

## Rare Clinical Manifestations; Priapism in Chronic Myeloid Leukemia-A Review

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### Abstract

Chronic myeloid leukemia (CML) is characterized by a chronic myeloproliferative disorder manifesting routinely with increased number of white blood cells and huge splenomegaly. Mostly it has an insidious nature with nonspecific set of symptoms such as tiredness, fever, or associated weight loss. At rare occasions priapism can also happen in course of CML. Its pathogenesis is ascribed to hyper leukocytosis and resultant increased viscosity. The treatment for such crises often involves oncologic and urology intervention. Due to the rarity of the manifestation of priapism in CML patients, the management remains controversial. Majority of the authors advocate CML-specific therapy (chemotherapy) alone, whereas some advocate additional urological intervention. It is not only a medical emergency but also a urological one, needing prompt therapy. In this review we tried to explain the importance of diagnosing this rare clinical challenge in time and taking the possible available measures to deal with it in terms of necessary work-up and management of such patients.

**Keywords:** Chronic Myeloid Leukemia (CML); Priapism; Chronic Myeloproliferative Disorder

### Introduction

Priapism is a condition marked by prolonged painful and imperishable erection without culmination as ejaculation. This makes it a medical emergency that might lead to notably formidable prognosis owing to higher risk of impotence associated with this emergent condition despite efforts to implement suitable management. Some of the hematologic disorders that might lead to this emergency include chronic lymphocytic leukaemia, Sickle cell anemia, chronic myeloid leukemia, chronic lymphocytic leukaemia and acute lymphoblastic leukemia [1,2].

In adult subjects suffering from leukemia, the incidence of priapism might be up to five percent while in young children it is all the more rarer. Priapism in such cases occur due to the blood disorders leading to veins being blocked owing to formation of small fragments of emboli and hyper viscosity of blood (resulting from sharp soaring count of circulating leukocytes). As discussed already that priapism is characteristically an involuntary phenomenon (without sexual stimulation), occur for extended time duration leading to painful penile

erection. Priapism is broadly categorized as two types: one is ischemic type and the other one is of non-ischemic origin. Non-ischemic priapism results from pelvic trauma or associated genital trauma resulting in formation of an arteriovenous fistula within penile circulation. On the other hand, ischemic type of priapism covers majority of the priapism cases encountered in clinical practice. Sickle cell disease seems to be leading cause of this type of priapism in younger children. In adults, idiopathic cause accounts for majority of these cases and only up to 20% of ischemic priapism cases results from various hematological disorders. As mentioned already that it might occur in subjects who have hyper leukocytosis (in adult leukemic subjects approximately 1 - 5%). Out of all leukemia cases presenting with priapism, chronic myeloid leukemia (CML) makes up 50% of the proportion. It is not only a medical emergency but also a urological one, needing prompt therapy. In this review we will try to explain the importance of diagnosing this rare clinical challenge in time and taking the possible available measures to deal with it in terms of necessary work-up and management of such patients [3,4].

### Materials and Methods

We did search on PubMed, Medline database publications using: Chronic myeloid leukemia, Priapism, Emergency treatment and surgical treatment options. The publications included were case reports, reviews, books and research studies regarding the subject matter over last 20 years.

### Discussions and Literature Review

CML patients habitually manifest itself with some vague symptoms such as loss of weight, temperature, associated night sweats, abdominal pain or sensation of fullness and bone pain. In addition to these, few subjects suffering from CML can manifest symptoms owing to phenomenon known as leukostasis (for example, thromboembolic events, loss of hearing sensation, resultant neurologic deficits and priapism). On very rare occasions, mere priapism can be a presenting feature in cases of hematological malignancies; CML comprises only nearly half of these cases. Priapism if manifest itself is basically an atypical feature underlying systemic disease.

**Types of priapism:** They are generally classified into two broader types: one is a high flow (non-ischemic) while the other one is low flow (ischemic) type. Majority of cases are of the low flow priapism type-It is an emergency scenario from urology point of view. As mentioned earlier, it takes place due to venous congestion and pooling of blood in corpora cavernosa. This happens as a result of deposition of excessive leukemic cells in dorsal penile veins and eventually the corpora cavernosa as well. There is another mechanism as well, that leukemic infiltration might involve sacral nerves [5-11]. Whatever the mechanism of low flow priapism, it eventually results in tissue injury, irreparable damage, fibrosis-all ending in loss of the penile function-if left untreated for 24 hours.

