OMCR

Oxford Medical Case Reports, 2015;3, 229–231

doi: 10.1093/omcr/omv020
Case Report

CASE REPORT

Priapism and clozapine use in a patient with hypochondriacal delusional syndrome

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Abstract

Priapism is a urological emergency that results in a penile or clitoral engorgement, having several triggers by the use of medications, including psychiatric drugs, such as antipsychotics and antidepressants. The most common priapism presentation is the ischemic type that can result in the fibrosis of *corporus cavernosus*, with a significant risk of persistent erectile dysfunction. It is believed that, in the case of antipsychotic use, priapism is mediated by an imbalance in alpha-1-adrenergic blocking, with large variation affinity for alpha-1-adrenergic receptors among antipsychotics. This case report contributes to the study of this rare but severe side effect. Priapism can limit both treatment adherence and the reproductive future of our patients. We describe a case report of a patient with a delusional hypochondriac syndrome who had multiple priapism episodes using clozapine 50 mg/daily. In conclusion, we make brief comments on priapism management, a hard clinical dilemma.

INTRODUCTION

Priapism is defined as an engorgement of penis or clitoris, usually painful and prolonged (e.g. 3–4 h) [1, 2], unrelated to sexual stimulus or desire. It is a urologic emergency and there are several etiologies that require substantial differential diagnosis from occlusive vessel diseases to perineal metastatic implants. Among different triggers, priapism secondary to drugs owns a great relevance, such as cocaine, marijuana and alcohol [3]. Psychotropic medications such as antidepressants and antipsychotics can contribute to such idiosyncratic events [4]. Apart from psychotropics, other medications may cause a prolonged penile erection, such as anticoagulants, antihypertensives and intracavernosal medicines. Antipsychotics are responsible for about half of the venous priapism cases triggered by pills [5].

Although priapism may be considered a rare adverse event, such urologic emergency requires agility on its management. Delayed treatment may culminate in persistent erectile dysfunction from 30 to 90% patients [6].

Medication-induced priapism is usually ischemic, due to imbalance in alpha-1-adrenoreceptors (A1As), inducing intracavernosal blood stasis. The change in penile blood flow may worsen due to pathways related to nitric oxide, culminating in a vicious circle that is only broken by a surgical intervention for withdrawing the blood, by aspiration, surgical shunting or by pharmacologically injecting A1A agonists to reduce local acidosis and prevent ischemia, avoiding penile fibrosis [5, 6]. The antipsychotic A1A receptor's affinity is variable and the occurrence of priapism is considered as an idiosyncratic reaction, with poor or no dose-dependent and time-dependent correlations [7].

Received: October 18, 2014. **Revised:** February 11, 2015. **Accepted:** February 20, 2015

Many reports show that priapism can happen due to typical and atypical intake of antipsychotics, related to therapeutic use or overdose (suicide attempt) [4]. Among typical drugs, there are cases associated with the use of the chlorpromazine, levomepromazine, haloperidol [5, 8] and zuclopentixol [5]. Among atypical antipsychotics are ziprasidone, risperidone, clozapine [8, 9], quetiapine [4, 5, 7, 8, 10], aripiprazole [7] and olanzapine [7, 9]. No reports associated with amisulpride and pipothiazine were found [5].

Motivated by the abovementioned case report, we decided to discuss this rare adverse effect—a tough and unexpected clinical and therapeutic dilemma that could possibly harm both treatment adhesion and patients' reproductive future. This case report was conducted, following the institutional ethical rules. Informed consent of the patient was taken before the case was submitted to publishing considerations.

CASE REPORT

V.S.N., 31 years old, who discontinued high school education, and is an ex-bricklayer assistant, protestant, cared by his sister. He returned to the psychiatric outpatient ambulatory in 2013, where he had been followed from 1998 to 2010 before moving to another town. He was readmitted to our service after repeatedly visiting the hospital's emergency department with somatic complaints without clinical findings after several investigations: 'I have a severe inflammation in my bladder, my kidneys are crumbling to dust, I feel a stone on the left side, everything's fully choked inside my body, my skin smells like putrefied meat'.

Symptoms began 15 years ago accompanied by social isolation, anhedonia, paranoia, avolition, excessive and bizarre somatic concerns, with kinesthetic hallucinations, and loss of labor interests culminating in a significant hypochondriac existence. Without disease insights, he peregrinated too many hospitals seeking for 'physicians that would cure the disease that is going to kill me'.

