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1 2	High-Flow Priapism following Chlorpromazine Induced Low-Flow Priapism
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7 Abstract

⁸ Priapism is defined as a penile erection that persists more 4 hours or longer and is unrelated

⁹ to sexual activity. The three main subtypes are low flow (ischemic), high flow (nonischemic)

¹⁰ and stuttering (intermittent or recurrent) priapism. Alpha-1 antagonistic activities of some

¹¹ antipsychotics, especially chlorpromazine, have been reported to be responsible for

¹² development of low-flow priapism. Chlorpromazine has the greatest alpha-adrenergic affinity

¹³ among the conventional antipsychotic agents and the most frequently reported to be

 $_{14}$ $\,$ associated with priapism. We report a case of priapism after a first single dose of

¹⁵ chlorpromazine (Neurazine ® 100 mg tablet, Misr Co. For Phramind-Egypt). The case was

¹⁶ presented first by neglected low-flow priapism that had been converted to high-flow priapism

¹⁷ due to injury of a branch of the cavernosal artery, during aspiration and irrigation treatment

¹⁸ procedure, proved by blood gas testing of the aspirated penile blood, penile color duplex

¹⁹ Doppler ultrasonography and selective left internal pudendal arteriogram. This conversion is

 $_{\rm 20}~$ an uncommon complication of such procedure.

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22 Index terms—

²³ 1 High-Flow Priapism following Chlorpromazine Induced Low ²⁴ Flow Priapism

Mohamed Saad Hegazy ? & Mustafa MR ? Abstract-Priapism is defined as a penile erection that persists more 4 hours or longer and is unrelated to sexual activity. The three main subtypes are low flow (ischemic), high flow (nonischemic) and stuttering (intermittent or recurrent) priapism. Alpha-1 antagonistic activities of some antipsychotics, especially chlorpromazine, have been reported to be responsible for development of low-flow priapism.

Chlorpromazine has the greatest alpha-adrenergic affinity among the conventional antipsychotic agents and the most frequently reported to be associated with priapism. We report a case of priapism after a first single dose of chlorpromazine (Neurazine ® 100 mg tablet, Misr Co. For Phramind-Egypt).

The case was presented first by neglected low-flow priapism that had been converted to high-flow priapism due to injury of a branch of the cavernosal artery, during aspiration and irrigation treatment procedure, proved by blood gas testing of the aspirated penile blood, penile color duplex Doppler ultrasonography and selective left internal pudendal arteriogram. This conversion is an uncommon complication of such procedure.

³⁷ 2 I. Case Report

24-year-old male patient presented with priapism to our Andrology Department, Kobry El-Koba Military Armed
Forces Medical Complex, Cairo-Egypt. He was fully awake, sitting calm and alert. On, Inspection, the penis
was fully erected and has a dorsoventral oscillatory movement (atrial pulse). Although the shaft was very rigid

41 on palpation, the glans penis was semi rigid with no tenderness. Patient is not married, not known to have

hypertension, sickle cell trait, history of malignancy. He denied any previous episodes of priapism, recent sexual
 activity or arousal, use of phosphodiesterase inhibitors or perineal trauma.

