THE TURKISH JOURNAL ON ADDICTIONS
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CASE REPORT

Disulfiram Encephalopathy Presenting with Delirium, Epilepsy, and a Manic Episode: A Case Report

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Main Points

- Disulfiram can cause encephalopathy presenting with delirium, epilepsy, and mania.
- Disulfiram-associated encephalopathy and disulfiram-induced psychosis should be considered in disulfiram-using patients with neuropsychiatric symptoms.
- The patient developed a manic episode after initial symptoms resolved, with a family history suggesting genetic vulnerability to bipolar affective disorder.
- Monitoring for severe neuropsychiatric side effects in patients on disulfiram is important, particularly for those with a psychiatric history or a family history.

Abstract

Disulfiram is an agent used in the treatment of alcohol use disorder and causes a disulfiram-ethanol reaction, which can result in serious adverse effects when taken with alcohol. Although rare, disulfiram can cause neuropsychiatric side effects even in the absence of alcohol consumption. This article presents a case of delirium, epileptic seizures, and a subsequent manic episode that developed on the 30th day of disulfiram treatment. A 50-year-old male patient diagnosed with alcohol use disorder and started on disulfiram treatment presented on the 30th day of treatment with complaints of disorientation, paranoid thoughts, agitation, and speech impairment. Following intramuscular haloperidol administration, the patient experienced a generalized tonic-clonic seizure. No evidence of alcohol or other substance use was found on examination. Electroencephalography revealed epileptiform activity. Disulfiram was discontinued, and antipsychotic/antiepileptic treatment was initiated. The patient was discharged on the fifth day but returned 2 days later with insomnia, increased speech, and grandiose delusions. The patient had a family history of bipolar disorder, and clinical evaluation suggested that he was in a manic episode. Valproic acid was added to the treatment, and the patient was discharged after improvement of symptoms. Cases of delirium, epilepsy, or mania associated with disulfiram use have been reported in the literature; however, there are no reports of these three clinical presentations occurring together. It is thought that disulfiram may have triggered these neuropsychiatric effects by inhibiting the dopamine β-hydroxylase enzyme and thereby increasing dopamine levels. This case is noteworthy as the first reported case of delirium, epilepsy, and mania developing in association with disulfiram.

Keywords: Delirium, disulfiram, encephalopathy, epilepsy, mania

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Received: May 2, 2025
Revision Requested: June 22, 2025
Last Revision Received: June 24, 2025
Accepted: July 20, 2025
Publication Date: September 15, 2025

Introduction

Disulfiram, one of the medications used in alcohol use disorder (AUD), exhibits aversive effects through a reaction called disulfiram-ethanol reaction (DER) when used in combination with alcohol, manifesting various adverse effects (Lanz et al., 2023). Especially when administered under observation (supervision), the effectiveness of disulfiram therapy lies

Cite this article as: Uçar Hasanlı, Z., Danışman, M., Zengin İspir, G., & Sezer Katar, K. (2025). Disulfiram encephalopathy presenting with delirium, epilepsy, and a manic episode: A case report. *Addicta: The Turkish Journal on Addictions*, 12(3), 320-323.

DOI:10.5152/ADDICTA.2025.25426

in involving family members capable of monitoring the patient (Axelrath, 2024).

The tolerable mild side effects of disulfiram therapy include dizziness, headache, impotence, and altered taste perception. On the other hand, disulfiram use can lead to neuropsychiatric side effects such as delirium, psychosis, lack of concentration, memory impairment, ataxia, and seizures (Lanz et al., 2023).

This article aims to contribute to the literature by presenting a case of disulfiram-related encephalopathy with sudden-onset disorientation, restlessness, disorganized speech, persecution delusions, and subsequently developing a manic episode following a seizure on the 30th day of disulfiram therapy.

Case Presentation

Consenting to disulfiram therapy under the diagnosis of AUD, a 50-year-old married male with a history of recurrent depression diagnoses and antidepressant medication use was discharged from the clinic with supervised disulfiram treatment under the observation of his spouse. On the 30th day of disulfiram therapy, he was brought to the clinic by his relatives due to disorganized speech, disorganized behavior, persecution delusions that started the day before, and increased psychomotor agitation. His relatives measured his blood pressure at home as 180/105 mmHg. In the initial mental status examination, his orientation to place, time, and person was impaired, and his cooperation was limited. The patient's speech rate had increased, and he had paranoid delusions.

