

Non surgical treatment of recurrent or stuttering priapism in sickle cell children

Jianmin Liu, MD, Mared A. Al-Hothari, BD, Faiz A. Mahboob, BD.

Sickle cell is a recessively inherited condition in which synthesis of hemoglobin is abnormal. The disease is characterized by chronic anemia, susceptibility to infection, and bouts of severe pain and organ dysfunction. The disease causes microvascular occlusion, which is manifested in most organ systems. There is a 6.4% incidence of priapism among sickle cell clinic patients.

Priapism is a prolonged painful erection for more than 6 hours. It is not related to sexual activity and occurs most commonly in patients with sickle cell disease, and it is a relatively frequent complication that results from the pooling of blood in the corpora cavernosa, causing obstruction of the venous outflow. Stuttering or recurrent priapism occurs often in patients with sickle cell trait or disease and in patients without sickle cell disease with prior episodes. The patient usually presents with a painful, spontaneous erection of several hours' duration. Physical examination reveals the penis to be rigid and mildly tender; the glans penis, however, is usually flaccid.

Although the main reservoir of sickle cell disease is tropical Africa and Madagascar, where the incidence may be as high as 40%, it is relatively common in Turkey, Greece and other Mediterranean countries including North Africa. The priapism in sickle cell anemia is relatively common in Yemenis. From November 2001 to March 2003, we treated 3 recurrent or stuttering priapism child patients. One 12-year-old boy had sudden, painful penile erection for more than 8 hours. There was a history of priapism 6 months previous. Another 12-year-old boy had painful, persistent penile erection that lasted more than 2 days with a history of priapism 3 times before; and a 13-year-old boy had painful, intermittent erection for 2 days with persistent penile erection for more than 20 hours. Examination revealed pale, dehydrated, anicteric adolescents with full non-pulsatile penile erection and engorged superficial penile veins. The color of penis was gray purple. The glans penis and corpus spongiosum were soft. The corpora cavernosa were fully rigid and tense with congested blood and tender to palpation and with a cool feeling. The urethral meatus, scrotum and rectum were normal. They had been diagnosed as suffering from sickle cell anemia, with genotype hemoglobin SS. There was no history of recent drug ingestion or neuro-psychiatric disturbance. Investigations showed a hemoglobin of 6.8-9.1 g/dl, white blood cell count $12.2-15.3 \times 10^9/l$ (neutrophils 60-68%, lymphocytes 30-35%, monocytes 3-5%, basophils 0-1%, eosinophils 0-1%); platelets

220-250,000/mm³; blood smear showed numerous sickled cells and occasional target cells but no parasitemia. Blood biochemistry was normal. Other investigations were normal, and the diagnosis of low-flow recurrent or stuttering priapism was made. We performed aspiration of the corpora and intravenous injection with an alpha-adrenergic agonist ephedrine bilaterally. We performed initial aspiration of the corpora via a 21-gauge butterfly needle, followed by injection of 50 mg ephedrine, a pure alpha-adrenergic stimulant, until detumescence took place. The ephedrine solution was made by mixing 50 mg/ml of ephedrine with 19 ml of normal saline. Intracavernous injection and irrigation with diluted alpha-adrenergic solution every 5 minutes until detumescence after aspiration of 10-20 ml of blood. At the same time as the injection we pressed the penis 2-3 times promoting detumescence until the penis became warmer and reddish. After 15-30 minutes, the erectile penis became flaccid, and 2 priapisms were converted into nonischemic priapism, and then sustained detumescence was noted. The 13-year-old boy's priapism recurred 2 times, 6 hours later and the next day, then we used an 18-gauge needle aspirating corpora cavernosa through the glans to evacuate the sludged blood, injected ephedrine 50 mg twice under anesthesia, then the erectile penis became flaccid. At the same time, 5% dextrose and Ringer's solution were given to adjust the occult misbalance of acid-base and electrolyte. Blood transfusion was applied to the patients receiving aspiration of corpora cavernosa. After the injection, erectile penis became flaccid, and 2 priapism were converted into nonischemic priapism, and then sustained detumescence was noted the next day; recovery was sustained and complete. The 13-year-old boy's priapism recurred the next day, after aspirating corpora cavernosa, injecting ephedrine 50 mg twice, the erectile penis was flaccid. Sustained detumescence was noted on the second post-admission day; recovery was sustained and complete. No acute hypertension, headache, palpitation and cardiac arrhythmia occurred after injection of alpha-adrenergic agents, and no bleeding, hematoma, infection and urethral injury were found in these patients.

