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Chlorpromazine-Induced Priapism in A 22-Year-Old Undergraduate Managed Conservatively in A Psychiatric Setting

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ABSTRACT

Introduction: Priapism which is a urological emergency caused by the use of antipsychotic drugs like Chlorpromazine, can occur at all ages, from newborn to the elderly, irrespective of dose, route of administration, intake duration, the etiology, and prior history of penile erections.

Case Presentation: A 22-year-old Nigerian undergraduate, in one of the Universities in the South East, was referred on account of the use of cannabis, alcohol, and codeine, with an associated history of abnormal behavior, low mood, weepy spells, guilt feelings, and poor sleep. A diagnosis of Mental and Behavioral Disorder secondary to Polysubstance Dependence (Cannabis, Alcohol, Shisha, Codeine, Crack) with co-morbid Severe Depression with Suicidal ideations, was made. Investigations done included Complete blood count, Malarial parasite test and Widal test, Serum Electrolyte, Urea and Creatinine, Retroviral screening, and HBsAg. The patient after the first dose of Intramuscular Chlorpromazine developed a painful penile erection (Priapism), which changed the clinical picture. A referral made to a Urologist was declined, as he was recommending that the patient be referred, which was not possible in the immediate term. Ice packs were administered in the region of the penis, that there was reversal of the painful engorgement of the penis. The time between the onset of the side effect and resolution of the engorgement was 3 hours, which was within the golden hours allowed in order to avoid complications.

Conclusion: This possibility of priapism due to antipsychotic use, and lessons from its conservative management, makes it imperative that physicians and patients, must be alert and knowledgeable about this life-threatening adverse drug reaction and this awareness would help in reducing priapism-related adverse sequelae.

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Introduction

Priapism is a rare pathological condition, characterized by a persistent and painful penile erection that persists beyond four (4) hours and is not related to sexual stimulation [1]. Priapism is considered a serious adverse drug reaction because it requires urgent intervention to preserve the erectile ability of corpora cavernosa [2]. Priapism may occur at all ages, from newborn to the elderly, it can even occur in impotent patients, and the erectile state is limited to the cavernous bodies, not affecting the corpus spongiosum or the glans [3]. This emergency condition has different presentations, etiologies, pathophysiology, and treatment algorithms [4]. It has been reported that both vascular and neural mechanisms are implicated in the pathophysiology of priapism, but it is not clear which initiates the process [5]. Evidence-based data reports that priapism is mainly classified into three main types: ischemic (low flow or veno-occlusive) priapism, arterial (high flow or non-ischemic) priapism, and stuttering (recurrent or intermittent) priapism. Ischemic (veno-occlusive or low flow), is being reported to be the most frequent type and is found in nearly 50% of cases of Priapism [5]. However, another more recent study recorded 95% of cases of Ischemic priapism [6]. In the etiology of priapism, the drugs most frequently implicated are psychotropic drugs (phenothiazines and trazodone), antihypertensives (mainly prazosin), and heparin [5]. Drugs are responsible for the onset of 25 to 40% of cases of priapism [7]. Drug-induced priapism, otherwise known as Iatrogenic priapism, is usually considered a clinically relevant cause of veno-occlusive priapism [8]. This type of priapism is commonly caused by the administration of certain drugs or as a result of drug-drug interaction [9]. Several causes have been attributed to causing veno-occlusive priapism, and this includes the use of antipsychotic drugs [10]. Its noteworthy that ADRs to antipsychotics are among the

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major challenges in the treatment of patients with psychotic disorders [11]. This is because antipsychotics, are well-known to cause potentially serious and life-threatening adverse drug reactions (ADRs) [12]. One such adverse drug reaction, caused by the use of antipsychotics, is Priapism [13]. In a related study, the observed pattern of signals indicates a relationship between alpha1 affinities of antipsychotics and the occurrence of priapism [2]. These signals for possible risk for priapism were present for chlorpromazine, quetiapine, risperidone, ziprasidone, and aripiprazole [2]. Chlorpromazine, which is our drug of concern in this report, is a conventional antipsychotic, that is commonly used for its sedative properties, in patients with abnormal behaviors, amongst other uses [14]. The mechanism causing priapism, associated with the use of chlorpromazine, includes peripheral alpha-1 blockade, and its central serotonin-like actions [15]. These complexities surrounding the mechanism of priapism are further buttressed by the fact that the dose, route of administration, and intake duration that can cause priapism and the etiology while using chlorpromazine is not clarified [16]. It has also been reported that sometimes, there may be etiological complexities, which may cause a delay in the diagnosis of antipsychotic-induced priapism, and the problem of establishing a link between priapism and one particular ingredient of a drug combination [17]. A case of an unusual complication of antipsychotic medication, chlorpromazine, leading to, priapism, that developed after intramuscular administration of a single dose of chlorpromazine, managed conservatively in a 22-year-old undergraduate, is presented in this report.

