A Case of Catatonia Induced by Disulfiram

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ÖZET

Disülfirama bağlı olarak gelişen bir katatoni olgusu

Katatoni, sınıflandırma sistemlerinde daha çok şizofreninin bir alt grubu olarak değerlendirilmiş olsa da, birçok genel tıbbi durum, nörolojik hastalık ya da bazı ilaçlara bağlı olarak da ortaya çıkabilir. Disülfiram, alkol bağımlılığı tedavisinde caydırıcı etkisi nedeniyle kullanılabilen bir ajandır. Psikoz ve deliryum gibi nöropsikiyatrik yan etkilere neden olabilir. Katatonik sendrom disülfiramın çok nadir görülen bir yan etkisidir. Bu yazıda, kliniği bilişsel işlevlerde bozulma ile başlayan ve katatonik sendroma dönüşen bir vaka sunulmaktadır. Hastanın alkol kötüye kullanımı dışında psikiyatrik öyküsü yoktu ve son 1 aydır, reçetesiz temin ettiği disülfiramı kullanıyordu. Hastaya, disülfirama bağlı katatoni tanısı ile elektrokonvülsif tedavi uygulandı. Tam düzelme sağlanan ve ilaçsız izlenen vakanın iyilik hali devam etti. Bu çalışmada, örnek vaka çerçevesinde katatoni kavramı tartışılmaktadır.

Anahtar kelimeler: Disülfiram, katatoni, elektrokonvülsif tedavi

ABSTRACT

A case of catatonia induced by disulfiram

Although catatonia has predominantly been evaluated as a subtype of schizophrenia, many of general medical conditions, some of neurological diseases or medications may cause catatonia. Disulfiram is an agent that is being used in the treatment of alcohol dependency by its aversive effect. It may cause neuropsychiatric side effects such as psychosis or delirium. Catatonic sydrome is a rare side effect of disulfiram. This paper aimed to report a case turning into catatonic syndrome following cognitive deterioration. The patient had no prior psychiatric history except alcohol abuse and was using disulfiram in the last month. With the diagnosis of "catatonia induced by disulfiram", electroconvulsive therapy was applied. Full remission was obtained and the patient have been followed up without any medication. Concept of catatonia is discussed in this context.

Key words: Disulfiram, catatonia, electroconvulsive therapy

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INTRODUCTION

Catatonia was predominantly evaluated as a subtype of schizophrenia throughout the 20th century, and was primarily associated with schizophrenia in diagnostic classification systems (1). Catatonic symptoms can also be seen, however, in affective disorders; catatonia has in fact occasionally been observed more frequently in such disorders than in schizophrenia (2). Moreover, the literature includes examples where catatonia has been caused by many general medical conditions, such as endocrinal disorders, infections, and electrolyte abnormalities (3-7); neurologic diseases (8); and various treatments (9-11).

The etiology of catatonia has not been fully described. It has been suggested that the motor symptoms of catatonia can be explained by basal ganglion modulation disorder caused by deficiency of cortical gamma-aminobutyric acid (GABA), which acts as the prime inhibitor neurotransmitter (12). This suggestion explains the therapeutic success of benzodiazepines (BZD), which increase GABA activity. Another suggested mechanism is the hyperactivity of glutamate, which is an excitatory neurotransmitter (13).

The primary treatment options are BZDs and electroconvulsive therapy (ECT), independently of etiology or intensity (14-16). In a study carried out using ECT, 30 patients with idiopathic catatonia, 19 patients with catatonia induced by schizophrenia, and 16 patients with catatonia induced by depression, responded to the treatment positively (17). While the number or pattern of catatonic symptoms do not have any impact on the treatment results, the prognosis of short-term treatment is quite good. But the long-term prognosis is rather associated with the cause of catatonia (1). Even though the underlying condition is psychotic, antipsychotic treatments are not recommended as the first-line treatment option for catatonic syndromes due to the risk of neuroleptic malign syndrome (NMS) (18).

