

Diagnosing Urothelial Carcinoma from Delirium: A Near Miss

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Abstract

Urinary tract infection (UTI) is a common cause of delirium in the elderly. Although diagnosis of delirium secondary to UTI is relatively straightforward, a lack of thorough investigation could result in missing underlying factors and medical conditions that may require immediate clinical/surgical intervention. Case of a 77-year-old male with delirium diagnosis and multiple psychiatric hospital admissions is reported here. This patient with multiple medical disorders and anxiety was admitted to psychiatric facilities on three different occasions with multiple psychiatric diagnoses including delirium. After a month of hospital stay and thorough medical and radiological examinations, the cause of refractory delirium was identified as multifactorial including urothelial carcinoma. Although UTI and urinary retention are common in the elderly, this case shows the importance of multifactorial diagnoses in cases of prolonged or refractory delirium to avoid delays in appropriate treatment.

Keywords

geriatric, delirium, urothelial carcinoma, bacteriuria, cystocerebral, cystitis

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Introduction

Delirium is classified by the *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition (DSM-5) as a disturbance in attention and awareness that develops over a short period of time that tends to fluctuate in severity with at least one additional disturbance in cognition (American Psychiatric Association, 2013). It is a highly prevalent syndrome that affects at least 15% of hospital inpatients (Shenkin et al., 2019). However, it is often poorly identified, as at least 57% of cases are missed, and often persisted even after discharge in 45% of cases (Cole et al., 2009; Pendlebury et al., 2015; Shenkin et al., 2019). This suggests that the classical thought of delirium being transient may not always hold true. Nevertheless, delirium must be addressed not only to treat underlying conditions, but also to prevent associated poorer outcomes including falls, medical complications, increased hospital stay, worsening cognitive function, and mortality, especially in the elderly who are at higher risk of developing delirium (Cole et al., 2009; Davis et al., 2017; Pendlebury et al., 2015).

Diagnosing delirium secondary to UTIs as seen commonly in elderly is relatively straightforward, but not necessarily thorough, resulting in missing underlying medical conditions (Ariathianto, 2011; Nicolle et al., 1987). Known as cystocerebral syndrome, significant urinary retention can precipitate or exacerbate delirium, especially in elderly, but responds rapidly with bladder

decompression (Liem & Carter, 1991; Rosen et al., 2015; Waardenburg, 2008). The following case report details and highlights the importance of looking past a simple diagnosis of UTI to evaluate for underlying serious medical conditions including urothelial carcinoma that may contribute to delirium.

Case Report

An elderly 77-year-old Caucasian male with past medical history including gastroesophageal reflux disorder (GERD), benign prostatic hyperplasia (BPH), herpes simplex, erectile dysfunction, and anxiety presented to an emergency department (ED) with complaints of panic attacks, poor sleep, weight loss, confusion, and inability to care for himself. On initial assessment, he was malodorous and disheveled with noted memory difficulties, cognitive problems, and disorganization. A CT head was obtained that was unremarkable, but his urinalysis (UA) was suggestive of an UTI.

He was diagnosed with acute stress disorder, major depressive disorder (MDD), and other specified anxiety

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disorder and transferred to a non-medical psychiatric facility on an involuntary basis. He was started on nitrofurantoin for the UTI, and tamsulosin for BPH. He displayed waxing and waning symptoms of confusion but was coherent in thought and later signed for voluntary treatment on day 3 of his admission. His diagnosis was later changed to delirium secondary to cystitis, other specified anxiety disorder, and acute simple cystitis. A repeat UA suggested possible UTI; however urine culture was negative. Upon concerns of cheeking medications, nitrofurantoin was changed to ceftriaxone (1-g; IM) injection for 3 days for possible UTI. On day 9, hypertension was noted with blood pressure of 180/104, which was brought down with clonidine (0.1-mg once) followed by amlodipine (5-mg daily). The patient had no prior history of hypertension. On day 10, the patient appeared coherent and rational and refused additional workup and medications. Due to his voluntary status and no history of aggressive behavior he was discharged home without any psychotropic medications.

The day after discharge, the patient was brought back to the ED after being found near his house, naked, with paranoid ideations. His UA again suggested UTI although his urine culture showed no growth. The patient was admitted to the medical floor. The CT of the abdomen and pelvis revealed asymmetric thickening and calcification of the right lateral wall of the bladder diverticulum containing multiple layering bladder calculi. Cytology showed atypical urothelial cells and the UroVysion test was positive for aneuploidy and homozygous 9P21 deletion associated with urothelial carcinoma. Prostate-specific antigen was 14.12, and urology recommended Foley placement and 1-month outpatient follow up. After 4 days, the patient was transferred to the non-medical psychiatric facility due to disorganized thoughts and depressed affect. Olanzapine 2.5-mg was started for visual and auditory hallucinations. After 3 days, the patient was transferred back to the ED after pulling out his Foley with resultant bleeding.

