

SECONDARY ENURESIS & BODY DYSMORPHIC DISORDER IN A CAUCASIAN MALE WITH CATATONIC SCHIZOPHRENIA: A case report

Nuruz Zaman, Milind Karale & Mark Agius

South Essex Partnership University Foundation NHS Trust, UK

SUMMARY

We describe a patient with Schizophrenia and secondary enuresis. The enuresis settled with resolution of his psychotic symptoms but later re-emerged after starting Clozapine. We explore the mechanisms of incontinence in Schizophrenia and those due to Clozapine. This case highlights the need to inquire about incontinence in patients with schizophrenia prior to prescribing clozapine.

Key words: schizophrenia – enuresis – clozapine – incontinence - body dysmorphic disorder

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Introduction

Urinary incontinence in patients with schizophrenia can present with daytime urinary leakage, urge incontinence and bed wetting. The association between bedwetting and schizophrenia has been noted since the pre neuroleptic era when Kraepelin reported a group of schizophrenic patients with resistant incontinence. Various mechanisms have been postulated for this association. The ventricular enlargement (hydrocephalus), selective neuronal loss with gliosis, and dopamine dysregulation in schizophrenia may indicate a neurological basis to the incontinence. These anatomical lesions might interrupt the pathways of bladder control or cause neurotransmitter dysfunction (de Groat & Kawatani 1985). The mechanisms of incontinence in schizophrenia might be similar to the possible mechanisms for incontinence seen in certain neurological conditions like hydrocephalus and Parkinson's where basal ganglia abnormalities with dopamine deficiency is accompanied with detrusor hyperreflexia. Groat and Kawatani postulated that the incontinence results from neurological (organic) brain disease which may interfere with the normal modulating influence of cerebral cortex and diencephalon causing detrusor hyperreflexia (de Groat and Kawatani, 1985).

It is also noted that urinary incontinence during the first psychotic episode is more common in schizophrenia (34%) than in other psychoses (14%) and those with schizophrenia are more likely to have experienced pre-morbid social impairments and enuresis (late onset of urinary continence). Patients with Schizophrenia had higher rates of childhood enuresis (21%) compared with Siblings (11%) or controls (7%) (Hyde et al. 2008.)

We describe a patient with Schizophrenia and secondary enuresis. The enuresis settled with resolution of his psychotic symptoms but later re-emerged after starting Clozapine. We explore the mechanisms of incontinence in Schizophrenia and those due to

Clozapine. This case highlights the need to inquire about incontinence in patients with schizophrenia prior to prescribing clozapine.

Case Report

Mr AP is a 21 year old man who was referred to an child and adolescent outpatient clinic at the age of 17 with a six month history of not coping with training and educational tasks. He had low mood, poor self esteem, occasional aggressive outbursts and certain compulsion like repeatedly checking doors, windows and mirrors. He walked with his hand over his nose and perceived people to be laughing at his nose. He had started wetting his bed despite attaining primary bladder control.

He was diagnosed with Body Dysmorphic Disorder and Adolescent Anxious Avoidant behaviour and was commenced on Amisulpiride 200mg nocte.

His symptoms, including nocturnal incontinence, responded to Amisulpiride and he remained symptom free for nearly two years when he stopped his medication. This time he presented with bizarre postures, self neglect, monosyllabic speech and withdrawn behaviour. Examination revealed catalepsy and posturing in absence of paranoia and perceptual abnormalities. He was stabilised on Amisulpiride 100mg and Risperidone 1mg twice daily and discharged.

Mr AP was re-admitted 6 months later with paranoia, significant self neglect and responding to auditory command hallucinations. He had lost 2 kg in weight and required electroconvulsive therapy. He was started on Clozapine due to poor response to Risperidone, Quetiapine, Haloperidol and Amisulpiride. He was stabilised on a daily dose of 500mg of clozapine, with serum levels of 350-500 ng/mL. Although his positive symptoms responded to Clozapine, he started displaying ambivalence and posturing. Nocturia was noticed on most nights. There was an increase in the frequency for micturation with no

symptoms of haematuria, dysuria or sensations of full bladder. Physical examination did not reveal any abnormality. Serum electrolytes, creatinine, glucose and urine microscopy showed normal results. MRI Brain was negative. A further kidney ultrasound and Urological review suggested incontinence symptoms were contributed by Clozapine.