The genitourinary tract is most commonly affected by hematuria, urinary tract infection and priapism but other more serious sequelae have been identified in sickle cell disease.¹ The diagnosis and management of sickle cell disease has advanced rapidly with a significant increase in the life expectancy of affected patients and recognition of a greater number of genitourinary complications. Renal function may be mildly altered or lost completely. Patients with sickle cell disease are at increased risk for urinary tract infection. Priapism is a painful complication of sickle cell disease that is poorly understood and challenging to treat and prevent. Testicular infarction has also been noted. Furthermore,

renal medullary carcinoma, a highly lethal tumor, develops almost exclusively in young patients with sickle cell trait. Sickle cell disorder accounts for approximately 28% of all cases of priapism; 42% of adults and 64% of children with sickle cell disease eventually develop it. Although high-flow priapism in patients with sickle cell disease has been reported, the majority of cases are of the low-flow type. Priapism is an uncommon problem in childhood. Most of the reported cases are in boys with sickle cell disease or leukemia. Stuttering or recurrent priapism occurs often in patients with sickle cell trait of disease and in patients without sickle cell disease with prior episodes. The mechanism is unknown although alteration of adrenoceptors or scarring of intracavernous venules might be partially responsible. Red cell sickling and later sludging of blood occurs within the corpora cavernosa, perhaps as a result of abnormal endothelial adherence, the relatively acidic state of the corpora during erection, mild acidosis accompanying hypoventilation during sleep, or mild trauma with masturbation and intercourse. When the venous channels are maximally compressed during nocturnal penile tumescence, the sludged red blood cells can then block the microscopic subtunical venules and trigger diffuse veno-occlusion. Anecdotally, pediatric patients have been known to achieve erectile capability subsequently, but adults often do not recover it. The natural history of sickle cell priapism is one of recurrence. Almost all cases are of the low-flow type. Priapism is considered a failure of the detumescence mechanism, which may be due to excess release of contractile neurotransmitters, obstruction of draining venules, malfunction of the intrinsic detumescence mechanism, or prolonged relaxation of intracavernosal smooth muscle. There are essentially 2 main types of priapism: high-flow (non-ischemic) and low-flow (ischemic). Low-flow priapism is the more common form, and it is associated with a decrease in venous outflow and vascular stasis that, in turn, causes tissue hypoxia and acidosis. This form of priapism is usually quite painful because of tissue ischemia. Penile blood aspirated from cavernous spaces appears dark in color. Immediate treatment is necessary, or penile fibrosis will ensue.

Diagnosis. Priapism is the persistence of erection that does not result from sexual desire and fails to subside despite orgasm. It can occur in all age groups, including the newborn, but the peak incidence occurs between the ages of 5 and 10 and 20-50 years. In the younger group, priapism is most often associated with sickle cell disease or neoplasm. Most incidents occur during nocturnal penile tumescence when the smooth muscle is relaxed, and the venous channels are maximally compressed. Typically, priapism affects only the corpora cavernosa (very rarely the corpus spongiosum is also involved). Although no definitive distinction has been made between prolonged erection and priapism, the authors prefer to refer to erection of more than 6 hours duration

as priapism because, in the low-flow type, ischemia and acidosis occur at that time.

The diagnosis of priapism is usually based on history and physical examination. A blood sample should be obtained for hemoglobin S determination and to rule out leukemia. Urinalysis and urine culture should also be obtained to rule out urinary tract infection, and intracavernous blood gases, technetium-99m scan and echo Doppler findings, to differentiate low-flow and high-flow type priapism; color-coded duplex ultrasound scan of the cavernous arteries and the corpora cavernosa to exclude trauma-induced high-flow priapism. Sickle cell priapism often occurs in teenagers, and recurrence is very common. Acute low-flow (veno-occlusive) priapism, if lasting more than several hours, is usually painful because of changes associated with tissue ischemia. In contrast, most cases of high-flow (arterial priapism) are painless and usually follow perineal injury or direct injury to the penis. On physical examination, the corpora cavernosa are fully rigid in low-flow priapism and partial too fully rigid in high-flow priapism. The glands and corpus spongiosum are not involved, except in very rare cases of tricarporal priapism. A thorough physical examination should include rectal, abdominal and neurologic examinations. Chronic priapism and acute intermittent (stuttering) priapism may be more difficult to diagnose because of atypical physical findings.

Treatment. Priapism must be considered a urologic emergency. Treatment is aimed at the primary cause of priapism if it can be identified. The goal is to abort the erection, thereby preventing permanent damage to the corpora, which would lead to impotence, and to relieve pain. Treatment should be prompt and conservative; medical management should always be tried before resorting to surgery as priapism often recurs in these patients. There is ample evidence that the risk of fibrosis and impotence increases with time. Generally, the incidence of impotence is less if erection is aborted in less than 24 hours. We gave the recurrent or stuttering priapism patients aspiration of the corpora and intracavernous injection with alpha-adrenergic agonist ephedrine bilaterally, and achieved a detumescence of erectile penis immediately and then sustained detumescence was noted on the second post-admission day; recovery was sustained and complete. We took measurements to adjust the occult misbalance of acid-base and electrolytes and gave a blood transfusion to the patient who received aspiration of the corpora cavernosa. Many doctors have applied various methods and agents, such as adrenergic agonists (etilefrine), antiandrogen, immunosuppressive agent (hydroxyurea) and methylene blue (MB), a guanylate cyclase inhibitor, to the priapism patients and received a significant consequence. Dahm² used antiandrogen to treat patients with recurrent and refractory priapism. All patients were successfully treated with low dose antiandrogens without major side effects. They considered that recurrent priapism in young men as a potentially