Three weeks before the patient came to us, he experienced agitation and insomnia for which he took a first 44 single dose of chlorpromazine (Neurazine ® 100 mg tablet, Misr Co. For Phramind.-Egypt). He had observed a 45 prolonged penile erection 5 hours after taking chlorpromazine. The patient did not give a care for his priapism 46 for the first 18 hours. However, as his penile erection became painful and did not resolve spontaneously and 47 after repeated ejaculation trials, he went to ER of Embaba General Hospital in next 24 hours. He was in obvious 48 physical pain and reported that the erection had remained rigid throughout the entire 36hrs since becoming 49 tumescent. Urologists had performed two sessions of intra-corporeal injection of 1 mg ephedrine, drainage, and 50 irrigation with sterile saline that were not sufficient to obtain de-tumescence and they transferred the patient 51 to Andrology Specialty Center and Department, Kasr El-Ainy Faculty of Medicine, Cairo University in the next 52 day. Andrologists admitted the patient and diagnosed him to have a lowflow priapism by penile duplex Doppler 53 ultrasonography with multiple intra-cavernosal fibrosis and echogenic blood clots. Corporal aspiration revealed 54 dark, red blood with a pH of 7.24, pO2 of 20, and pCO2 of 65, consistent with low-flow, ischemic priapism. Since 55 then, intra-corporeal injection of 1 mg ephedrine, drainage, and irrigation with sterile saline were handled at a 56 57 rate of 3 cycles per session for 2 sessions over the first 24hrs and de-tumescence was achieved with some residual 58 corporal edema. Unfortunately, the corporal bodies were again fully erect, but surprisingly not painful. Many 59 sessions of intra-corporeal injection of alpha-adrenergic receptor agonists with aspiration and ice-pack compression 60 in between were done for the next consecutive 6 days without improvement. They discharged the patient thereafter 61 as the patient refused surgical intervention. As long as erection was inevitable yet; patient came to us on day 23 rd since becoming tumescent and he 62

was admitted in our andrology in-patient unit, where basic laboratory investigations including: complete blood 63 counts, coagulation profile, electrolytes, hepatic and renal function and sickle cell tests were done. All laboratory 64 investigations were normal except for mild leukocytosis (TLC=14.2). Penile arterial blood gas (ABG) from 65 the lateral base of the corporal body was obtained. The latter was consistent with high-flow priapism (bright 66 red blood with a pH of 7.45, pO2 of 90, and pCO2 of 35). Penile duplex Doppler ultrasonography revealed 67 bilateral echogenic, distorted cavernosa reflecting significant bilateral corporal fibrosis and the sinusoids are 68 typically not compressible with probe pressure and engorged with sinusoidal thrombosis. Doppler assessment of 69 the both left and right cavernosal artery, revealed significantly reduced arterial flow (<10 cm/s) giving picture of 70 71 low-flow priapism except for a turbulent arteriocavernosal fistula which was determined with high-velocity and 72 low-resistance flow (>90 cm/s) within the left proximal corpus cavernosus (peri-lacunar) (fig. ??) giving a picture of high-flow priapism. Selective left internal pudendal arteriogram confirmed a large fistula arising from the peri-73 lacunar area of left corpus cavernosus (fig. ?? This treatment strategy is continued, except for the antibiotic 74 (only 7 days), and priapism is not resolved yet, the rigidity is decreased by 20%, which is retained whenever 75 sexual arousal is present and decreased back by 20% after masturbation. Follow up was handled monthly for 76 18 months without any other complications except for the persistent penile erection, which is still surprisingly 77 tumescent. The case will be presented later on to report the efficacy of the new non-surgical treatment strategy 78

79 we followed.

⁸⁰ 3 II. Discussion

Priapism is defined as a penile erection that persists for 4 hours or longer and is unrelated to sexual activity that was first described in medical literature in 1845 1. The corpus cavernosa consist of vascular spaces called sinusoids, which include smooth muscles on their walls. Arterioles in the penis that supply blood to the corpus cavernosa are in a tonic state during flaccid periods 2. The three main subtypes are low flow (ischemic), high flow (non-ischemic) and stuttering (intermittent or recurrent) priapism 3. The identification of priapism subtype is important as delayed emergent medical interference (particularly in low flow ischemic subgroup) can result in persisting erectile dysfunction 1,3,4.

Patients with low-flow priapism will often present with rigid corpus cavernosa and pain, whereas those with high-flow priapism will often present with tumescent but not rigid corpus cavernosa and seldom report pain. The most considerable modalities to distinguish lowand high-flow priapism are blood gas testing and color Doppler ultrasonography 5. Low flow priapism is characterized by a reduced venous outflow, hypoxia, rising PaCO2 and acidosis that can cause progressive ischemia within the cavernosal tissue with timedependent changes in the corporal metabolic environment. This lead to smooth muscle irreversible injury and necrosis to the erectile tissue with consequent fibrosis of the corporas 3,6.

