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Stuttering priapism in a case of Sickle Cell Disease – A case report

Amol Andhale[1], **Abhijit Dhale**[2], **Sourya Acharya**[3]✉, **Anuj Varma**[4], **Nakul Kadam**[5]

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Author Affiliation:
[1]Resident, Dept of Medicine, Jawaharlal Nehru Medical College and Datta Meghe Institute of Medical Sciences (Deemed to be University) Sawangi (Meghe) Wardha-442001 Maharashtra, India
[2]Professor, Dept of Urosurgery, Jawaharlal Nehru Medical College and Datta Meghe Institute of Medical Sciences (Deemed to be University) Sawangi (Meghe) Wardha-442001 Maharashtra, India
[3]Professor and HOD, Dept of Medicine, Jawaharlal Nehru Medical College and Datta Meghe Institute of Medical Sciences (Deemed to be University) Sawangi (Meghe) Wardha-442001 Maharashtra, India
[4]Asso. Prof, dept of Medicine, Jawaharlal Nehru Medical College and Datta Meghe Institute of Medical Sciences (Deemed to be University) Sawangi (Meghe) Wardha-442001 Maharashtra, India
[5]Asst. Prof, dept of Medicine, Jawaharlal Nehru Medical College and Datta Meghe Institute of Medical Sciences (Deemed to be University) Sawangi (Meghe) Wardha-442001 Maharashtra, India

✉**Corresponding author**
Professor and HOD, Dept of Medicine, Jawaharlal Nehru Medical College and Datta Meghe Institute of Medical Sciences (Deemed to be University) Sawangi (Meghe) Wardha-442001 Maharashtra, India;
Email: souryaacharya74@gmail.com

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ABSTRACT

Priapism is a painful penile erection unrelated to sexual desire. It can be graded as low flow (ischemic) or high flow (non-ischemic). Low-flow priapism accounts for most cases of priapism in SCD individuals. Stuttering priapism is an ischemic variant characterized by short repeated episodes of intermittent, self-restricted priapism, which are also known as chronic ischemic priapism. Each episode usually lasts for two to three hours. The common hematologic conditions associated with priapism are sickle cell disease, leukemia, thalassemia, multiple myeloma, thrombotic thrombocytopenic purpura. We report a case of a 17 year old male, who had recurrent episode of stuttering priapism over 3 to 4 years and finally presented to us with an episode of ischemic priapism lasting for more than 36 hours.

Keywords: priapism, penile erection, ischemic, sickle cell

1. INTRODUCTION

Priapism is a common complication of sickle cell disease (SCD) in men (penile erection in the absence of sexual activity or desire). Priapism is characterized as a chronic, sexually unrelated penile erection. The vast majority of cases of priapism in individuals with SCD are triggered by low-flow priapism. Over time, repeated episodes have caused permanent damage and erectile dysfunction. Priapism is therefore considered to be a medical emergency in which prompt diagnosis and adequate treatment are vital to the maintenance of normal functioning.

Low-flow priapism – Low-flow priapism (also called ischemic or venocclusive priapism) accounts for more than 95% of SCD. (Anele et al., 2015) It is linked to reduced or absent blood flow in the penile arteries caused by high pressure in the corporal sinuses of the cavernosa, causing severe rigidity and discomfort, similar to contrast syndromes in other parts of the body. Although ischemic priapism may last for any amount of time, the longer the erection period, the more likely it is to cause permanent damage to the penile tissue. Episodes lasting up to 4 hours (sometimes called big episodes) are of particular concern because of the greater risk of permanent tissue damage associated with ischemia during this period of time. Tissue necrosis

and scarring may occur beyond 24 hours, leading to erectile dysfunction (ED). Stuttering priapism – Stuttering priapism is an ischemic variant characterized by brief, recurring, acute, self-limited priapic episodes (Morrison et al., 2012). Every episode normally takes up to few minutes to three hours. The episodes are traumatic and not linked to sexual desire, as are other forms of ischemic priapism.

ED (Erectile dysfunction) is commonly characterized as the inability to achieve or maintain an erection that is sufficiently firm for coitus. ED is a common complication of priapism in SCD and is the product of repeated ischemia-inducing tissue damage episodes that interfere with normal vascular changes resulting in erection (Halawani et al. 2020). Penis' basal, flaccid state is sustained by inputs from the sympathetic nervous system that create high vascular, smooth muscle tone. Penile erection usually occurs in response to parasympathetic nervous system inputs (e.g., genital stimulation, or psychosexual excitement). Such parasympathetic inputs improve blood flow to the penis through the cavernous and helical arteries, filling the sinusoids and contributing to distension of trabecular cavernosal tissue (Bivalacqua et al., 2012). Distension of the cavernosal tissue, in effect, decreases venous outflow and enables sustained engorgement (Anele et al., 2015).