Case Presentation

The patient is a 22-year-old Nigerian undergraduate, in one of the Universities in the South East, referred from a hospital in Port Harcourt to a private psychiatric and rehabilitation facility on account of the use of cannabis, alcohol, and codeine, with an associated history of abnormal behavior, low mood, weepy spells, guilt feelings, and poor sleep pattern, all of 3 years duration. In the history of presenting complaints, the illicit use of cannabis was associated with a progressive increase in the amounts taken over time. He was also using cannabis as an additive to her food, Alcohol was used in different strengths ranging from beer to brandy and whisky. The whisky or brandy can be taken about 25 shots a day, accompanied by 3 or 4 bottles of beer. Abnormal behavior was associated with irritability and verbal and physical aggression. On one of the occasions, he almost strangulated his dad with his bare hands. Threats to his mother and aunt were also reported. The patient always blamed his parents, especially his dad for his ordeal, and he was always threatening to give him money to finance his drug habits. The dad revealed, that he had, before the presentation, used his 200-level school fees to learn internet fraud, popularly referred to in Nigerian parlance as 'Yahoo Yahoo', and his 300-level undergraduate fees for social activities, which included; joining and financing the activities of an outlawed organization (Cult group), night clubs and confessed to having multiple sex partners, and night clubbing. According to his account, he finally decided to change after reading the book, 'POWER TO CHANGE FOR SUCCESS'. The patient dissociated himself from friends and destroyed his SIM CARD. He also left the highbrow lodge where he was living, earlier financed with proceeds from internet fraud, for a cheaper apartment before the presentation. There was associated history of low mood, guilt feelings, lack of sleep, fear of the unknown, nightmares, and suicidal thoughts. He decided to seek medical help when people started noticing the change in his behavior, and his awareness that the substance, was affecting his brain and studies.

Past Psychiatric History, showed that this is the patient's first psychiatric consultation as she had been previously seen by general medical practitioners. In the Past Medical History, there was no history of Hypertension, Asthma, epilepsy, Diabetes Mellitus, or Sickle Cell Disease. Their family History revealed that he is the only child of his parents, in a monogamous setting. The mother is a middle-aged medical worker with a tertiary level of education. His father has a tertiary level of education and works as a supervisor in a private security firm. In their Personal history, his pregnancy was planned and labor was not complicated. Early childhood was not difficult. At the time he presented in the clinic, he was a 300-level undergraduate whose academics and psychosexual history had been complicated, with emotional trauma and multiple sex partners, with confessed patronage of commercial sex workers. Although internet fraud and membership in outlawed groups are illegal, he had never had any issues with law enforcement agents and had neither been detained before nor incarcerated, when the forensic history was assessed. Pre-morbid personality, he was said to be calm, respectful, lovable, and actively religious. Mental Status Examination, in the appearance and behavior, a well-dressed but fairly groomed young man, with occasional weepy spells, poor eye contact, and there were no abnormal involuntary movements. The speech was noted to be normal in tone, volume, and rhythm, coherent and relevant. The mood of the patient was labile. It was also noted during the examination that there was no formal thought disorder but the content of thought was essentially that of suicidal ideations, without any obvious delusions, and no perceptual abnormalities were noted. Under cognition, the patient was fully oriented to time, place, person, and circumstance. Attention, concentration, comprehension, calculation ability, and abstraction were within normal range. In addition, immediate recall, and long and short memory were within normal range. Fund of knowledge and abstract thinking were normal. Judgment was poor and Insight was full (believed he had a psychological problem and the drugs will be of benefit in his case). Neurological examination findings were normal. A diagnosis Mental and Behavioral Disorder secondary to Polysubstance Dependence(Cannabis, Alcohol, Shisha, Codeine, Crack) with co-morbid Severe Depression with Suicidal ideation, was made.

Plan

Investigations done included Complete blood count, Malarial parasite test and Widal test, Serum Electrolyte, Urea and Creatinine, Retroviral screening, and HBsAg screening, which were seronegative. The patient was managed using the bio-psycho-social model. Drug treatment was done using Intramuscular chlorpromazine, Intravenous Diazepam, and oral antipsychotic (Haloperidol), because of the abnormal behavior. The mood stabilizer used was Carbamazepine, which is also noted to reduce the craving for the substances. He was also given

an oral anti-depressant (Amitriptyline). Psychotherapy carried out involved psychoeducation, supportive psychotherapy, Motivational Enhancement Therapy, and Cognitive Behavioral Therapy (with emphasis on coping skills and assertiveness training). A family session was also held with the patient's family to educate them on the psycho-dynamic formulation of the illness and how the family can cope by listening to him, being more observant of changes in his mood and behavior, and offering support. Social treatment involved environmental manipulation or Milieu therapy, and Suicide caution. Group therapy was offered with a homogenous group of patients with similar presentations.

