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A mood disorder episode with an onset under chronic cannabis consumption and accompanied with psychotic features immediately after N,N-Dimethyltryptamine (DMT) use: case report

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ABSTRACT

A mood disorder episode with an onset under chronic cannabis consumption and accompanied with psychotic features immediately after N,N-Dimethyltryptamine (DMT) use: case report

N,N-dimethyltryptamine (DMT) is a serotonin agonist hallucinogen, similar to lysergic acid diethylamide (LSD). Synthetic production of DMT as well as extraction from several plants of South American flora is possible. DMT might induce feelings of unity with the cosmos and experiences of eternity, and it is a natural content of a traditional South American beverage –ayahuasca- which is consumed at shamanistic rituals. There is not any data on the abuse of DMT in Turkey to date. We here present a case characterised by sudden and dramatic changes in the clinical features of a hypomanic episode induced after three years of cannabis use, immediately after consuming DMT due to the addition of psychotic features.

Key words: N,N-dimethyltryptamine (DMT), cannabis, mood disorder

ÖZET

Esrar kullanımı sırasında başlayan ve N, N-dimetiltriptamin (DMT) kullanımı ile psikotik özellikler eklenen duygudurum bozukluğu: Bir olgu sunumu

N, N-dimetiltriptamin (DMT), liserjik asit dietilamid (LSD) benzeri serotonin agonisti bir hallüsinojendir. Sentetik olarak üretilmesinin yanı sıra, özellikle Güney Amerika'da yetişen pek çok bitkiden elde edilebilmektedir. Evrenle bütünlük ve sonsuzluk hissi gibi etkileri bulunan ve Güney Amerika yerlilerince geleneksel olarak şaman ayinlerinde de kullanılan "ayahuasca" isimli içeceğin içeriğinde de saptanan maddenin Türkiye'de kullanımına dair veri bulunmamaktadır. Bu makalede, 3 yıllık esrar kullanımı sonrasında ortaya çıkan bir hipomanik atak içerisindeyken, DMT kullanımı ile psikotik özelliklerin eklenmesi sonucunda, klinik tablonun ani ve dramatik biçimde değişmesi ile karakterize bir olgu sunulmuştur.

Anahtar kelimeler: N, N-dimetiltriptamin (DMT), esrar, duygudurum bozukluğu

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INTRODUCTION

N, N- dimethyltriptamine (DMT) is a hallucinogen which is a member of triptamine family. DMT was first produced synthetically in 1931 (1) and was later detected in a drink called "ayahuasca" which has traditionally been used by South American natives in shamanic rites (2). Ayahuasca is produced by mixing leaves of Psychotria viridis containing DMT and juice of Banisteriopsis caapi plant containing β-carboline which is strong monoamine oxidase-A (MAO-A) inhibitor. β-carboline prevents peripheral break-down of DMT and makes its oral use possible despite its own psychoactive properties (3).

DMT is synthesized in vivo in several tissues by indolethylamine N-methyltransferase in humans (4). After the discovery of hallucinogenic effects of DMT, and together with detection of its endogenous

production, different studies conducted with the hypothesis that it may have a role in the etiology of schizophrenia, brought out findings pointing increase in urinary DMT metabolites of schizophrenic patients, particularly in correlation with clinical worsening (5).

DMT is a prohibited substance in United States of America. DMT is broken down peripherally when not taken with a MAO inhibitor so it does not have oral bioavailability unless taken in excessive doses to overcome metabolic capacity of MAO. It can also be used by cigarette, breathing or injection as well (6). Using by "freebase (sliding folios)" has also been reported in web forums and people shared their opinions on this method as well (7).

It is well-known in the literature that relationship of cannabis with psychotic disorders such as schizophrenia is more distinct; however, there is need for more data about relationship of mood disorders and particularly manic attacks. Although it is generally accepted that cannabis increases manic symptoms, its manic episode triggering potential is under debate. Although it was stated in diagnostic systems such as DSM-IV-TR and ICD-10 that manic or hypomanic episodes cannot be explained by a substance such as cannabis directly, debate on the need of "cannabis-induced mania" concept is continuing (8).

In this report, a case who was experiencing hypomanic episode after cannabis use for 3 years and whose clinical course changed suddenly and dramatically by addition of psychotic features due to DMT use was presented.

