Priapism as an Initial Presentation of Chronic Myelogenous Leukemia

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Priapism is a prolonged, painful, and persistent erection unassociated with sexual arousal. Although the injection of intracavernosal vasoactive substances is the most common cause of priapism, nearly 20% of all cases relate to a hematologic disorder. Such hematologic conditions include sickle cell anemia, chronic myelogenous leukemia, chronic lymphocytic leukemia, and acute lymphoblastic leukemia.[1] In adult leukemic patients, the incidence of priapism is estimated to be approximately 5%.[2] This article discusses the case of a 21-year-old patient who presents with priapism and is found to have chronic myelogenous leukemia. Physiology of normal erectile function as well as the pathophysiology, diagnosis, and proper management of priapism are also reviewed.

CASE PRESENTATION

A 21-year-old man presents to the hospital complaining of a minimally painful erection that has lasted approximately 30 hours. The patient is concerned about the extreme duration of the erection. He denies recent intercourse, trauma, use of illicit drugs, use of medications, and radiation therapy. The patient also denies fever, sweats, and chills.

Physical Examination, Laboratory Evaluation, and Diagnosis

Physical examination reveals normal cardiovascular and pulmonary systems. The liver span is approximately 12 cm in the midclavicular line, and the spleen is palpable. On examination, the penis is erect and circumcised and the testicles are bilaterally descended. The glans is soft and does not appear ischemic. The corpora cavernosa are engorged. Digital rectal examination reveals a normal prostate without tenderness.

Urinalysis is normal. Because of the patient's young age and lack of predisposing causes for priapism, a complete blood count (CBC) with differential is ordered. The leukocyte count is 307,000/mm^3, platelet count is 650,000/mm^3, and hematocrit is 24%. Differential reveals 4% metamyelocytes, 18% myelocytes, and 11% banded neutrophils Peripheral smear demonstrates immature leukocytes in various stages of differentiation (**Figure 1**). Based on the CBC, the diagnosis of chronic myelogenous leukemia is made.

Urologist Consultation

Because of the long duration of the patient's priapism (30 hours), the absence of penile pain at the time of examination, and the lack of ischemia in the penis, a urology service is consulted concerning treatment. The urologist elects conservative management and suggests aggressive treatment of the underlying condition instead of corporal aspiration/irrigation.

Hospital Admission and Treatment

The patient is admitted to the hospital and receives intravenous fluid hydration, hypertransfusion, allopurinol (400 mg), and leukapheresis. Bone marrow biopsy is performed 4 days after hospital admission and confirms the diagnosis of chronic myelogenous leukemia. The priapism resolves 8 days after admission. After 20 days of chemotherapy with busulfan and hydroxyurea, the patient's leukocyte and platelet counts are 7800/mm^3 and 250,000/mm^3, respectively, and the patient is discharged home on self-injection of interferon-α. Presently, the patient's leukemia is in remission. He is able to achieve an erection with manual stimulation and maintains the ability to ejaculate. The patient is currently sexually inactive.

DISCUSSION

Priapism is a persistent, prolonged, typically painful erection unassociated with sexual stimulation. The word *priapism* derives from the name *Priapus,* the Greek god

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of hunting and the bountiful harvest. However, the condition of priapism is not synonymous with virility and robust health. In fact, the rate of permanent impotence following detumescence is approximately 50% in patients with priapism.[3] Priapism, although morbid in its own right, may also be a manifestation of other pathologies. In the patient in this case study, the priapism alerted physicians to a previously undiagnosed chronic myelogenous leukemia. Regardless of the etiology, priapism represents a urologic emergency with prognosis directly related to the promptness of treatment.[4–6]

Physiology

During a normal erection, parasympathetic tone increases and is mediated by fibers originating in the sacral plexus, which course anteriorly as the pelvic nerve. This parasympathetic tone leads to smooth muscle relaxation of the cavernae and helicine arteries; distention of the sinusoidal spaces and stretching of the tunica albuginea follows. Emissary subtunical venules are then compressed under the pressure in the cavernosal spaces. Detumescence is achieved by contraction of arteriolar and cavernosal smooth muscle, decreased blood pressure within cavernosal sinusoids, and increased venous outflow through emissary venules. Detumescence is mediated by norepinephrine.[7]

