

HYPERACTIVE DELIRIUM AS A COMPLICATION OF NICOTINE WITHDRAWAL: A CASE REPORT

MAJACZENIE JAKO POWIKŁANIE NIKOTYNOWEGO ZESPOŁU ABSTYNENCYJNEGO: OPIS PRZYPADKU

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Abstract

Introduction: Many active smokers want to quit and attempt to quit smoking throughout their lifetime of use. As practitioners, it is crucial to understand the difficulty of quitting smoking and offer support through nicotine replacement products as needed. Here we present a case report of a rare side effect of nicotine withdrawal: hyperactive delirium.

Case description: A 61-year-old Caucasian male was voluntarily admitted to the dual diagnosis psychiatric unit for active suicidal ideation and alcohol detoxification. The patient was started on alcohol detoxification protocol with a benzodiazepine taper. The patient exhibited increased agitation, visual hallucinations, irritability and disorientation. Due to the patient's onset of hyperactive delirium with the absence of any signs or symptoms of alcohol withdrawal, the treatment team reviewed the patient's substance use history. He reported smoking three packs of cigarettes per day for the past 20 years. The patient was immedi-

Streszczenie

Wprowadzenie: Wielu palaczy przez całe życie podejmuje próby rzucenia palenia. Dla nas, praktyków, kluczowe znaczenie ma zrozumienie trudności związanych z rzuceniem palenia i, jeśli to konieczne, oferowanie wsparcia w postaci nikotynowych produktów zastępczych. W artykule przedstawiono opis majaczenia z nasilonymi objawami – rzadko występującego przypadku skutku ubocznego odstawienia nikotyny.

Opis przypadku: 61-letni mężczyzna rasy kaukaskiej zgłosił się na oddział psychiatryczny podwójnej diagnozy z powodu myśli samobójczych i na detoksykację alkoholową. Leczenie rozpoczęto od detoksykacji alkoholowej z sukcesywnie zmniejszonymi dawkami benzodiazepiny. Pacjent wykazywał zwiększone pobudzenie, omamy wzrokowe, drażliwość i dezorientację. Ze względu na wystąpienie objawów majaczenia, przy braku innych objawów odstawienia alkoholowego, zespół terapeutyczny dokonał przeglądu jego historii używania substancji psychoaktywnych. Pacjent zgłosił

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ately treated with a nicotine patch and continued to receive a nicotine patch daily. Two days later, the patient denied recurrence of hallucinations, was behaviourally controlled, and was oriented to self, time, place, and situation. The patient was discharged back to his home in stable condition.

Commentary: A study revealed that patients undergoing sudden cessation of smoking were more likely to exhibit hyperactive delirium than non-smokers and that smoking cessation was an independent risk factor for hyperactive delirium. Healthcare providers should be aware of the more rare side effects of nicotine withdrawal especially when admitting patients in the acute condition.

Keywords: Tobacco use disorder, Hyperactive delirium, Nicotine withdrawal.

palenie trzech paczek papierosów dziennie przez ostatnie 20 lat. Natychmiast otrzymał plaster nikotynowy, który następnie był stosowany codziennie. Po dwóch dniach zniknęły omamy, pacjent kontrolował swoje zachowania, był skoncentrowany na sobie, zorientowany w czasie, miejscu i sytuacji. Został wypisany do domu w stanie stabilnym.

Komentarz: Badanie wykazało, że pacjenci, którzy nagle przestali palić papierosy, częściej byli narażeni na wystąpienie majaczenia niż osoby niepalące, a zaprzestanie palenia było niezależnym czynnikiem ryzyka pojawienia się tego rodzaju delirium. Pracownicy służby zdrowia powinni być świadomi tych rzadko występujących skutków ubocznych odstawienia nikotyny, zwłaszcza podczas przyjmowania pacjentów w stanach ostrych.

Słowa kluczowe: zaburzenia związane z używaniem tytoniu, delirium, nikotynowy zespół abstynencyjny.

■ INTRODUCTION

There are 1.1 billion tobacco users worldwide, with 7.7 million user deaths in 2019 [1]. Secondhand smoke causes more than 42,000 deaths in the United States annually [2]. Even though smoking rates have declined over the years, smoking continues to be the leading cause of preventable death in the United States [3]. Cigarette smoking costs the healthcare system more than 225 billion dollars per year [4]. Many active smokers do would like to quit smoking and attempt to quit throughout their tobacco use. It may take some up to 30 times to quit smoking [5]. Multiple attempts to quit smoking can be linked to numerous reasons from cravings and withdrawal side effects to lack of support. As practitioners, it is crucial to understand the difficulty of quitting smoking and offer support through nicotine replacement products, referrals to support groups or pharmaceuticals as needed. We present a case report of a rare side effect of nicotine withdrawal: hyperactive delirium. While nicotine withdrawal is a diagnosis in the Diagnostic and Statistical Manual of Mental Disorders, fifth edition, hyperactive delirium is not one of the listed known effects. The objective of this case report is to raise healthcare providers' awareness of one of the more rare side effects of nicotine withdrawal when admitting smokers to inpatient units or other long-term medical-care stays.