CASE PRESENTATION

Our case was a 19 year old male, was born in New York, came to Turkey 1.5 years after starting primary school in France and repeating his freshman year in computer engineering department of a university having foreign language curriculum. His father was a citizen of a Middle-Eastern country, was living at his home country and was unemployed. His mother was a retired engineer and citizen of Turkey. Patient's mother and father were officially divorced 1,5 years ago but there were long separation periods previously. His father was called from abroad because his mother was working and not interested in him. For this reason, he could come together with his father only twice when he was 10-11 years old and 13-18 years old. He graduated from a high school having foreign language curriculum in Turkey by his father's pressure. He has been using cannabis for 3 years, first rarely and irregularly and for 1.5 years 1-2 joints daily. He had no psychiatric admission before and also his father was reported to use mixed drugs in the past.

The patient was living with his father for 3-months abroad and returned back to Turkey 40 days before his admission to our hospital. On the evening of the day he returned home, he was found continuously swearing, claiming to be king, with increased speech, inappropriate dressing, excessive money spending, excessive joyfulness, dancing in the streets, being rapidly familiar and getting friends with people he did not know before. This condition was connected to his happiness of returning home by his mother and she did not seek any treatment. He used cannabis a few times after this and 15 days later he used DMT in a solution prepared by a friend with cannabis. After DMT use, symptoms such as being out of control and feeling of being directed by another power, seeing musical sounds in the sky, contacting creatures from outer space and mental preoccupation with "cosmos" emerged and he started to write down incomprehensible things in a social media website. He was extracting meanings from numbers. He was thinking that people could read his thoughts, people were saying numbers to him when he was walking in the street, and these numbers did not mean anything to him but mean something to people who said them. He also said that his friend who used DMT with him also focused on a point and get into a dreamy state like something was happening around him. His mother who connected his previous hypomanic symptoms to his joy and did not seek treatment before, started to look for treatment as she got worried due to sudden and dramatic clinical changes after DMT use. Cannabis metabolites were detected in his urine in a private hospital 20 days after DMT use. He was given a prescription but he did not use them and then convinced and brought to our hospital 3 days later.

His psychiatric examination was as follows when admitted to our hospital: He was alert, fully cooperated,

time orientation was deficient and psychomotor activity was slightly decreased, affect was mildly limited and associations were tend to loosen. Patient was inclined to excitation so he was hospitalized for diagnosis and treatment. His treatment was started with haloperidol 10 mg/day IM and biperidene 5 mg/day IM and, doses were escalated to haloperidol 20 mg/day IM and biperidene 10 mg/day IM because his excitation did not relieve. His oral treatment was maintained with risperidone 5 mg/day and valproic acid 250 mg/day. Although substance metabolites in the urine was found negative while he was staying at the hospital, cannabis level was found 48 ng/ml (normal value interval for cannabis is 0-50 ng/ml). Routine blood chemistry, complete blood count, thyroid function tests, VDRL, hepatitis and HIV markers, and activated EEG were all normal. In psychometric examination, no finding in favor of organicity was found in Bender-Gestalt test. He was discharged after twelve days of inpatient follow-up and treatment with valproic acid 1000 mg/day, risperidone 5 mg/day and biperidene 2 mg/day. At his follow-up visit 15 days later, although his clinical condition seemed to be better, he stated that people were still saying some numbers to him, world should have a network and people should communicate with that network but telepathy could still not be done and he was watching his works and occupations in television ads. In his follow-up visit 15 days later, he said that he now did not think that his thoughts were being read, he had had suspicions towards other people but now these suspicions went away and he was using his medications regularly. In the following visits his psychotic symptoms gradually remitted and at his last control visit his affect was euthymic, psychomotor activity and associations were normal and except for some touchiness he had no symptoms. His treatment was continued with risperidone 3 mg/day and valproic acid 1250 mg/day. Patient was followed for approximately 2.5 months with 5 follow-up visits and his informed consent was taken for this publication.

DISCUSSION

In a 10-year retrospective study by Doğanavşargil et al. (9) conducted in 325 patients, mixed substance use was found in approximately 30% of substance abusers admitted to dependence centers. In a 3-year follow-up study done with 4800 people in 2006, initial cannabis use is related with manic symptoms in follow-up and this relation is independent from initial manic symptoms and follow-up psychotic symptoms (10). Similarly, there was a hypomanic episode after 3 years of cannabis use in our case. Although it is not possible to understand exactly by data available whether there is a deterministic relationship between cannabis use and hypomanic episode in our case, he was diagnosed as affective disorder/not otherwise specified according to DSM-IV-TR because he had no history of a depressive or manic episode and hypomanic symptoms could not be related with any substance or a general medical condition. Psychiatric admission was during this hypomanic episode due to acute and dramatic change in clinical picture by DMT use and worrying of family.

