Catatonia in disulfiram intoxication – a case report and a brief overview of the literature

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Catatonic syndromes could accompany a variety of psychiatric and medical conditions. The most common conditions underlying catatonia are affective disorders followed by schizophrenia, but several medical conditions including intoxications affecting the central nervous system can also present with catatonic signs and symptoms. Therapeutic doses of disulfiram could induce catatonia with or without accompanying psychosis or mood disorder. A case of disulfiram intoxication manifesting with catatonia is reported here together with a brief overview of the literature. A patient was admitted to the toxicology ward after a suicide attempt with approximately 20 g of disulfiram. On transfer to the psychiatric ward, she was sitting still, in a semi-stuporous state and displayed motiveless resistance to instructions or attempts to move (active negativism). She was unresponsive to most of the questions (mutism), occasionally verbigerated 1-2 words and stared for more than 20 seconds between shifting attention. After developing a comatosus state her treatment continued at the toxicology ward, where a contrast-enhanced computer tomography scan revealed bilateral emollition of 1.5 cm diameter in both nucleus lentiformis at the level of the third ventricle. Following treatment her condition improved and she benefited of rehabilitation facility and a second psychiatric treatment. She was discharged free of neurological and psychiatric symptoms. In conclusion, we underscore the importance of accurate diagnosis of the underlying psychiatric or medical condition when encountering a fast emerging catatonic syndrome and focus first on treating the causative condition while simultaneously attempting symptomatic treatment of catatonia.

(Neuropsychopharmacol Hung 2016; 18(2): 110–114)

Keywords: disulfiram, intoxication, neuropsychiatric complications, catatonia

BACKGROUND

Over the past two decades there has been a growing interest in catatonia. The history, clinical presentation, nosology, prevalence and management options for the catatonic syndrome have been extensively reviewed (Fink & Taylor, 2003; Caroff et al., 2004). In contemporary conceptualization, catatonic phenomena are decoupled from schizophrenia and regarded as a syndrome that appears in a host of psychiatric and medical conditions including intoxications.

In ICD-10 (WHO, 1992) and DSM-IV (APA, 1994) catatonia still appeared as a subtype of schizophrenia and also as "Organic catatonia" (F06.1) in ICD-10 and as Catatonia due to General Medical Conditions in DSM-IV. This category was kept in DSM-5 (APA, 2013) while catatonia has become a specifier for both psychotic and affective disorders and also construed as a semi-independent subcategory named "Unspecified Catatonia" (293.89) in the Schizophrenia Spectrum and Other Psychotic Disorders chapter. (For the sake of brevity, in the following we use the term of 'organic catatonia'. Also, 'catatonia' and 'catatonic syndrome' will be used interchangeably in this paper).

Organic catatonia is estimated to take up about 20-30% of all cases of catatonia (Carroll & Goforth, 2004). Organic catatonia frequently goes undetected which explains that to date only single case reports have been published about this type of catatonia. Due to the pathological changes of the brain, organic catatonia may be less responsive to therapeutic interventions and therefore it may require particularly intensive treatment (Swartz et al., 2003).

Catatonia can accompany infections affecting the central nervous system (CNS), such as encephalitis lethargica (Dekleva & Husain, 1995), paraneoplastic encephalitis (Kaestner et al., 2008), anti NMDA encephalitis (Lawrence et al., 2014) or typhoid fever (Breakey & Kala, 1977). Toxic encephalopathy was also reported to trigger catatonic syndrome in LSD intoxication (Perera et al., 1995) and gamma hydroxyl butyric acid (GHB) withdrawal syndrome (Claussen et al., 2014).

Disulfiram (tetraethylthiouram disulfide) has been used in the treatment of alcohol addiction since 1948 (Hald et al., 1948) although with decreasing frequency (Mark et al., 2009). In addition to a number of adverse effects (e.g. fatigue, headache, gastrointestinal disturbances) therapeutic doses of disulfiram (=/< 500 mg/day) without alcohol exposure not infrequently induce acute psychosis (Liddon & Satran, 1967; de Melo et al., 2014). This is explained by the inhibitory effect of disulfiram on dopamine beta-hydroxylase thereby increasing the level of dopamine in the central nervous system (Sudilovsky, 1975).

The association between catatonia and disulfiram was observed by one of the pioneers of biological psychiatry, Rolf Gjessing (Gjessing, 1965). Therapeutic doses of disulfiram could induce catatonia with or without accompanying psychosis or mood disorder. A search of three major databases (PubMed, EMBASE and PSYCHINFO) yielded 7 case reports of disulfiram-induced catatonic syndrome, all of which were characterized by stupor, mutism and a few other psychomotor phenomena (Knee & Razani, 1974; Reisberg, 1978; Weddington et al., 1980; Fisher, 1989; Hajela at el., 1990; Schmuecker et al., 1992; Saddichha et al., 2011). The small number of cases does not permit to describe a consistent clinical presentation.

