CASE REPORT

Priapism in a patient with sickle cell trait using marijuana

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SUMMARY

A 22-year-old man with a history of multiple episodes of priapism presented to the emergency room with an erection lasting more than 48 h after conservative management failed at home. He had no known family history of sickle cell disease or trait. He was haemodynamically stable. Physical examination revealed an enlarged, tender penis. Laboratory data revealed a positive sickle solubility test. Haemoglobin electrophoresis revealed sickle cell trait and urine drug screen was positive for cannabinoids. Initial management was attempted with intracavernosal phenylephrine without any success. The patient underwent a limited El-Ghorab procedure on the right corpora cavernosa but the priapism did not resolve adequately. Two days later, the patient had to undergo a bilateral El-Ghorab procedure and achieved complete resolution of the priapism.

BACKGROUND

Priapism is a well-known complication of sickle cell disease (SCD) that could lead to erectile dysfunction and psychosocial problems. However, very few cases of priapism have been described in patients with sickle cell trait (SCT). In this article, we present a case of priapism in SCT followed by a detailed discussion about the natural history of SCT, its pathogenesis and the possible role of marijuana in precipitating an attack in SCT, its complications and management of priapism. It is very important for physicians to be aware of the initial management as any delay in care can result in permanent erectile dysfunction. The effects of cannabinoids (CBs) on human penile tissue and role of marijuana in priapism need to be investigated further.

CASE PRESENTATION

A 22-year-old man presented to the emergency room with a persistent painful erection for more than 48 h. He had six similar episodes in the past which were of very short duration and resolved with conservative management with ice packs at home. He denied any other medical history. He was of a mixed African-American, Caucasian and Native American descent. He was never diagnosed with SCD and had no known family history of SCD or trait. He admitted to tobacco, alcohol and marijuana misuse. He denied taking any over-the-counter or herbal medications.

Blood pressure was 125/82 mm Hg, heart rate 79/min, respiratory rate 18/min and temperature was 98.4°F. Physical examination revealed an enlarged, tender penis.

INVESTIGATIONS

Laboratory data revealed a normal haemoglobin (Hb) level of 14 g/dL. Rest of the laboratory data is summarised in table 1.

Peripheral blood smear showed rare sickled red blood cell (RBC), ovalocytes and normal-shaped RBC. The sickle solubility test was positive. Hb electrophoresis showed adult Hb (Hb A) 56% (reference range: 94–99%), Hb A2 2.7% (reference range: 2–3.5%) and sickle Hb (Hb S) 41.3% (reference range: <2%) confirming the diagnosis of SCT. Urine drug screen was positive for tetrahydrocannabinol.

TREATMENT

Intramuscular epinephrine and intracavernosal phenylephrine were tried without success. The patient underwent a corpora cavernosa-glans shunting (El-Ghorab procedure) on the right side. Significant fibrosis was noted under the skin of the glans on the right side during the procedure. The shunting was performed only on one side to preserve erectile function and aid a speedy recovery. Adequate resolution of the priapism was achieved. He was discharged home the same day.

The patient presented to the emergency room 2 days later, again with a painful erection. He was haemodynamically stable. Physical examination revealed a partial penile erection. He was taken to the operating room again and the El-Ghorab procedure was repeated on both sides. Intraoperative irrigation of the cavernosa with normal saline returned dark, old blood. The corpora cavernosa were milked to remove all traces of old blood. The priapism resolved completely by the end of the procedure.

OUTCOME AND FOLLOW-UP

The priapism resolved completely by the end of the procedure. Three-month follow-up revealed no further episodes of priapism but the patient's erectile function was severely affected. The patient was offered a penile prosthesis but he refused the same.

