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Case report

Sensory-motor axonal polyneuropathy involving cranial nerves: An uncommon manifestation of disulfiram toxicity

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ABSTRACT

Disulfiram (tetraethylthiuram disulfide) has been used for the treatment of alcohol dependence. An axonal sensory-motor polyneuropathy with involvement of cranial pairs due to disulfiram is exceedingly rare. The authors report a unique case of an extremely severe axonal polyneuropathy involving cranial nerves that developed within weeks after a regular dosage of 500 mg/day disulfiram. To the authors best knowledge, such a severe and rapidly-progressive course has never been described with disulfiram dosages of only 500 mg/day.

1. Introduction

Disulfiram (tetraethylthiuram disulfide) has been used for the treatment of alcohol dependence for more than fifty years [1].

Disulfiram is commonly used in dosages of 250–500 mg/day [1,2]. Although it is well tolerated by most patients, severe toxic effects are rare and involve hepatic (hepatitis) and nervous (encephalopathy, psychosis, optic and peripheral neuropathy) systems [1].

Every year, about one in 15,000 patients taking disulfiram will develop neuropathy [1,2]. Disulfiram peripheral neuropathy manifests as a sensory, motor or mixed axonal polyneuropathy that is partial or completely reversible after drug withdrawal [1–4].

The authors report a unique case of an extremely severe axonal polyneuropathy involving cranial nerves that developed within weeks after 500 mg/day disulfiram.

2. Case report

The authors describe a thirty-nine year old male with history of heavy alcohol intake (240 g/day) for eight years.

In early July 2014 he voluntarily decreased the alcohol consumption. After one month he decided to visit a psychiatrist for the treatment of alcohol dependence and started 500 mg/day disulfiram, 50 mg/day amisulpride, 15 mg/day oxazepam and 75 mg/day dosulepin. The last alcohol intake had occurred 48 h before starting disulfiram.

A month after starting the treatment, he began complaining of a tingling sensation and motor weakness over hands and feet that progressed over six weeks with speech impairment, difficulty in swallowing liquids and inability to walk.

The previous medical history was also relevant for tobacco consumption (20 pack-years for ten years). Other medical comorbidities and exposure to toxic substances/drugs were denied. The family history was irrelevant.

On initial evaluation he was found afebrile with a blood pressure of 145/69 mmHg and a regular pulse of 70 bpm. The general physical examination was normal. He was somnolent and disoriented. The cranial pair evaluation revealed bilateral, left-predominant, facial weakness (Fig. 1), dysphonia and dysphagia for liquids. The motor examination disclosed a symmetric distal-predominant muscle atrophy. Motor strengh evaluation revealed a symmetric and distal-predominant tetraparesis (grade 4 on cervical flexion/extension, shoulder abdution/adduction, forearm flexion/extension and hip/leg flexion/extension; grade 3 on finger adduction/abduction/opponency; grade 1 on foot dorsiflexion/plantar flexion). The aquilian and patellar osteo-tendinous reflexes were symmetricaly abolished and decreased, respectively, and the cutaneo-plantar reflexes were flexor. The sensory evaluation suggested a tactile/algic hypoesthesia with a symmetric glove-sock pattern (to the level of upper forearm and hip, respectively), hypopallesthesia and impaired proprioception. The gait revealed a marked bilateral *steppage* and he was only able to walk a few steps with bilateral support.

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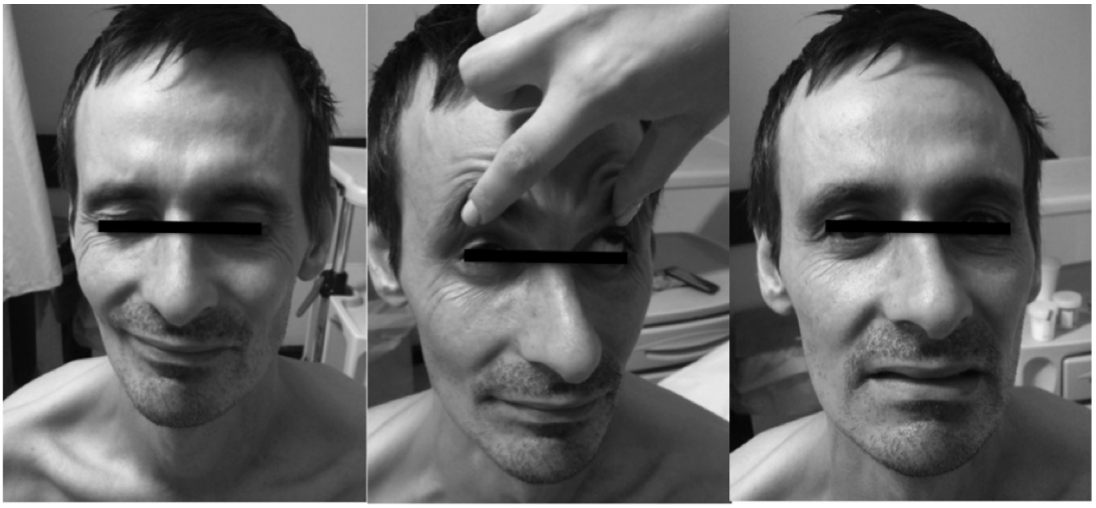