Progress

The patient after the first dose of Intramuscular Chlorpromazine developed a painful penile erection (Priapism), which changed the clinical picture and the course of management, making him smash his laptop computer, because of the pain. A referral made to a Urologist was declined, as he was recommending that the patient be referred, which was not possible in the immediate term. He was given Intramuscular diclofenac, Hydrocortisone, and Intravenous fluid Dextrose Saline, all of which did not bring succor to the condition the patient was experiencing. It was when Ice packs were administered in the region of the penis, that the dilation of the penile vessels caused by the cold, that there was reversal of the painful engorgement of the penis. The time between the onset of the side effect and resolution of the engorgement was 3 hours, which was within the golden hours allowed, to avoid complications.

The patient made significant clinical improvement both in the mood and psychotic symptoms and with motivation to stop the use of psychoactive substances, he was discharged one week after admission in stable health. A medical report was written to the University after about a year, certifying him medically and mentally sound to resume his studies, after 1 year of being maintained on his discharge medications. He has remained stable since discharge with no relapse noted since discharge, with his mental health and overall well-being ensured by the family support systems. On resumption of studies, there was an improvement in his academic performance.

Discussion

Conservative management though reported to have low effectiveness in Priapism was found to be an effective treatment modality, that saved the patient from distress, especially in a limited-resource hospital setting, like a psychiatric monoclinic. A recent study supports this in its conclusion, that conservative medical treatments are considered the first line of treatment in Ischemic Priapism, although there is no clear evidence regarding their efficacy [18]. The outcome of management of Priapism in this patient was good, even though according to Caprognosso et al, in 2022, conservative methods including ice packs, exercise, cold enema, and ejaculation depicted lower effectiveness in resolving priapism in 1-55% of cases. The findings in this report stress the fact that patients with priapism should be evaluated emergently to identify the sub-type of priapism. This is because priapism, as multiple reports have shown, requires prompt evaluation and usually requires emergency management [1,19]. Therefore, those with an acute ischemic event, as identified clinically in this report, should be provided early and prompt clinical intervention [20]. A previous study showed that Priapism is caused by disturbances in the mechanism controlling penile detumescence and the maintenance of penile flaccidity due to excess release of contractile neurotransmitters, malfunction of the intrinsic detumescence mechanism, obstruction of draining venules or prolonged relaxation of intracavernous smooth muscle, leading to a urological emergency [16]. That is why priapism, even from what happened in this study, is considered a urological emergency and it is advised that early measures, conservative and medical should be instituted immediately [21]. Surgical intervention with corpus cavernosum aspiration and pharmacological lavage with normal saline, and alpha-adrenergic agonists, are the most established medical treatment modality and it is advised to be instituted immediately, after the onset of priapism, in cases where it is indicated [22]. However, in this study, the patient's persistent painful erection resolved without any surgical intervention, since it was in a psychiatric setting and the Urologist called to review, declined, and asked for a referral, and also because the proximity to the urologist was doubtful, and time was of essence, the conservative measure of the use of ice packs was done, with good effects on the patient. It had been recommended in a related study that surgical shunts should be performed if non-surgical treatment had failed [6]. This patient under consideration, therefore, did not need a surgeon's attention or the use of drugs. The clinician in this study was faced with an unusual presentation, a surgical emergency, in a psychiatric ward, which initially challenged the competence and capacity of the available resources. It is a widely held evidence-based finding, that priapism is noted to be a challenging condition to manage for urologists since the etiology is often multi-factorial and the suggested treatment algorithms are based on small studies and expert anecdotal experience, perhaps due to the rarity of the disorder [4,23]. It can be associated with significant patient distress and sexual dysfunction if emergency care is not instituted early after the onset [24]. This is further stressed by the finding that this notable urological emergency, has over 90% of those who remain erect for 24 hours losing sexual function [25]. The longer time interval from the onset to the resolution of Ischemic Priapism was associated with a higher rate of erectile dysfunction at follow-up (30-70%), especially after 24 hours [18]. Furthermore, another study found that Ischemic priapism of more than 36 h is frequently associated with permanent erectile dysfunction [26]. The possibility of cannabis use as a risk factor in this patient being reported was highlighted in a case report which illustrates that a variety of illicit drugs had been associated with priapism but cannabis was first associated with priapism in a healthy 32-year-old African American man with a history of stuttering (recurrent) priapism secondary to mild cannabis substance use [25]. A case report suggests that topiramate might induce ischemic priapism, experienced in a patient with Bipolar Affective disorder, that led to a medical admission and surgical intervention directly or through interactions with other medications [27]. Clinicians, including psychiatrists, should be aware priapism resulting from antipsychotic drugs is rare and few cases were reported, but it