■ CASE DESCRIPTION

A 61-year-old Caucasian male with a past psychiatric history of major depressive disorder, alcohol-use disorder and tobacco use disorder and pertinent medical history of hypertension and mild intermittent asthma, self-presented to the emergency department with suicidal ideations and alcohol intoxication. The patient reported recent stressors including being fired from his job leading to active suicidal ideations with both intent and plan. The patient's vital signs including blood pressure and heart rate were within normal limits upon initial evaluation. His mental status exam revealed the patient was oriented to person, place, and time and was otherwise unremarkable except for active suicidal ideation. His blood alcohol level upon admission was 221 mg/dl. The patient required inpatient admission due to being a danger to himself or others and was voluntarily admitted to the dual diagnosis psychiatric unit for active suicidal ideation and alcohol detoxification. Due to the patient's history of chronic alcohol use disorder and blood alcohol level of 221 mg/dl on admission to the hospital, he was started on an alcohol withdrawal detoxification with a benzodiazepine taper to avoid potential alcohol withdrawal. He was started on lorazepam 1 mg every four hours, which was decreased to 0.5 mg every four hours after 4 days, and tapered again to 0.25 mg

every four hours after another 4 days until discontinued.

On day two of admission, the patient had an unwitnessed fall and his physical examination was unremarkable for any signs of trauma. On general assessment, the patient was oriented only to self and was experiencing visual hallucinations according to nursing staff, resulting in increased agitation and multiple attempts to leave the inpatient hospital unit. On day three of admission, the patient reported visual hallucinations that consisted of a nurse putting pills into his mouth with an ungloved hand behind the nurses' station. The patient was adamant that this was not a hallucination and that it did in fact happen. The patient continued to request to leave the unit because of the distress caused by his hallucinations. On day four of admission, the patient still reported hallucinations of a nurse putting pills in his mouth without gloves. The patient was increasingly irritable and demanding release home. The patient was oriented to self and place though he stated it was January when it was October. Upon review of records, the patient had remained adherent with the benzodiazepine taper that was started at the time of admission and he was not scoring on the Clinical Institute Withdrawal Assessment for Alcohol (CIWA) protocol, reflecting that he was not showing any signs of symptoms of alcohol withdrawal. Furthermore, the patient denied symptoms of alcohol withdrawal including anxiety, tremors, nausea, vomiting, paroxysmal diaphoresis, restlessness, tactile disturbances, auditory disturbances and headache. His heart rate and blood pressure remained within normal limits throughout his admission.

Due to the patient's onset of hyperactive delirium in the context of the absence of any signs or symptoms of alcohol withdrawal, the treatment team further reviewed the patient's substance use history. The patient denied any prior history of alcohol detoxification, rehabilitations or history of seizures or delirium tremens with alcohol cessation. When probed by the treatment team about his smoking history, the patient reported a history of smoking three packs of cigarettes per day for the past 20 years. The treatment team subsequently ordered a 21 milligram (mg) nicotine patch which was immediately applied to the patient. The following day, the patient had no recurrence of hallucinations and was still only oriented to self and place. The patient continued to receive a 21 mg

nicotine patch daily. Two days after the nicotine patch was applied, the patient continued to deny recurrence of hallucinations, was behaviourally controlled and had a linear thought process. Furthermore, the patient was oriented to self, time, place and situation. He denied suicidal ideation, intent, or plan and was future-oriented. The patient finished alcohol withdrawal detoxification and was no longer a danger to himself or others after stabilisation of medication. The patient was offered rehabilitation but preferred outpatient follow up. The patient was discharged back to his home in a stable condition and a follow up appointment was arranged with an outpatient psychiatric clinic.

■ COMMENTARY

Smoking is the practice of burning tobacco by the user's choice of medium with the purpose of inhaling the smoke that is tasted and subsequently absorbed into the bloodstream. Tobacco and cigarette smoking continue to be a public health issue considering that 23% of the world's population smokes cigarettes [6]. Given this information, it is important for clinicians to be aware of the possible withdrawal effects of nicotine cessation. Tobacco Use Disorder is a diagnosis in the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5), assigned to individuals who are dependent on the drug nicotine due to the use of tobacco products [7]. According to the DSM-5, there are 7 primary symptoms associated with nicotine withdrawal that include "irritability/anger/frustration, anxiety, depressed mood, difficulty concentrating, increased appetite, insomnia, and restlessness" [7]. Nicotine withdrawal can also cause psychiatric symptoms, also known as affective symptoms. Some of these symptoms include anxiety, depression, dysphoria and irritability to name a few. Furthermore, nicotine withdrawal manifests with somatic symptoms which include but are not limited to include tremors, low heart rate and gastrointestinal upset or discomfort [7]. Lastly, nicotine withdrawal cognitive symptoms manifest as difficulty concentrating and impaired memory [8]. However, the acute cessation of nicotine can rarely manifest as hyperactive delirium, such as in this patient's case.