Disulfiram intoxication could present with a host of neurologic and neuropsychiatric signs and symptoms (Krauss et al., 1991; Zorzon et al., 1995; Trélohan & Milea, 2011) including catatonic syndrome (Wilson, 1984). A patient with sudden onset of transient generalized dystonia following disulfiram intoxication causing bilateral pallidal and midbrain lesions was reported.

PET scan showed reduced metabolism at the striatum bilaterally (Cho et al., 2011). In another case pallido-nigral lesion manifested with severe oculogyric crisis (Lee et al., 2009). Unilateral pallidal lesion was found on MRI scan in a 38-year-old man, whose disulfiram intoxication resulted in cortical decerebration (de Mari et al., 1993). Acute vocal cord palsy (Bae, 2009) and reversible posterior encephalopathy (Coppens et al., 2011) have also been described following disulfiram intoxication.

A case of self-poisoning with disulfiram presenting with a catatonic syndrome is reported here.

CASE PRESENTATION

Ms A, a 33-year-old woman was admitted to the toxicology ward of a general hospital after a suicide attempt with approximately 20 g of disulfiram and an unknown amount of benzodiazepines. Routine laboratory tests, toxicology which did not include disulfiram and a CT scan were negative. Because of disorientation and prominent psychomotor symptoms, she was transferred to an acute psychiatric ward.

On transfer to the psychiatric ward, Ms A was sitting still, with minimal interaction, in a semi-stuporous state and displayed apparently motiveless resistance to instructions or attempts to move (active negativism). She was unresponsive to most of the questions (mutism), occasionally verbigerated 1-2 words and stared for more than 20 seconds between shifting attention. Her few words she uttered, was incoherent. She refused to eat and drink requiring parenteral nutrition.

Ms A was started on tiapride 300 mg/day and alprazolam 1.5mg/day that resulted in increasing somnolence and confusion over the next 24 hours. These drugs were withdrawn and parenteral fluid was started. A second brain CT scan was performed, again with negative result. Somnolence fast progressed to a comatose state with pinpoint pupils followed by a grand mal epileptic seizure thus she was transferred to an intensive care unit. Her Glasgow Coma Score was 1-T-4. Laboratory tests showed rhabdomyolysis: CPK: 7340 U/l, CKMB: 140 U/l, and myoglobin: 329.2 ng/ml. Repeated standard toxicological tests were negative. Over the next days, her alertness somewhat improved but she still remained semi-stuporous. A third, contrast-enhanced CT scan revealed bilateral emollition of 1.5 cm diameter in both nucleus lentiformis at the level of the third ventricle. EEG showed diffuse, high voltage, relatively regular and rhythmic 2.5-3 Hz delta activity that was unresponsive to pain stimuli. She had weak symmetrical deep reflexes, sluggish pupillary reflexes, positive oculo-cephalic reflex and only minimal grimaces to pain stimuli. Based on the clinical presentation, the collateral data including history of alcohol abuse and the result of the third CT scan the tentative diagnosis of disulfiram intoxication was made that presented with catatonia likely to be related to the brain damage. Intramuscular thiamine (200 mg/day), pyridoxine (50 mg/day) were started, together with famotidine (40 mg/day), nadroparine (0.4 ml/day), and ciprofloxacine (1000 mg/day) for an emerging pneumonia. Her vigilance and behavior slowly improved; sometimes she uttered a few words and followed instructions.

After 19 days at the toxicology ward Ms A was transferred to a rehabilitation facility for physiotherapy and speech therapy. Over the subsequent 6 weeks the previously experienced low limb numbness and weakness subsided and she could be transferred back to the psychiatric ward for further treatment.

On the second psychiatric admission Ms A could give a coherent account of her suicidal thoughts that appeared 2 weeks before her suicide attempt; by then she had become increasingly paranoid and withdrawn for a few months.

In addition to heavy alcohol use, Ms A's psychiatric history was remarkable for a suicide attempt at the age of 18, cocaine and marijuana use in her twenties and a spontaneously recovered postpartum depression.

At that point, the psychiatric diagnosis of psychotic depression was made that was behind Ms A's suicide attempt. After another 35 days of pharmacotherapy with 100 mg quetiapine and 20 mg of paroxetine, Ms A was discharged free of neurological and psychiatric symptoms with the advice to remain on the above mentioned maintenance medication. During the second psychiatric admission, repeated neuropsychological tests revealed only transient mild cognitive impairment.