Disulfiram is an agent used in the treatment of alcohol addiction or abuse due to its alcohol-aversive effect. This agent may cause the accumulation of acetaldehyde metabolized from alcohol in toxic amounts, by inhibiting the acetaldehyde dehydrogenase enzyme. Disulfiram also acts on the dopaminergic system; diethyldithiocarbamate, the breakdown product of disulfiram, blocks the dopamine β-hydroxilase enzyme and inhibits the conversion of dopamine into noradrenalin and may cause neuropsychiatric side effects such as delirium, paranoid conditions, lack of concentration, memory impairment, depression, ataxia, and dysarthria (19,20). In addition to these side effects, cases of catatonia induced by disulfiram have been reported, though rarely (10,21-23). This paper presents a case of catatonia induced by disulfiram, a rare clinical condition that may therefore have been difficult to diagnose in clinical practice but that responded positively to treatment.

CASE REPORT

The case was 37-year old married male; he was a high school graduate and had a job. The patient had no prior psychiatric history, but on June 4, 2010 he suddenly exhibited symptoms such as the inability to collects his thoughts, confusion, and mistaking addresses he normally knew. As his complaints persisted, he went to the hospital the next day. He defined his complaints as "I cannot put together and remember what is being said, I cannot catch what is being talked about." He had never had disorientation in time or people recognition. Although he was referred to the neurology department, he did not go there. Within a few hours, he started making absurd and irrelevant sentences, avoiding members of his household, and going in and out the door repeatedly. He kept saying, "Do not take me there, I cannot see my children any more, my head is empty," locking the door, and exhibiting paranoid behaviour. On June 6, 2010, the patient was again taken to hospital, having closed his eyes and started to not respond to verbal stimulants. With a pre-diagnosis of delirium tremens (DT) and alcohol withdrawal, because of his history of alcohol use, the patient was administered diazepam and referred to the Bakırköy Research and Training Hospital for Psychiatry, Neurology and Neurosurgery (BRTHPNN) for hospitalization. During his examination in the psychiatric emergency ward of BRTHPNN, the patient did not respond to tactile, verbal, and painful stimulants and neurology consultation was requested. No pathology was detected, however, in the neurological examination. Anamnesis obtained from his family revealed that the patient had given up alcohol 35 days earlier and for 30 days had been taking a medication called "Antabus®," which they had bought on their own. The DT diagnosis was changed and the patient was hospitalized in the 12th Psychiatric Ward of BRTHPNN on June 7, 2010 for diagnosis and treatment.

In the psychiatric examination carried out during admission to the ward, the patient was in a stupor with mutism and negativism and suffered urinary incontinency. Findings such as flexibilitas cerea, echopraxia, and automatic obedience were added to his clinical condition over the course of the day. On the whole he was apathetic. The family reported that the patient had been using alcohol for 8 years, that he had increased his consumption in the last year to 3 to 4 bottles of beer every other day, that he had not drunk alcohol for more than a month, and that he had been using disulfiram – which they had bought from the pharmacy without a prescription – at a dose of 500 mg/day for the last month, upon the recommendation of his relatives. He had never drunk alcohol every day, and even stopped drinking during Ramadan while he was fasting, and he had never used any illicit substances. While no withdrawal symptoms had been defined, he said that he had not drunk any alcohol while using the medication. The patient was subjected to detailed biochemical (liver, kidney, thyroid function tests, and electrolytes) and blood count tests. The abnormal findings detected were as follows: AST: 50 IU/L (5-45), ALT: 62 IU/L (5-40), Creatinine Kinase (CK): 861 IU/L (20-200), White Blood Cells: 13.100 10^3/μL (4.300-10.300). The high CK was attributed to injections and the high AST and ALT to alcohol use. Urine analysis did not reveal any alcohol or illicit substance metabolites. Electroencephalography (EEG), cranial magnetic resonance imaging (MRI), and neurology consultation were requested for advanced testing purposes and lumbar puncture (LP) was performed. Since the results of EEG, cranial MRI, and

LP examinations were within normal limits, neurologic pathology was not considered necessary. With the diagnosis of "catatonic syndrome induced by disulfiram," an ECT was planned, the patient's relatives were informed accordingly, and their consent was obtained.