The other broad type of priapism high flow (of arterial origin). It is mostly a sequela of trauma to penile or perineal region. Trauma leads to formation of fistula between the penile cavernosal artery and the corpus cavernosum, leading the way to enhanced arterial inflow into the system of sinusoids in penile cavernosa [5-7].

**Age of presentation:** Priapism might affect any age; nevertheless two age peaks have been defined from the literature. One age peak occur in the range of 5 - 10 years, mainly occurring secondary to sickle cell disease in children. There is a second peak too that is prone to affect patients in age range of 20 to 50 years [7].

**Causes of priapism:** In a nutshell few of the causes leading to priapism include conditions such as trauma, fat embolism, dialysis, fabry disease, vasculitis, autonomic neuropathy, cauda equine compression, spinal cord stenosis. Hematological origin causes are sickle cell anemia, thalassemia and leukemia. Then rarely metastatic infiltration to the penis or other malignant conditions. Certain pharmacologic agents such as psychotropic drugs (phenothiazines and trazodone), antihypertensive (mainly prazosin) and heparin. Some of the other rare conditions involve some specific spider bites amyloidosis, infective condition such as mycoplasma pneumonia. It is important to note here that many of the priapism cases are of idiopathic category while only 20% can be ascribed to hematologic diseases [7,8].

**Mechanism of priapism in CML:** Congestion of the corpora cavernosa occurring due to mechanical compression of the abdominal veins by the enlarged spleen; Sludging of leukaemic cells in the corpora cavernosa and the penile dorsal vein; infiltration of the sacral nerves and central nervous system with leukaemic cells [1,4,8,10].

**Diagnosing priapism:** Correct differentiation of ischemic and non-ischemic priapism is a matter of significance as both types have a different line of action for management of the patient presenting with priapism. Apart from the basic history, physically examining the patient and sending baseline laboratory investigations, also take sample for corpora cavernosa blood gas analysis. Base line investigations comprising complete blood picture, serum electrolytes and renal function tests, coagulation status. Drugs screen can be undertaken in suspected history, if needed. Penile Doppler ultrasound should be done as soon as possible [6,7]. On physical examination it is to be noticed that patients suffering from low-flow priapism mainly manifest with painful and turgid penile shaft however glans is soft. On the other hand, painless and a partially rigid penis denotes high-flow priapism. In addition to the physical examination another vital tool that helps in differentiating the high flow from low flow priapism, is intra-cavernosal sample for blood gas analysis. In case, blood gas analysis results are within normal, point towards making diagnosis of high-flow priapism. Then coming to the radiological investigation, Doppler ultrasonography can be performed immediately to delineate an arterial to-cavernosal fistula (characteristic of high-flow priapism cases) [9-11].

**Treatment of priapism:** Literature and clear guidelines are not sufficient in the context of treating patient suffering from priapism in presence of an underlying hematological malignancy. Some guidance given by near past recommendations assert on initiating immediate administration of intra-cavernous therapy for treating the emergency of priapism followed by systemic treatment of the cardinal disorder (malignancy). The initial management of priapism comprise immediate aspiration of penile cavernosa together with an injection of alpha adrenergic (epinephrine or phenylephrine).

**Therapeutic aspiration technique:** Therapeutic aspiration with additional intracavernous injection of sympathomimetics are implied urgently in treatment of priapism. A penile block might be utilized for this but can be omitted too. Block is performed with 10 to 20 ml quantity of 1% lignocaine that is infiltrated just below the symphysis pubis in order to block the dorsal nerves of penis. After applying a tourniquet to the base of the penis, 16 or 18 gauge intra-venous catheter is inserted laterally into the corpus cavernosum through the penile skin (taking care to avoid injury to dorsal neurovascular bundle and urethra). On the other hand, the cannula can also be inserted via glans penis thus reducing chances of skin bruising. Due to the interconnectivity of the two corpora cavernosa, unilateral aspiration is enough. Cavernosal blood is aspirated with alternate injection of heparinized saline. This cycle is repeated till 1 hour and up to 50 ml of blood can be aspirated. Aspiration alone achieves a success rate reaching approximately thirty percent [12,16-21].

**Adjunct intracavernosal injections:** Injecting phenylephrine into cavernosa might be attempted concomitantly. However, it is pertinent to note that it too has several risks and side effects such as tachycardia, malignant hypertension and cardiac arrhythmia (especially in patients with history of cardiovascular ailment). Usually, phenylephrine has to be diluted in normal saline solution (concentration of 100 - 200 mg/mL). Then it is slowly injected maintaining a rate of 1 mL every five minutes under strict blood pressure monitoring [9-13].