Low-flow priapism occurs when the venous outflow from the penis is impaired; the penile compartment has elevated pressure that prevents normal blood circulation, leading to hypoxia, acidosis and tissue ischemia. Nitric oxide (NO) signaling is a significant mediator of erection; it induces smooth muscle relaxation in response to parasympathetic inputs. NO is formed by NOS in neuronal and endothelial cells, using arginine and oxygen as precursors (Donaldson et al., 2014). NO spreads readily into smooth muscle cells in cavernosal artery and sinusoidal space where it stimulates guanylate cyclase, resulting in increased cyclic guanosine monophosphate (cGMP). cGMP-dependent protein kinases produce signals that eventually decrease intracellular calcium, leading to smooth muscle relaxation, vasodilatation, and increased blood flow to penis.

The erectile response ends when phosphodiesterases (PDEs; particularly PDE-5, the erectile dysfunction drug target) hydrolyze and inactivate cGMP, leading to smooth muscle contraction. This process doesn't seem to function normally in certain SCD individuals. This may be because NO signaling often controls PDE-5 protein expression; when NO is chronically reduced (as in individuals with SCD), PDE-5 levels are lower and erection termination set point is changed (Bivalacqua et al., 2012; Kato, 2012). Increased priapism risk in setting a low NO state is counterintuitive as penile erection requires high NO rates. In cases of chronically low NO and low PDE-5, the penile vasculature may become hypersensitive to other sources of cGMP and may lack a mechanism to hydrolyze cGMP and end an erection.

Individuals with SCD have reduced NO-levels. This is due to chronic hemolysis that releases free hemoglobin into the plasma, serving as a potent NO scavenger (Kato et al., 2012; Kato et al., 2007). Hemolysis also releases arginase into circulation; arginase depletes NO by metabolizing arginine into ornithine. Excess superoxide anion, a by-product of oxidative stress, can also minimize NO. In a case-control study analyzing data from participants in the Sickle Cell Disease Cooperative Study (CSSCD), individuals with a history of priapism had evidence of more clinically serious SCDs, including higher levels of stroke, acute chest syndrome, and acute painful episodes, as well as elevated hemolysis laboratory markers such as lower hemoglobin, higher reticulocyte production, Reduced NO bioavailability to lead to pulmonary hypertension in SCD

2. CASE REPORT

A 17 year old male, a diagnosed case of SCD, presented to us with painful penile erection of 36 hours duration. SCD was diagnosed 10 years back. Since then the patient was on tab. folic acid 5 mg/day and tab. Zinc 25 mg/day. On asking leading questions the patient revealed about 6 episodes of priapism over 3 to 4 years each lasting less than 3 hours. He used to visit local practitioner for the attacks who would give some medications. This time the priapism did not respond to the medications and the patient thought it would resolve on its own. When the pain increased and he did not get relief waiting for such long, his father decided to come to this hospital.

On examinations: Pulse-108/min, regular. Blood pressure - 100/70 mm hg, right arm supine position. Icterus present, clubbing, and lymphadenopathy are absent. CVS, RS, Per Abdomen and CNS examination was normal. Local examination of penis revealed an enlarged, tender penis Fig 1.

Routine investigations revealed Hb – 9.8 gm%, WBC – 29000 / cu.mm, Platelet count was 2.12 lakhs/cu.mm, Total bilirubin – 5.8 mg/dL , Urea – 29 mg/dl, creatinine – 0.2. mg/dl, Sodium – 147 mEq/lit, Potassium – 5.1 mEq/lit. Total protein was 7.9 g/dl, serum albumin-3.8 g/dl. Repeat Hb- electrophoresis revealed "SS" pattern.

Management was started with aspiration of blood from the corpus cavernosum, with saline irrigation, followed by injection of an alpha-adrenergic agonist, but detumescence was not achived within 12 hours. So a surgical T-shunt was performed. The corpora cavernosa were milked to remove all traces of old blood. The priapism resolved completely by the end of the procedure (Fig. 2 a, b).

