

Unexpected behavioral changes in geriatric patients: “how to recognize delirium, when it does not recognize itself”: report of a case

Abstract

Background and overview: An 80-year old female with a history of surgery, cardiovascular disease, metabolic disease, urinary tract infection, and multiple medications, including levofloxacin reported to the urgent care department with signs and symptoms of delirium.

Case description: The patient was unaware of why she was present at the urgent care department and referred to the staff as “devils and witches” and uttered obscenities at the staff. Attempts to get the patient to be cooperative were futile and the patient eventually left the urgent care against the advice of the staff. The patient returned some weeks later, alert, and responsive and with no memory of her prior attendance at the clinic. He granddaughter reported that prior to coming to the clinic; the patient was hospitalized with urinary tract infection and treated with levofloxacin.

Results: The required extractions were done on the patient at the last appointment, with no problem.

Conclusions and practical implications: Delirium should be considered as a possible explanation for patients who are acting strangely and using obscenities in a dental setting. Particularly if such patients have metabolic or cardiovascular disease, history of surgery, infections, or receiving antibiotic treatment. If central nervous system toxicity to the antibiotic is suspected, then cessation of the medication should restore the patient to neurologic equilibrium.

Keywords: antibiotics, drug interaction, cardiovascular disease, anxiety disorder

Volume 2 Issue 2 - 2015

Edwards L,¹ Amos S,² Thurman T,² Johnson C,³ Warner B,¹ Johnson CD⁴

¹Department of Diagnostic Sciences, University of Texas School of Dentistry, USA

²University of Texas School of Dentistry, USA

³Texas Southern University, USA

⁴Department of General Dentistry and Dental Public Health, University of Texas School of Dentistry, USA

Correspondence: Edwards L, Associate professor, Department of Diagnostic Sciences, University of Texas School of Dentistry, 7500 Cambridge Street, Houston, Texas 77054, USA, Tel 713-486-4109, Email Lincoln.Edwards@uth.tmc.edu

Received: March 18, 2015 | **Published:** April 25, 2015

Abbreviations: CDC, center for disease control; HIPAA, health insurance portability and accountability act; GABA, gamma-amino butyric acid

Introduction

The United States is experiencing a tremendous growth in its geriatric populations of individuals aged 65 years and older. This rapid growth is largely due in part to two independent factors; first, the baby boomers coming of age, with the leading edge of the boomers turned 65 in 2011. Second, individuals are living longer as a consequence of the advances in modern medicine. The Center for Disease Control (CDC) predicts that by 2050, it is anticipated that Americans aged 65 or older will number nearly 89 million people.¹ More than a quarter of all Americans and two of three older Americans have multiple chronic conditions, and treatment for this population consumes nearly 66% of the country's health care budget. Individuals with chronic diseases are prone to have other health challenges including mental illness, dementia or other cognitive impairments.² These multiple maladies necessitate treatment by multiple health care specialists, a variety of treatment regimens, and prescription medications that may not be compatible. Thus individuals with multiple chronic conditions are at an increased risk of conflicting medical advice, unnecessary and duplicative tests and adverse drug reactions. One adverse drug reaction that is accompanied by devastating risks, yet

poorly understood is delirium. Contrasting symptoms of dementia and delirium are listed in (Table 1). Traditionally the distinction between delirium and dementia has been made on the basis of acuteness of action and temporal course.³ Koponen and colleagues⁴ points out that delirium may be a harbinger of an underlying, undiagnosed dementia or cognitive defects that persists may be related to medical problems, direct neurotoxicity of delirium or to the effects of medication. One such medication is levofloxacin, a third-generation fluoroquinolone. We report the case of an 80-year-old female who presented to the urgent care clinic with levofloxacin therapy-psychosis.