**Prolonged episode of priapism:** In case of prolonged erection, more invasive therapy such as resorting to creation of surgical shunt can be considered. If timely diagnosis is made and patient might make full recovery from priapism with more chances of intact sexual function on long-term basis. Use of timely surgical intervention if indicated for priapism and accompanying treatment protocol followed for underlying CML (such as using cytoreductive therapy) might bring satisfactory outcome [11-16].

### Role of leukapheresis

Leukapheresis is a technique in which circulating blood is separated into liquid and blood cells that is followed by elimination of WBCs while putting back the remaining components into the circulation of patients. There are some side effects inherent with this procedure

such as hypothermia and electrolyte disturbances. Electrolyte monitoring and corrections are to be strictly followed. In addition to this, body temperature should also be monitored and maintained.

Till now not more than 2 dozen cases could be reported for priapism secondary to complication of underlying CML. Some authors reported that these special conditions required surgical interventions in form of shunting procedure in case of failure of the initial aspiration of cavernosal blood and phenylephrine injection [13-18]. Despite the initial measures taken the priapism might return owing to the underlying hyperleukocytosis in such special cases. In one case even in the face of best medical efforts by utilizing ample intravenous hydration and concomitant regime of Cytarabine and Hydroxyurea, it required to wait for 4 days to lessen the WBC count to a level lower than  $50 \times 10^9/L$ . In such very demanding scenario leukapheresis could be a helpful option. In past, in few cases, utilizing leukapheresis was a successful tool for achieving detumescence without requirement of additional surgical procedures such as shunting surgery. Veljković D., *et al.* utilized this concept of leukapheresis for single cycle each on three successive days. In yet another case reported by another author, seven sessions. Ergenc H., *et al.* mentioned their experience in a different manner as they utilized only one session (three hours duration) to attain complete detumescence [14-16]. In these special cases subjects' WBC count were surpassing  $300 \times 10^9/L$ . It was utilization of this leukapheresis concept that they were in position to reduce enormous WBC count below level of  $100 \times 10^9/L$  after a single session. It should be kept in mind however that leukapheresis is not commonly available option in many centers globally. In such cases, the oncologic regimen of treatment can be limited to utilization of chemotherapy and concomitant hydration.

A very sparse data is available till now regarding apposite management pathway for subjects suffering from priapism secondary to CML. Some of the guidelines in this regard mentioned to start systemic treatment of an underlying disorder (CML). Systemic therapies for such patients comprise of cytoreductive therapies including high-dose hydroxycarbamide, tyrosine kinase inhibitors (TKIs). These can be used alone or in combination with utilization of leukapheresis in order to diminish the detrimental effects of hyperviscosity. As described already the emergency is dealt with by Intra-cavernous treatment [17-20]. Treatment of priapism in such special cases where there is underlying CML calls for a very judicious and timely multi-disciplinary efforts from hematology, oncology and urology teams. Depletion therapy of WBC by utilizing hydration, chemotherapy and leukapheresis can be helpful in decreasing blood viscosity [19-21].

### Surgical options of treatment

- a. **Shunt procedures:** Winter shunt procedure is a form of cavernoglanular shunt. Other of such cavernoglanular shunts encompass the T-shunt, Ebbehøj, and Al-Gorab shunts. All of these shunts are types of distal shunts. Sometimes proximal shunts are needed called as the Quackles and caverno-venous shunts. A distal shunt is usually preferred. However, in some conditions distal shunt might be inappropriate because of the condition of edema or tissue damage. Proximal shunt is less preferably utilized owing to its inherent complications such as more chances of urethral fistula, erectile dysfunction or pulmonary embolism [20-22].
- b. **Early penile prosthesis:** Early penile prosthesis implantation is advocated in situations such as shortened, damaged tissues and a non-erectile penis. Aside from the quick resumption of sexual activity, early implantation might be of benefit as it can help circumvent formation of dense fibrosis that can lead to shortened penis [22].

### Conclusion

A launching manifestation of CML as priapism is rare and unusual phenomenon. All emergency physicians must keep a low threshold for timely intervention for managing such a rare case. Keeping in view the dismal outcomes if priapism and the underlying CML remains improperly managed, it is imperative to manage such a rare clinical case in unison with the oncological and urological team.

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