Fulminant encephalopathy with unusual brain imaging in disulfiram toxicity

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A 35-year-old man presented to the emergency department with a history of 1 generalized tonic clonic seizure 1 week prior, followed by altered sensorium. He was admitted for these complaints to an outside hospital and transferred to our institution, as he had not regained consciousness. There was no fever in the preceding month. His relatives said that he had a drink with friends on the day he developed seizures. He had been alcohol dependent for 6 months, but was abstinent for 6 months after rehabilitation.

On evaluation, the patient’s limbs exhibited withdrawal response and the patient experienced eye opening to deep painful stimuli, but he did not blink to threat or track movement. He was hemodynamically stable. Breathing was deep, slow, and labored, and respiratory rate was 12 per minute. Hypotonia involving all limbs with diminished deep tendon reflexes and absent Babinski sign were noted. Pupils were bilaterally equal and reactive to light. There was no nystagmus or ophthalmoplegia. There were no clinical signs of raised intracranial tension or meningeal irritation. Acute intoxication and metabolic encephalopathy were the differential diagnoses considered. Routine investigations, serum ammonia, and CSF were normal. Arterial blood gases revealed severe metabolic acidosis with 7.031 pH and bicarbonate 6 mmol/L. Contrast-enhanced CT brain revealed bilateral symmetric hypodensities involving globus pallidi and internal capsule. Laboratory tests, CT brain, and MRI were done in our center. Fluctuation in blood pressure was recorded, ranging from 150/80 to 84/50 mm Hg and pulse from 70/min to 115/min, with profuse sweating. He was managed with an antiseizure drug (phenytoin), antibiotics, acidosis correction, and mechanical ventilation. There was no further convulsion. History was revisited for exposure to any drugs. The detoxification center where he had received treatment was contacted. They endorsed use of oral disulfiram for treating alcohol dependency. He had been weaned off alcohol gradually and implanted with 1 g of disulfiram subcutaneously in the right iliac fossa as maintenance therapy.

In view of this history, imaging findings were revisited. MRI brain revealed extensive bilateral symmetric hyperintense signal on fluid-attenuated inversion recovery (FLAIR) and T2, with corresponding hypointense signal on T1 in bilateral frontal subcortical white matter, temporal lobes, midbrain, upper pons, posterior half of lower pons, thalamus, and basal ganglia (except bilateral globus pallidi and posterior limb of internal capsule, which shows heterogeneous hypointense and hyperintense signal on T2/FLAIR with isointensity on T1) (figure). There was enlargement of occipital and temporal horns of the lateral ventricles and enhancement in the globus pallidi, with susceptibility-weighted imaging showing blooming in globus pallidus. There was no diffusion restriction. Findings were suggestive of acute toxic encephalopathy. Screening of spine MRI revealed no abnormality. Nerve conduction study revealed severe bilateral symmetrical axonal sensorimotor polyneuropathy. Local ultrasound of the right iliac fossa showed multiple small pellets in subcutaneous plane. Pellets were removed by surgical consult under local anesthesia. The patient showed neurologic improvement on the second day post removal of disulfiram implant with Glasgow Coma Scale improving to E3V1M5. He started responding to commands with gestures, but died of respiratory infection and sepsis. Time period between seizure and death was 7 weeks.
**Discussion**

Disulfram causes CNS as well as peripheral nervous system toxicity due to its toxic metabolites. Case reports of basal ganglia and crus cerebri involvement have been described. There are reports of parkinsonism and dystonia in chronic disulfram toxicity. Our patient had fulminant encephalopathy as well as severe peripheral neuropathy. Disulfram accumulates in adipose tissue and readily crosses blood–brain barrier owing to its high lipid solubility. It is metabolized into toxic and nontoxic metabolites. Toxic metabolites are diethyldithiocarbamate and carbon disulfide. Toxic metabolites cause acute and chronic toxicity. Copper chelation by diethyldithiocarbamate is responsible for inhibition of dopamine β-hydroxylase, which converts dopamine into norepinephrine. Dopamine excess is responsible for psychosis and choreoathetosis in disulfram toxicity. Copper deposition in basal ganglia is a possible mechanism for development of parkinsonism and dystonia. The disulfram reaction responsible for unpleasant effects after alcohol consumption is different from disulfram toxicity: the disulfram reaction occurs as a result of accumulation of acetaldehyde in blood due to irreversible inhibition of enzyme aldehyde dehydrogenase. Acetaldehyde is produced from ethanol by alcohol dehydrogenase. Symptoms of disulfram reaction are flushing of face, headache, vertigo, nausea, vomiting, palpitations, and pruritus. Thus this case emphasizes the importance of understanding the difference between disulfram toxicity and disulfram reaction. This case also highlights the fact that both central and peripheral neurotoxicity by disulfram can be insidiously progressive as well as abrupt.

**Author contributions**

Dhanashree Peddawad: study concept and design, writing, acquisition of data, critical revision of the manuscript for important intellectual content. Shashank Nagendra: acquisition of case data, critical revision of the manuscript for important intellectual content. Rudrarpan Chatterjee: acquisition of data, critical revision of the manuscript for important intellectual content. Hina Faldu: study supervision. Akash Chheda: study supervision.

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**References**

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