In bifrontotemporal ECT sessions, propofol (1 mg/kg) was administered as an anesthetic agent and succinylcholine (0.5 mg/kg) as a muscle relaxant. In all sessions, sufficient time for epileptic seizures was achieved. After the first session of ECT, as the symptoms of mutism, negativism, and akinesia were replaced by catatonic excitation symptoms (echolalia, echopraxia, meaningless talk and gestures, and hyperactivity), lorazepam of 7.5 mg/day was added to the treatment. After lorazepam treatment, the excitation symptoms lessened. Lorazepam was reduced to as low as 3 mg/day, because sedation was high and this complicated the evaluation of the clinical condition and eventually it was decided to administer lorazepam when it is required while the ECT continued. After the third session, almost full remission was achieved. A total of 5 ECT sessions was administered. Given the full remission achieved after the third session and its stability until the end of the fifth session, and to avoid side effects, ECT was discontinued. A week later, the patient was discharged in full remission, with the decision of follow-up care without any medication. During follow-up interviews held in the second, fourth, and sixth weeks after discharge, full remission continued.

DISCUSSION

This paper reported a case of catatonic syndrome induced by the use of unprescribed disulfiram, purchased from a pharmacy without medical advice. The patient had a prior history of alcohol abuse. The symptoms first affected the cognitive functions, then paranoid symptoms emerged, and 36 hours after the clinical manifestation, the patient was in catatonia.

Studies in the literature reported delirium induced by disulfiram-ethanol interaction and encephalopathy manifestations induced by disulfiram (24,25). Since our patient had not drunk alcohol while he was taking disulfiram, the possibility of disulfiram-alcohol interaction was eliminated. Similarly, since the patient did not have a prior history of substance use and tests did not reveal any findings related to substance use, any clinical manifestation induced by substance use was also eliminated. Although the initial sudden disruptions in cognitive functions such as concentration and memory suggested a delirium manifestation induced by disulfiram, our evaluation of the dominant manifestation with mutism, negativism, akinesia, and flexibilitas cerea finalized the diagnosis as catatonia induced by disulfiram.

The patient had been pre-diagnosed with DT and alcohol withdrawal in another center. The basic characteristics of DT are delirium manifestation within a week after the individual quits drinking or reduces intake, its occurrence after heavy alcohol use of 5 to 15 years, and co-existence of autonomic hyperactivity, hallucinations, and illusions with delirium (26). Given that our patient's alcohol use was not at dependency level, that he had had many alcohol-free periods with no withdrawal syndromes whatsoever, and that he had not drunk alcohol for more than a month, we excluded the diagnosis of DT or withdrawal syndrome.

Since the patient did not have prior psychiatric history and the clinical manifestation had an acute onset, the diagnosis of catatonia induced by a psychiatric disorder was also eliminated.

This case emphasizes the importance of anamnesis in diagnosis and treatment. The history of alcohol abuse and the unsettled manifestation with delirium-like onset may have led to the diagnosis of DT at first examination. Furthermore, a definitive diagnosis cannot be made at first examination because catatonia is less known than other clinical manifestations. Classification systems do not have specific diagnosis criteria for catatonia. Its classification by duration and symptom cluster, just like delirium, will increase the recognition level and therefore the treatability of the syndrome (1).

In catatonia treatment, BZDs are considered the first option, while for cases that respond insufficiently or do not respond at all to BZDs, ECT is used. Some cases respond to BZDs within a few hours. Studies suggest that the treatment should start with BZDs, but if there is no immediate response despite the sufficient dose, this treatment should be ended and ECT should be started quickly (16,18,27). Due to the risk of NMS, antipsychotics are not recommended as a

first-line treatment option, even though the underlying condition is psychotic (18). In case of resistance to the first-line treatments, atypical antipsychotics can be considered, if the patient has a history of chronic psychotic disorder or if psychotic symptoms are also manifested alongside catatonic ones. Even in such a case, medications with high potency should be avoided and the patient should be closely monitored for side effects which may be induced by antipsychotics (16, 18). Since our patient had previously been administered intravenous diazepam with the pre-diagnosis of DT but did not experience any improvement in his clinical condition, and since we needed a quick response because the patient was refusing oral intake, ECT was started and during ECT treatment, additional lorazepam treatment was utilized for the manifestation of catatonic excitation. The clinical manifestation of our patient was in dramatic remission after the third ECT session. Since this clinical remission continued steadily, ECT was ended after the fifth session and the patient was discharged to be followed up without any medication.

Another important issue in this case is the over-the-counter sale of non-prescription medications. Even medications that should only be used with sufficient knowledge, attention, and experience can be purchased in pharmacies without a prescription. This may cause unexpected side effects, which, in turn, may lead to delayed diagnosis and treatment, just as seen in this case.

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