Table 1 Contrasting Symptoms of delirium and dementia

	Mental State	Symptoms	Onset
Delirium	Varying degree of confusion	Disorientation, hallucinations, agitation, apathy, withdrawal, impairment in memory and attention Altered level of consciousness Disorganized thinking	Sudden onset; most cases remit with correction of underlying medical condition
Dementia	Memory impairment	Disorientation, agitation	Chronic slow onset

Case report

An 80 year old black female patient reported to the University of Texas, School of Dentistry's Urgent Care Clinic on several occasions. She was referred by her physician for dental evaluation of several painful teeth. She stated that her last comprehensive dental care was done at least 10 years ago. Her medical history was significant for a diabetic coma, stroke and heart attack 3 years ago, resulting in her being hospitalized for 6 weeks. She also stated that she had a seizure, associated with malignant hypertension 3 years ago, for which she was also hospitalized for 4 weeks. She also reported a fractured orbital bone resulting from a fall, for which she was treated on an outpatient basis.

Treatment with Lisinopril (10mg) resulted in an episode of angioedema for which she was hospitalized for 1 week, almost 18 months ago. The patient was managed for her type II diabetes with HumalogKwikPen (Insulin Lispro) 100 units/ ml, and Lantus (SoloStar) 100 units prior to bed. Several drugs were used to manage her hypertension, including Hydralazine (25mg TID), Losartan (100mg), Atenolol (50mg TID) and Hydrochlorothiazide (25mg). Other medications taken by the patient include, Atorvastatin (40mg; for hypercholesterolemia), Phenytoin (50mg BID; for seizures), Levothroid (Levothyroxine sodium 50 mcg for hypothyroidism), Xanax (prn for anxiety) and aspirin as a preventative. Her vital signs over six visits were generally within normal limits. Radiographs indicated moderate periodontal disease, several non-restorable teeth (# 3 and 8) and carious lesions were noted on teeth # 9, 11, 28, 29. Her dental history included an upper and lower partial for replacement of teeth: #'s 1,2,14,15,1,17,1,29,30,31,32. She reported the teeth were extracted over the years with the last lower molar approximately 20 years ago.

Questionable actions

The visit in question (# 6 over several months) started with the patient arriving 4 hours early for her appointment. She appeared uncharacteristically disheveled and seemed to be unclear as to why she was at the office. She began the appointment with shouts and obscenities. She called the staff "devils and witches". Office protocols dictated activation of the emergency procedures. Our response team: evaluation of her vitals which included: blood pressure, 132/78/94, respiration was 21/ minute, temperature 100.2. Several attempts were made to evaluate her blood glucose and apply oxygen; however she became extremely agitated and left the clinic against our professional recommendation without further incident. Subsequent attempts to contact the patient failed. Six weeks after the appointment in question, the patient returned to the urgent care clinic with her granddaughter. She had no memory of her last visit and requested that we complete her evaluation as requested by her physician. The granddaughter stated that prior to her previous appearance at the clinic, her grandmother had been hospitalized for 3 weeks due to a urinary tract infection, for which she received treatment with I.V. Levaquin (levofloxacin) for 2 days. The patient had several severe episodes of delirium which included hallucination. Her primary care physician's advised that she had been treated with 50mg of Xanax TID P.R.N., for management of anxiety, if symptoms presented. The patient resumed her normal appearance, was engaging, inquisitive, and presented with no memory of her last visit. Her vitals were within normal limits and the last 2 extractions were completed without incidence. HIPAA, the federal Health Insurance Portability and Accountability Act of 1996, defines

protected health information "minimum necessary information" in a separate paragraph if needed or I can just provide the code citations for those terms as defined in the HIPAA law. When treating a patient who is not consentable due to a medical condition or medication causing altered mental status or delirium and you need to ensure this person seeks appropriate medical treatment, the following question arises: Can a dentist, without violating HIPAA Privacy laws, disclose protected health information regarding the patient's current medical condition and mental incapacity to a patient's family member or friend in order to facilitate the patient seeking the proper medical treatment? The answer is yes; when your patient is suffering from an altered mental status or delirium, effectively rendering the patient incapacitated and unable to consent to the disclosure of Private Health Information, PHI, the HIPAA privacy rules permit limited disclosure of PHI. This issue is addressed in HIPAA section 164.510 (b) (3) titled Limited uses and disclosures when the individual is not present. This section states, "If the individual is not present, or the opportunity to agree or object to the use or disclosure cannot practicably be provided because of the individual's incapacity or an emergency circumstance, the covered entity (defined to include health care providers) may, in the exercise of professional judgment, determine whether the disclosure is in the best interests of the individual and, if so, disclose only the protected health information that is directly relevant to the person's involvement with the individual's health care." Pursuant the "minimum necessary" information provisions of HIPAA, the information disclosed to the family member should be limited to only that information necessary to address the patient's condition which has rendered them not consentable.