Hyperactive delirium is a state of increased arousal that can present with symptoms of agita-

tion, restlessness and, at times, aggressiveness [9]. One study set out to assess if there is a risk of developing hyperactive delirium in tobacco users during inpatient hospitalisations secondary to abrupt tobacco and nicotine cessation. The study concluded that patients who underwent sudden cessation of tobacco and nicotine while hospitalised were more likely to exhibit symptoms of hyperactive delirium than hospitalised non-smokers [10]. The study concluded that smoking cessation in tobacco users was an independent risk factor for hyperactive delirium in the inpatient setting [10]. Nicotine withdrawal has been shown to result in a combination of psychiatric, somatic, and/or cognitive symptoms which reflects changes in cholinergic transmission throughout various areas of the brain and anatomical structures [11]. It has been shown that there is down-regulation and desensitisation of nicotinic acetylcholine receptors in the brains of chronic smokers [10]. When a chronic smoker suddenly ceases cigarette smoking, the unoccupied state of nicotinic acetylcholine receptors is what causes withdrawal symptoms [10]. Similarly, delirium also results from changes in cholinergic

transmission and deficits while imbalances in dopamine, serotonin, and gamma-aminobutyric acid pathways have also been implicated [10]. Given that the pathophysiology of nicotine withdrawal and delirium have overlapping deficits within similar neurotransmitter symptoms, it is not surprising that sudden nicotine cessation increases risk of hyperactive delirium.

Given that the patient was undergoing detoxification from alcohol with a benzodiazepine taper and was consistently not scoring on the CIWA, his hyperactive delirium was attributed to the abrupt cessation of nicotine withdrawal especially in the context of the patient smoking three packs of cigarettes per day for the past 20 years. Furthermore, the cessation of delirium in this patient after application of a nicotine patch led the treatment team to attributing these symptoms to nicotine withdrawal. Overall, this demonstrates that clinicians who treat nicotine-using patients should be aware of potential nicotine-withdrawal side effects, including the more rare side effect of hyperactive delirium, when admitting patients to inpatient units or any other long term health care stays.

Conflict of interest/Konflikt interesów

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Ethics/Etyka

The work described in this article has been carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) on medical research involving human subjects, Uniform Requirements for manuscripts submitted to biomedical journals and the ethical principles defined in the Farmington Consensus of 1997.

Treści przedstawione w pracy są zgodne z zasadami Deklaracji Helsińskiej odnoszącymi się do badań z udziałem ludzi, ujednoliconymi wymaganiami dla czasopism biomedycznych oraz z zasadami etycznymi określonymi w Porozumieniu z Farmington w 1997 roku.

References/Piśmiennictwo

1. Institute for Health Metrics and Evaluation. *Smoking and Tobacco*. IHME 2019. <https://www.healthdata.org/smoking-tobacco> (Accessed: 21.10.2022).
2. Max W, Sung HY, Shi Y. Deaths from secondhand smoke exposure in the United States: economic implications. *Am J Public Health* 2012; 102(11): 2173-80. DOI: 10.2105/AJPH.2012.300805.
3. Hall W, Doran C. How much can the USA reduce health care costs by reducing smoking? *PLoS Med* 2016; 13(5): e1002021. DOI: 10.1371/journal.pmed.1002021.

4. Xu X, Shrestha SS, Trivers KF, Neff L, Armour BS, King BA. U.S. Healthcare spending attributable to cigarette smoking in 2014. *Prev Med* 2021; 150: 106529. DOI: 10.1016/j.ypmed.2021.106529.
5. Chaiton M, Diemert L, Cohen JE, Bondy SJ, Selby P, Phipipneri A, et al. Estimating the number of quit attempts it takes to quit smoking successfully in a longitudinal cohort of smokers. *BMJ Open* 2016; 6: e011045. DOI: 10.1136/bmjopen-2016-011045.
6. Adams TN, Morris J. Smoking. *StatPearls* 2022. <https://www.ncbi.nlm.nih.gov/books/NBK537066> (Accessed: 23.05. 2023).
7. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders: DSM 5*. Washington: American Psychiatric Association; 2013.
8. Heishman SJ, Kleykamp BA, Singleton EG. Meta-analysis of the acute effects of nicotine and smoking on human performance. *Psychopharmacol* 2010; 210: 453-69.
9. Van Velthuisen EL, Zwakhalen S, Mulder WJ, Verhey F, Kempen G. Detection and management of hyperactive and hypoactive delirium in older patients during hospitalization: a retrospective cohort study evaluating daily practice. *Int J Geriatr Psychiatry* 2018; 33(11): 1521-9. DOI: 10.1002/gps.4690.
10. Park H, Kim KW, Yoon IY. Smoking cessation and the risk of hyperactive delirium in hospitalized patients: a retrospective study. *Can J Psychiatry* 2016; 61(10): 643-51. DOI: 10.1177/0706743716652401.
11. McLaughlin I, Dani JA, De Biasi M. Nicotine withdrawal. *Curr Top Behav Neurosci* 2015; 24: 99-123. DOI: 10.1007/978-3-319-13482-6_4.