Pathophysiology

Priapism can be classified according to two pathophysiologic states, high-flow and low-flow. Low-flow priapism, the more common of the two states, occurs when venous drainage from emissary venules is blocked or decreased and leads to intracavernosal stasis. Low-flow priapism may be secondary to sludging of blood caused by hematologic malignancies, venous compression from penile hematoma or solid malignancy, or neurogenically mediated failure of smooth muscle constriction. In the low-flow state, intracavernosal blood quickly becomes depleted of oxygen, leading to hypoxia, hypercarbia, and acidosis.[3,4] Aspiration of intracavernosal blood may reveal necrobiotic cells with agglutination of erythrocytes in cases of leukemic priapism.[8] Sickled erythrocytes may be seen in cases of sickle cell anemia.[2,7] Stasis of blood leads to tissue ischemia with irreversible fibrosis and induration of the cavernosal spaces within 24 to 48 hours of onset.

Nelson and Winter[6] reviewed 48 cases of priapism and found that nearly 100% of patients with priapism of 6 to 12 hours' duration who underwent surgical detumescence to relieve the condition experienced return of erectile function and that patients with priapism for more than 3 days had little chance of recovering erectile function. Long-term follow-up revealed cases of late failure of erectile function months after the priapism occurred, reflecting the potential for a higher rate of impotence than currently recognized.[6] Rapid institution of therapy is essential to reverse the histologic changes that occur during low-flow priapism. The risks of permanent impotence should be made clear to patients prior to treatment.[6,9]

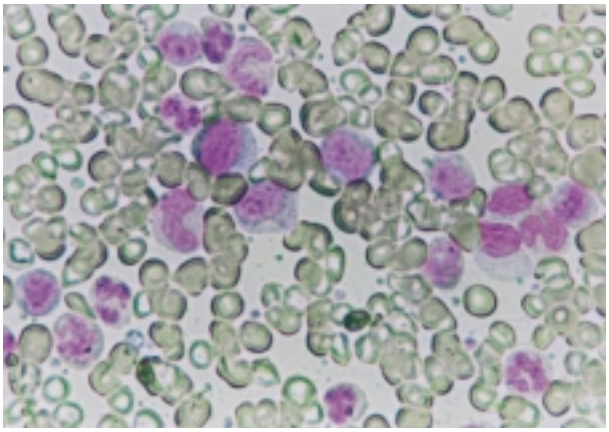

Figure 1. Peripheral smear shows cells of all stages in granulocytopoietic development, X 40.

High-flow priapism is rare and often caused by perineal trauma. Such an injury (eg, a fall from a bicycle) results in a pudendal fistula between an artery and cavernosa. In cases of high-flow priapism, regulation of arterial inflow by the helicine arteries is bypassed and outflow from emissary venules cannot compensate for the increased sinusoidal pressures. Lack of ischemia in these patients results in a relatively painless erection, in contrast to patients with low-flow priapism. Oxygenation of the penile tissues is preserved because of the increase in arterial perfusion. For these reasons, high-flow priapism is not considered a true emergency and therapy can be instituted on a more elective basis. Therefore, differentiation between high-flow and low-flow priapism is critical in order to develop a treatment plan that optimizes the chance of future potency.[3,4,10,11]

Etiology and Incidence

The population of patients with priapism can be divided into pediatric and adult cases. In children, the most common cause for priapism is a hematologic disorder such as sickle cell anemia (67%). Leukemia and idiopathic events are the next most common causes of priapism in children.[12]

In adults, the most frequent causative factor is intracavernosal injection of vasoactive substances, which

Table 1. Differential Diagnosis of Priapism

Idiopathic causes
Drugs
Heparin
Warfarin
Labetalol
Prazosin
Nifedipine
Guanethidine
Trazodone
Phenothiazine (antipsychotic agents)
Hematologic disorders
Sickle cell anemia
Leukemia
Fanconi's anemia
Lymphoma
Thrombocythemia
Metabolic disorders
Amyloidosis
Gout
Diabetes
Renal failure
Nephrotic syndrome
Trauma
Tumors
Neurologic disorders
Inflammation
Kawasaki syndrome

include different combinations of phentolamine, papaverine, and prostaglandin E_1 for the treatment of impotence.[4,5,9] In a review of 105 cases, Winter and McDowell[12] found that, in adult cases of priapism deemed idiopathic, medication history was frequently positive for neurologic drugs. In addition to these agents, many other drugs have been implicated in priapism in adults; a recent case is suspected to have been caused by vancomycin.[13]