Ms A consented in written form to the publication of her case history.

CONCLUSIONS

Ingestion of disulfiram is an unusual way of suicide attempt; to the best of our knowledge only 6 case reports were published in the last 20 years (Zorzon et al., 1995; Bae, 2009; Lee et al., 2009; Cho et al., 2011; Jerónimo et al., 2009; Tartara et al., 2013) but none of them mentioned catatonia. Our case presented with a retarded catatonia syndrome. Treatment was initiated with a benzodiazepine and a low-dose second generation antipsychotic, but the patient's condition deteriorated. In this case arriving to a diagnosis was a challenging task, as the intracerebral lesions appeared with a 3-day delay and the clinical picture, the catatonic syndrome, was not specific.

While the therapeutic effectiveness of benzodiazepines in catatonia is well documented (Sienaert et al., 2014), in this case benzodiazepines aggravated the patients' condition by contributing to the development of a comatose state. This underlines the fact that in organic catatonia administration of the standard treatment options, benzodiazepines and/or electroconvulsive therapy should be applied cautiously. Instead, a flexible, individualized approach to the management of organic catatonia should be considered. In addition to supportive measures like rehydration and antibiotics, the diagnosis and possible treatment of the underlying medical condition that leads to the catatonic syndrome are the first priority.

In conclusion, we underscore the importance of accurate diagnosis of the underlying psychiatric or medical condition when encountering a fast emerging catatonic syndrome and focus first on treating the causative condition while simultaneously attempting symptomatic treatment of catatonia. Careful history and a catatonic syndrome should raise the suspicion of subcortical brain damage caused by, among other agents, disulfiram intoxication. Early specific and symptomatic therapeutic intervention of disulfiram intoxications is vitally important because almost complete recovery is within reach.

List of abbreviations

APA American Psychiatric Association
CNS central nervous system
CPK creatine phosphokinase
CPK-MB creatine phoosphokinase – myocardial band
CT computer tomography
DSM Diagnostic and Statistical Manual of Mental Disorders
EEG electroencephalography
GHB gamma hydroxybutyric acid
ICD International Classification of Diseases
LSD lysergic acid diethylamide
MRI magnetic resonance imaging
NMDA N–metyl-D-aspartate
PET positron emission tomography

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Diszulfirám mérgezéshez társuló katatónia – esetismertetés és rövid irodalmi áttekintés

Kataton tünetegyüttes számos neuropszichiátriai és belgyógyászati betegséghez társulhat. A katatónia alapjául szolgáló leggyakoribb kórképek az affektív betegségek, melyeket a szkizofrénia követ, de a központi idegrendszert érintő számos betegséghez – mint például az intoxikációkhoz – társultan is jelentkezhetnek kataton tünetek. A diszulfirám terápiás dózisai kiválthatnak pszichózishoz vagy hangulatzavarhoz társuló, vagy ezektől független kataton tüneteket. Jelen tanulmányunkban egy katatónia formájában megjelenő diszulfirám intoxikáció esetét ismertetjük rövid irodalmi áttekintéssel. A páciens toxikológiai osztályos felvételére kb. 20g diszulfirámmal történt öngyilkossági kísérletet követően került sor. Pszichiátriai osztályra történő átszállításakor mozdulatlanul, stupor közeli állapotban ült, felszólításnak és mozgatási kísérletnek ellenállt (aktív negativizmus). A kérdések többségére nem adott választ (mutizmus), időnként egy-egy szót ismételt (verbigeráció), és mereven nézett maga elé. Kómás állapot kialakulását követően kezelése a toxikológiai osztályon folytatódott, ahol egy következő kontrasztanyagos koponya CT 1,5 cm-es kétoldali lágyulást írt le a lencsemagokban, a harmadik agykamra szintjén. Az alkalmazott kezelés hatására állapota javult és rehabilitációs, valamint egy második pszichiátriai osztályos kezelésre is sor került. Emissziója neurológiai és pszichiátriai szempontból tünetmentesen történt. Következtetésként alá kívánjuk húzni a gyors ütemben kibontakozó kataton tünetegyüttes hátterében húzódó neurológiai vagy belgyógyászati betegség pontos diagnosztizálásának és az elsődleges oki kezelésnek a fontosságát a katatónia tüneti kezelése mellett.

Kulcsszavak: diszulfirám, mérgezés, neuropszichiátriai szövődmények, katatónia