Mr AP was otherwise born via a normal delivery, achieving appropriate milestones with no reported head injuries or neurological deficits in childhood. Initial schooling was un-remarkable. His mother has a history of Depression with Psychosis and his younger sister is known to services for Depersonalisation Derealisation syndrome

Mr AP does not suffer from any medical illness. He is a non smoker, with no history of illicit drug use and very occasional alcohol use. The patient was not a strong tea or coffee drinker. There is no significant history in childhood other than divorce of his parents when he was eleven.

Discussion

We present a case of a young schizophrenic male who initially presented with body dysmorphism and anxiety symptoms with secondary incontinence. His incontinence and psychiatric symptoms resolved with antipsychotic medication. His incontinence re-emerged after treatment with Clozapine.

Bladder dysfunction is noted in patients with schizophrenia (Kraepelin 1919.) In Schizophrenia, the bladder dysfunction has been attributed to Detrusor hyperreflexia, even in the absence of other recognized disease (Gupta & Bonney 1995.) It is possible that the incontinence at the onset of his illness was considered to be a part of his psychiatric symptomatology and was not investigated separately.

Bladder dysfunction has been attributed to neuroleptic medication including Clozapine (Aronowitz et al. 1995), although it is reported that Clozapine can resolve incontinence in schizophrenia (Kumar 2007.) In Mr AP, it appears that the incontinence was a feature of schizophrenia (as it appeared prior to neuroleptic medication). However, the cause of incontinence was not investigated at that time and it is possible that the incontinence could have been a result of other pathology.

In his third rephase, incontinence re emerged after starting Clozapine. Nocturnal enuresis secondary to clozapine treatment occurs in 0.23% (Aronowitz et al. 1995) to 27% (Centorrino et al. 1994) of patients. Patients are sometimes embarrassed to report this side-effect, leading to an underestimation of its incidence (Warner et al. 1994).

The pathophysiological mechanism of incontinence secondary to Clozapine treatment is un-clear. Proposed mechanisms have included, (a) sedation preventing waking from sleep to empty the bladder (Steingard 1994); (b) clozapine acting as a potent anticholinergic

antagonist, leading to urinary retention and subsequent overflow incontinence (Aronowitz et al. 1995); (c) clozapine induced seizures; (d) diabetes secondary to clozapine (e)potent anti-alpha-adrenergic effects of clozapine (Fuller et al. 1996.) Clozapine induced enuresis is considered to be a late side-effect, which is not correlated to the plasma level of the drug (Centorrino et al. 1994.) Mr AP has normal blood sugars, ruling out diabetes as a cause and has not had clozapine induced seizures.

A few studies have shown that Clozapine can in fact cause improvement in incontinence in schizophrenia by acting on a complex central neural network involving suprapontine brain structures associated with voluntary voiding control (Kumar et al. 2007). Moreover, anticholinergic side effects, may actually suppress Detrusor Hyperreflexia resulting in improvement in incontinence (Ambrosini 1984). No change in incontinence was noted with continued use of clozapine in Mr AP.

Lin (1999) showed that there were no statistically significant differences in age, sex, clozapine dose, duration of clozapine use, duration of illness, age at onset of schizophrenia, or concurrent treatment with other psychiatric medications between a cohort developing urinary incontinence and non-urinary incontinent control group (Lin 1999). Warner et al. in 1994 showed in his series of 12 patients on clozapine that the incontinence can resolve spontaneously

The links between negative symptoms, enuresis and urinary incontinence during psychotic episodes suggest that these symptoms might result from a common neural mechanism, possibly involving aspects of prefrontal cortical function (Hollis 2003)

Lesion studies have associated acquired frontal lobe lesions in adulthood with the development of urinary incontinence (Sakakibara et al. 1999). The findings from subjects with Schizophrenia and controls are in agreement with the proposition that the frontal lobes are intimately involved in the development and maintenance of volitional bladder control.