Sickle cell disease accompanies priapism in 23% of adults; 38% to 42% of these patients have experienced one or more previous episodes of priapism, which may not have been treated.[5] Malignant penile infiltration from primary cancers of the bladder, prostate, rectosigmoid colon, and kidney is another cause of priapism in adults. Priapism may also occur in patients with spinal cord injury as well as in patients with direct local trauma to the perineum. Hematologic malignancy is less common in adults (2% to 5%) than in children, and leukemias and a greater variety of lymphomas are more frequently reported in adults. Priapism as a result of hematologic malignancy is most likely caused by venous obstruction from microemboli/thrombi as well as hyperviscosity caused by the increased number of circulating leukocytes in mature and immature forms.[6,9,12]

Diagnosis and Treatment

A differential diagnosis of priapism is presented in **Table 1**. Differentiating between high-flow and low-flow priapism is the most critical step in the diagnostic work-up. This distinction can usually be accomplished by a thorough history and physical examination. A treatment algorithm is presented in **Figure 2**.

High-flow priapism. In patients with high-flow priapism, a history of perineal or penile trauma is almost always elicited, although at least one case of nontraumatic high-flow priapism has been reported.[3] In cases of high-flow priapism, the patient may complain of pain originating from the trauma, but the erection is typically painless. The next step in diagnosis is a cavernosal blood gas determination.[3,8,9,10] If cavernosal blood gas values return as arterial, the diagnosis of high-flow priapism is confirmed. In such cases, color flow Doppler imaging has been shown to be a sensitive modality for localizing the damaged vessel.[4,8,14] At this point, superselective transcatheter embolization of the ruptured artery using autologous clot is the most common intervention, and resolution of the priapism occurs in 100% of patients, 86% of whom experience long-term potency.[15] Surgical ligation and observation have also demonstrated good long-term potency results and are still advocated by some physicians.[14]

Low-flow priapism. In patients with low-flow priapism, a history of sickle cell disease or use of intracavernosal injection agents is most commonly elicited. Approximately 6% of children with sickle cell disease experience one episode of priapism during childhood, whereas 40% of adults with sickle cell disease experience one episode of priapism.[6,12] Therefore, a prior history of priapism should be sought in adult patients. In children, the physician must maintain a high index of suspicion for sickle cell disease. Sporadic, spontaneously resolving leukemic priapism has also been reported in both children and adults.[16,17] An initial CBC frequently reveals evidence of hematologic malignancy, and subsequent management focuses on treatment of the underlying neoplasm. In the absence of patient history and without evidence of trauma, a thorough drug

