Case Report: Priapism as The Clinical Presenting Feature of Chronic Myeloid Leukemia: Case Report and 20-Year Literature Review [version 2; peer review: 2 approved]

Previously titled: 'Case Report: Priapism as The Clinical Presenting Feature of Chronic Myeloid Leukemia: Case Report and 20-year Literature Review'

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Abstract
Priapism in chronic myeloid leukemia (CML) appears to be an infrequent manifestation as well as a crucial emergency. Here, we report an 18-year-old male presenting with a persistent erection of the penis for 20 days. We evaluated and compared the reported cases within 20 years discussing the management of priapism in CML. Cytoreductive therapy followed by leukapheresis, the administration of tyrosine kinase inhibitor, and intra-cavernosal blood aspiration may resolve the symptoms of priapism. Early intervention for cytoreduction and aspiration are the pivotal keys to successfully impeding the complications.

Keywords
priapism, chronic myeloid leukemia, cytoreduction, penile-aspiration, cancer
Introduction

Priapism is a urological emergency due to persistence of an erection lasting more than 4 hours, whether or not it is related to sexual influence. Priapism is a rare condition with an incidence of 1–5 cases per 100,000 people per year. Penile erection in priapism is regularly painless. There are two types of priapism, which are low-flow priapism and high-flow priapism. Low-flow priapism is provoked by a pathological condition of low venous blood flow causing stasis in the penile vessels. This condition is an emergency condition that can result in cell damage and fibrosis, thus it often requires immediate therapy. Meanwhile, high-flow priapism is caused by increased blood flow to the sinusoid arteries without offsetting the flow to the veins. One of the causes of high-flow abnormalities is penile injury, while low-flow priapism is commonly caused by blood disorders such as sickle cell anemia and chronic myeloid leukemia (CML).

Priapism accounts for 20% of the hematological abnormalities while 1–5% of priapism are due to leukemia. The theory behind a priapism is the dysregulation of nitric oxide (NO) in penile vascularization. This occurs due to changes in NO synthase enzyme activity which decrease NO production by the corpora cavernosa. This ischemic condition induces platelet aggregation, thrombus, and tissue damage. Decreased NO interferes with smooth muscle tone and generates the priapism. Hyperviscosity conditions due to leukocytosis and adenosine-opiorphins abnormalities is also involved in this condition.

Currently, the approach to treat CML patients with priapism uses a combination of systemic therapy (chemotherapy with hydroxyurea or tyrosine kinase inhibitors and leukapheresis) and local intracavernosal therapy. Some cases with late manifestations cause erectile dysfunction, gangrene and penile abscess. This case report and review aims to discuss the clinical characteristics and outcomes of CML patients who experience priapism.

Case

An 18-year-old unmarried male student, presented at the ER complaining of persistent erection of the penis. The patient complained of persistent erected penis for 20 days before admission. There was no phase without an erection in between. Previously, there was neither history of trauma to sexual stimulation, nor consumption of certain drugs. The patient also complained of mild genital pain along with the onset of erection. There were no complaints about discoloration of the penis; becoming reddish, bluish, or pale, also there was no numbness. The patient could urinate normally (see Figure 1).

The patient complained of tinnitus in his right and left ears for 15 days accompanied by blurred vision. The patient also felt that his left side of stomach was slowly enlarging for 5 months. There was no bleeding and fever. Before coming to the

Figure 1. Penis at day 2, day 6 (after intracavernosal blood aspiration), and day 9.
ER, the patient was hospitalized at the regional hospital and received a blood transfusion and was diagnosed with a blood disorder.

Physical examination revealed no anemia and icterus. The spleen was palpable showing Schuffner 4 and Hackett 3. There was no enlargement of the lymph nodes. His laboratory findings were: hemoglobin 10.4 g/dL; leucocytes 421,000 cells/mm³; platelets 407,000 cells/mm³; white blood cells differential 4.3/6.8/81.3/4.9/2.7; blood urea nitrogen 9 mg/dL; serum potassium 0.5 mg/dL; uric acid 6.5 mg/dL. Peripheral blood smear showed normochromic anemia, normocytic anisopikilocytosis, leukocytosis (3% myeloblasts, 6% promyelocytes, 4% myelocytes, 2% metamyelocytes, 5% stab neutrophils, 63% segment neutrophils, 6% eosinophils, 6% basophils, 5% lymphocytes, 2% monocytes, atypical lymphocytes (+)) concluded as CML. The patient received hydroxyurea 2000 mg once daily at night, paracetamol 500 mg TID, and an urgent leukapheresis.

