British Journal of Medicine & Medical Research
21(3): 1-5, 2017; Article no.BJMMR.33433
ISSN: 2231-0614, NLM ID: 101570965

SCIENCEDOMAIN *international*
www.sciencedomain.org

Delirious Mania: Recognition and Successful Treatment with Donepezil

Laurie Jo Moore[1*], Mila Goldner-Vukov[2] and Rachel Huso[1]

[1]Department of Psychiatry, Loma Linda University, California, USA.
[2]Department of Psychiatry, Belgrade University, Serbia.

Authors' contributions

This work was carried out in collaboration between all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/BJMMR/2017/33433
Editor(s):
(1) Mohamed Essa, Department of Food Science and Nutrition, Sultan Qaboos University, Oman.
Reviewers:
(1) Ludgleydson Fernandes De Araújo, Federal University of Piaui, Brazil.
(2) Alicia García Falgueras, The Official College of Psychologists, Madrid, Spain.
Complete Peer review History: http://www.sciencedomain.org/review-history/18950

Case Study

Received 15th April 2017
Accepted 30th April 2017
Published 6th May 2017

ABSTRACT

Aims: Presentation of a case of severe delirious mania with resolution of delirium after treatment with donepezil.
Presentation of Case: KA was a 44 y/o Australian female with a history of bipolar affective disorder with psychotic manic episodes. Two weeks prior to her psychiatric admission she was admitted to a medical ward after an overdose (OD) of acetaminophen. On review, it appeared that this OD may have been the beginning of an unrecognized delirious mania. The patient was sent home and returned 2 weeks later for a prolonged psychiatric admission with multiple medical comorbidities. Psychiatric management and medical care were provided in intensive settings and despite adequate treatment and improvement in mood symptoms, her delirium did not resolve. Immediately upon institution of donepezil, her delirium resolved. After a period of stability, donepezil was stopped. Her delirium returned and donepezil was reinstituted with resolution of normal cognitive function.
Discussion: The DSM 5 criteria for Delirium and some inherent difficulties using these criteria are discussed. A review of the literature of delirious mania is presented which shows unresolved controversies but an evolving recognition of this disorder. A Cochrane Review shows no benefit in the use of acetylcholinesterases in the treatment of delirium. However, the multiple etiologies and

**Corresponding author: E-mail: Laurie.Moore2@va.gov, lauriejomoore.ljm@gmail.com;*

pathological processes involved in delirium may require unique and individual recognition and management.
Conclusion: This case suggests that the use of donepezil is strongly recommended in the treatment of delirious mania. Further study is required to clarify in this challenging disorder.

Keywords: Delirious mania; Bell's mania; bipolar disorder; donepezil; delirium.

1. INTRODUCTION

The authors have had a lifelong interest in both bipolar disorder and delirium. A patient they treated with schizoaffective disorder and delirium required a 9-month admission and responded to addition of donepezil 5 mg at bedtime. (Unpublished data). This stimulated an interest in the use of donepezil in the treatment of delirious mania.

2. PRESENTATION OF CASE

KA was a 44 y/o Australian female with a Samoan mother and German father. She was single, had a daughter and granddaughter and lived with her mother. She had a history bipolar affective disorder with manic episodes associated with psychotic features. She had a recent medical admission with impaired liver and renal function following an overdose of acetaminophen. She was treated for one week, sent home and returned two weeks later in a persisting delirious state that had gone unrecognized by her doctors. She suffered from diabetes mellitus, hypertension, gastroesophageal reflux disorder and had a longstanding right-sided foot drop. On admission to the Psychiatric Intensive Care Unit (PICU) she was delirious, disorganized, agitated, and responding to internal stimuli. She was yelling, screaming, throwing herself on the ground and smearing faeces. After arriving at the hospital, she fell and a neurological exam and computerized tomography (CT) of the head were normal. She required seclusion to provide immediate medical management of her diabetes and a urinary tract infection. Medication that had been effective in the past was started including quetiapine 200 mg every morning and 300mg at bedtime and amisulpride 100mg every morning and 200 mg at bedtime. A consult was obtained with the psychiatrist supervising electroconvulsive therapy (ECT) who recommended against it. Lithium 500 mg at bedtime was then initiated and increased to 500 mg BID with a level of 1.1 mmol/L. As a result of uncontrolled aggression, she required an injection of Acuphase 150 mg (zuclopenthixol acetate, a conventional antipsychotic that causes sedation for 3-5 days). She was transferred to a medical ward when her blood pressure fell to 83/50 and while on this unit she was given haloperidol and developed severe extra pyramidal symptoms. Her QTc was followed regularly because of the risk of using multiple antipsychotics and fluctuated between 478-491. When she returned to PICU, she was screaming, pacing and attempted to assault the staff. Haloperidol was stopped, olanzapine was titrated up to 30 mg daily, lithium continued and because of minimal improvement, sodium valproate was started at 20 mg/kg, then 30 mg/kg. Her serial clock drawings were bizarre and disorganized and her Mini Mental State Examination (MMSE) remained around 21/30.