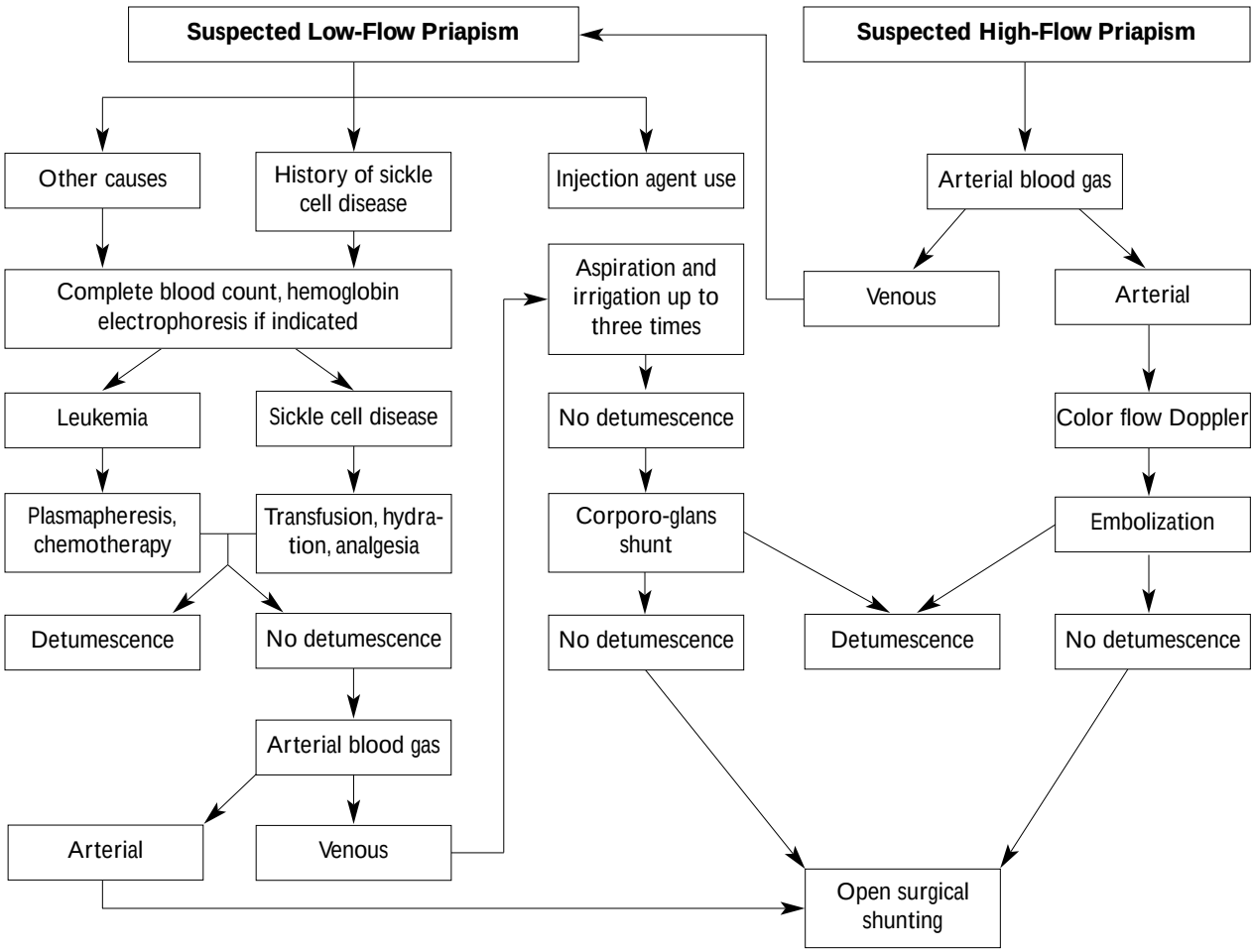

Figure 2. Treatment algorithm for suspected high-flow and low-flow priapism.

history should be elicited and the previously mentioned etiologies of priapism should also be considered.

On physical examination, the patient's erection is painful and may be violaceous or indurated. Typically, the paired cavernosa are rigid while the glans remains flaccid. A thorough abdominal examination may reveal splenomegaly. In a study of nine cases of leukemic priapism, all patients exhibited some degree of splenomegaly.[8,16,17] Inguinal lymphadenopathy and prostatic nodules may alert the physician to other malignancies.

If history of sickle cell anemia is elicited and confirmed by hemoglobin electrophoresis, initial therapy should consist of hydration, correction of acidosis and hypoxia, and treatment of any factors that predispose to sickle cell crisis. Exchange transfusion may be required to reduce sickled hemoglobin to less than 30% and to increase the hemoglobin concentration to more than 10 mg/dL.[4,9] If exchange transfusion fails, corporal aspiration and injection of phenylephrine may be attempted,[4,5,9] which, if unsuccessful, should be followed by a cavernosa-to-glans shunt. Nondetumescence after installation of the initial shunt should be followed by creation of a larger, proximal cavernosa-to-spongiosa shunt (eg, Al-Ghorab or Quackels). If all other therapies fail, a final surgical option is the creation of a sapheno-cavernosal vein bypass.[1,2,4,5]

If no history of sickle cell disease is found, then hemoglobin electrophoresis should be performed in pediatric patients suspected to have the disease. In adults, or in children whose sickle preparation is negative, detumescence may be attempted by aspiration of 60 mL of blood followed by injection of 500 µg of phenylephrine. If detumescence does not occur, then the diagnosis of low-flow priapism should be confirmed by either penile blood gas analysis or color flow Doppler study. The low-flow state is typically associated with a pH of less than 7.25, partial pressure of carbon dioxide greater than 60 mm Hg, and partial pressure of oxygen

less than 30 mm Hg, or decreased flow in one or both of the pudendal arteries.[3,4] If low-flow priapism is confirmed, then phenylephrine injection may be repeated up to three times. If detumescence still does not occur then the same series of surgical shunting used in high-flow priapism should be used. In either high- or low-flow priapism, intermittent, pediatric pneumatic cuff compression applied to the penis postoperatively decreases stasis of blood in the penile tissues and is considered helpful in resolving the erection.[3,5]