DISCUSSION

Epidemiology

SCT affects approximately 2.5 million people in the USA and 300 million people worldwide.[1] The condition is more prevalent in sub-Saharan Africa, middle-east, Mediterranean countries and parts of

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Table 1 Complete blood panel

Laboratory	Patients value	Reference range
Haemoglobin	14	13–15 g/dL
Haematocrit	40.3	40–50%
Red blood cells	4.43	4.6–6.8×10^6/μL
Leucocytes	9.4	3.6–10.3×10^3/μL
Mean corpuscular volume	91	80–98 fL
Mean corpuscular haemoglobin	31.6	25–34 pg
Mean corpuscular haemoglobin concentration	34.7	31–36 g/dL
Red cell distribution width	14.1	11–16.3
Platelets	204	140–420×10^3/μL

India.[2] It offers a survival advantage against *Plasmodium falciparum*.[3] SCT does not alter life expectancy.[4]

Aetiology and genetics

A glutamic acid to valine substitution at the sixth position of one of the β-globin chains of human Hb A results in the formation of Hb S. Homozygosity of this mutation (Hb SS) results in SCD and inheritance of only one Hb S allele results in Hb AS and the resulting condition is SCT. SCD is transmitted in an autosomal recessive fashion.

Pathogenesis

The pathogenesis of SCT and SCD is identical. Deoxy Hb S is poorly soluble and polymerises to form elongated rope-like fibres in hypoxic or acidic environments which decrease the RBC elasticity and lead to the classical sickle shape. The sickle-shaped RBC cannot manoeuvre the capillaries and lead to vaso-occlusive crisis which in turn leads to tissue ischaemia and acidosis which further propagate the vicious cycle. The degree of polymerisation depends on the relative concentration of Hb S, Hb A and Fetal Hb within the RBC. The proportion of Hb S within the RBC in SCT is less compared with SCD which explains the relative rarity of acute vaso-occlusive episodes in patients with SCT compared with SCD.

Screening/diagnosis

All newborns are screened for SCD in the USA. All positive results are reported to the State Department of Health. Adults presenting with symptoms suggestive of sickle haemoglobinopathy are screened with the sickle solubility test which can detect sickle Hb concentration as low as 8–10%. The screening tests cannot distinguish between SCT and SCD. Hb electrophoresis or high-performance liquid chromatography is performed for confirmation.

Clinical features of SCT

SCT is mostly asymptomatic. Tsaras *et al*[1] classified the clinical complications of SCT as (1) definite: renal medullary carcinoma, haematuria, renal papillary necrosis, hyposthenuria, splenic infarction, exertional rhabdomyolysis, exercise-related sudden death and protection against severe falciparum malaria; (2) probable: complicated hyphema, venous thromboembolism (VTE), fetal loss/demise and low birth weight; (3) possible: acute chest syndrome, asymptomatic bacteriuria in pregnancy and proliferative retinopathy and (4) unlikely: stroke, cholelithiasis, priapism, leg ulcers and avascular necrosis of the femoral head.

There has been growing concern over the past several decades about the association of SCT and exercise-related morbidity and mortality in collegiate athletes and military recruits. The strongest epidemiological data supporting this association comes from an epidemiological review of over two million military recruits during 1977–1981. It showed that among the African-American recruits, those with SCT were 27.6 times more likely to suffer sudden unexplained death than those without Hb S; and among all recruits, those with SCT were 39.8 times more likely to suffer sudden unexplained death than those without sickle haemoglobinopathy.[5] These deaths were believed to be secondary to exercise-related rhabdomyolysis, heat stroke, acute kidney injury, disseminated intravascular coagulation and cardiac arrythmias.[1 2] The College of American Pathologists (CAP) recommends athletic programmes offer screening for SCT status in all athletes at risk for this disease as part of preparticipation physical examinations. The National College Athletics Association (NCAA) has made SCT screening mandatory for all student–athletes participating in division I and II sports in the USA.[6]

Although VTE was reported to be associated with SCT, a recent study by Pintova *et al*[7] involving 12 429 pregnant women showed no increase in incidence of VTE in African-American patients with SCT when compared with either pregnant non-SCT African-American patients or pregnant Caucasian patients. Renal manifestations of SCT include decreased ability to concentrate urine (hyposthenuria) and painless haematuria which appear to be secondary to microinfarction of the renal medulla. SCT is also associated with increased incidence of renal medullary carcinoma. Splenic infarction and autosplenectomy are more common in patients with SCD. In SCT, splenic infarction is generally seen in people who exercise at high altitudes. The clinical associations of SCT are summarised in table 2.