In Mr AP we postulate that incontinence was a presentation of schizophrenic illness which improved with treatment of schizophrenia. Clozapine caused re emergence of incontinence in a person vulnerable to develop incontinence due to schizophrenic process.

Conclusion

In conclusion, we described a patient with Schizophrenia and secondary enuresis. We highlight the potential neurological mechanisms of incontinence in Schizophrenia and those due to Clozapine treatment. Despite recognition of incontinence in Schizophrenia for some time, more studies are required to identify the actual basis. This case highlights the need to inquire about incontinence in patients with schizophrenia prior to prescribing Clozapine.

References

1. Ambrosini PJ (1984) A pharmacological paradigm for urinary incontinence and enuresis. *J Clin Psychopharmacol.* 4(5):247-53.
2. Aronowitz JS, Safferman AZ, Lieberman JA (1995) Management of clozapine-induced enuresis. *Am J Psychiatry.* 152(3):472.
3. Centorrino F, Baldessarini RJ, Kando JC, Frankenburg FR, Volpicelli SA, Flood JG (1994) Clozapine and metabolites: concentrations in serum and clinical findings during treatment of chronically psychotic patients. *J Clin Psychopharmacol.* 14(2):119-25.
4. De Groat WC, Kawatani M (1985) Neural control of the urinary bladder: Possible relationship between peptidergic inhibitory mechanisms and detrusor instability. *Neurourol Urodyn* 4(4):285-300
5. Fuller MA, Borovicka MC, Jaskiw GE, Simon MR, Kwon K, Konicki PE (1996) Clozapine-induced urinary incontinence: incidence and treatment with ephedrine. *J Clin Psychiatry* Nov;57(11):514-8.
6. Gupta S, Bonney WW, Sethi PS, Hunter DR (1995) Preliminary report: detrusor hyperreflexia in schizophrenia. *Neurourol Urodyn.* 14(4):371-8.
7. Hollis C (2003) Developmental precursors of child- and adolescent-onset schizophrenia and affective psychoses: diagnostic specificity and continuity with symptom dimensions. *Br J Psychiatry.* 182:37-44.
8. Hyde TM, Deep-Soboslay A, Iglesias B, Callicott JH, Gold JM, Meyer-Lindenberg A, Honea RA, Bigelow LB, Egan MF, Emsellem EM, Weinberger DR (2008) Enuresis as a premorbid developmental marker of schizophrenia. *Brain.* 131(Pt 9):2489-98. Epub 2008 Jul 31.
9. Kraepelin, E. (1919) *Dementia Praecox* (trans. R. Barclay). Edinburgh: Livingstone.
10. Kumar A, Chadda RK, Kumar N, Balan S, Prakash Srinivasan S (2007) Clozapine for the treatment of neurogenic bladder. *Neurourol Urodyn.* 26(4):537-9.
11. Lin CC, Bai YM, Chen JY, Lin CY, Lan TH. (1999) A retrospective study of clozapine and urinary incontinence in Chinese in-patients. *Acta Psychiatr Scand.* 1999 Aug;100(2):158-61.
12. Sakakibara R, Hattori T, Uchiyama T, Yamanishi T. (1999) Urinary function in elderly people with and without leukoaraiosis: relation to cognitive and gait function. *J Neurol Neurosurg Psychiatry.* Nov;67(5):658-60.
13. Steingard S (1994) Use of desmopressin to treat clozapine-induced nocturnal enuresis. *J Clin Psychiatry.* Jul;55(7):315-6.
14. Warner JP, Harvey CA, Barnes TR (1994) Clozapine and urinary incontinence. *Int Clin Psychopharmacol.* 9(3):207-9.

Correspondence:

Dr Milind Karale, Consultant Psychiatrist
South Essex Partnership University Foundation NHS Trust
Weller Wing, Bedford Hospital, Bedford, MK42 9DJ, UK
E-mail: Milind.Karale@blpt.nhs.uk