In cases of hematologic malignancy, controversy has existed regarding the optimal treatment of leukemic priapism. Earlier series of case reports show successful detumescence with local radiation therapy, open surgical shunting, or combination of the two treatments.[6,12,16] More recent literature has focused on the use of cytoreductive modalities such as chemotherapy or combination chemotherapy and leukapheresis.[8,17] Because of the relatively rare occurrence of leukemic priapism and the small number of case series, there is no standard treatment protocol at this time. Chemotherapy or radiotherapy may first be attempted.[7] If detumescence is not achieved, then surgical shunting should be considered. Other physicians have suggested a more specific time course. Suri et al[16] recommend that chemotherapy and leukapheresis should be initiated immediately. A similar conclusion was reached by Becker et al,[8] who recommended chemotherapy and leukapheresis followed by surgical shunting if detumescence is not "immediately obvious." These articles seem to suggest an early, more aggressive use of surgery. Such urgent treatment is not always necessary in cases of leukemic priapism because of the generally poor prognosis of most cases of leukemia.[5] However, in pediatric patients with priapism, 50% of cases are caused by chronic granulocytic leukemia, which carries a more favorable prognosis and greater life expectancy than other leukemias.[2] In such cases, an aggressive treatment protocol may provide a greater chance of maintaining normal erectile function. In the patient in this case study, surgical shunting was a less favorable option because of the patient's response to chemotherapy and leukapheresis. Further review of such cases with long-term follow up is necessary to more precisely define an optimal treatment protocol.

SUMMARY

Based on this case and a brief review of the literature, several recommendations can be made for diagnosing and treating patients with priapism. Early diagnosis of priapism should focus on distinction between high-flow and low-flow priapism. Subsequent treatment must be instituted quickly to optimize probability of long-term potency. Further experience is necessary to define the best use of surgery in the resolution of leukemic priapism. Finally, these authors recognize the importance of the CBC to screen for the possibility of hematologic malignancy when the history and physical examination fail to elucidate an obvious cause of priapism. **HP**

REFERENCES

1. Schreibman SM, Gee TS, Grabstald H: Management of priapism in patients with chronic granulocytic leukemia. *J Urol* 1974;111:786–788.
2. Steinhardt GF, Steinhardt E: Priapism in children with leukemia. *Urology* 1981;18:604–606.
3. Lue TF, Hellstrom WJ, McAninch JW, Tanagho EA: Priapism: a refined approach to diagnosis and treatment. *J Urol* 1986;136:104–108.
4. Harmon WJ, Nehra A: Priapism: diagnosis and management. *Mayo Clin Proc* 1997;72:350–355.
5. Magoha GA: Priapism: a historical and update review. *East Afr Med J* 1995;72:399–401.
6. Nelson JH, Winter CC: Priapism: evolution of management in 48 patients in a 22-year series. *J Urol* 1977;117: 455–458.
7. Benson GS: Priapism. In *American Urological Association Update Series,* vol XV, lesson 11. Baltimore, MD: 1996: 85–91.
8. Becker HC, Pralle H, Weidner W: Therapy of priapism in high counting myeloid leukemia—a combined oncological–urological approach. Two case reports. *Urol Int* 1985;40:284–286.
9. Mulhall JP, Honig SC: Priapism: etiology and management. *Acad Emerg Med* 1996;3:810–816.
10. Bastuba MD, Saenz de Tejada I, Dinlenc CZ, et al: Arterial priapism: diagnosis, treatment, and long-term follow-up. *J Urol* 1994;151:1231–1237.
11. Hakim LS, Kulaksizoglu H, Mulligan R, et al: Evolving concepts in the diagnosis and treatment of arterial high flow priapism. *J Urol* 1996;155:541–548.
12. Winter CC, McDowell G: Experience with 105 patients with priapism: update review of all aspects. *J Urol* 1988;140:980–983.
13. Czachor JS, Garzaro P, Miller JR: Vancomycin and priapism. *N Engl J Med* 1998;23:1701.
14. Ilkay AK, Levine LA: Conservative management of high-flow priapism. *Urology* 1995;46:419–424.
15. Kim SC, Park SH, Yang SH: Treatment of posttraumatic chronic high-flow priapisms by superselective embolization of cavernous artery with autologous clot. *J Trauma* 1996;40:462–465.
16. Suri R, Goldman JM, Catovsky D, et al: Priapism complicating chronic granulocytic leukemia. *Am J Hematol* 1980;9:295–299.
17. Kumar L, Sagar TG, Majhi U, Shanta V: Priapism in leukaemia—report of three cases. *J Assoc Physicians India* 1990;38:229–230.