is an important condition [23]. Antipsychotic drugs including, chlorpromazine, thioridazine, and risperidone have been reported as a causative factor of priapism [28]. Concerning priapism induced by chlorpromazine, just a few reported cases have been mentioned in literature and most of them were due to overdose, long-term therapy of psychiatric illness or interaction as well as Combined use of antipsychotics, psychostimulants, antidepressants, and mood stabilizers such as Risperidone, quetiapine, methylphenidate and Trazadone [14]. In this patient, administration of the Chlorpromazine was via the intramuscular route, administered by the nursing staff. leading to Iatrogenic priapism, which is a notable cause of veno-occlusive priapism [8]. Available literature shows only one case of priapism was reported after self-administered chlorpromazine via the trans-urethral route [29]. In addition, only a few case reports have discussed priapism occurring after a short-term administration of chlorpromazine, as our case report, which occurred after a single low-dose intramuscular administration of the drug [14]. The complexities in the management of priapism are because it has remained controversial and continued to pose challenges to urologists. It is noteworthy that Priapism management depends on the type of priapism, with medical treatment (corporal aspiration and injection of sympathomimetics) reported to be the mainstay of treatment, but if it fails, surgery is indicated for ischemic priapism [8]. In other to avoid complications, the management of ischemic priapism should achieve resolution as promptly as possible [20]. Recent and more thorough knowledge of the pathophysiological basis of priapism and the clear differentiation between the low flow veno-occlusive priapism and high-flow arterial priapism have significantly improved the diagnostic protocol for patients with priapism [22]. It is advocated therefore that treatment of the acute ischemic patient must be based on patient objectives, available resources, and clinician experience, as was the case in this patient being reported [4]. Consequently, a single pathway for managing the disorder of priapism condition is oversimplified and no longer appropriate. The importance of investigations and the consequences of their unavailability can delay the diagnosis and early intervention had been variously mentioned. In this regard, Color doppler ultrasound evaluation and cavernosal blood gas determinations have become mandatory and had greatly improved specific diagnoses [22]. Lab investigations like Complete Blood Count, reticulocyte count, Hemoglobin-electrophoresis, psychoactive medication screening, and urine toxicology, also help to rule out the other causes of Priapism like; sickle cell disease, leukemia, and drug abuse [23,30]. In light of the above findings in this study, awareness of these associations and an appreciation of the potentially serious consequences of this disorder may assist clinicians in choosing psychotropic agents that minimize the risk of developing priapism [3]. Patients who are to receive psychotropic medications be forewarned about priapism and patients must be questioned concerning the prior occurrence of prolonged erections since a history of delayed detumescence is present in approximately 50% of subsequent cases of priapism [9]. The possibility of this adverse drug reaction to antipsychotic use makes it imperative that physicians must be alert and knowledgeable about this life-threatening adverse drug reaction [12,31]. Patients taking trazodone and/or antipsychotics need to be aware of the priapism risk; awareness among prescribers would help in reducing priapism-related detrimental sequelae [32]. Early diagnosis and proper, and institution of rapid management in such cases, could lead to favorable prognoses and better outcomes.

Conclusion

Given its time-dependent and progressive nature, priapism is a situation that both urologists emergency medicine practitioners, and clinicians must be familiar with conservative, medical and surgical management. It is a condition that often requires early emergency treatment to spare erectile function of those affected. Clinicians should be aware of this rare side effect because of the severity of its complications and the difficulty of its management, especially in non-stabilized psychotic patients and resource poor-settings.

Recommendation

Clinicians should be guided by the Urology Guideline on Priapism, which addresses the role of imaging, adjunctive laboratory testing, early involvement of urologists when presenting to the emergency room, discussion of conservative therapies, and enhanced data for patient counseling on risks of erectile dysfunction, its surgical complications and the crucial nature of multidisciplinary approach in the management of Priapism.

Consent

Written informed consent was obtained from the patient and parents for publication of this case report.

Ethical Approval

Informed consent, protection of privacy, and other human rights were ensured in the course of this report. Approval was gotten from the private hospital, where the patient was reviewed. This confirms that this study is neither against the public interest nor violates the conditions for the release of patient information allowed by legislation.

Author's Contribution

Nwaopara Uche, designed the manuscript and the introduction, Nwaopara Uche, and Watson-Aputu, F, were involved in the management of the patient, Nwaopara Uche and Nwaopara Beatrice were involved in the discussion. All authors read and accepted the publication of this article.

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