Pathogenesis of priapism

Low-flow (ischaemic) priapism is a very rare presentation of SCT (Hb AS) although it is common in SCD (Hb SS). Priapism is defined as an unwanted erection lasting more than 4 h. High-flow (non-ischaemic) priapism occurs secondary to trauma to the cavernosal artery. It is generally painless and is not considered a medical emergency. Low-flow (ischaemic) priapism is considered a medical emergency. A report of 46 cases of priapism was published in 1974 in which 7 of the 24 African-Americans had SCT.[8] A few case reports have been published linking priapism to SCT. The underlying pathology seems

Table 2 Organ system and related clinical manifestations of sickle cell trait (SCT)

Organ system	Possible manifestations of SCT
Central nervous system	Stroke
Ocular	Hyphaema, proliferative retinopathy
Respiratory	Acute chest syndrome, pulmonary embolism
Cardiovascular	Exercise-related arrhythmia
Gastrointestinal	Cholelithiasis, high altitude and exercise-related splenic infarction
Renal	Hyposthenuria, isosthenuria, renal medullary carcinoma
Genitourinary	Priapism, urinary tract infections
Musculoskeletal	Exercise-related rhabdomyolysis, avascular necrosis of femoral head, leg ulcers
Pregnancy	Fetal loss/demise, asymptomatic bacteriuria

to be stasis of blood in the corpora cavernosa during normal erection, hypoxia leading to sickling of the RBC within the venous sinusoids obstructing the egress of blood. Reduced levels of nitric oxide in the penile tissue secondary to phosphodiesterase 5 (PDE5A) gene dysregulation have also been proposed as an alternative mechanism.[9] Increased levels of adenosine in the penile tissue have also been shown to cause priapism[10] leading to penile fibrosis[11] in murine models. The spongiosa and the glans are spared. Most of the episodes are self-limiting, a condition called stuttering priapism, but recurrent episodes can lead to necrosis of cavernosal smooth muscle leading to fibrosis and erectile dysfunction.

Role of marijuana

Marijuana has been traditionally associated with priapism,[12–14] although the exact mechanism is not fully elucidated. A few case reports of priapism in patients using marijuana have been described.[12 13] Increased parasympathetic outflow due to CB1 receptor mediated sympathetic outflow inhibition and inhibition of Ca^{2+} mobilisation in vascular smooth muscles resulting in penile smooth muscle relaxation with pooling of blood have been proposed as the possible mechanisms.[12] The effect of cannabis on human penile tissue has not been studied extensively. The association of cannabis and priapism is still unclear and needs to be investigated further.

Management of priapism

Conservative measures at home include voiding, masturbation, analgesics, ice packs or a warm bath. Standard of care for early presentation (within 4–12 h since onset) includes intracorporeal phenylephrine, aspiration and irrigation of the corpora cavernosa with normal saline and/or injecting selective α1 agonists like phenylephrine. Etilephrine, an α agonist, has also been shown to result in good clinical outcomes in adults with recurrent priapism.[15] Exchange transfusion can be performed in SCD but it does not seem to have any role in SCT.

Surgical management is reserved for patients who do not achieve detumescence even after 12 h with first-line therapy or patients who present very late in the course of the disease. The basic principle involves creating a shunt from the cavernosa to the distal glans (Winter or El-Ghorab procedure or T-shunt[16]) to improve the egress of stagnated blood. The main side effect of the procedure is erectile dysfunction and patients often require a penile prosthesis in the future. Proximal spongiosal-cavernosal (Quackels or Sacher procedures) or cavernosal-saphenous (Grayhack procedure) shunting is generally reserved for patients who fail the distal shunt procedures.

Learning points

- Priapism is a very rare clinical manifestation in sickle cell trait (SCT).
- Initial management of priapism (less than 12 h since onset) involves aspiration/irrigation of penile tissue with normal saline and/or α- blocking agents like phenylephrine or etilephrine.
- If patient fails conservative management (more than 12 h since onset) or presents late in the course of the disease, surgery should be considered.
- SCT screening is advised in student–athletes participating in division I and II sports in the USA to prevent exercise-related deaths.
- The role of marijuana in priapism needs to be investigated further.

Competing interests None.

Patient consent Obtained.

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