Figure 1 howing enlarged, tender penis

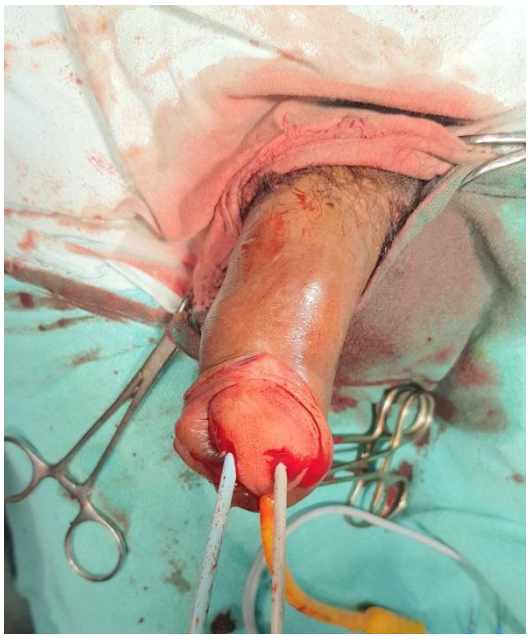

Figure 2 (a) Showing Surgical corpora cavernosa-glans T-shunts

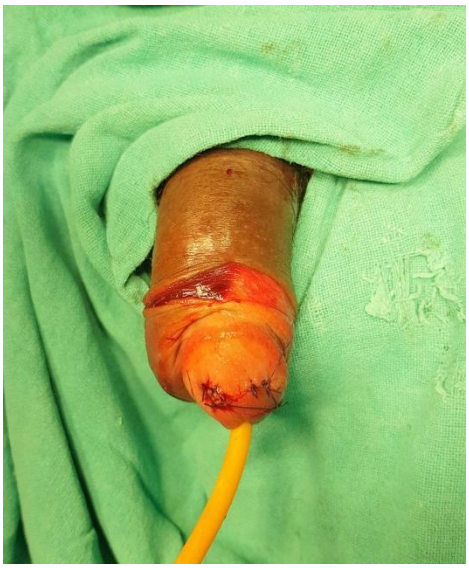

Figure 2 (b) Detumescence penis

Post operatively patient was started on IV antibiotics, opioids analgesics and tab. Finasteride 5 mg OD. USG local site of penis showed normal penial artery flow. Left cavernosal artery showed reduces flow and right cavernosal artery flow could not be visualized probably due to severe edema of carpora cavernosa fig. 3 a, b. In view of impaired flow in right cavernosal artery a proximal shunt surgery was done. The patient was discharged.

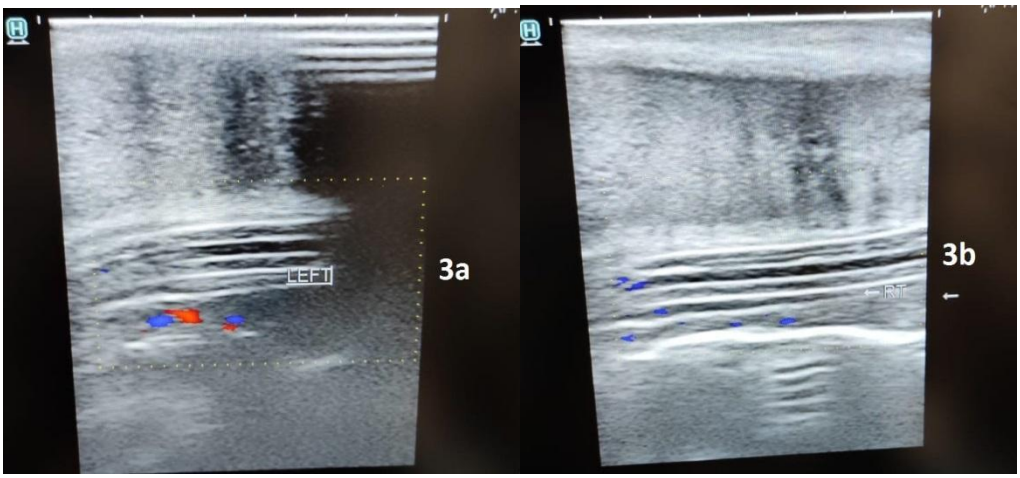

Figure 3 (a) showing normal penial artery flow. b) Left cavernosal artery shows reduce flow and **b)** Right cavernosal artery flow could not be visualized probably due to severe edema of carpora cavernosa.