95 Alpha-1 antagonistic activities of some antipsychotics, especially chlorpromazine, have been thought to be 96 responsible for development of priapism. Based on their ability to block the ?-adrenergic receptors of sinusoidal 97 smooth muscles, they lead to a reduction in resistance and uncontrolled blood flow into the corpora cavernosa 98 2,7,8. Chlorpromazine has the greatest alpha-adrenergic affinity among the conventional antipsychotic agents and the most frequently reported to be associated with priapism 7.8. It had been reported that, priapism 99 occurred in a patient after he had taken one 25-mg tablet of chlorpromazine (the lowest dose to produce this 100 complication). On contrary, another patient developed priapism after he had been using chlorpromazine for 3 101 years. In our case report, the patient developed low-flow priapism after taking his first single 100-mg tablet of 102 chlorpromazine. This shows that priapism can occur after short-term or long-term and even after high or low 103

dose therapy with chlorpromazine 9. So, it is believed that low-flow priapism is not a dose-or duration-specific
 complication to chlorpromazine as has been reported in different studies 2,7,8,10,11.

High-flow priapism is a persistent erection caused by unregulated cavernous arterial inflow 4. The usual cause 106 of high-flow priapism is blunt perineal trauma. However, it may be associated with metastatic malignancy to the 107 penis, with acute spinal cord injury and occasionally may complicate low-flow priapism after shunt procedures 4,12 108 . Moreover, high-flow priapism caused by iatrogenic needle trauma during pharmacological agent injections in the 109 cavernosal body, as a treatment of early cases of low-flow priapism, is considered as an uncommon complication of 110 such procedure. This may occur due to a lacerated cavernous artery or one of its branches leading to a high-flow 111 fistula between the artery and the lacunar spaces of the sinusoidal tissue 13,14. During priapism, the edematous 112 corporal state, septal and/or intra-corporal fibrosis may anchor the cavernous arteries to a more eccentric place 113 immediately adjacent to the intercorporal septum. These arteries are therefore become relatively fixed and are 114 possibly more susceptible to needle injury during corporal aspiration as happened in our case report 13. 115

¹¹⁶ 4 III. Conclusion

It seems hard to predict the dose and/or duration that may cause priapism with antipsychotic medications, especially chlorpromazine, as discussed before. Among patients treated for low-flow priapism, who retain penile tumescent, a penile ABG determination and penile ultrasound are essential for early detection of converted priapism from low to highflow priapism. Selective internal pudendal arteriogram is the golden standard technique to diagnose and treat (arterial embolization) high-flow priapism due to arterial fistulae. However, in our case, nonsurgical treatment strategy is continued for about 2 years. This acquires a promising strategy as it has reduced the risk of corporal fibrosis and its complications such as irresponsive penile erection on sexual excitation.

¹²⁴ 5 IV. Recommendations

Clinicians should be familiar with infrequent serious adverse events of antipsychotic medications especially chlorpromazine. Performing the corporal aspiration, irrigation and injections of alpha-adrenergic receptor agonists in low-flow priapism, under the guidance of penile duplex Doppler ultrasonography to prevent injury of corporal vessels during procedure and thus preventing conversion of low-flow priapism into high-flow one.Further prospective studies on larger number of cases are recommended in order to evaluate the effectiveness of non-surgical systemic oral medications versus the invasive surgical procedures especially in neglected cases of priapism.



Figure 1: Figure 1 Figure 2 High



Figure 2: Figure 4 HighFigure 9 Figure 10 High-

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Figure 3:



Figure 4:



Figure 5:



Figure 6:



Figure 7:



Figure 8:

					-
10).Medical	interference	was	postponed		(no
embolization)	according	to	the	patient's	
decision.					

Figure 9:

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