Upon the relatives' confirmation of regular disulfiram intake and absence of any alcohol consumption, the patient was initially treated with intramuscular haloperidol 5 mg under the preliminary diagnosis of disulfiram-induced psychotic reaction. Ten minutes after the administration of haloperidol, the patient experienced a generalized tonic-clonic seizure lasting for 2 minutes. The patient's blood pressure was measured at 170/110. A dose of 10 mg diazepam was administered in a bolus form, and the disulfiram therapy was discontinued. The patient had postictal confusion and was admitted to the intensive care unit (ICU). On the same day, the patient had another seizure and received intravenous (IV) diazepam again.

The brain computed tomography and laboratory tests were normal. Ethanol was detected as <10, and gamma glutamyl transferase (GGT) was found to be 46. Substance metabolites were not seen in the urine analysis. The cranial magnetic resonance imaging revealed no pathological findings or diffusion restriction. With a Clinical Institute Withdrawal Assessment for Alcohol, Revised (CIWA-AR) value of 7, the patient was diagnosed with disulfiram encephalopathy accompanied by delirium and epilepsy, and the treatment was arranged with haloperidol 10 mg/day and quetiapine 25 mg/day. The patient was consulted by internal medicine, infectious diseases, and neurology specialists to rule out organic etiology during this period. No additional recommendations were made by internal medicine or infectious diseases specialists. Electroencephalography (EEG) was requested by the neurology department. The EEG performed on the second day of ICU was interpreted as an "epileptiform anomaly characterized by slow and sharp waves in the fronto-centro-temporal regions."

After the second day in the intensive care unit, without experiencing seizures anymore and with stabilized vital signs, except for a slight increase in speech rate, the patient was discharged on the fifth day with a treatment of quetiapine 25 mg/day, having discontinued haloperidol. No additional treatment was recommended by neurology specialists at discharge.

Two days later, the patient was re-admitted to the clinic complaining of insomnia, increased speech, and racing thoughts, with a preliminary diagnosis of a manic episode. During the psychiatric examination upon re-admission, increased and pressured speech, racing thoughts, increased goal-directed activities, and grandiose delusions were observed. The Young Mania Rating Scale was calculated as 20, and olanzapine 5 mg was initiated. The patient's complaints intensified on the second day of this re-admission, and the Young Mania Rating Scale increased to 35. The treatment was adjusted to olanzapine 20 mg, haloperidol 10 mg, quetiapine 300 mg, and valproic acid 1250 mg (valproic acid blood level on the fifth day: 73 mg/L).

As the manic symptoms improved, after a detailed anamnesis was obtained from the patient and their relatives, it was discovered that the patient's deceased mother had a history of bipolar disorder and lithium treatment. Having shown improvement with a decrease in the Young Mania Rating Scale to 5 during the 2-week hospitalization period, the patient was discharged on valproic acid 1250 mg/day, olanzapine 20 mg/day, and quetiapine 300 mg/day. The definitive diagnosis for the patient was confirmed as disulfiram encephalopathy, presenting with delirium, epilepsy, and a manic episode.

Written informed consent was obtained from the patient for this case report.

Discussion

In patients diagnosed with AUD, the occurrence of delirium or epileptic seizures should first prompt consideration of alcohol withdrawal syndrome (AWS) (Day & Daly, 2022). In the presented case, the patient discharged with supervised disulfiram therapy showed average GGT values, a CIWA-AR score of 7, and a history indicating no alcohol consumption, leading to the divergence from the diagnoses of Delirium Tremens (DT) and epilepsy attributed to AWS.

Cases of seizures following DER or singular use of disulfiram have been reported in the literature (Nogueira et al., 2021). These seizures often do not recur upon discontinuation of disulfiram. Although the mechanism of how disulfiram induces seizures is unknown, even without the synergistic effect of alcohol consumption, the seizure threshold may be lower due to decreasing norepinephrine levels and increasing dopamine levels in the brain. Additionally, disulfiram may lead to EEG changes resembling delirium due to hypoxia in the central nervous system (Kulkarni & Bairy, 2015).

Researchers have observed that 37.5% of patients experiencing seizures had hypertension, too, and within 6 weeks after treatment, there was a decline in both seizures and hypertension symptoms (Kulkarni & Bairy, 2015). After discontinuation of disulfiram therapy in patients experiencing seizures related to its

use, the recurrence of seizures is not expected. The EEG findings, hypertension, regression of delirium, and seizures after discontinuation of disulfiram therapy and initiation of antiepileptic agents in the presented case align with these reported findings in the literature (Heung et al., 2018). In this case, it's hypothesized that disulfiram, through a possible shared neurobiological basis like dopamine β-hydroxylase inhibition, might have been closely associated with seizures, hypertension, and a manic episode (increased dopamine) (Gupta & Spoorthy, 2022).