He had never used psychoactive abuse substances, and had no hemoglobinopathies and pelvic injuries. He had already used haloperidol 10 mg/daily irregularly for a couple of months but developed dystonia. During daily irregular risperidone 4 mg intake, his improvement was negligible and he maintained his negative symptoms, such as delusions and kinesthetic hallucinations. His best therapeutic response was observed during irregular clozapine 400 mg/daily for 8 years, with improvement of delusional hypochondriac symptoms and slightly persistent negative symptoms (isolation and flatted affection). He stopped clozapine at 2010 when he had moved to a small town in order to live with another sister and lost ambulatory follow-up. There are no priapism reports on his medical records during his treatment.

After failure on ambulatory follow-up at 2013, he was readmitted to psychiatry care treatment at the University Hospital as part of his therapeutic project that proposed clozapine reintroduction. At that time, the patient was not taking any medications. He at that time had the same delusional hypochondriac symptoms and no insight: 'I feel my flesh stink; the cancer is going to kill me, everything is fully choked inside myself'. He complained of abdominal and suprapubic pain at the first week at the psychiatric ward. He restricted his feeding saying 'everything in his body was inflamed'. Physical and laboratory examinations were without abnormalities, including abdominal ultrasound, upper endoscopic studies, electrolytes, blood tests and serologies.

On his fifth hospitalization day, while he was using clozapine 50 mg/daily, he had his first priapism episode with little pain lasting 5 h. This episode resolved after rigorous hydration. The following day, he suffered another similar event, nevertheless lasting shorter. The clinical staff decided to suspend clozapine and observe. After 2 days, another episode occurred, for a shorter period of time. He still complained of perineal and suprapubic pain, but now relating the priapism events with delusional ideas: 'the disease is worsening, testicles are decreasing, my penis is choking, so as my kidneys and bladder'. We interpreted that 'residual priapism' was linked to the possible presence of clozapine active metabolites in the serum of that patient. Unfortunately, at that time, the access to clozapine blood level monitoring was not available in the hospital.

After priapism episodes, one of his family members told us that the patient had already had previous priapism episodes during clozapine irregular intake (~100–400 mg daily) between 2002 and 2010. Based on the hypothesis that priapism tendency with clozapine intake was high in that case, and excluded the possibility of multiple antipsychotics interactions, as we maintained the patient using only one antipsychotic by time, we decided to introduce and observe olanzapine intake, until the actual 20 mg daily. That decision was based on the fact that olanzapine may have lower affinity to A1A receptor [5, 7, 11], possibly linked to the antipsychotic-induced priapism pathophysiology. Since then, during the rest of incare and aftercare (about 1 year) follow-up treatment, no more priapism episodes were observed.

DISCUSSION

Alpha-1-Adrenergic receptor antagonism may lead to arteriole dilation that causes blockade of venous drainage due to an increase of the intracavernosal pressure, and triggers venous stasis because of venous collapse. Anti-erection mechanism gets damaged and penile or clitorial engorgement is perpetuated [5].

A recent case report suggests that some patients may have a biological and/or genetic tendency to develop drug-induced priapism [12]. Maybe that is the case of a patient, possibly with clozapine. We also argue that further studies on the connection between biological tendencies and drug-induced priapism should be investigated [12].

Penile detumescence or flaccidity is a process mediated by the sympathetic autonomic nervous system; intracavernosal A1A antagonism inhibits it and therefore increases the time of penile erection. Antipsychotics have different profiles of A1A receptor affinity [13]. For this purpose, study results are used, as of the Richelson *et al.* [5, 11], which are made *in vitro*, then compared with values among various antipsychotics. Regarding that literature information, there are more therapeutic possibilities for a safe choice to patients with more risk of priapism occurrence that need to use antipsychotics.

During follow-up of patients in the use of antipsychotic medications, clinicians should pay close attention to risk factors to priapism that are in the sequence list [12]. As soon as it happens, it is essential to make a meticulous investigation to find out the possible etiologies: hemopathies, hepatic injuries, metabolic alterations, psychoactive substance use (mainly, cocaine), perineal neoplasia or trauma and drugs interaction (including antipsychotic combinations).

This case report has the purpose to discuss this rare adverse event, but very severe, mainly between clinicians and psychiatrists who deal with antipsychotics drugs [14].

ACKNOWLEDGEMENTS

All the authors participated in the report elaboration and approved the final edition. F.D.C. (first author), K.T.S.A. and P.D.

are members of a psychiatry incare and outcare staff responsible for the patient's care, and worked together in writing this case report with a brief review. We thank Dr KB Ashok for helping reading the text and suggesting changes to make it clear and accurate.

CONFLICT OF INTEREST STATEMENT

None declared.

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