She was admitted in mid-November and was still in the hospital over the holiday season. On New Year's Day she impulsively left the ward without permission to celebrate at a nearby casino and returned with an elevated blood alcohol level. Her cognitive function continued to be impaired despite treatment with two mood stabilizers and two antipsychotic medications. Donepezil 5 mg at bedtime was added to her treatment empirically and she showed a dramatic improvement with a MMSE score of 29/30, a perfect clock drawing and normal short term memory. Lithium and sodium valproate were adjusted, olanzapine was discontinued due to her diabetes and amisulpride was increased to 800 mg at bedtime. Her manic symptoms abated and she agreed to an implanon birth control device (showing improved insight). Since her manic episode appeared to have resolved, donepezil was discontinued. However, her cognition immediately deteriorated and donepezil was reinstituted with rapid stabilization. She continued to improve and after successful overnight leave with family she was discharged home.

3. DISCUSSION

Delirium is a complex neuropsychiatric syndrome with fluctuating symptoms that is poorly recognized. It may go unrecognized 95% of the time with 1/3 to 2/3 of psychiatrists and

neurologists failing to diagnose it. This is particularly alarming because in inpatients delirium is associated with a 5.5 times increased risk of mortality (22-75% of patients) [1].

In the authors' opinion delirium suffers from the 'Dot Point Mentality', the reduction of a complex syndrome into a list of symptoms that fail to convey an adequate understanding of the disorder. The DSM-5 criteria include: "A. A disturbance in attention (i.e., reduced ability to direct, focus, sustain and shift attention) and awareness (reduced orientation to the environment). B. The disturbance develops over a short period of time (usually hours to a few days), represents a change from baseline attention and awareness and tends to fluctuate in severity during the course of the day. C. An additional disturbance in cognition (memory deficit, disorientation, language, visuospatial, or perception). D. The disturbance in Criteria A and C are not better explained by another pre-existing, established, or evolving neuropsychiatric disorder and do not occur in the context of a severely reduced level of arousal, such as coma. E. There is evidence from the history, physical examination, or laboratory findings that the disturbance is a direct physiological consequence of another medical condition, substance intoxication or withdrawal (i.e., due to a drug of abuse or to a medication) or exposure to a toxin, or is due to multiple etiologies." [2] Awareness, for example, is a concept that philosophers, theologians and physicists grapple with in endless discourse. We believe a reductionist approach leaves most clinicians disadvantaged in their attempts to understand the fundamental nature of delirium.

The descriptions of Lipowski [3] in his textbook on delirium are elucidating. He describes the following concepts: 1) the highest integrative functions of the brain are disorganized and render a patient incapable of thinking and acting in a goal-directed manner. 2) Global cognition is impaired including thinking, remembering and perceiving along with an increasing difficulty in focusing and maintaining attention. 3) The patient's grasp of their situation is faulty with a reduced capacity to act in a purposeful manner and instead they show erratic behaviour interfered with by cognitive distortions and poorly controlled impulses. 4) There is an intrusion of dream-like thinking into ordinary consciousness with patients frequently awakening at night from dreams that continue as hallucinations and delusions which patients accept as real. Since patients are usually disoriented and not making sense of their surroundings, they often try to go home where they believe they will feel safe.

Lipowski [3] identified the general cause of delirium as a dysfunction of the Reticular Activation System, an area predominantly controlled by acetylcholine. More recent studies have identified abnormalities: in the right prefrontal cortex (that may explain difficulty making sense of novel situations and be associated with psychotic symptoms due to an increase in right-sided dopamine release), in the superior right posterior parietal area (that impairs attention to both the self and environment), in the ventromedial temporal parietal fusiform cortex, the lingual gyrus, the basal ganglia, the right anterior thalamus and the thalamic-subcortical and temporolimbic-frontal-subcortical connections that contribute to disorganization of mental information and behaviour, visuospatial impairment, psychotic experiences and emotional arousal. [1] In delirium, overall, right brain dysfunction is prominent with impaired visual attention and visual memories. This means that the Clock Drawing and Trail Making Test which measure right hemisphere function are more effective screening measures than the MMSE which assesses left-brain function [1].

Delirious Mania was first described by Calmiel in 1832 and Luther Bell provided the first comprehensive description in 1849 in 40 patients out of 1700 consecutive admissions to McLean Hospital. Kraepelin categorized mania into 3 categories in 1921: acute, delusional and delirious [4]. Klerman proposed staging of mania form normal, neurotic, hypomanic, manic and delirious viewing the severity as a progression [5].

Unfortunately, delirious mania has been described in a variety of way with different terms that may not relate to the same phenomena. The following topics summarize both historical and current understanding:

1) Bell's mania identified in 1934 was also called typhomania, acute delirious mania, delirium grave, acute delirium, specific febrile delirium and collapse delirium. Bell described a sudden onset, exceedingly great over activity, a marked sleeplessness, a great push of speech with statements disconnected due to rapidity of flow, disconnected and poorly systematized delusions, transient

hallucinations bordering on illusions, and the appearance of confusion that was not always consistent. Fatal outcome resulted in ¾ of cases in 3-6 weeks' time due to cardiovascular failure [4].