Although rare, disulfiram-associated delirium and psychosis typically manifest within the first few months of disulfiram therapy (Das et al., 2017). The development of delirium in individuals using disulfiram is often associated with a DER or a psychotic process (Ghosh et al., 2019). Similarly, disulfiram-associated psychosis usually accompanies the clinical picture of delirium (Iwashige & Shibasaki, 2006).

Lidden and Satran classified three groups of disulfiram-related psychotic reactions: primarily delirium features without significant psychotic traits (Group 1); significant depression, manic, or paranoid features in addition to delirium (Group 2); and depressive, acute manic, or psychotic traits without delirium (Group 3). Of 52 cases of disulfiram psychosis, only five were actual psychosis cases, while others were toxic delirium associated with disulfiram use (Liddon & Satran, 1967). In this case, the initial presence of delirium symptoms alongside psychotic features, followed by the resolution of delirium and the emergence of manic episodes, aligns with these findings in the literature. The inhibition of dopamine β-hydroxylase by disulfiram may result in increased dopamine levels in the Central Nervous System (CNS), leading to psychotic symptoms (Mandula et al., 2024) and mood alterations (Ceylan et al., 2007).

The literature presents cases of manic episodes following disulfiram use (Ceylan et al., 2007; Gupta & Spoorthy, 2022; İnaltekin & Yağcı, 2022; Li & Shen, 2008; Lin et al., 2020; Mackie & Clark, 1994; Maşalı et al., 2009). Manic episodes were observed in two of these cases with a disulfiram dosage of 1500 mg/day (Ceylan et al., 2007; Li & Shen, 2008), in three cases with therapeutic doses (500 mg/day) during the first month (Maşalı et al., 2009), second month (Gupta & Spoorthy, 2022), and at the fifth month (İnaltekin & Yağcı, 2022), and in another case with a lower dose (200 mg/day) in the second month (Lin et al., 2020). Two of these cases also had delirium accompanying manic episodes (Li & Shen, 2008; Mackie & Clark, 1994). In psychotic conditions associated with disulfiram, including mania, clinicians should consider avoiding prolonged, unnecessary use of antipsychotics as the psychotic condition tends to regress 1 – 14 days (average interval: 7.5 days) after disulfiram discontinuation (Das et al., 2017).

Maşalı et al. (Maşalı et al., 2009) presented a patient with increased speech and grandiose delusions on the 30th day of disulfiram treatment and received haloperidol but, upon symptom improvement, was discharged without medication on the 7th day. However, a week later, the patient's manic symptoms recurred. Similarly, the patient was discharged after the improvement of psychotic symptoms following haloperidol and quetiapine treatment on the fifth day of ICU admission but was re-admitted on the second day post discharge with a diagnosis of a manic episode. Discontinuation of disulfiram in psychotic conditions, including mania, should be considered, as disulfiram can have effects for up to 2 weeks, and premature termination of treatment may lead to relapses (Maşalı et al., 2009).

The higher prevalence of psychiatric complications associated with disulfiram in Eastern countries raises the possibility of genetic factors playing a role in disulfiram-induced psychosis. Patients with a family history of psychosis might have a higher likelihood of a genetic background for disulfiram-induced psychosis (Melo et al., 2014). Although this case has a family history of bipolar disorder, the occurrence of the first manic episode not in the expected 20s or 30s but at 50 years old raises the suspicion that the manic episode might be due to disulfiram treatment.

While cases have been reported of disulfiram-associated delirium, psychosis/mania, epileptic seizures, or concurrent delirium and psychosis, encountering a case with concomitant disulfiram-induced delirium, epilepsy, and mania during the same period is unprecedented. This case holds the distinction of being the first case where disulfiram-induced delirium, epilepsy, and manic attacks co-occurred due to disulfiram use.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

Informed Consent: Written informed consent was obtained from the patient who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – Z.U.H., M.D., G.Z.İ., K.S.K.; Design – Z.U.H., M.D., G.Z.İ., K.S.K.; Supervision – N/A; Resources – N/A; Materials – Z.U.H., M.D., G.Z.İ., K.S.K.; Data Collection and/or Processing – Z.U.H., M.D., G.Z.İ., K.S.K.; Analysis and/or Interpretation – N/A; Literature Search – N/A; Writing Manuscript – Z.U.H.; Critical Review – Z.U.H., M.D., G.Z.İ., K.S.K.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