The patient underwent leukapheresis once per day (three times since initial admission) with gradual improvement. Unfortunately, on the fourth day of treatment the patient felt a penis erection again with pain on a scale of 0–5. Local examination of the genitalia showed a maximal erected penis, with no discoloration indicative of hyperemia, cyanosis, or pallor. Blood gas analysis showed pH 6.95, pCO₂ 64 mmHg, HCO₃ 14 mEQ/L, BE -18 unit. We concluded that the patient had ischemic priapism. Therefore, the patient underwent intracavernous aspiration producing 150 mL blood. Not long after that, the patient’s penis returned to an erection with bleeding from the puncture wound. We then decided to give leukapheresis to the patient.

On the eighth day of treatment, the erection improved with pain scale of 1. Quantitative BCR–ABL examination showed a positive result of 65%, thus the administration of hydroxyurea was stopped and replaced by imatinib 400 mg once daily at night. On the twelfth day of treatment, the erection completely resolved and the patient was successfully discharged from the hospital.

Discussion
This review presents data on patients who have priapism due to CML (see Table 1). Priapism occurred in the age ranging from 9–53. Patients usually had episodes of priapism for 18 h to 7 days. Not all patients with priapism showed a typical clinical examination of CML in the form of splenomegaly, but all of these patients had a hyperleukocytosis profile with a leukocyte count >200,000 cells/mm³. Some of them are equipped with data of peripheral blood smear with excessive blast and identification of BCR–ABL gene. A study by Minckler et al. was the only one reporting a resolved erection with a cold shower, whilst most other cases needed medical intervention. Although the duration of symptoms varied, four cases reported complications following an episode of priapism. Patients with unfavorable outcomes once received hydroxyurea, imatinib but failed to undergo urological emergency therapy such as intra-cavernosa aspiration, surgical intervention, and embolization.

The patient in our study was 18 years old. However, based on the literature, patients in every age group are at risk of developing priapism. There are two peaks in the age distribution that tend to experience this condition. The peak in earlier age is between 5 and 10 years, especially in patients with sickle cell disease. Meanwhile, the second peak is at sexually active phase between 20 and 50 years. Apart from hypercoagulability, this condition may also be related to the abuse of erectile drugs.

History and physical examination are important when encountering cases of priapism. Laboratory tests are required to check for impaired coagulation and serum electrolytes. Some patients who are at high risk for priapism include users of intracorporal injection therapy for erectile dysfunction, coagulation disorders such as sickle cell disease and CML. In CML, hyperleukocytosis is thought to be the prime cause of priapism. The main mechanism is the aggregation of leukemic cells in the corpora cavernosa and dorsal veins of the penis. Other than that, mechanical pressure in the abdominal veins due to the enlargement of the spleen might also increase the risk.

The data needed in the management of patients with this case are erection duration, pain scale, trauma, complete blood count, peripheral blood smear, penile blood gas analysis, bone marrow and polymerase chain reaction for BCR–ABL if necessary. In CML, the most common type of priapism is the ischemic one (veno-occlusive). Patients usually complain of painful, rigid erection, with reduced to no cavernous blood flow at all. Priapism that lasts for more than 4 hours indicates a compartment syndrome and may require emergent medical intervention.

