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CASE REPORT

"A hard pill to swallow": a case series of chlorpromazine-induced priapism

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Priapism is a rare but potentially serious adverse effect of several medications including chlorpromazine, which is commonly used in the treatment of refractory migraine. We describe three cases of ischaemic priapism occurring in men following intravenous chlorpromazine administration for migraine relief. These cases highlight an important but under-recognised complication that can result in long-term erectile dysfunction if not promptly managed. Clinicians should maintain a high index of suspicion for this adverse effect and ensure patients are appropriately counselled regarding the need for urgent medical review should symptoms arise.

Key Words: priapism, chlorpromazine, side effect, case report

Introduction

Priapism is a urological emergency with potentially serious consequences; however, its aetiology and implications are often under-recognised in general medical practice. Amongst a range of other precipitating causes, chlorpromazine—commonly prescribed for the treatment of migraines—has been reported as a rare but clinically significant cause. The literature remains limited on the association and pathophysiological mechanism of chlorpromazine-induced priapism. In this case series, we describe three patients who developed ischaemic priapism following the administration of chlorpromazine. In the first case, a patient received a second hospital-administered dose of chlorpromazine despite developing priapism after the initial infusion. The second case involved two separate episodes of priapism triggered by a single chlorpromazine dose. The third patient presented with recurrent episodes of priapism several months after his initial dose, prompting investigation for other possible causes. These cases highlight the need for increased clinical awareness of chlorpromazine as a potential precipitant of ischaemic priapism, particularly in patients with no other risk factors. Informed consent was obtained from each patient.

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Case Series

Case 1

A 72-year-old Caucasian man presented to the Emergency Department of Manning Base Hospital in New South Wales, Australia, with a unilateral pulsatile headache preceded by an aura and associated nausea and vomiting. His medical history included provoked pulmonary embolism and migraines, typically triggered by general anaesthesia or sedation. Regular medications included vitamin D and calcium supplements, rabeprazole, and tramadol as needed. Initial management with metoclopramide and paracetamol was ineffective. He was subsequently administered 12.5 mg of intravenous chlorpromazine diluted in a litre of normal saline over 30 min, which resulted in resolution of his headache within one hour. He was discharged home. The following day, he represented 15 h after the onset of a spontaneous and sustained penile erection. A dorsal penile nerve block was performed, 100 mL of blood was aspirated from

the corpus cavernosum using a 19-gauge butterfly needle, without achieving sustained detumescence. Cavernosal blood gas analysis confirmed ischaemic priapism, with a pH of 7.07 and lactate of 8 mmol/L. Administration of a total of 750 mcg of intracavernosal phenylephrine in 250 mcg increments resulted in complete detumescence and resolution of pain. During this presentation, the patient also reported symptoms consistent with a recurrence of migraine. Given the prior efficacy of chlorpromazine, a second dose was administered in the Emergency Department. Fortunately, no recurrence of priapism was observed following re-exposure.

Case 2

A 68-year-old male presented to the Emergency Department at John Hunter Hospital, a metropolitan hospital in Newcastle, Australia, four hours after waking with a sustained and excruciatingly painful penile erection. His medical history included type 2 diabetes mellitus and hypercholesterolaemia. He had a similar presentation three weeks earlier, when he developed a prolonged erection 15 h after receiving an intravenous chlorpromazine infusion for a right-sided migraine. On that occasion, he was treated with a dorsal penile nerve block, bilateral cavernosal aspiration, and 200 mcg of phenylephrine. Cavernosal blood gas showed a pH of 6.72 and a lactate of 23 mmol/L, consistent with ischaemic priapism. During the current presentation, a dorsal penile block was applied with 5 mL of 1% lignocaine. Cavernosal blood gas again confirmed ischaemic priapism, with a pH of 6.73 and a lactate of 25 mmol/L. Two 200 mcg aliquots of 10 mg/mL intracavernosal phenylephrine were administered with good effect, followed by aspiration of 300 mL of blood, resulting in complete detumescence. The patient was discharged with a prescription for pseudoephedrine 60 mg tablets and was advised to seek urgent medical attention should symptoms recur.

Case 3

A 39-year-old man presented to the Emergency Department of St George Hospital in Sydney, Australia, with a 4-day history of an intense throbbing headache over the left eye. His past medical history included bipolar disorder and attention-deficit hyperactivity disorder. Regular medications included sertraline, dexamphetamine and lithium. He was administered 12.5 mg of intravenous chlorpromazine and was discharged after his migraine symptoms improved. Two days later, he re-presented with a 17-h history of a spontaneous and persistent penile erection unrelieved by ejaculation and application of ice. Examination revealed a tender and erect penis. A dorsal penile nerve block was applied and cavernosal blood gas confirmed ischaemic priapism with a pH of 6.9 and a lactate of 6.1 mmol/L. Due to persistent tumescence, three further aspirations were performed with intermittent aliquots of 100 mcg/mL intracavernosal phenylephrine, yielding a total of 300 mL of blood. After a period of observation, complete detumescence was achieved and the patient was discharged.

