Letter to the Editor

Confusion in Sobriety: A Case Study on Disulfram Encephalopathy in a Middle-Aged Male Patient

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Dear Editor,

Disulfram has been established as one of the few pharmacological treatments for alcohol dependence since 1947. Rare neuropsychiatric complications associated with disulfram have been reported in case studies, but these were related to intoxication and drug interaction with other medications. Here we report a case of encephalopathy in a middle-aged Chinese man who was taking disulfram alone at therapeutic dose.

A 50-year-old Chinese cargo terminal worker suffered from long-standing alcohol dependence, which was complicated by liver parenchymal disease and marital tension. Otherwise he had no other physical or psychiatric comorbidity. After completing in-patient medically assisted detoxification in a psychiatric hospital, he was prescribed disulfram for relapse prevention. He was arranged to take 400 mg every Monday and Wednesday, then 600 mg every Friday under direct supervision by a nurse at out-patient clinic.

In the first 2 weeks after discharge, he was mentally stable and resumed duty successfully. Then he developed acute mental confusion 1 day after taking disulfram without any alcohol use. He was admitted to a general hospital and mental state examination revealed irrelevant speech, irritable mood and auditory hallucination. He was disoriented to time, place and person. Physical examination was unremarkable with no sign of alcohol withdrawal, Wernicke–Korsakoff syndrome, head injury or liver failure. All investigations, including serum ethanol level, urine toxicology, complete blood count, liver and renal function tests, electrolyte profile, serum glucose level, clotting profile, serum ammonia, thyroid function test, serum vitamin B12 and folate level, syphilis serology, computed tomography of the brain and electroencephalography, revealed no clear pathology. Disulfram was discontinued and the patient was empirically treated with oral lorazepam and intravenous thiamine supplement. He recovered gradually over 2 weeks of time, with complete resolution of mental confusion before discharge.

The patient continued to experience memory impairment which made it difficult for him to resume normal duty a few weeks later. He scored 25 out of 30 in Mini Mental State Examination, which was comparable with his performance before disulfram treatment. He had a few episodes of self-limiting anterograde amnesia lasting for one to two days. He had lapsed into drinking beer a few times but soon returned to abstinence. His mental state remained stable with no recurrence of acute confusion.

Patients with disulfram encephalopathy usually present with disorientation, memory impairment, affective changes and lability. Grasp and snouting reflexes, ataxia and motor perseveration may be detected in physical examination, while autonomic signs are absent. Further investigations may show diffuse slowing in electroencephalogram, with various anatomical involvements on imaging e.g. posterior reversible encephalopathy syndrome (parieto-occipital region), basal ganglia. The condition usually occurs towards the beginning of disulfram therapy (around first few months after commencement), independent of the dose of disulfram used. It may evolve over a period of few days. Patients usually have full recovery after disulfram is withdrawn.

There are several proposed hypotheses of the pathophysiology. Disulfram itself increases extracellular level of glutamate, which is an excitatory neurotransmitter and neurotoxic in excess. It increases cell membrane permeability, provokes loss of dopamine and results in release of vesicular glutamate, which leads to further neurotoxicity. Disulfram also inhibits glutamine activity, which may relate to slowing in electroencephalogram and frontal release signs (Park and Riggio, 2001).

The two metabolites of disulfram are also possible culprit underpinning the encephalopathy. Diethylthiocarbamate is a copper chelator that inhibits dopamine beta-hydroxylase, which converts dopamine to noradrenaline. Excessive dopamine content or increased dopaminergic tone at limbic and frontal regions of the brain causes symptoms similar to that of schizophrenia. It blocks superoxide dismutase and hence reduces the enzyme’s availability to eliminate free radicals (Hekkilä et al., 1976). Carbon disulphide is the other metabolite of disulfram which precipitates a neuropsychiatric syndrome (delirium, ataxia, peripheral neuropathy, Parkinsonism). This syndrome can be difficult to distinguish from disulfram encephalopathy (Laplane et al., 1992).

Co-administration of other medications may also precipitate disulfram encephalopathy, for example, tranylcypromine and griseofulvin, which are inducers of disulfram metabolism.
There is no definite epidemiological data for disulfram encephalopathy. Its incidence is estimated to be 1–20% (Park and Riggio, 2001). While the diagnosis of disulfram encephalopathy can be difficult, clinical teams may implement multiple measures to reduce its impact. It may be prevented through careful selection of patients. Patient who has deranged liver function, heart disease, psychiatric comorbidities, history of dangerous impulsive behaviour or high risk of suicide may not be suitable. Reliable supervision of drug taking should be provided either by significant others or healthcare professionals. Doctors must remain vigilant against potential drug interaction with disulfram. Early detection of any acute change in mental state, especially in early stage of therapy, is important. Cessation of disulfram is recommended in case of suspicion about disulfram encephalopathy.

CONFLICT OF INTEREST STATEMENT

None declared.

REFERENCES