The American Urological Association recommends that systemic treatment of an underlying disorder should not be the only one therapy for ischemic priapism. In this case, the patient had an erectile episode since 20 days before the admission. This phenomenon was likely due to the compartment syndrome, hence the intra-cavernous aspiration was required.
| No | Author | Country | Year | Age | Duration of priapism | Diagnosis of CML | Treatment of CML | Treatment of priapism | Outcome of the treatment |
|----|--------|---------|------|-----|----------------------|-----------------|-----------------|----------------------|-------------------------|
| 1  | Gaye et al. | Senegal | 2020 | 46  | 48 hours             | White Blood Cell: 526000/mm³, Platelets: 412000/mm³, Myelogram result: bone marrow hyperplasia, Karyotyping: Translocation between chromosomes 9 and 22 | Imatinib (the dosage wasn’t mentioned) | Aspiration of corpora cavernosa, injection of phentylephrine, hydroxy carbamide | Success |
|    |        |         |      |     |                      |                 |                 |                      |                         |
|    |        |         |      |     |                      | White Blood Cell: 82000/mm³, Platelets: 81000/mm³, BMA: acute myeloid leukemia | Vincristine and Prednisolone | penile skin refrigeration, rehydration, puncture of corpora cavernosa, injection of phentylephrine | Success |
| 2  | Rajabto et al. | Indonesia | 2020 | 44  | 4 days               | Physical exam: pale skin, conjunctival pallor, leukemic retinopathy in both eyes. Schuffer 2 | IV fluid, Allopurinol 300 mg, Sodium bicarbonate 500 mg 3 times daily, hydroxyurea 1 gram three, Imatinib 400 mg times a day | aspiration of penile corpus, injection of epinephrine | suffered ED |
|    |        |         |      |     |                      | Labs: anemia, hyperleukocytosis, microcytic hypochromic, anisopoikilocytosis, fragmentocytes, polychromic erythrocytes, a left shift, platelet count (355,000/μL), and hyperleukocytosis (399.560/μL). |                         |                       |                       |
|    |        |         |      |     |                      | Positive BCR-ABL1 | BMA: hypercellularity |                         |                         |
| 3  | Dhar et al. | India | 2019 | 52  | 4 hours              | Physical examination: massive splenomegaly of 8 cm below the left costal margin along with hepatomegaly of 3 cm below right costal margin. Blood count: left sided granulopoeis, total leucocyte count of 239×10⁹/L and platelet count of 625×10⁹/L. | Hydroxyurea 500 mg TDS, Imatinib OD, Allopurinol 300 mg OD, adequate hydration | needle aspiration --> didn’t work, went for Winters procedure | Success |
| No | Author | Country  | Year | Age | Duration of Priapism | Diagnosis of CML | Treatment of CML | Treatment of Priapism | Outcome of the Treatment |
|----|--------|----------|------|-----|----------------------|------------------|------------------|-----------------------|------------------------|
| 4  | Becerra et al. | Mexico | 2018 | 52  | 6 day evolution | WBC: 282,000, platelets: \(368 \times 10^3/mm^3\) | dasatinib 100 mg/day +G15 | corpora cavernosa irrigation and surgery penis shunts | Success |
|    |        |         |      |     |          | BMA: acute phased CML | | translocation t(9;22)(q34; q11.2) with P210 BCR-ABL1 fusion transcriber | |
| 5  | Khan et al. | Pakistan | 2018 | 16  | 264 hours | Leukocyte count: \(614.8 \times 10^9\), platelets \(709 \times 10^9/L\), peripheral smear: myeloid hyperplasia, neutrophilia. BMA: myeloid hyperplasia. Detection of BCR-ABL | Hydroxyurea, allopurinol | Glans-cavernosal shunt | Achieved detumescence, No info on ED |
| 6  | Qu et al. | China | 2018 | 18  | 72 hours | Hepatosplenomegaly 2-3 cm under arcus costae, blood count: white blood cell (WBC) \(257 \times 10^9/L\) and platelets (PLT) \(5450 \times 10^9/L\) | Imatinib | Caverosa-corpus spongiosum shunt | No ED at 3 months follow up |
| 7  | Clark et al. | USA | 2018 | 13  | 3 days | Blood count: WBC count of \(350,000/mL (350 \times 10^9/L)\) and platelet count of \(450 \times 10^9/mL \) \(450 \times 10^9/L\). Flow cytometry of blood: granulocytosis with no increase in blasts | Leukapheresis, IV fluids, hydroxyurea, allupurinol, Imatinib | Phenylephrine injection, three times corporeal irrigation | Improved with phallus rigidity and tenderness |
|    |        |         |      |     |          | BMA: Philadelphia chromosome | | | |
| 8  | Kumar et al. | India | 2018 | 47  | 5 days | Hepatosplenomegaly, WBC: \(279 \times 10^9, 91.2\%\)BCR | Hydroxyurea, Imatinib | Aspiration and irrigation with phenylephrine, Winter’s T Shunt | Successful treatment |
| 42 |        |         |      | 7 days | Splenomegaly 6 cm below costal margin, WBC: \(390 \times 10^9/L, 70.7\%\) BCR-ABL ratio | Hydroxyurea, Imatinib | Aspiration and irrigation | Successful treatment |
| 28 |        |         |      | 6 days | No hepatosplenomegaly, WBC: \(206 \times 10^9/L, 75.3\%\)BCR-ABL ratio | Hydroxyurea, Imatinib | Aspiration and irrigation with phenylephrine, Winter’s T Shunt | Successful treatment |
| No | Author | Country | Year | Age | Duration of priapism | Diagnosis of CML | Treatment of CML | Treatment of priapism | Outcome of the treatment |
|----|--------|---------|------|-----|---------------------|-----------------|------------------|----------------------|------------------------|
| 9  | Sun et al. | USA     | 2018 | 27  | 8 years, persistent erection 9 hours | Labs: anemia, WBC 450,010/mm³, Platelets 509,000/mm³, Peripheral blood smear: hyperleukocytosis with absolute neutrophilia and a peripheral blast count of 2%. Bone marrow aspirate and biopsy: hypercellular marrow with 4% blasts. BCR-ABL did not reveal clonal evolution. | Leukapheresis, hydroxyurea 500 mg daily, allopurinol 300 mg daily, Imatinib 400 mg daily, Corpus body aspiration, 1 dose of phenylephrine injection | Successful treatment |
| 10 | Huei et al. | Malaysia | 2018 | 28  | 48 hours | Hepatomegaly 2 cm below right costal margin, splenomegaly, anemia, WBC 294,000/μL, Platelets 94,000/μL, Peripheral blood smear: hyperleukocytosis, blast cells | Leukapheresis, intravenous Cytarabine | Hydroxyurea, allopurinol, intravenous Cytarabine, Intracavernosal aspiration, phenylephrine irrigation --> detumescent --> recurrent erection --> corpoglandular shunt | Successful treatment |
