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Research Article

**POLYPHARMACY INDUCED DELIRIUM: A CASE REPORT
HIGHLIGHTING THE IMPORTANCE OF A THOROUGH
PSYCHIATRIC HISTORY AND PHYSICAL EXAMINATION**

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Article Received: July 2019**Accepted:** August 2019**Published:** September 2019**Abstract:**

A combative, aggressive 65-year-old female was brought to the emergency room (ER) after found wandering in the streets. Agitated, confused, disoriented in a delirious state, she was admitted to Psychiatric ER for diagnostic clarification. All labs except low platelets were within normal limits (WNL). Imaging did not show any changes. She was not a known neuro-cognitive disorder patient. Poly-pharmacy was ruled in as the etiology of the delirium, highlighting the importance of careful prescribing, especially in older persons. Moreover, this case highlights the importance of having expert knowledge in (a) the prescribing of psychotropic medication to include mechanism of action, side effects, and interactions, (b) treating delirium, and (c) the importance of a thorough history and physical examination. From this case report, the authors recommend consulting psychiatry as a standard of care in treating delirium.

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INTRODUCTION:

Delirium is defined as a transient, usually reversible, cause of mental dysfunction, and manifests clinically with a wide range of neuropsychiatric abnormalities [1]. Delirium can occur in any patient population, either young or old; however, it occurs more commonly in patients who are elderly and who have a neurocognitive disorder [1]. Decreased or change in baseline cognition, attention or awareness are clinical hallmarks of delirium and often manifests with a waxing and waning type of confusion[1]. Symptoms include clouding of consciousness, difficulty maintaining or shifting attention, disorientation, illusions, hallucinations, fluctuating levels of consciousness, dysphasia, dysarthria, tremor, asterixis in hepatic encephalopathy, uremia, and motor abnormalities[1].

The diagnosis of delirium is clinical. No laboratory test can diagnose delirium.

Diagnostic criteria: *The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)* diagnostic criteria for delirium is as follows[2]:

- a. Disturbance in attention (i.e., reduced ability to direct, focus, sustain, and shift attention) and awareness.
- b. Change in cognition (e.g., memory deficit, disorientation, language disturbance, perceptual disturbance) that is not better accounted for by a preexisting, established, or evolving dementia.
- c. The disturbance develops over a short period (usually hours to days) and tends to fluctuate during the day.
- d. There is evidence from the history, physical examination, or laboratory findings that the disturbance is caused by a direct physiologic consequence of a general medical condition, an intoxicating substance, medication use, or more than one cause.

Typically anti-psychotics are used as first-line agents in treating delirium[3,4]. However, as a bit of irony, there is evidence that up to 30% of the cases of delirium in elderly hospitalized patients is caused by medication toxicity to include psychotropic medications [5]. Hospitalized patients and elderly are more at risk of developing cognitive impairment as a result of taking medications. Both age and associated disease states in the elderly, especially as it relates to both brain neurochemistry and drug metabolism are factors making this population at risk[5]. Cases of drug-induced delirium can result from central nervous system (CNS) toxicity with or without dose-dependent manner and with interference of

neurotransmitter function[5]. Drug-induced delirium can also be an idiosyncratic complication and/or secondary to iatrogenic complications of medication use [5].

Although any drug theoretically can cause delirium, psychoactive drugs are important causes of delirium [5]. Drugs with cholinergic properties such as those used in the Alzheimer's disease spectrum treatments have associated risk in causing delirium [5,6]. So antipsychotics which often have anti-cholinergic properties which can cause delirium. Medication-induced delirium is thought to be a temporary psychiatric disorder resulting from a reduced central cholinergic transmission, combined with an increased dopaminergic transmission [5].

