated the link between acute psychosis and mania associated with cannabis.[1,19–21] The most prominent symptoms elicited are auditory hallucinations, paranoid feelings of being persecuted, depersonalization, derealization, anxiety, grandiosity, irritability.[3,9,10,22] The debate remains as to whether or not cannabis can cause schizophrenia and bipolar disorder in an otherwise healthy individual. We presented a case of a young individual, who was previously healthy and was high functioning, pursuing a bachelor's degree in chemistry with a 3.3 grade-point average. His case is unique because we had the opportunity to observe him firsthand longitudinally over a four-month period, saw how cannabis use can cause psychotic symptoms, and followed him through his course as he developed a more severe affective and psychotic disorder.

Clinicians have hypothesized several contributing factors including "heavy usage, length and age of users, and psychotic vulnerability."[6] In the report by Johns,[3] it was felt that adolescents are more vulnerable to the mental effects of cannabis because they may "experience emotional problems that cue cannabis use" and secondly, regular use may "interfere with learning and personal development." Although our patient had no genetic predisposition with a negative family history of any psychiatric illness, he did start smoking cannabis during his adolescence. As there is an increase in the use of cannabis among younger individuals and a rise in schizophrenia in this younger population, we must be aware of the potential harm of cannabis abuse.[23] During his first psychotic break, he presented to the clinic with delusions of being persecuted, auditory hallucinations, and grandiosity, which have been well documented as prominent symptoms secondary to cannabis abuse. He soon recovered without any use of medications. The only insightful data we could gather about his vulnerability, aside from age of onset with cannabis use, was from his MMPI. The report gave evidence as to the nature of his personality. This was an individual who had elements of paranoia, grandiosity, risk of addiction, and antisocial traits. According to Regier et al,[15] 83.6 percent of individuals with antisocial personality disorder also have comorbid drug misuse. It seems that Mr. X's cannabis use heightened these personality characteristics and may have been a contributing factor to his psychotic break. After his first discharge, he was nonadherent and did not follow up with the university psychiatrist. Review of literature has shown that cannabis use was consistently associated with relapse and nonadherence to treatment in psychotic patients.[24] This makes it difficult to manage these types of patients with increasing relapses, hospitalizations, and progressive worsening of symptoms.

When he was admitted the second time, his behavior was more exaggerated than the first hospitalization. Being that his drug test came back positive for cannabis, we felt strongly that this was another case of cannabis-induced psychosis. Based on pharmacokinetics, a single dose of Δ9-THC may last for an absolute period of 30 days.[2] However, when his symptoms had not abated after one month with no treatment, we changed our working diagnosis to bipolar disorder with psychosis being that he showed both affective and psychotic symptoms. Mr. X stayed at GBHC for a total of four months and was not treated the first two months. His behavior soon changed after starting olanzapine and divalproex sodium. He had a more stable mood and less internal preoccupation. Since his symptoms resolved with these medications, we feel that the cannabis affected his neurochemical system in a chronic way causing him to have long-term problems. As our case report demonstrates, there are individuals who are otherwise healthy, with no genetic predisposition, who can be diagnosed with a psychiatric illness purely with cannabis abuse. This goes along with the first hypothesis that cannabis use causes psychotic symptoms in an otherwise healthy individual, which would not have occurred with abstinence. One would argue that someone who had a first episode psychosis with cannabis use is itself a risk factor for having a subsequent psychotic or mood disorder. These are the patients we should follow closely to help prevent from having long-term consequences secondary to cannabis abuse.

As our case report demonstrates, there are individuals who are otherwise healthy, with no genetic predisposition, who can be diagnosed with a psychiatric illness purely with cannabis abuse.

REFERENCES

1. Leweke F, Koethe D. Cannabis and psychiatric disorders: it is not only addiction. *Addict Biol*. 2008;13(2):264–275.Review.
2. Ashton C. Pharmacology and effects of cannabis: a brief review. *Br J Psychiatry*. 2001;178:101–106.
3. Johns A. Psychiatric effects of cannabis. *Br J Psychiatry*. 2001;179:270–271. Review.
4. Sewell R, Ranganathan M, D'Souza D. Cannabinoids and psychosis. *Int Rev Psychiatry*. 2009;21(2):152–162.
5. D'Souza D, Sewell R, Ranganathan M. Cannabis and psychosis/schizophrenia: human studies. *Eur Arch Psychiatry Clin Neurosci*. 2009 Jul 16. [epub ahead of print]
6. Amar B, Potvin S. Cannabis and psychosis: what is the link? *J Psychoactive Drugs*. 2007;39(2):131–142.
7. Thomas H. Psychiatric symptoms in cannabis users. *Br J Psychiatry*. 1993;163:141 Review.
8. Thomas H. A community survey of adverse effects of cannabis use. *Drug Alcohol Depend*. 1996;42(3):201–207.
9. Arseneault L, Cannon M, Witton J, et al. Causal association between cannabis and psychosis: examination of the evidence. *Br J Psychiatry*. 2004;184;110–117.
10. Hall W. Cannabis use and psychosis. *Drug Alcohol Rev*. 1998;17(4):433–444.
11. Degenhardt L, Hall W. Is cannabis use a contributory cause of psychosis? *Can J Psychiatry*. 2006;51(9):556–565.
12. Degenhardt L, Hall W, Lynskey M. Testing hypotheses about the relationship between cannabis use and psychosis. *Drug Alcohol*

Depend. 2003;71(1):37–48.
13. Szymanski H. Prolonged depersonalization after marijuana use. *Am J Psychiatry*. 1981;138(2):231–233.
14. Keshaven M, Lishman W. Prolonged depersonalization following cannabis abuse. *Br J Addict*. 1986;81(1):140–142.
15. Regier D, Farmer M, Rae D, et al. Comorbidity of mental disorders with alcohol and other drug abuse. Results from the Epidemiologic Catchment Area (ECA) Study. *JAMA*. 1990;264(19):2511–2518.
16. Strakowski S, DelBello M, Fleck D, et al. Effects of co-occurring cannabis use disorders on the course of bipolar disorder after a first hospitalization for mania. *Arch Gen Psychiatry*. 2007;64(1):57–64.
17. Henquet C, Krabbendam L, de Graaf R, et al. Cannabis use and expression of mania in the general population. *J Affect Disord*. 2006;95(1-3):103–110. Epub 2006 Jun 21.
18. Lutz B. From molecular neurodevelopment to psychiatry: new insights in mechanisms underlying Cannabis-induced psychosis and schizophrenia. *Eur Arch Psychiatry Clin Neurosci*. 2009;259(7):369–370.
19. Kroll P. Psychoses associated with marijuana use in Thailand. *J Nerv Ment Dis*. 1975;161(3):149–156.
20. Bartolucci G, Fryer L, Perris C, et al. Marijuana psychosis: a case report. *Can Psych Assoc J*. 1969;14(1):77–79.
21. Talbott JA, Teague JW. Marijuana psychosis: acute toxic psychosis associated with the use of cannabis derivatives. *JAMA*. 1969;210:299–302.
22. Van Os J, Bak M, Bijl RV, et al Cannabis use and psychosis: a longitudinal population-based study. *Am J of Epidemiology*. 2002;156: 319–327.
23. Hall W, Degenhardt L.Cannabis use and the risk of developing a psychotic disorder.*World Psychiatry.* 2008;7(2):68–71.
24. Zammit S, Moore TH, Lingford-Hughes A, et al. Effects of cannabis use on outcomes of psychotic disorders: systematic review. *Br J Psychiatry*. 2008;193(5):357–363.