Hallucinogens are evaluated in two groups in the literature: serotonin agonists of lysergic acid diethylamide (LSD) type and N-methyl D-aspartate (NMDA) antagonists of ketamine type. DMT and other indolealkylamines are accepted as LSD group hallucinogens. This classification is also used in experimental schizophrenia models. For example, Daumann et al (11) tested "inhibition of return" phenomenon which tests not shifting attention to visual fields which were scanned and found unimportant after administering intravenous DMT and ketamine in healthy volunteers. It was found that response durations were prolonged and "inhibition of return" was impaired only under DMT effect. Inhibition of return phenomenon is impaired in patients with paranoid schizophrenia but this effect is not observed in unidentified type of schizophrenia (12). In the study of Gouzoulis-Mayfrank et al. (13) which compared effects of DMT and ketamine in healthy volunteers, participants identified DMT effect as visual hallucinations, synesthesia, paranoid thoughts and thought flow disturbances and it was found that there were significant increases in positive symptoms under DMT effect and in negative symptoms under ketamine effect after assessment with SAPS (the Scale for the Assessment of Positive Symptoms) and SANS (the Scale for the Assessment of Negative Symptoms). These symptoms

were interpreted as appropriate modeling of DMT for paranoid type schizophrenia and ketamine for unidentified and catatonic types schizophrenia. Strong antipsychotic efficacy of clozapine which has stronger antagonistic effects on serotonin than dopamine supports the use of DMT which is a serotonin agonist for schizophrenia modeling (14).

Although it is known that DMT should be taken with a MAO inhibitor to be effective orally it is classified under "designer drug" category that means structurally changed as also mentioned in DSM-IV-TR (15). For this reason, the substance which our case used as DMT was thought to have been modified and processed in order to be effective for oral use.

People who used natural ayahuasca which contains DMT and β-carboline which is a MAO-A inhibitor were reported to experience their surrounding is trembling and shining, rapid passing over of images, sensation that time does not flow and "eternity" (2). DMT users also reported that they visit other universes, speak with aliens/creatures from outer space and talk about deep changes in existence perception and scary and compelling powers (16). In the case we reported, clinical course evidently changed following DMT use. The symptoms DMT caused in our case, such as being directed by another power, seeing musical sounds in the sky, contacting creatures from outer space and excessive preoccupation with cosmos, were not previously present and are consistent with the literature. Synesthesia (i.e., mixture of sensations like seeing musical sounds in the sky) is mentioned in hallucinogen intoxication in DSM-IV-TR (15). Seeing musical sounds in the sky in our case after DMT use suggests hallucinogen use.

Autonomic symptoms and signs such as mydriasis, hyperthermia, tachycardia and hypertension can be seen due to DMT use but due to both absence of a specific antidote and short duration of symptoms, no intervention is needed generally except routine follow-up (17). No autonomic symptoms or sign was observed in our case. Median lethal dose for humans was calculated as 1,6 mg/kg for intravenous use (112 mg for a person of 70 kg.) and 8 mg/kg for oral use (560 mg for a person of 70 kg.); mean effective dose was reported as 27 mg orally (2).

Although DMT is a hallucinogen used for modeling of schizophrenia, its effects on general mental health is under debate. Jacop and Presti (18) proposed that DMT exerts anxiolytic effect in small doses but if this dose is increased (or taken) then hallucinogenic effects occur. In studies done in communities using ayahuasca traditionally, it was found that incidence of schizophrenia is less than 1%, general psychiatric symptoms tend to decrease by ayahuasca use and even cognitive skills such as verbal fluency, verbal memory and arithmetical skills are slightly better compared to controls (19).

As our case provided DMT from Turkey, we think that we may encounter other cases using DMT in the future. After our application to General Directorate of Security we were informed that there is not any statistical data related with DMT (dimethyltriptamine), this is a new psychoactive substance and being controlled in EU according to United Nations Convention and there is no capturing data about this substance in their records (20).

CONCLUSION

This the first report about DMT use in Turkey as far as we know. We hope that this case report will be a reminder that psychoactive substances may have different psychogenic effects and in multiple substance use patterns, different substances should be asked carefully. Routine toxicology panels do not consist of DMT yet and its acute autonomic effects may not be observed during psychiatric interview due to its rapid elimination. For this reason, careful examination of symptoms which are non-routine and not previously observed during history taking will substantially contribute to clinical approach.