Discussion

This case report illustrates the association between delirium, medical conditions and medications used to treat such conditions. According to Inouye et al.,^{5,6} the geriatric population faces a greater risk of psychiatric challenges due to factors such as pharmacotherapy, infections, cardiovascular diseases, metabolic conditions, trauma and surgery. All these factors are manifested in our patient of interest. Of particular interest to dental professionals are the neurotoxin adverse reactions of antimicrobials. These reactions tend to be unexpected and unpredictable, however an awareness of the antimicrobials agents that are associated with neurotoxin adverse effects may be helpful in diagnosis by the physician and management by both physician and dentist, when there is an occurrence of such incidents. Symptoms of CNS toxicity could be mistaken for a worsening progression of an infection, in which case the practitioner may be tempted to continue the use of antimicrobial agent, resulting in possible harm to the patient. The physiological changes in the pharmacokinetic properties of drug absorption, protein binding, distribution, metabolism and elimination predispose the elderly to adverse drug reaction. Fluoroquinolone such as levofloxacin are commonly used to treat urinary tract infections in medicine⁷ and in dentistry, agents such as ciprofloxacin may be used as an adjunct in the treatment of aggressive periodontitis due to Enterobacteriaceae. Neurotoxicity occurs in 1% -2% of patients taking fluoroquinolones⁸ and is reported as headache, insomnia, dizziness, and hallucinations. The structural similarity between quinoline and gamma-amino butyric acid (GABA), the major inhibitory neurotransmitter in the brain, may account for the majority of neurologic adverse effects. Quinoline can displace GABA from its receptor binding site, thereby acting as GABA antagonists. Fluoroquinolone also appear to interact with the N-methyl-D-aspartate receptor.^{8,9} Patients should be aware that consumption

of theophylline and caffeine while taking Fluoroquinolones could increase the potential for CNS stimulation by these agents; particularly ciprofloxacin.¹⁰ Use of Non-Steroidal Antiinflammatory Agents such as ibuprofen can impair blood flow to the kidney and increase the concentration of fluoroquinolones, and therefore the potential for adverse drug reactions. Other antimicrobials agents that are prescribed by dentists such as clarithromycin¹¹ and azithromycin¹² are associated with delirium, more so with clarithromycin, but resolution of CNS symptoms after discontinuation of antibiotic therapy was much longer with azithromycin, maybe on account of its longer half-life. The beta-lactam ring shares structural similarities with GABA and therefore has the potential to inhibit GABA transmission in the CNS and producing symptoms of CNS toxicities. When dosed appropriately, CNS toxicities associated with penicillin are rare, however piperacillin and tazobactam are associated with several cases of CNS toxicities.^{13,14} Among the cephalosporin, cefepime poses the greatest risk for CNS toxicity because of good CNS penetration, high doses used and GABA antagonism.

Metronidazole is another agent that has utility both in medicine and dentistry. In dentistry, Metronidazole is used to treat gram-negative anaerobic pathogens implicated in orofacial infections and chronic periodontitis. Sometimes Metronidazole is combined with a beta-lactam antibiotic for more serious infections or for aggressive periodontitis. In medicine, Metronidazole is used to treat *Clostridium difficile* associated diarrhea, protozoal infections such as amebiasis or giardiasis, vaginosis and anaerobic infections.⁷

In the vast majority of cases reported in the literature, the patients return to neurologic and physiologic baseline once the causative medication is withdrawn.¹⁵⁻¹⁷ Delirium is related to high doses of drug relative to poor renal function. This condition is seen more in the elderly who are therefore at greater risk of developing CNS drug toxicities. Dental practitioners should therefore be aware of the association between delirium and the drugs that they prescribe, and should alert family members to be on the lookout for signs of delirium in at risk patients, and be prepared to report these to the dentist.