| 11 | Minckler et al. | USA | 2017 | 18  | 3 month intermittent | WBC: 588×10⁹/L, Platelets: 109×10⁹/L | Hydroxyurea transition to imatinib 400 mg daily | Penile irrigation and aspiration | Successful |
| 12 | Nerli RB et al. | India | 2016 | 19  | duration: 24 hours | WBC 296,810, Platelet 936,000/mm³, BM/ A: hypercellular, increased megakaryocytes | Hydroxyurea 1.5 gram daily, Imatinib 40 mg daily, Allopurinol 300 mg daily | Irrigation, decompression | Successful |
| No | Author               | Country | Year | Age | Duration of priapism | Diagnosis of CML                                                                 | Treatment of CML                                  | Treatment of priapism | Outcome of the treatment |
|----|----------------------|---------|------|-----|----------------------|--------------------------------------------------------------------------------|--------------------------------------------------|-----------------------|------------------------|
| 13 | Ergenc H et al.     | Turkey  | 2015 | 18  | duration: 72 hours   | Hepatosplenomegaly 2-3 cm under arcus costae, anemia, WBC 100,000, platelets 1,002,000/mm, peripheral blood smear: immature leukocytes. BMA: hypercellularity with myeloid hyperplasia, positive BCR-ABL translocation | Imatinib 400 mg once daily, allopurinol 300 mg once daily, leukapharesis | not mentioned         | Success                |
| 14 | Shaeer et al.      | Egypt   | 2015 | 21  | 6 days               | palpable splenomegaly, WBC 410000, Philadelphia chromosome translocation         | Leukapharesis, Imatinib 400 mg daily              | failed several cavernosal aspiration and injection of epinephrine → penile prosthesis | No complication throughout 6 months-follow up |
| 15 | Osorio et al.       | Spain   | 2014 | 24  | 14 hours, the second episode. The first episode was 4 months ago | WBC: 177.15 × 10^9, platelet was not mentioned, cytogenic diagnosis: showing CML | Imatinib                                         | Corpora cavernosa aspiration, intracavernosa fenilefrin injection | not mentioned          |
|    |                      |         |      |     |                      |                                                                                   |                                                  |                        |                        |
| 29 |                      |         |      |     | 6 hours, the second episode. The first episode was less than a month ago | WBC: 402.24 × 10^9, platelet was not mentioned positive BCR-ABL                     | Hydroxyurea                                      | Corpora cavernosa aspiration, intracavernosa fenilefrin injection | not mentioned          |
| 16 | Hazra et al.        | India   | 2013 | 14  | 24 hours             | Splenomegaly 6 cm below the left costal margin, anemia, WBC 226900, platelets 310,000/uL, Peripheral blood smear: immature leukocytes in various stages. BMA: CML. | Hydroxyurea 50 mg/kgBB/day, Allupurinol 300 mg/day | Cavernosal aspiration and phenylephrine irrigation | No recurrence at 2-months-follow-up |
| 17 | Veljkovic et al.    | Serbia  | 2012 | 16  | 24 hours             | Splenomegaly 4 cm below costal margin, WBC 320 × 10^9/L, Platelet (Plt) 417 × 10^9/L BMA: extreme hypercellularity, BCR/ABL positive | Leukapharesis, cytoreductive chemotherapy          | Leukapharesis          | No follow up            |
| No | Author            | Country | Year | Age | Duration of priapism | Diagnosis of CML                                                                 | Treatment of CML                                                                 | Treatment of CML                                                                 | Outcome of the treatment |
|----|-------------------|---------|------|-----|----------------------|--------------------------------------------------------------------------------|--------------------------------------------------------------------------------|--------------------------------------------------------------------------------|-------------------------|
| 18 | Paladino et al.   | Spain   | 2011 | 16  | 48 hours             | Splenomegaly, WBC 312,000, PLT 60,000/mm³, BMA: showing CML                    | Corpora cavernosa drainage                                                     | Terbutaline 0.125 mg subcutaneously IV fluid 3L/day, allopurinol, Imatinib, hydroxyurea 4g/day, Imatinib, leukapheresis | Erectile dysfunction      |
| 19 | Gupta et al.      | India   | 2009 | 12  | 48 hours             | Hepatosplenomegaly below the costal margins, anemia, WBC: 346,10⁹/L, platelet count of 40,000/mm³, peripheral blood smear: immature leukocytes, Cytochemistry: Philadelphia chromosome, BCR-ABL transcritp was positive | Hydroxyurea 4g/day, IV fluid 3L/day, allopurinol, Imatinib, leukapheresis         | Allopurinol, Imatinib, Terbutaline 0.125 mg subcutaneously IV fluid 3L/day, allopurinol, Imatinib, leukapheresis | Resolved by 24 h         |
| 20 | Ilais Tazi       | Morocco | 2009 | 33  | duration: 22 hours   | Palpable splenomegaly 4 cm below left costal margin, WBC: 400,000/mm³, peripheral blood smear: immature leukocytes, Karyotype analysis: Ph¹ chromosome, myeloid hyperplasia | Imatinib                                                                     | Aspiration               | Successful              |
| 21 | Castagnetti et al.| Italy   | 2008 | 9   | several days         | Splenomegaly, anemia, WBC: 395,000, Philadelphia chromosome, BCR-ABL +         | Hydroxyurea 1.5mg/m²/day, Cyclophosphamide 250 mg/m²/day for 2 days, leukapheresis | Hydroxyurea 1.5mg/m²/day, Cyclophosphamide 250 mg/m²/day for 2 days, leukapheresis | Fully resolved after 1 month |
| 22 | Yoshida et al.    | Japan   | 2007 | 29  | 96 hours             | mild splenomegaly, WBC: 263,000, PLT: 110,000/mm³                           | LMWH 90 units/kg SQ BID for 1 month, Metamizole, Imatinib, Metamizole, Morphine | LMWH 90 units/kg SQ BID for 1 month, Metamizole, Imatinib, Metamizole, Morphine | Fully resolved after 3 months |
| 23 | Lopez et al.     | Spain   | 2004 | 29  | 10 hours             | Hepatosplenomegaly 49 days, WBC: 414,10⁹/L, BMA: hypercellularity, PLT: 1100 x 10⁹/L | Corpora cavernosa aspiration, phenylephrine injection | Corpora cavernosa aspiration, phenylephrine injection | no evidence of recurrent |

