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NON-LETHAL AMITRIPTYLINE OVERDOSAGE MIMICKING BRAIN DEATH

Konstantinos N. Fountoulakis[1], Theofilos Theodorou[2], Maria-Valeria Karakasi[1] & Ioannis Nimatoudis[1]

[1]Third University Department of Psychiatry, AHEPA University General Hospital, Department of Mental Health, Aristotle University, Faculty of Medicine, Thessaloniki, Greece

[2]First Department of Neurology, Aristotle University, Faculty of Medicine, Thessaloniki, Greece

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Dear Editors,

This is to highlight the possibility of amitriptyline overdosage incidents presenting with a clinical picture of consciousness disorder mimicking brain death. This is a clinical possibility that should be included in the differential diagnosis upon arrival of such incidents in the emergency room.

The opportunity to report this differential diagnostic comment was the overdose of an outpatient who was being treated in the outpatient psychiatric office of our psychiatric department. The 39-year-old woman, with refractory schizoaffective disorder, a psychiatric family history of psychosis, multiple hospitalizations and one previous suicide attempt, presented to the emergency department as a possible suicide attempt (was found unconscious by her mother).

On arrival she had Glasgow Coma Scale E1V1M4, heart rate 130 beats/min, blood pressure 137/59 mmHg, abnormal ECG with prolonged P-R, pH: 7.321, pCO2: 43.8 mmHg, pO2: 48 mmHg and oxygen saturation 80. Her eye pupils were midsized, poorly and sluggishly reactive to bright light. The oculocephalic reflex was not detectable. There was bilateral exotropia, with both eyes abducted, imitating the Wall-eyed ophthalmoplegia. Noxious stimuli produced non-purposeful, abnormal movements of all extremities. Plantar reflex (Babinski) seemed abnormal unilaterally (left) but this was not definite. Brain CT was normal. There were high serum levels for nortiazepam, lidocaine, phenothiazines and amitriptyline.

Although her clinical condition was almost identical to brain death, on the third day after her admission the neurological examination was completely normal and the days that followed she gained verbal communication. However a weak later she was still dysarthric, and at times confused and disoriented. Ten days after her admission she had fully recovered without any residual symptoms or signs and reported that she had taken approximately 100 tablets of perphenazine plus amitriptyline (Minitran 2/25 mg/tab) in order to commit suicide.

Cases of amitriptyline overdose have been reported, causing consciousness disorders, accompanied by a variety of ocular motor disorders, such as internuclear ophthalmoplegia, total external ophthalmoplegia, or complete loss of brain stem reflexes mimicking brain death (Delaney & Light 1981, Yang & Dantzker 1991, v. Stuckrad-Barre et al. 2002, Kansal et al. 2017). Similar pictures have been reported with perphenazine overdose (Cook et al. 1981). Ophthalmoplegia and loss of vestibular reflexes have been reported after consumption of a total dose of amitriptyline from 1.0 to 1.5 g (Roberge & Krenzelok 2001), while sedation and imitation of brain death has been associated with a total intake of 500 mg to 9 g (Kansal et al. 2017). The current case consumed approximately 2.5 g.

The sedative action of amitriptyline has been associated with antihistaminic and anticholinergic action (Tasaka et al. 1989, Espana & Scammell 2011), while anticholinergic action in the brain stem is probably responsible for ophthalmoplegia and dysfunctions of the vestibulocular and oculocephalic reflexes (v. Stuckrad-Barre et al. 2002). Animal studies have identified acetylcholine neurons in several areas of the brain stem that may participate in ocular movements, including somatic motor cranial nerve nuclei, prepositus hypoglossi nucleus, and the medial vestibular nuclei. The literature suggests an important role for cholinergic transmission in the physiology of eye horizontal gaze (Zhang et al. 2014).

It has been reported that after amitriptyline overdosage, consciousness is usually recovered after 24 hours to 5 days (Roberge & Krenzelok 2001) and this was more or less the case with the current incident.

It has been suggested (Plum & Posner 2015) that the pupillary light reflex is normal in case of coma due to metabolic causes but when there is an oculomotor dysfunction this is indicative of structural damage. However, drug induced cases of complete loss of brain stem reflexes should always be taken into account.

CONCLUSION

The clinical significance of the present case is that the initial differential diagnosis included stroke, metabolic-drug induced coma as well as conversion disorder. The presence of ophthalmoplegia excluded conversion disorder while, on the contrary, the oculocephalic reflex was not useful. It seems that pharmacological agents in overdosage can mimic the picture of brain death, and this should be considered carefully especially in cases of suspected suicide.

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Correspondence:
Maria-Valeria Karakasi, MD
Third University Department of Psychiatry, AHEPA University General Hospital,
Department of Mental Health, Aristotle University, Faculty of Medicine
1, Stilponos Kyriakidi str, GR 54124 Thessaloniki Greece
E-mail: valeria28289@hotmail.gr