Andrology

Quetiapine-induced Priapism Requiring Frequent Emergency Admissions: A Case Report

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ABSTRACT

Priapism, a rare but well-known adverse reaction of first and second generation anti-psychotics, has been hypothesized to be associated with blockade of alpha 1 receptors. However, genetic abnormalities or heritability of affected cytochrome P450 alleles has not been ruled out as a causal mechanism. A case is presented with three episodes of priapism within 17 days while taking standard FDA (Food and Drug Administration) approved doses of quetiapine. Cytochrome P450 3A4 genotype testing was performed and resulted with normal enzymatic activity. This case further eliminates enzymatic metabolism as a possible cause of priapism, thus strengthening the alpha one receptor blockade hypothesis.

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Case report

A divorced 48 year old Caucasian male presented to the emergency department with a painful erection of nine hours duration which woke him from sleep. He denied recent sexual activity or arousal, use of phosphodiesterase inhibitors, sickle cell trait or anemia, malignancy history, perineal trauma, or illicit drug use which was confirmed by negative toxicology screening. He admitted use of smokeless tobacco. Medical and psychiatric history included hypertension, hypercholesterolemia, and schizoaffective disorder. He was maintained on quetiapine 800 mg nightly for the past 10 years with brief periods of non-compliance and medication changes. The most recent period of non-compliance was eight months prior to presentation at which time he was admitted to an inpatient psychiatric unit. Since discharge, he reported full compliance with quetiapine 800 mg nightly, clonazepam 1 mg three times daily, atenolol 100 mg daily, hydrochlorothiazide 12.5 mg daily, and pravastatin 40 mg nightly. Over-the-counter medications taken include aspirin 81 mg daily and aspirin-caffeine powder packets for occasional headaches. Compliance was confirmed by pharmacy records and pill count. Physical examination revealed a fully erect penis, circumcised phallus, and moderate tenderness throughout. No erythema or induration was present, and bilateral testicles were soft. The remaining genitourinary examination was unremarkable.

He appeared fully awake and alert. No signs of quetiapine overdose including somnolence, tachycardia, respiratory depression, or hypotension were present. Laboratory data confirmed normal complete blood counts, electrolytes, and hepatic function. Urine gas chromatography-mass spectroscopy (GCMS) was positive for nicotine, cotinine, lidocaine, and quetiapine metabolite. Given cytochrome P450 3A4 is primarily responsible for quetiapine's metabolism, genotype testing was obtained. The cytochrome P450 study was done to rule out any enzymatic or genetic abnormality interfering with metabolism of the above medications.1,2 Urology was consulted and aspirated 15 cc of dark, red blood from the bilateral corpora after local anesthesia with 1% lidocaine. The patient was given 1000 mcg of phenylephrine and 750 mg of levofloxacin orally. Aspiration of the corporal bodies resulted in gradual detumescence and relief of the patient's pain. After a three hour observation, he was medically cleared for discharge from the emergency room. As this was the patient's third episode of priapism within 17 days, psychiatry was consulted for recommendations as his priapism was speculated to be related to his psychotropic medications. The previous two episodes had similar presentations to the one described and resolved with improvement in pain after the procedure by urology. Further history revealed two episodes of priapism within one month approximately one year ago while taking chlorpromazine. The patient was unaware of other medications taken in addition to chlorpromazine. Following these occurrences, his primary psychiatrist promptly stopped chlorpromazine, and symptoms did not recur until 17 days ago. During these episodes, the patient denied recent sexual activity or arousal, use of phosphodiesterase...
inhibitors, perineal trauma, or illicit drug use. Taking this history into consideration, psychiatric consultation recommended not exceeding the recommended daily dose of quetiapine, reducing clonazepam 1 mg to twice daily, and following up promptly with his primary psychiatrist within 1 week for directions on discontinuing quetiapine and cross-titrating to another anti-psychotic medication. He was instructed to return to the emergency department if another episode occurred.

**Comments**

We report this case linking quetiapine, a second generation anti-psychotic medication to priapism as there is limited data on anti-psychotics and their link with priapism in the literature. Previous cases involved a single ingestion or overdose of quetiapine outside the therapeutic range or stable daily dosage within the therapeutic range lacking further laboratory data or genetic testing linking hepatic functioning or other medication interactions to the possibility of causing priapism. In contrast to other cases, cytochrome P450 3A4 genetic testing was performed as our patient clearly has a propensity for priapism with use of daily dosed anti-psychotics including his prior history one year ago. Furthermore, the patient denied taking more than the recommended daily dose of quetiapine and the absence of other side effects that have been previously linked to quetiapine overdose including somnolence, tachycardia, respiratory depression, and hypotension. Any use of illicit substances or other medications were ruled out by GCMS. As quetiapine and clonazepam are significant cytochrome P450 3A4 substrates, cytochrome genetic testing allowed a closer examination of the patient’s enzymatic functioning. We hypothesized there were likely malfunctioning hepatic cytochrome enzymes with a major role in the medications’ metabolism either inherited or acquired (Table 1). Upon review of his cytochrome lab results, the patient had CYP 3A4 CC genotype, which predicts normal enzyme activity. Direct polymorphism analysis of the CYP 3A4 allele was performed by a polymerase chain reaction (PCR) based on 5'-nuclease assay using fluorescently labeled detection probes, which does not detect all CYP 3A4 genetic variants. As a result of CYP testing, enzymatic and metabolizing abnormalities are less likely the mechanism of the patient’s frequent emergency department visits. These results do not exclude hepatic enzyme genetic abnormalities or confounding medication interactions as the cause, only less likely in this patient. This suggests quetiapine’s alpha 1 adrenergic antagonist properties are the most likely cause of this patient’s priapism.

**Conflict of interest**

The authors declare no conflicts of interest.

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