Table 1. Continued
| No | Author | Country | Year | Age | Duration of priapism | Diagnosis of CML | Treatment of CML | Treatment of priapism | Outcome of the treatment |
|----|--------|---------|------|-----|---------------------|-----------------|------------------|----------------------|------------------------|
| 24 | Ponniah et al. | United Kingdom | 2004 | 19 | 18 hours | WBC 513,109/L | Leukapheresis | failed cavernosal aspiration + leukapheresis | No ED on follow up |
| 25 | Dogra et al. | India | 2003 | 18 | 10 days | hepatosplenomegaly, anaemic, WBC 320000, PLT was not mentioned | Intravenous hydration, furosemide, sodium bicarbonate, hydroxyurea, allopurinol, leukapheresis | Winters Procedure | impotent and enlarged penis at 3-months follow up |
| 26 | Meng-Wei Chang et al. | Taipei | 2003 | 21 | 19 hours | Hepatomegaly 6 cm below right arcus costae, Splenomegaly 7 cm below left arcus costae, anemia, WBC 216800, Platelet 1746,000/mm^3 | Interferon alfa-2a (6 MIU/veil), allopurinol 300 mg daily | Aspiration, epinephrine irrigation | Success |
| 27 | Guerra et al. | Spain | 2002 | 53 | 12 hours | WBC 510000, BMA: myeloid hyperplasia, karyotype analysis: chromosome Ph1 | Hydroxyurea | Corpora cavernosa aspiration | Successful treatment |
| 28 | Murayama et al. | Japan | 2001 | 14 | 4 days | WBC 510000, BMA: myeloid hyperplasia, karyotype analysis: chromosome Ph1 | Urokinase, hydroxyurea | Embolization of bilateral pudendal artery | Reduced sexual potency |
| 29 | Rojas et al. | Chilli | 1998 | 22 | duration: 36 hours | none | WBC 510000, BMA: myeloid hyperplasia, karyotype analysis: chromosome Ph1 | Surgical intervention | Unsuccessful (post-treatment sexual dysfunction) |
The intra-cavernous aspiration procedure can be accomplished by giving the anesthetic injection first under the symphysis pubis. The penis is tied with a tourniquet followed by insertion of a 16–18-Gauge bivalve intravenous catheter into the corpus cavernosum. When the two corpora are fused, aspiration of 20–30 mL of blood can be undertaken. This procedure has 30% chances of success.8,9