Over the following 12 months, the patient re-presented to the Emergency Department on five further occasions with recurrent episodes of priapism, each lasting up to 14 h prior to presentation. In the first three episodes, ischaemic priapism was confirmed on cavernosal blood gas, necessitating aspiration and intracavernosal pseudoephedrine. In the two most recent episodes, detumescence was achieved spontaneously with oral analgesia and pseudoephedrine. During this period, the patient trialled a several interventions including sildenafil 25 mg daily, baclofen, regular pseudoephedrine, and cessation of dexamphetamine but found minimal therapeutic benefit. He was referred to a urologist with a special interest in andrology for further management.

Discussion

Priapism is defined as a prolonged penile (or clitoral) erection that occurs in the absence of sexual stimulation or desire.[1] Ischaemic priapism, the most common subtype, constitutes a urological emergency. The incidence has been estimated at 1.5 cases per 100,000 person-years, although this is likely an underestimation, with higher rates reported in certain at-risk populations.[2]

A variety of aetiologies have been identified for ischaemic priapism, with medication use representing the most common cause, accounting for at least 25% of cases.[3] Implicated agents include intracavernosal injections for erectile dysfunction, inappropriate use of phosphodiesterase-5 inhibitors (e.g., sildenafil), antipsychotics, antidepressants (including trazadone and selective serotonin reuptake inhibitors), phenothiazines (particularly chlorpromazine), alpha-adrenergic antagonists, and total parenteral nutrition.[4] Antipsychotic medications alone have been implicated in 15%–26% of medication-induced priapism.[5] In our third case, the patient's regular use of sertraline, a selective serotonin reuptake inhibitor, may have contributed to the development of recurrent priapism. Recreational drug use, particularly cocaine and excessive

alcohol consumption, has also been associated with prolonged tumescence.[2] Other recognised causes include haematologic disorders (e.g., sickle cell disease, glucose-6-phosphate dehydrogenase deficiency and thrombophilias), malignancies involving the genitourinary or gastrointestinal tract, and pelvic or perineal trauma.[2,6,7]

Prolonged ischaemic priapism carries a significant risk of subsequent erectile dysfunction, with reported rates as high as 90% when the episode persists beyond 24 h.[2,8] Tissue damage is believed to begin as early as four to six hours after onset of tumescence, and the likelihood of erectile dysfunction is strongly correlated with the duration of the episode.[8] Chlorpromazine is a typical antipsychotic used in the management of schizophrenia, but it is also indicated for the treatment of anxiety, nausea, acute migraine, intractable hiccups, and severe behavioural disturbances in children with hyperactivity and excessive motor activity.[9] Among its reported adverse effects, sexual dysfunction—including erectile dysfunction (in up to 20%–50% of patients), ejaculatory disturbances, reduced libido, and priapism—has been well documented.[9] Although chlorpromazine exerts peripheral alpha-1 adrenergic blockade and central serotonin-like effects, the exact mechanism by which it precipitates priapism remains unclear.[1,9] To our knowledge, the cases presented here are the first reported instances of priapism occurring after such a low intravenous dose of chlorpromazine. This is particularly relevant in light of current guidelines for intractable migraine, which recommend up to two intravenous infusions of 12.5 mg chlorpromazine.[10] In our first case, a second dose was administered despite the patient actively receiving treatment for priapism, highlighting a potential lack of clinical recognition of this serious side effect. Without appropriate counselling and early recognition, patients may delay presentation and miss the therapeutic window for effective intervention, increasing the risk of long-term erectile dysfunction.

In summary, ischaemic priapism is a urological emergency that requires early recognition and timely intervention to prevent long-term complications. Prescribers should be aware of medications associated with an increased risk of priapism, including chlorpromazine, and ensure that patients are appropriately counselled on this risk. For individuals with a history of priapism, clinicians shoulder consider alternative therapies and exercise caution when prescribing chlorpromazine or other high-risk agents.

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Author Contributions

Matthew Kwon: Conceptualisation, Methodology, Writing—Original Draft, Writing—Review & Editing; Kathleen Lockhart: Conceptualisation, Writing—Original Draft, Writing—Review & Editing, Visualisation; Hugh Reid: Conceptualisation, Visualisation; Avi Raman: Conceptualisation, Methodology, Visualisation, Supervision. All authors reviewed the results and approved the final version of the manuscript.

Availability of Data and Materials

Not applicable.

Ethics Approval

This case series was approved by the Hunter New England Local Health District Research Ethics Committee (AU202506-04). Informed consent was obtained from each patient.

Conflicts of Interest

The authors declare no conflicts of interest to report regarding the present study.

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