Fig. 1. Bilateral facial weakness observed on voluntary eye occlusion (right), forced eye occlusion (middle) and when trying to smile (left).

Table 1
Nerve Conduction Studies.

Height: 180 cm Skin temperature: 31 °C				
Motor nerve	Distal Latency (DL), ms	Amplitude (A), mV	Conduction Velocity (CV), m/s	F-responses, ms
Right Median (record: APB)				
Forearm	–	–	–	–
Arm (proximal)	–	–		
Left Median (record: APB)				
Forearm	–	–	–	–
Arm (proximal)	–	–		
Right Ulnar (Record: FDI)				
Forearm	3,6	1,8	52,5	30,2
Arm (proximal)	7,6	1,6		
Left Ulnar (Record: FDI)				
Forearm	3,4	2,0	52,0	29,8
Arm (proximal)	7,2	1,8		
Right Tibial (Record: AHB)				
Foot	5,8	0,5	41,1	58,8
Leg	15,3	0,3		
Left Tibial (Record: AHB)				
Foot	–	–	–	–
Leg	–	–		
Right Peronial (Record: EDB)				
Foot	6,4	0,5	35,6	–
Leg	15,4	0,1		
Left Peronial (Record: EDB)				
Foot	6,6	0,6	36,2	–
Leg	15,8	0,2		
Sensory nerve	Distal Latency, ms	Amplitude, uV	Conduction Velocity, m/s	
Right Median (2nd digit)	3,6	14,0	44,0	
Left Median (2nd digit)	3,4	17,0	46,2	
Right Ulnaris (5th digit)	3,2	14,0	44,0	
Left Ulnaris (5th digit)	3,1	16,0	46,6	
Right Radial	1,9	32,0	52,6	
Left Radial	1,9	34,0	52,6	
Right Superficial Peroneal	2,6	4,0	38,5	
Left Superficial Peroneal	3,6	4,6	38,9	
Right Sural	3,5	1,8	34,3	
Left Sural	3,0	2,5	40,0	

Notes: APB– abductor pollicis brevis; EDB – Extensor digitorum brevis; FDI – First dorsal interosseous; AHB – Abductor hallucis brevis; (–) – Not detected.
The borderline values in DL of peroneal and ulnar CMAP and the decreased CV of peroneal CMAP and sural/superficial peroneal SNAP are due to the axonal degeneration and low skin temperature. EMG and the study of facial nerves were not performed.
Reference values for NCS: Motor nerves – Median (APB): DL ≤ 4,4 A ≥ 4 CV ≥ 49. Ulnar (FDI): DL ≤ 4,5 A ≥ 7 CV ≥ 49. Tibial (AHB): DL ≤ 5,8 A ≥ 4 CV ≥41. Peroneal (EDB): DL ≤ 6,5 A ≥ 2 CV ≥ 44. Sensory nerves – Median (2nd digit): DL ≤ 3,5 A ≥ 20 CV ≥ 50. Ulnaris (5th digit): DL ≤ 3,1 A ≥ 17 CV ≥ 50. Radial: DL ≤ 2,9 A ≥ 15 CV ≥ 50. Superficial peroneal: DL ≤ 4,4 A ≥ 6 CV ≥ 40. Sural: DL ≤ 4,4 A ≥ 6 CV ≥ 40.

Routine laboratory screening was normal. Copper and vitamins B12, E, B1 and B6 showed normal results. Hemoglobin A1c accounted 4,5% and Hepatitis B, C, HIV, syphilis and borrelia serology were negative. An extensive immunologic study, including antiganglioside and antineuronal antibodies, was negative. Cerebrospinal fluid examination disclosed 1 cell/uL, 64 mg/dL glucose