Systemic therapy is often used to reduce hyperviscosity is cytoreductive therapy such as high-dose hydroxycarbamide and tyrosine kinase inhibitors (TKI) with or without apheresis procedures. Hydroxycarbamide can be given 2–6 grams divided into four doses per day. This can reduce leukocytes by almost 60% in 24–48 h. In addition, TKI, such as imatinib, can be administered as soon as the diagnosis is confirmed. The recommended dose of imatinib is 400 mg once daily in the chronic phase, 600–800 mg once daily in the accelerated phase, and 800 mg once daily in a blast crisis.9 Generally, IRIS study describes the effectiveness of imatinib therapy for complete hematological response (CHR), major cytogenetic response (McyR) and complete cytogenetic response (CcyR).4

Leukapheresis can promote a rapid decrease in intravascular leukemic cells, improve tissue perfusion and prevent leukostasis (generally show pulmonary and central nervous system manifestations). Once leukapheresis is given, it possibly can reduce the leukocyte count by 30–60%. However, compared to the chemotherapy, several previous studies have shown that this procedure had high all-cause mortality. According to 2016 apheresis guidelines, category 2 (second-line therapy) is recommended for grade 1B of acute myeloid leukemia (strong recommendation, moderate quality evidence), while category 3 (unclear role of apheresis) is recommended for acute lymphoblastic leukemia cases grade 2C (weak recommendation, low quality evidence). In this guideline, leukapheresis is not recommended for chronic myeloid leukemia.10 Several cases of priapism in this case review reported a successful combination of leukapheresis with systemic oral CML therapy. A study by Rojas et al. was the only one reporting a failed leukapheresis.

This case report and review presents a comparative presentation of patient characteristics, clinical characteristics of CML, laboratory profile, and therapeutic intervention for CML with priapism. Clinical presentation and early intervention are pivotal keys to achieve favorable outcome and prevent complications. Systemic intervention combined with intraurethral therapy may add the success rate (see Figure 2).

Eventually, further discussion and study on other causes of priapism is essential as a meta-analysis stated that priapism might also be related to lymphoproliferative disorders.32

| Treatment: | N  | %  |
|-----------|----|----|
| Cytoreduction | 19 | 54% |
| Tyrosine Kinase Inhibitor | 17 | 49% |
| Leukapheresis | 13 | 37% |
| Penile aspiration | 19 | 54% |
| Penile aspiration and sympatomimetic | 10 | 29% |
| Penis-Shunt | 6 | 17% |

| Outcome: | |
|---------|---|
| Success | 22 | 63% |
| Erectile dysfunction | 3 | 9% |
| Not mentioned | 4 | 11% |

**Figure 2. Treatment and outcome from priapism and CML.**
Consent
Written informed consent for publication of their clinical details and/or clinical images was obtained from the patient.

