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Priapism Associated with Olanzapine

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Abstract: Priapism is a rare but serious adverse effect of psychotropic drugs where antipsychotic agents were implicated in 15 to 26% of priapism associated with medications. Among atypical antipsychotic, clozapine, risperidone and olanzapine have been reported to be associated with the condition. The patient was a 24 years old male referred to the OPD Clinic at Zare Psychiatry Hospital in 2007 with symptoms of delusion of control, delusion of persecution, delusion of somatic and auditory hallucination, for the last year. He had priapism following the use of olanzapine. Serotonin-Dopamine Antagonist (SDA) should be proscribed with care because of this rare yet serious complication, especially in cases with previous history of priapism following the use of psychotropic drugs.

Key words: Priapism, olanzapine, serotonin-dopamine antagonist, antipsychotic, sexual adverse

INTRODUCTION

Priapism is a rare but serious adverse effect of psychotropic drugs (Compton and Miller, 2001), which is attributed to the blockade of α -adrenergic receptors at corpora cavernosa (Segraves, 1989). Among psychotropic drugs, antipsychotic drugs are common causative agents (Compton and Miller, 2001). Antipsychotic agents were implicated in 15% to 26% of priapism associated with medications (Thompson *et al.*, 1990). Among atypical antipsychotic, clozapine, risperidone and olanzapine have been reported to be associated with priapism (Rosen and Hanno, 1992; Seftel *et al.*, 1992; Emes and Millson, 1994; Maizel *et al.*, 1996; Tekell *et al.*, 1995; Nicolson and McCurley, 1997; Diermenjian *et al.*, 1998).

Priapism associated with olanzapine, was first reported in 1998 (Diermenjian *et al.*, 1998; Heckers *et al.*, 1998). Since then olanzapine - induced priapism has been described in several case reports. To our knowledge, this case is the tenth report of priapism associated with olanzapine (Diermenjian *et al.*, 1998; Heckers *et al.*, 1998; Childers and Schwartz, 1999; Compton *et al.*, 2000; Jagadheesan *et al.*, 2004; Mattews and Dimsdale, 2001; Kuperman *et al.*, 2001; Songer and Barslay, 2001) (Table 1).

CASE REPORT

The patient was a 24 years old male seeking a psychiatric consult with symptoms of delusion of

control, delusion of persecution delusion of somatic and auditory hallucination, referred to the OPD clinic at Zare Psychiatry Hospital in 2007. In the year prior to presentation he was under treatment with 20 mg haloperidol augmented with lithium which resulted in no reasonable recovery and referred for symptoms of drug induced Parkinsonism. For the first 2 weeks, drugs were discontinued and after recovery from drugs side effects, 2 mg risperidone combined with trihexyphenidyl were prescribed. Doses of risperidone were gradually increased and due to insomnia it was changed to single dose of 6 mg at night. After two months, the patient presented with the complaint of non sexual stimulation painful erection starting from 8 am to 8 pm. Therefore the dose of risperidone was decreased to 4 mg day⁻¹. The patient experienced priapism for three consecutive periods and recovered without any other treatment. Clinical examination and history of patient did not demonstrate any pathologic condition. After 45 days, the patient presented at this stage with complaint of non sexual stimulation painful erection (lasting 8 h). This was relieved by an injection of diazepam. Considering the prolonged priapism and its recurrence, risperidone was discontinued in spite of giving good therapeutic response and 2.5 mg olanzapine was administered.

He experienced priapism for 14 h upon taking one dose of olanzapine. The patient did not report immediately despite the strong recommendation in spite of being recommendation to do so.

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It highlights three important questions related to the development of drug-induced priapism. (1) what are the etiologies and the mechanisms? (2) What is the correlation to dose and length of drug treatment? (3) What are the potential risk factors for priapism?

The final common pathway in the pathophysiology of priapism is decreased venous out flow from the corpora cavernosa of the penis. This can be caused by (a) physical obstruction of the venous system (b) decreased venous flow due to blood dyscrasias or (c) blocking the sympathetically controlled detumescence of the penis at the level of postsynaptic α_1 receptors. It is thought that the ability of drugs to block α_1 receptors correlates with their risk of priapism. If the antiadrenergic effect is unopposed by an anticholinergic effect, the balance of sympathetic tone (related to detumescence) and parasympathetic tone (related to erection) is disturbed. This hypothesis helps explain the onset of priapism due to drugs (e.g., trazodone and chlorpromazine), which have more antiadrenergic than anticholinergic properties. However, clozapine has strong anticholinergic properties and has been reported to cause priapism (Rosen and Hanno, 1992; Seftel *et al.*, 1992).