devastating condition that may result in irreversible penile fibrosis. Hormonal manipulation using estrogens and gonadotrophin-releasing hormone analogues has been successful in treating episodes of priapism refractory to other treatment forms, but it is associated with significant adverse effects, particularly to the loss of libido and erectile function. The role of antiandrogens in the treatment of men with refractory priapism should be evaluated in the setting of a controlled study. Al-Jam'a and Al-Dabbous³ used the immunosuppressive agent hydroxyurea to treat the priapism associated with sickle cell disease. This therapy for sickle cell disease may prevent these complications in the future.¹ DeHoll⁴ and his colleagues described the use of intracavernous MB a guanylate cyclase inhibitor, or internal pudendal artery embolization for the treatment of priapism. The results confirmed that MB is effective for pharmacologically induced priapism. During treatment, the agent being injected should be diluted to prevent necrosis of cavernous tissue, the dose of agent should be controlled to avoid acute hypertension, headache, palpitation and cardiac arrhythmia from alpha-adrenergic agents, care should be taken to be tender to decrease bleeding, hematoma, infection, and urethral injury from needle puncture. Infections are usually in the form of cellulites. Therefore, strict asepsis in carrying out penile irrigation and use of antibiotics are both mandatory to avoid this potentially disastrous complication. Having ruled out other causative factors, one should treat the patients by aggressive hydration, oxygenation, and metabolic alkalization to reduce further sickling. Supertransfusion and erythropheresis should be used as second-line therapy. Irrigation and injection should be performed promptly. Sedation followed by enemas of ice-cold saline solution may induce subsidence of the erection. Red blood cell exchange transfusion⁵ can, without increasing the whole-blood viscosity quickly replace abnormal erythrocytes and raise the hematocrit resulting in improved delivery of oxygen to hypoxic tissues. Unfortunately, transfusion can also be associated with complications. Hyperbaric oxygen also has been suggested for these patients.

We considered that priapism in sickle cell patients is a recurrent, low-flow priapism and a urologic emergency. Recognition, diagnosis and prompt treatment of the disease is important to prevent complications such as fibrosis and impotence. The goal of treatment is to abort the erection, thereby preventing permanent damage to the corpora and to alleviate pain. Treatment should be prompt and conservative, medical management should always be tried before resorting to surgery; almost all cases can be successfully aborted with injection of a dilute alpha-adrenergic agonist, provided treatment begins within 12 hours of onset. Intracavernous injection of an alpha-adrenergic agonist remains the most effective treatment for low-flow priapism and is almost 100% effective if the priapism is treated within 12 hours of onset. Various methods and agents, such as

adrenergic agonists (etilefrine), antiandrogen, immunosuppressive agent (hydroxyurea) and guanylate cyclase inhibitor (MB) can be used in the patients effectively. Measurements to adjust the occult misbalance of acid-base and electrolyte should be given simultaneously. Blood transfusion should be applied to the patient who received aspiration of corpora cavernosa.

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From the Department of Urology (Liu), Affiliated Hospital of Bengbu Medical College, Anhui, People's Republic of China, and Bin-Khaldoon General Hospital (Al-Hothari, Mahboob), Al-Hawta-Lehej, Republic of Yemen. Address correspondence and reprint requests to Dr. Jianmin Liu, Department of Urology, Affiliated Hospital of Bengbu Medical College, Bengbu, Anui, People's Republic of China, 233004. Tel. +86 (552) 2059902. E-mail: liu_john_jm@hotmail.com

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The effects of cardiac rehabilitation in patients with coronary artery disease

Abbas Afrasiabi, MD, Mehrnoosh Toofan, MD,
Leila Pirzad, MD, Susan Hassanzadeh, MS, Habib Pirzad, MD.

Cardiac rehabilitation (CR) has been recommended after acute myocardial infarction and coronary artery bypass surgery. Comprehensive cardiac rehabilitation programs usually consist of exercise, education regarding nutrition, smoking cessation and psychosocial support. The goals of these programs shall return patients to a productive lifestyle and to reduce risk of cardiac events or death. The aim of this prospective randomized trial was to investigate influences of supervised comprehensive cardiac rehabilitation on exercise capacity, psychological factors and plasma lipid profiles in patients with coronary artery disease.

Patients survived after first acute myocardial infarction (AMI), coronary artery bypass graft (CABG) and percutaneous transluminal coronary angioplasty (PTCA) included in this trial if the following criteria were found: History of recent (4-6 weeks ago) first acute myocardial infarction, no conduction abnormality, physically and medically stable and no contraindications to perform exercise. From September 2000 through July 2001, 76 patients were referred to CR programs. All