3. DISCUSSION

"Priapism" comes from Priapus meaning; the lord of fertility, gardening, desire and presents with a gigantic phallus (Papadopoulos & Kelami, 1988). Priapism is characterized as a continuous penis erection unrelated to sexual stimulation. Priapism can occur any time. However, some studies identify a bimodal incidence distribution. The ranges given are 5-10 years in children and 20-50 years in adults (Cherian et al., 2006). Priapism can be ischemic (low-flow or veno-occlusive), nonischemic Priapism (high-flow or arterial), and stuttering priapism (recurring or intermittent).

Ischemic priapism is the most common form, causing > 95% of cases (Broderick et al., 2010). It is characterized by pronounced limitation of cavernous arterial flow (Rees et al., 2002). If left untreated, ischemic priapism can cause ischemia, necrosis and subsequent penis fibrosis and erectile dysfunction (Rees et al., 2002). Stuttering priapism is a form of ischemic priapism most prevalent in patients with sickle cell disease. It has a similar appearance to ischemic priapism, and is characterized by recurring episodes that typically resolve by themselves but last less than three hours (Kheiranish et al., 2011). The underlying pathophysiology of this condition points to the deficiency of endothelial nitric oxide in the penis which causes downstream effectors to be downregulated (Kheiranish et al., 2011). This allows the cavernous, smooth muscle regulation to work at a lower level. Thus, any form of stimulus can cause an erectile episode for an extended period of time.

A variety of diagnostic methods can diagnose priapism. History and physical inspection are important in this regard. Analyzing blood gases can distinguish arterial and ischemic forms. It has $pO2 < 40$ mmHg, $pCO2 > 60$ mmHg and $pH < 7.25$. Color duplex ultrasound also plays a role in differentiating the two forms and can distinguish 70% of arterial priapism cases (Hakim et al., 1996). There are several approaches to handle stuttering priapism which include medical and surgical modalities. Prolonged cases and progress to ischemic form require immediate treatment using corporal aspiration along with phenylephrine injections (Montague et al., 2003). Prophylactic therapy can be used in patients with repeated episodes. Both may be hormone-releasing hormone (GnRH) agonists or antagonists in nature, diethylstilbestrol, or ketoconazole. Other potential effects include pseudoephedrine, digoxin, terbutaline, etilefrine, phosphodiesterase-5 (PDE5) inhibitors, and gabapentin (Kheiranish et al., 2011).

In a prospective study administering finasteride to 35 individuals with SCD and recurrent priapism, the frequency of episodes decreased (Rachid-Filho et al., 2009). The initial dosage was 5 mg daily, reduced after 40 days to 3 mg daily and 80 days to 1 mg daily. Where the conservative solutions are exhausted and the episode does not resolve, surgical options such as a shunt between corpora cavernosa and glans or corpus spongiosum may be considered (Kheiranish et al., 2011). If the patient still has priapism even after shunting, implantation of a penile prosthesis can help preserve sexual function and penile length (Ralph et al., 2009).

The initial management of this case was done by corporal aspiration followed by phenylephrine injection. As detumescence was not achieved, a surgical T- shunt was carried out which established detumescence. Prophylactically 5 alpha reductase inhibitor

(Fenesteride) was prescribed. Our patient presented to us after 72 hours (big episode), so the parient's father was counseled about permanent erectile dysfunction and the requirement of penile prosthesis.

4. CONCLUSION

Stuttering priapism is an ischemic variant characterized by brief, recurring, acute, self-limited priapic episodes. Every episode normally takes up to few minutes to three hours. The episodes are not linked to sexual desire. The pathophysiology of this type of priapism is not fully understood. A mechanism based on dysregulation of nitric oxide and 5 alpha reductase inhibitor in the corporal smooth muscle has been proposed. It is a serious medical emergency condition if untreated, early treatment may decreases the further complications.

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Authors' contributions

Sourya Acharya, Amol Andhale: Primary author read and approved the final manuscript.

Abhijit Dhale, Anuj Varma, Nakul Kadam: This work carried out in collaboration among all authors. All authors read and approved the final manuscript.

Conflict of Interest

The authors declare no conflict of interest.

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Abbreviations

Sickle cell disease	SCD
Erectile dysfunction	ED
Nitric oxide	NO
Cyclic guanosine monophosphate	cGMP
phosphodiesterases	PDE

Informed consent

Written & Oral informed consent was obtained from all individual participants included in the study. Additional informed consent was obtained from all individual participants for whom identifying information is included in this manuscript.

Data and materials availability

All data associated with this study are present in the paper.

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