REFERENCES

1. Manske RHF. A synthesis of the methyltryptamines and some derivatives. Can J Res 1931; 5:592–600.

2. Gable RS. Risk assessment of ritual use of oral dimethyltryptamine (DMT) and harmala alkaloids. Addiction 2007; 102:24-34.

3. McKenna DJ. Clinical investigations of the therapeutic potential of ayahuasca: rationale and regulatory challenges. Pharmacol Ther 2004; 102:111-129.

4. Thompson MA, Moon E, Kim UJ, Xu J, Siciliano MJ, Weinshilboum RM. Human indolethylamine N-methyltransferase: cDNA cloning and expression, gene cloning, and chromosomal localization. Genomics 1999; 61:285-297.

5. Ciprian-Ollivier J, Cetkovich-Bakmas MG. Altered consciousness states and endogenous psychoses: a common molecular pathway? Schizophr Res 1997; 28:257-265.

6. Freye E, Levy JV (editors). Dimethyltryptamine (DMT) a Psychedelic. In: Pharmacology and Abuse of Cocaine, Amphetamines, Ecstasy and Related Designer Drugs. Newyork: Springer, 2009, 219-221.

7. Freebaze DMT. DMT and Ayahuasca. Drugs Forum. http://www.drugs-forum.com/forum/showthread.php?t=9127.

8. Richardson TH. Cannabis use and mental health: A review of recent epidemiological research. International Journal of Pharmacology:IJP 2010; 6:796-807.

9. Doğanavşargil GÖ, Sertöz ÖÖ, Coşkunol H, Şen G. EÜTF Psikiyatri Anabilim Dalı bağımlılık tedavi biriminin hasta verilerinin on yıllık geriye dönük olarak incelemesi: madde kullanan hastaların sosyodemografik özellikleri. Bağımlılık Dergisi 2004; 5:115-120 (Article in Turkish).

10. Henquet C, Krabbendam L, de Graaf R, ten Have M, van Os J. Cannabis use and expression of mania in the general population. J Affect Disord 2006; 95:103-110.

11. Daumann J, Heekeren K, Neukirch A, Thiel CM, Möller-Hartmann W, Gouzoulis-Mayfrank E. Pharmacological modulation of the neural basis underlying inhibition of return (IOR) in the human 5-HT2A agonist and NMDA antagonist model of psychosis. Psychopharmacology 2008; 200:573-583.

12. Carter CS, Robertson LC, Chaderjian MR, O'Shora-Celaya L, Nordahl TE. Attentional asymmetry in schizophrenia: the role of illness subtype and symptomatology. Prog Neuropsychopharmacol Biol Psychiatry 1994; 18:661-683.

13. Gouzoulis-Mayfrank E, Heekeren K, Neukirch A, Stoll M, Stock C, Obradovic M, Kovar KA. Psychological effects of (S)-ketamine and N,N-dimethyltryptamine (DMT): a double-blind, cross-over study in healthy volunteers. Pharmacopsychiatry 2005; 38:301-311.

14. Horacek J, Bubenikova-Valesova V, Kopecek M, Palenicek T, Dockery C, Mohr P, Höschl C. Mechanism of action of atypical antipsychotic drugs and the neurobiology of schizophrenia. CNS Drugs 2006; 20:389-409.

15. Amerikan Psikiyatri Birliği. Ruhsal Bozuklukların Tanısal ve Sayımsal Elkitabı Yeniden Gözden Geçirilmiş Tam Metin, 4. baskı (DSM–IV–TR). Köroğlu E (Çeviri ed.) Ankara: Hekimler Yayın Birliği, 2007, 267-418 (Article in Turkish).

16. DMT. Hallucinogens Part 2. Ask Pat. http://askpat.colostate.edu/ViewHotTopic.aspx?HotTopicID=38#5.

17. Richardson WH, Slone CM, Michels JE. Herbal drugs of abuse: an emerging problem. Emerg Med Clin North Am 2007;25:435-457.

18. Jacob MS, Presti DE. Endogenous psychoactive tryptamines reconsidered: an anxiolytic role for dimethyltryptamine. Med Hypotheses 2005; 64:930-937.

19. McKenna DJ. Clinical investigations of the therapeutic potential of ayahuasca: rationale and regulatory challenges. Pharmacol Ther 2004; 102:111-129.

20. Personal communication from bilgiedinme@egm.gov.tr.