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A Case of Recurrent Priapism in the Context of Quetiapine Use, Discontinuation, and Rechallenge

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Keywords

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Priapism has been described in case reports as an extremely rare, idiosyncratic adverse event resulting from treatment with both first- and second-generation antipsychotic medications¹. Peripheral alpha-1 adrenergic blockade has been hypothesized as the causal mechanism². This mechanism is consistent with how priapism is classically associated with trazodone³, an antidepressant medication that also has alpha-1 antagonistic properties⁴. Prior case reports of priapism associated with quetiapine use have involved total daily doses of 600 mg or greater^{5–9}; one case involved a single overdose of 675 mg¹⁰ (and in a seventh case the dose of quetiapine was not reported¹¹). No case reports have cited lower doses of quetiapine as the putative causal agent. We report here a case of priapism associated with quetiapine use, with a treatment course complicated by concomitant methamphetamine, cocaine, and marijuana abuse.

CASE REPORT:

A 46 year-old gay-identified Caucasian male presented to our outpatient psychiatry clinic with a chief complaint of anxiety and insomnia. He related his anxiety to financial concerns, and because of this he was often unable to sleep without taking zolpidem regularly. He described a history of multiple major depressive episodes, interspersed with periods of increased irritability, reduced need for sleep, and excessive involvement in pleasurable activities. He also reported ongoing methamphetamine dependence and marijuana abuse, as well as sporadic abuse of cocaine, ecstasy, opioids, and hallucinogens. His past medical history included HIV, diagnosed six years prior. His medications included escitalopram, zolpidem, lamivudine/zidovudine, and nevirapine. Lab testing did not reveal hematologic or hypercoagulable disorders, or any infection other than HIV.

He was initially started on quetiapine at 50 mg daily to treat his symptoms of insomnia and anxiety, for several reasons: a diagnosis of a bipolar spectrum illness was clouded by his refusal to curtail his use of mood-altering substances, other non-habit forming hypnotic agents had been unsuccessful in treating his symptoms of insomnia, and his ongoing

polysubstance abuse and dependence placed him at greater risk for developing dependence on a benzodiazepine agent. Concurrently the dose of escitalopram was increased from 10 mg to 15 mg daily.

Three months after the escitalopram dosage increase, the patient presented to clinic with a baseline mental status examination, except for expansive affect and rapidity of speech. He also reported recent methamphetamine use, but in light of the initial differential diagnosis, treatment-emergent hypomania remained a concern. Therefore the dose of escitalopram was reduced back to baseline, and the dose of quetiapine was increased to 100 mg daily.

Approximately 15 months after initiating treatment with quetiapine, the patient began experiencing intermittent morning erections lasting 2–4 hours apiece then resolving spontaneously. He did not report these to the prescribing physician and continued taking quetiapine. During this time he continued to abuse methamphetamines, marijuana, and cocaine, despite repeated attempts to engage him in substance abuse treatment. Five months later, after using “a ton of cocaine” one evening, he had a painful erection lasting 10–12 hours, whereupon he presented to the emergency department. Urine toxicology screening was positive for cocaine and marijuana, and he was treated with drainage and intracavernosal phenylephrine injection. The patient stopped taking quetiapine and reported this to his physician six weeks later, who also recommended discontinuing treatment with quetiapine.

Over the next five months, the patient did not report any episodes of priapism. He then re-presented to our clinic with a chief complaint of difficulty sleeping despite self-medicating with 40–60 mg of zolpidem daily. He also stated that he had been on a drug binge, using methamphetamines on a daily basis, and marijuana intermittently, throughout the previous five months. The patient was counseled about his continuing use of illicit substances and was warned about the potential adverse effects of using excessive doses of zolpidem, but he again declined substance abuse treatment. This posed a difficult treatment dilemma because bipolar spectrum illness remained on the differential diagnosis, the patient had failed other hypnotic agents, and benzodiazepine hypnotic agents posed significant safety risks in light of his zolpidem abuse. Olanzapine was considered for its utility in treating bipolar illness, comparable sedative properties, and lesser alpha-1 antagonism; however, in a recent literature review, a greater number of case reports described an association between olanzapine use and priapism¹. Moreover, it was unclear whether the episode of priapism had actually been caused by quetiapine treatment, since the patient’s use of cocaine¹² was more proximally correlated with the incident. Quetiapine had improved the patient’s sleep in the past. The patient was therefore cautiously re-started on quetiapine at a minimal dose of 25 mg daily.

One month later, he again developed a painful, prolonged erection, whereupon he presented to the emergency department for treatment. Drainage of the penile shaft yielded dark colored blood, consistent with low flow priapism. The priapism resolved with intracavernosal injection of saline and phenylephrine.

DISCUSSION:

Although the patient continued to use illicit drugs, notably cocaine¹², throughout the course of his treatment, the quetiapine treatment challenge-discontinuation-rechallenge scenario described in this case suggests that low flow priapism may be an idiosyncratic adverse event associated with quetiapine treatment. Quetiapine has rarely been described as a cause of priapism^{5–11}, perhaps because of its intermediate affinity for alpha-1 adrenoceptors as compared to other atypical antipsychotic medications¹³. Notably, some teaching cases have even suggested using quetiapine for patients at risk for developing priapism¹⁴.

Ascertaining the cause of priapism in this case is difficult, as the patient continued to abuse methamphetamines, cocaine, and marijuana throughout the treatment course. All three illicit substances have been associated with priapism^{7, 12, 15}. Of the seven previously published case reports of priapism associated with quetiapine use, two cases involved concomitant abuse of methamphetamines⁷, cocaine¹¹, and marijuana¹¹. Additionally, the patient took escitalopram throughout the treatment course. Although the episodes of priapism were not temporally correlated with the patient's changing dose of escitalopram (which remained relatively constant) and escitalopram is not known to cause priapism, it should be noted that the racemate citalopram has been associated with priapism¹⁶.

Certain aspects of this case merit further comment and comparison to other cases reported. First, the patient received daily doses of quetiapine far lower than the 600 mg (and greater) doses described previously^{5–10}. Second, the priapism occurred 15 months after treatment with a 100 mg daily dose, and then again one month after re-challenge at a dose of 25 mg daily. To the extent that quetiapine was the causal agent, this case suggests that priapism can occur across a range of doses of quetiapine (consistent with what has been described in the context of other psychotropic medications^{17, 18}) and that the relationship may be unrelated to the duration of treatment (again consistent with prior case reports, which have described latency periods ranging from one day to 18 months^{5–10}).

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