References

Axelrath, S. (2024). Disulfiram should remain second-line treatment for most patients with alcohol use disorder. *Journal of Addiction Medicine*, *18*(6), 617 – 618. [CrossRef]

Ceylan, M. E., Turkcan, A., Mutlu, E., & Onal, O. (2007). Manic episode with psychotic symptoms associated with high dose of disulfiram: A case report. *Journal of Clinical Psychopharmacology*, *27*(2), 224 – 225. [CrossRef]

Das, N., Mahapatra, A., & Sarkar, S. (2017). Disulfiram induced psychosis: Revisiting an age-old entity. *Asian Journal of Psychiatry*, *30*, 94 – 95. [CrossRef]

Day, E., & Daly, C. (2022). Clinical management of the alcohol withdrawal syndrome. *Addiction*, *117*(3), 804 – 814. [CrossRef]

Melo, R. C., Lopes, R., & Alves, J. C. (2014). A case of psychosis in disulfiram treatment for alcoholism. *Case Reports in Psychiatry*, *2014*, 561092. [CrossRef]

Ghosh, A., Basu, D., Pradeep, C., & Subodh, B. (2019). Disulfiram-induced psychosis at a therapeutic dose and in clear sensorium: Two case demonstrations. *Journal of Mental Health and Human Behaviour*, *24*(1), 57 – 59. [CrossRef]

Gupta, P., & Spoorthy, M. S. (2022). Disulfiram induced mania – A case report. *Indian Journal of Psychiatry*, *64*(Suppl. 3), S677.

Heung, J., Poon, J. Y.-K., Tung, C.-K., Yeung, S.-W., & Lam, M. (2018). Confusion in sobriety: A case study on disulfiram encephalopathy in a middle-aged male patient. *Alcohol and Alcoholism*, *53*(4), 497 – 498. [CrossRef]

İnaltekin, A., & Yağcı, İ. (2023). Mania as a result of using disulfiram at the prescribed amount during the fifth month of maintenance therapy: A case report. *Addicta: The Turkish Journal on Addictions*, 10(1), 20-22.

Iwashige, T., & Shibasaki, M. (2006). Disulfiram-induced delirium: A case report. *Nihon Arukoru Yakubutsu Igakkai Zasshi*, *41*(6), 535 – 540.

Kulkarni, R. R., & Bairy, B. K. (2015). Disulfiram-Induced de novo convulsions without alcohol challenge: Case series and review of literature. *Indian Journal of Psychological Medicine*, *37*(3), 345 – 348. [CrossRef]

Lanz, J., Biniaz-Harris, N., Kuvaldina, M., Jain, S., Lewis, K., & Fallon, B. A. (2023). Disulfiram: Mechanisms, applications, and challenges. *Antibiotics*, *12*(3), 524. [CrossRef]

Li, M.-Y., & Shen, Y.-C. (2008). Manic episode with psychosis following a lower than recommended dosage regimen of disulfiram. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *32*(1), 311 – 312. [CrossRef]

Liddon, S. C., & Satran, R. (1967). Disulfiram (Antabuse) psychosis. *American Journal of Psychiatry*, *123*(10), 1284 – 1289. [CrossRef]

Lin, Y., Tsai, P.-C., & Cheng, Y.-C. (2020). High-dose disulfiram-induced delirium and manic features: A case report. *Taiwanese Journal of Psychiatry*, *34*(2), 96 – 97. [CrossRef]

Mackie, J., & Clark, D. (1994). Cannabis toxic psychosis while on disulfiram. *British Journal of Psychiatry*, *164*(3), 421 – 421. [CrossRef]

Mandula, S. K., Mukherjee, D., Chakravarty, P. J., & Bhattacharya, S. (2024). Disulfiram-induced psychosis still an important clinical entity: A case series. *Industrial Psychiatry Journal*, *33*(Suppl 1), S229 – S232. (doi:[CrossRef]

Maşalı, B., Atış, Y., & Yeşilbursa, D. (2009). Sürdürüm Dozunda Disülfiram Kullanımına Bağlı Mani Olgusu. *Klinik Psikofarmakoloji Bülteni*, *19*(Suppl. 1): S270-S272.

Nogueira, V., Mendes, M. A., Pereira, I., & Teixeira, J. (2021). Disulfiram-induced epileptic seizures. *BMJ Case Reports*, *14*(3), e236296. [CrossRef]