After the bleeding was stabilized, another Foley was placed and the patient was admitted to the medical psychiatric ward. For agitation, mood, and psychosis, valproate 500-mg daily and olanzapine 2.5-mg nightly and for sleep and appetite, mirtazapine 15-mg was prescribed. Sertraline was trialed but later discontinued due to inefficacy. Due to cheeking or refusal, medication compliance was difficult. After failing a void trial, urology recommended outpatient procedure. While waiting, the patient was started on amoxicillin (500-mg TID \times 5 days) due to suprapubic pain and *Enterococcus faecalis*-positive urine culture. On day 22, the patient had outpatient cystoscopy and underwent a transurethral resection of bladder tumor (TURBT) followed by cystolitholapaxy the next day. Pathology revealed high-grade papillary urothelial carcinoma without detrusor or lamina propria intrusion. Cefepime (2-mg/IV q8 hours.) was prescribed for 7 days after bladder calculi grew

Pseudomonas aeruginosa and *Enterococcus faecalis*. During this hospitalization, the patient continued to exhibit waxing and waning confusion. Following his urologic procedures, Foley removal was unsuccessfully attempted twice. On day 35 of his current hospitalization, urology recommended a second surgery with resection of diverticula in 6 weeks to 6 months. Patient's diagnosis was changed to delirium, multifactorial, due to infection, and/or urinary outlet obstruction vs. unspecified neurocognitive disorder, carcinoma of bladder s/p TURBT, and urinary retention. While the patient still exhibited waxing and waning confusion, he was less disorganized, was not reporting pain, and his mental status improved enough that he was discharged to his son and guardian after 60 days of hospitalization.

Discussion

Without a diagnosis of delirium, this patient may have been treated primarily for psychiatric symptoms and a diagnosis of urothelial carcinoma may have been missed. Initially the patient's delirium was attributed to simple cystitis and was treated accordingly during his first admission (Table 1). However, the second admission 1 day after his discharge revealed concerns for an underlying medical condition. Due to his initial diagnosis of delirium, additional medical workup was performed revealing asymmetric thickening and calcification of the bladder diverticulum and bladder calculi, with a possible diagnosis of bladder neoplasm. This suggests that his delirium was likely attributed to urinary retention versus UTI, or a combination of the two. Urinary retention is hypothesized to contribute to delirium due to bladder distension from resultant increased sympathetic tone and catecholamine surge triggered by the tension on the bladder wall (Waardenburg, 2008), which could potentially induce altered mental status (Saga et al., 2013). His one episode of hypertension, while controlled on amlodipine (5-mg daily), may have also been related to this sequence of events. However, the increased sympathetic tone and catecholamine surge has never been proven biochemically (Waardenburg, 2008). In fact, there is limited literature regarding cystocerebral syndrome (Blackburn & Dunn, 1990; Blè et al., 2001; Liem & Carter, 1991; Saga et al., 2013; Waale et al., 2001; Waardenburg, 2008; Young et al., 2008), which suggests the need for additional research to determine potential factors involved in delirium secondary to urinary retention.

While the delirium and urinary retention fits cystocerebral syndrome, his delirium was likely attributed to chronic urinary retention, as the patient did not have complete decompression of his bladder after Foley (18-fr) insertion or after his first TURBT. Additionally, his delirium was multifactorial including the recurrent growth of *Pseudomonas/Enterococcus* in his urine and urothelial carcinoma. Furthermore, it was difficult to

Table 1. Hospital Admissions, Clinics, and Treatments.

Treatment timeline	Urinalysis/CT	Urine culture
First ED admission (day 1)	RBC: 18, WBC: 14 Bacteria: Rare Leukocyte esterase: (-) Nitrites: (-)	Mixed growth of three or more organisms is indicative of faulty collection or contamination
First psychiatric admission (day 1–10)	RBC: 28, WBC: 26 Bacteria: Rare Leukocyte esterase: (-) Nitrites: (-) Blood: Small	No growth
Second ED admission (day 11)	RBC: 27, WBC: 27 Bacteria: Few Leukocyte esterase: (-) Nitrites: (-) Blood: Small	No growth
Second hospitalization (day 11–17)	RBC: 562, WBC: 19 Bacteria: Rare Leukocyte esterase: Trace Nitrites: (-) Blood: Large	No growth
Medical floor (day 11–14)	CT of the abdomen/pelvis: asymmetric thickening and calcification of the right lateral wall of the bladder diverticulum	No growth
Psychiatry unit (day 14–17)	UroVysion test: Positive-abnormal aneuploidy and homozygous 9p21 deletion	
Third ED admission (day 17)	RBC: 4740, WBC: 222 Bacteria: None Leukocyte esterase: Moderate Nitrites: (-) Blood: Large	>100,000 col/ml <i>Pseudomonas aeruginosa</i> 10,000 to 100,000 col/ml <i>Enterococcus faecalis</i>
Third psychiatric hospitalization (day 18–38)	RBC: 162, WBC: 126 Bacteria: Occasional Leukocyte esterase: Moderate Nitrites: (-) Blood: Small	>100,000 col/ml <i>Enterococcus faecalis</i>
Day 22	Outpatient cystoscopy, transurethral resection of bladder tumor	
Day 23	Cystolitholapaxy	
Third psychiatry hospitalization (close to discharge; day 38–60)	RBC: 26, WBC: 1467 Bacteria: Many Leukocyte esterase: Large Nitrites: (-) Blood: Large	>100,000 col/ml <i>Pseudomonas aeruginosa</i> >100,000 col/ml <i>Enterococcus faecalis</i>
Day 60	Discharged	

determine the patient's degree of cognitive dysfunction as evidenced by the changes in diagnosis. However, as research has suggested, delirium is a strong predictor for dementia and/or worsen pre-existing cognitive function (5). In addition to UTIs, urinary retention is also common in the elderly and should be considered as a risk factor for delirium. The importance of this case is that delirium can be multifactorial and additional workup procedures should be considered in cases of prolonged or refractory delirium to avoid delays in diagnoses, especially serious cancers such as urothelial carcinoma as in this patient's case.

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Patient Consent

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