2) In contemporary reports Lee et al described excitement, altered consciousness with and without catatonia, lethal catatonia, malignant catatonia, excited catatonia and delirious catatonia [6]. These and other investigators warn that catatonic delirious mania can be life-threatening and advise that it responds well to ECT and benzodiazepines. Propofol has been suggested as an alternative for overly agitated patients who refuse ECT. [6,7].
3) Mash describes the Excited Delirium Syndrome (ExDS) first identified with the cocaine epidemic also associated with methamphetamine and designer cathinone abuse [8].
4) Bipeta and Khan describe delirious mania as excitement, grandiosity, emotional lability, psychosis, insomnia, altered consciousness and disorientation. They estimate that 5-20% of patients with bipolar disorder suffer from delirious mania. They present a cogent argument for accepting the concept of delirious mania [9].
5) Delirious mania has been recognized after a cerebrovascular accident (CVA) [10].
6) Sampson et al completed an RTC after total hip replacement in 33 patients that showed donepezil did not significantly decrease the incidence of delirium [11].
7) Delirious mania has been recognized as a cultural phenomenon in the presentation of "Jinn Possession" in a Pakistani patient [12].
8) Donepezil has been suggested primarily in case reports to benefit cognitive impairment in some patients following traumatic brain injury (TBI) [13,14]. Injuries involving the right hemisphere particularly basoventral, anterior temporal, orbitofrontal, caudate and thalamus are associated with the development of mania. This right-sided association is recognized but bilateral lesions are more common. [14] The recognition of delirious mania remains a potential consequence of TBI.
9) A Cochrane Review of the use of Cholinesterase Inhibitors for delirium concluded there was no evidence from controlled trials to support the efficacy of cholinesterase inhibitors in the treatment of delirium [15].

4. CONCLUSION

Evidence is emerging to support the recognition of delirious mania as a distinct disorder associated with bipolar disorder, following CVA and possibly TBI. There may be diverse presentations with and without catatonia. This case presents a compelling argument to support a trial of donepezil in patients with delirious mania.

CONSENT

All authors declare that written informed consent was obtained from the patient (or other approved parties) for publication of this paper.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Trzepacz PT, Meagher DJ, Wise M. Neuropsychiatric Aspects of Delirium. In: Yudofsky SC, Hale RE Ed. Essentials of neuropsychiatry and clinical neurosciences. American Psychiatric Press, Inc., Washington, DC: American Psychiatric Publishing; 2004.
2. Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. Washington DC: American Psychiatric Publishing; 2013.
3. Lipowski ZJ. Delirium: Acute confusional state. NY: Oxford University Press; 1990.
4. Kraines SH. Bell's Mania. Am J Psychiatry. 1934;91(1):29-40.
5. Klerman GL. The spectrum of mania. Compr Psychiatry. 1981;22:11-20.
6. Lee B, Huang S, Hsu W, Chiu N. Clinical features of delirious mania: A series of five cases and a brief literature review. BMC Psychiatry. 2012;12:65.
7. Jacobowski NL, Heckers S, Bobo WV. Delirious mania: Detection, diagnosis, and clinical management in the acute setting. J Psychiatr Pract. 2013;19(1):15-28.

8. Mash D. Excited delirium and sudden death: A syndromal disorder at the extreme end of the neuropsychiatric continuum. Frontiers in Physiology. 2016; (7):435.
9. Bipeta R, Khan MA. Delirious mania: Can we get away with this concept? A Case report and review of the literature. Hindawi Publishing Corporation: Case Reports in Psychiatry. 2012;Article ID 720354.
10. Bobo WV, Murphy MJ, Keckers SH. Recurring episodes of bell's mania after cerebrovascular accident. Psychosomatics. 2009;50(3):285-288.
11. Sampson EL, Raven PR, Ndhlovu PN, Vallance A, Garlick N, Watts J, et al. A randomized, double-blind placebo-controlled trial of donepezil hydrochloride (Aricept) for reducing the incidence of postoperative delirium after elective total hip replacement. Int J Geriatr Psychiatry. 2007;22:343-349.
12. Khan Q, Sanober A. Jinn possession and delirious mania in a Pakistani woman. Am J Psychiatry. 2016;173(3): 219-230.
13. Arciniegas DB, Anderson CA, Topkoff J, McAllister TW. Neuropsychiatric disease and treatment. 2005;1(4):311-327.
14. Arciniegas DB, Frey KI, McAllister TW. Cognitive impairment. In: Arciniegas DB, Zasler ND, Vanderploeg RD, Jaffee MS editors. Management of Adults with Traumatic Brain Injury; 2013.
15. Overshott R, Karim S, Burns A. Cholinesterase inhibitors for delirium (Review). The cochrane collaboration. The Cochrane Library. 2008;1.

Peer-review history:
The peer review history for this paper can be accessed here:
http://sciencedomain.org/review-history/18950