Our patient did not have any medical conditions known to be associated with priapism.

Urologic examination trial didn't show any pathologic findings, but he had a history of priapism during previous treatment with risperidone before taking olanzapine treatment.

Although most reports attribute drug-induced priapism to a single drug (5 out of 9), the possibility that priapism is attributable to a combination of medicines should be considered (Table 1).

First, priapism after physical obstruction of the venous system and concomitant drug treatment has been

reported. Second, decreased blood flow, due to blood dyscrasias, may not always be ruled out in cases of drug-induced priapism. Third and most important, drug interaction may lead to priapism. Such interactions may occur at the level of protein-binding and drug metabolism (pharmacokinetic interaction or at the level of receptors (pharmacodynamic interaction). Our case took only one drug though.

Drug-induced priapism dose not correlate with either the dose or the length of treatment, for example, priapism associated with trazodone has been reported for dosages ranging from 50 to 400 mg qd and for treatment lasting from 1 day to 18 months (Warner *et al.*, 1987). Also priapism associated with olanzapine has been reported for dosages ranging from 2.5 to 10 mg qd and for treatment lasting from single dose to one year (Table 1).

The onset of priapism after a single dose or within 24 h of a new medication is rare (Segraves, 1989; Thompson *et al.*, 1990) however, the onset of priapism after a single dose or within 24 h of olanzapine is not rare, because 5 out of 9 case reports were single dose or within 24 h and 2 out of 5 had previous history of drug induce priapism (Table 1). Our patient had previous history of risperidone induced - priapism and took 2.5 mg olanzapine in single dose. Rapidly developing priapism, as occurred in our patient as well as cases some other patients might be caused by the addition of another risk factor to a cavernosus venous system already vulnerable to decreased outflow (Table 1).

Clinicians should assess the likelihood of developing priapism before starting any medication know to be associated with priapism (Table 2).

If priapism occurs, urological consultation should be thought seeked immediately. Not uncommonly, urological intervention is delayed by the patients hesitanceto report

Table 1: Summary of case reports on olanzapine-induced priapism

Year	Journal	Age	Diagnosis	Dose day ⁻¹ (mg)	Length of treat. previous history priapism	Comorbid with medical disease	With other drugs	Emergency surgery
1998 May/Jan.	Psychosomatic	68	BMD	5	Signal dose No	Yes	Yes gabapentin benazepril	Yes
1998 Aug.	J. Clin. Psychopharmacology	46	Schizophrenia (paranoid)	15	2 week No	No	No	No
1999 April	J. Clin. Psycho pharmacology	27	Schizophrenia (paranoid)	15	2 week No	No	No	Yes
2000 April	Am. J. Psychiatry	43	Schizo affective	25	One day Yes	No	Yes thiothient divalproex	No
2001 April	J. Clin. Psychopharmacology	26	Schizophrenia (disorganized)	10	Single dose No	No	No	No
2001 May-June	Psychosomatic	51	Schizo affective	100	Single dose Yes	No	Yes gabapantin	Yes
2001 Dec.	AMJ Psychiatry	35	Schizo affective	10	Single dose No	No	No	Yes
2003 Jul.-Aug.	Psychosomatic	45	Schizophrenia	10	One year No	No	No	Yes
2004 May	Aust. N. Z. Psychiatry	30	BMD	5	One week No	No	Yes lithium	Yes
Author	This Journal	24	Schizophrenia	5	Single dose Yes	No	No	

Table 2: Conditions associated with priapism

Physical obstruction	Decreased blood flow	Drugs
Trauma, Solid tumors, Spinal-cord injuries, Stroke, Others	Sickle cell disease, Leukemia, Multiple myeloma, Nephrotic syndrome, Hyper viscosity states	Antipsychotics, Phenothiazines, Butyrophenones, Risperidone, Clozapine, Olanzapine, Antidepressants, Anticoagulants, Heparin, Warfarin, Antihypertensives, Prazosin, Labetalol, Guanethidine, Hydralazine, Anxiolytics, Phenoxybenzamine

prolonged erection and priapism. Patient education about the risk of priapism is essential to avoid the long term complications, including impotence and possibly penile gangrene.

However, while the condition is far from common, clinicians should be aware of the Serotonin-Dopamine Antagonists' (SDA) ability to induce priapism, especially in cases with previous history of priapism following the use of psychotropic drugs.

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