Conclusion

Patients who report to dental offices demonstrating "strange" behavior including the use of inappropriate language should have their medical records carefully examined for possible links to delirium. Fluoroquinolone, beta lactam, Macrolides, Metronidazole are associated with delirium and CNS toxicities in general. If a particular medication is suspected, then consultation between the dentist and physician should result in discontinuation of the offending drug, and hopefully a return of the patient to stable baseline. Alternative agents can be used to treat the existing condition where necessary. Family members should be informed of possible signs of delirium so that they will be able to report such signs to the health care providers. Since treatment requires consent, then when dealing with a patient experiencing an altered mental state, one must question the validity of consent. The HIPAA laws do authorize the discussion of protected Health Information to an appropriate party when and if the welfare of the patient is at risk. Healthcare workers should strictly adhere to the sage paradigm, "Never treat a stranger", even more so, if delirium is suspected.

Funding

None.

Acknowledgments

None.

Conflicts of interest

The authors declare that there was no conflict of interest.

References

1. http://www.cdc.gov/features/agingandhealth/state_of_aging_and_health_in_america_2013.pdf
2. Multiple Chronic Conditions: A Strategic Framework—Optimum Health and Quality of Life for Individuals with Multiple Chronic Conditions. Washington, DC: US Dept of Health and Human Services: 2010.
3. Meagher D, Trzepacz PT. Phenomenological distinctions needed in DSM-V: delirium, Subsyndromal delirium, and dementias. *J Neuropsychiatry Clin Neurosci*. 2007;19(4):468–470.
4. Koponen HJ, Sirvio J, Lepola U, et al. A long-term follow-up study of cerebrospinal fluid acetylcholinesterase in delirium. *Eur Arch Psychiatry Clin Neurosci*. 1994;243(6):347–351.
5. Inouye SK, Charpentier PA. Precipitating factors for delirium in hospitalized elderly persons. Predictive model and interrelationship with baseline vulnerability. *JAMA*. 1996;275(11):852–857.
6. Inouye SK, Zhang Y, Jones RN, et al. Risk factors for delirium at discharge: development and validation of a predictive model. *Arch Intern med*. 2007;167(13):1406–1413.
7. Saczynski JS, Marcantonio ER, Quach L, et al. Cognitive trajectories after postoperative delirium. *N Engl J Med*. 2012;367(1):30–39.
8. Francis J, Martin D, Kapoor WN. A Prospective Study of Delirium in Hospitalized Elderly. *JAMA*. 1990;263(8):1097–1101.
9. Mattappalil A, Mergenhagen KA. Neurotoxicity with antimicrobials in the elderly: a review. *Clin Ther*. 2014;36(11):1489–1511.
10. Tome AM, Filipe A. Quinolones: review of psychiatric and neurological adverse reactions. *Drug Saf*. 2011;34(6):465–488.
11. Schmuck G, Schurmann A, Schluter G. Determination of the excitatory potencies of fluoroquinolones in the central nervous system by an *in vitro* model. *Antimicrob Agents Chemother*. 1993;42(7):1831–1836.
12. Stahlmann R, Lode H. Safety considerations of fluoroquinolones in the elderly: an update. *Drugs Aging*. 2010;27(3):193–209.
13. Bandettini di Poggio M, Anfosso S, Audenino D, et al. Clarithromycin-induced neurotoxicity in adults. *J Clin Neurosci*. 2011;18(3):313–318.
14. Cone LA, Padilla L, Potts BE. Delirium in the elderly resulting from azithromycin therapy. *Surg Neurol*. 2003;59(6):509–511.
15. Bassilios N, Restoux A, Vincent F, et al. Piperacillin/Tazobactam inducing seizures in a hemodialysed patient. *Clin Nephrol*. 2002;58(4):327–328.
16. Tong MK, Siu YP, Yung CY, et al. Piperacillin /tazobactam-induced acute delirium in a peritoneal dialysis patient. *Nephrol Dial Transplant*. 2004;19(5):1341.
17. Chow KM, Szeto CC, Hui AC, et al. Retrospective review of neurotoxicity induced by cefepime and ceftazidime. *Pharmacotherapy*. 2003;23(3):369–373.