The cholinergic and the dopaminergic systems interact not only with each other but with glutamatergic and gamma-amino-butyric acid (GABA) pathways [7]. The cerebral cortex, striatum, substantia nigra, ventral tegmental area, and thalamus are all implicated in mental status changes seen in delirium [7]. The thalamus acts as a filter, allowing only the relevant information to travel to the cortex. Psychoactive medications frequently prescribed to hospitalized patients (e.g; benzodiazepines, opioids, antipsychotics) can compromise the thalamic functioning, leading to sensory overload and hyperarousal [7]. Literature [7] proposes that drug-induced delirium would result from the transient thalamic dysfunction caused by exposure to medications that interfere with central glutamatergic, GABAergic, dopaminergic, and cholinergic pathways at critical sites of action [7]. A list of drugs believed to cause or prolong delirium or confusional states is seen in the appendix.

CASE PRESENTATION:

This is a case of 65 years old female (Ms. M) who was brought in the ER by the police. She was found wandering in the streets and knocking on strangers' doors. On presentation, she was increasingly confused, disoriented, restless, and agitated. Ms. M had a psychiatric history of being intermittently treated for bipolar disorder. She was sleepless for several nights. She was admitted in psychiatric ER with the presumption of having an exacerbation of her bipolar disorder.

On evaluation, Ms. M had waxing and waning level of consciousness with intermittent episodes of wakefulness. She was restless, trying to climb out of bed, and trying to pull her nasogastric tube and intravenous lines. Her long term memory was deranged, and she had difficulty in sustaining her

attention. On Physical Examination, no focal neurological deficit was found. While in the hospital, she was started on haloperidol 5mg as needed for behavioral control and safety. Laboratory tests revealed blood glucose of 104 mg/dl, hemoglobin of 10.7 g/dl, and her platelet count was low at 70,000. The rest of her tests, complete blood count, urinalysis, and comprehensive metabolic panel were within normal limits. Both brain CT and MRI Brain did not show any changes. She was too paranoid about performing any neuropsychiatric testing.

At the time of evaluation, Ms. M's regular medication regimen was Hydroxyzine (25 mg three PO times a day) Temazepam (30mg PO at bedtime), Mirtazapine (15 mg PO at bedtime), Gabapentin (400 mg PO three times daily), Valproic Acid (500 mg PO twice daily), Lorazepam (0.5mg PO three times daily), Topiramate (50 mg PO twice daily). Ms. M was subsequently diagnosed with medication-induced delirium. Polypharmacy was tapered and discontinued constituting a medication washout.

Haloperidol was continued due to her agitation and delirium. Valproic Acid was continued for her Bipolar disorder. She showed gradual improvement of her behavioral and cognitive functioning. She was discharged home with her sedatives weaned off. On follow up visit one week after her discharge, she continued to do well with no behavioral or cognitive sequelae. Her mini-mental status (MMSE) score on follow up visit was WNL.

DISCUSSION:

Delirium is common in older persons in hospitals and long-term care facilities, and it may indicate a life-threatening condition [8]. Estimates of the prevalence of delirium vary based on the population studied the timeframe in which delirium is assessed and the method of assessment[8]. Nearly 30 percent of older medical patients experience delirium at some time during hospitalization [9]. Drug toxicity causes or contributes to approximately 30 percent of all cases of delirium [9,10]. It has been noted to occur in 11-42% of medical inpatients [11]. Benzodiazepines, anticholinergics, and antipsychotics, in particular, are considered an important cause of delirium[9,10].

Delirium has been described for hundreds of years, and many case reports and studies have been written on medication-induced delirium. The current case highlights a learning point described by Kosari SA (2014)[11]:

“Delirium is a multifactorial disorder that can be precipitated by any medical condition in a

susceptible person; therefore, a comprehensive history and physical (H&P) examination are imperative to guide diagnostic investigations.”

The current case also highlights the importance of expertise and coordination of care among physicians (and non-physician providers) in psychotropic prescribing. It was not clear in the case as to how Ms. M arrived at such a complicated psychiatric medication regimen. It is surmised that with multiple providers and multiple medications, medications are added superfluously, without a thorough history, and without proper communication among physicians.

The authors of the current case contend that a high level of psychiatry expertise is required for psychotropic management of psychiatric patients. The authors also contend that because delirium is a multifactorial disorder, and psychotropic medications can be dangerous, expert psychiatric consultation is required. This case highlights just how dangerous psychotropic medications can be. Delirium predisposing factors such as dementia, stroke, Parkinson's disease, advanced age, and sensory impairment[11] must be fully understood by both physicians and non-physician providers prescribing psychotropics. Delirium precipitating factors such as poly-pharmacy, infection, dehydration, immobility, malnutrition, and the use of urinary catheters [11] must be fully elucidated in the H&P. The current case highlights that psychotropic medication management of psychiatric patients and treating delirium needs to either be at the level of residency-trained psychiatrists or non-physician providers with physician-level oversight.

A thorough psychiatric H&P is especially important in managing delirium. Delirium is a very common medical condition encountered throughout the world and is one of the most frequent reasons psychiatrists are consulted [12]. The H&P needs to be at the level described in Markowitz, J. D., & Narasimhan, M. (2008) [12] where the physician should search for contributing causes, obtain a complete history, including a careful review of medication usage and illicit drug history, and perform full physical and neurological exams. In performing this H&P, the detailed science of neurobiology and neuropathogenesis needs to be fully appreciated to be thorough.

In treating delirium, the authors of the current case recommend consulting a psychiatrist as a standard of care. Psychiatrists understand the neurotransmitters most strongly implicated in delirium pathogenesis such as acetylcholine and dopamine [12]. While

decreased acetylcholine and anticholinergic activity are presumed to play a role in delirium, hyperactivity in the dopamine system is also implicated in the pathogenesis of delirium [12]. Psychotropic medications work on these neurotransmitter systems. Less is known about the role of serotonin and gamma-aminobutyric acid (GABA) in delirium pathogenesis. Although these neurotransmitters are involved in the mechanism of action of medications such as anti-depressants and sedatives used in psychiatry [12]. Excess glutamate activity or decreased histamine activity also may be etiologic factors in delirium [12], and certain psychotropic medications involve these neurotransmitters.

CONCLUSION:

In summary, the author's of the current study would like to add to the learning point of Kosari SA (2014) by adding the following addendum:

"Delirium is a multifactorial disorder that can be precipitated by any medical condition in susceptible persons; therefore a comprehensive history and physical (H&P) examination are imperative to guide diagnostic investigations" and expert level psychiatric consultation should be the standard of care.

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IMAGES AND TABLES:

Table 1: Drugs believed to cause or prolong delirium or confusional states (1-12)

Analgesics	
SAIDs	Corticosteroids
Opioids (especially meperidine)	
Antibiotics and antivirals	Dopamine agonists
Acyclovir	Amantadine
Aminoglycosides	Bromocriptine
Amphotericin B	Levodopa
Antimalarials	Pergolide
Cephalosporins	Pramipexole
Cycloserine	Ropinirole
Fluoroquinolones	Gastrointestinal agents
Isoniazid	Antiemetics
Interferon	Antispasmodics
Linezolid	Histamine-2 receptor blockers
Macrolides	Loperamide
Metronidazole	Herbal preparations
Nalidixic acid	Atropa belladonna extract
Penicillins	Henbane
Rifampin	Mandrake
Sulfonamides	Jimson weed
Anticholinergics	St. John's wort
Atropine	Valerian
Benztropine	Hypoglycemics
	Hypnotics and sedatives

Diphenhydramine	Barbiturates
Scopolamine	Benzodiazepines
Trihexyphenidyl	Muscle relaxants
Anticonvulsants	Baclofen
Carbamazepine	Cyclobenzaprine
Levetiracetam	Other CNS-active agents
Phenytoin	Disulfiram
Valproate	Cholinesterase inhibitors (eg, donepezil)
Vigabatrin	Interleukin-2
Antidepressants	Lithium
Mirtazapine	Phenothiazines
Selective serotonin reuptake inhibitors	
Tricyclic antidepressants	
Cardiovascular and hypertension drugs	
Antiarrhythmics	
Beta blockers	
Clonidine	
Digoxin	
Diuretics	
Methyldopa	