Data availability
All data underlying the results are available as part of the article and no additional source data are required.

References

1. Rodgers R, Latif Z, Copland M: How I manage priapism in chronic myeloid leukaemia patients. Br J Haematol. 2012; 158(2): 155–64. PubMed Abstract | Publisher Full Text
2. Shaer Ok, Shaer KZ, Abdelrahman IF, et al.: Priapism as a result of chronic myeloid leukemia: case report, pathology, and review of the literature. J Sex Med. 2015; 12(3): 827–34. PubMed Abstract | Publisher Full Text
3. Paladino N, Roldán D, Caram MS: Priapism secondary to chronic myeloid leukemia. J Clin Apher. 2004; 19(3): 82–3. PubMed Abstract | Publisher Full Text
4. Sun HH, Zhang JH, DeWitt-Foy M, et al: Unusual Presentation of Priapism Associated with Acute and Chronic Myeloid Leukemia in Two Patients: Emergency Management. Case Rep Emerg Med. 2020; 2020: 3962432. PubMed Abstract | Publisher Full Text | Free Full Text
5. Minckler MR, Conser E, Figueroa JJ, et al.: Priapism Secondary to Chronic Myeloid Leukemia. Urology. 2017; 109(5): e104–8. PubMed Abstract | Publisher Full Text
6. Veljkovic D, Kuzmanovic M, Mišić D, et al.: Leukapheresis in management hyperleucocytosis induced complications in two pediatric patients with chronic myelogenous leukemia. Transfus Apher Sci. 2012; 46(3): 263–7. PubMed Abstract | Publisher Full Text
7. Neri R, Magdum PV, Hiremath SC, et al.: Priapism – A Rare Presentation in Chronic Myeloid Leukemia: Case Report. Urol Case Rep. 2016; 4: 8–10. PubMed Abstract | Publisher Full Text | Free Full Text
8. Chang MW, Tang CC, Chang SS: Priapism – a rare presentation in chronic myeloid leukemia: case report and review of the literature. Chang Gung Med J. 2017; 2017; 30(4): 288–92. PubMed Abstract
9. Rajabto W, Jirananon J, Pratithitha LB, et al.: Priapism as Leukostasis Manifestation in Chronic Myeloid Leukemia. Acta Med Indones. 2020; 52(4): 420–2. PubMed Abstract
10. Schwartz C, Panmananaban A, Aquil N, et al.: Guidelines on the Use of Therapeutic Apheresis in Clinical Practice-Evidence-Based Approach from the Writing Committee of the American Society for Apheresis: The Seventh Special Issue. J Clin Apher. 2016; 31(3): 149–62. PubMed Abstract | Publisher Full Text
11. Dhar J, Dhar J, Chhabra G, et al.: Priapism as a Debut Presentation of Chronic Myeloid Leukemia. J Coll Physicians Surg Pak. 2019; 29(1): 78–80. PubMed Abstract | Publisher Full Text
12. Becerra-Pedraza LC, Jiménez-Martínez LE, Peña-Morfin I, et al.: Priapism as the initial sign in hematologic disease: Case report and literature review. Int J Surg Case Rep. 2018; 43: 13–7. PubMed Abstract | Publisher Full Text | Free Full Text
13. Khan A, Shafiq I, Shah MH, et al.: Chronic myeloid leukaemia presenting as priapism: A case report from Khyber Pakhtunkhwa. J Pak Med Assoc. 2018; 68(5): 942–4. PubMed Abstract
14. Qu M, Lu X, Wang L, et al.: Priapism secondary to chronic myeloid leukemia treated by a surgical cavernosa-corpus spongiosum shunt: Case report. Asian J Urol. 2019; 6(4): 373–6. PubMed Abstract | Publisher Full Text | Free Full Text
15. Clark AJ, Hsu P, Darves-Bornaz A, et al.: Priapism in a 13-year-old Boy. Pediatr Rev. 2018; 39(12): 617–9. PubMed Abstract | Publisher Full Text | Free Full Text
16. Kumar P, Rahman K, Kumari S, et al.: Priapism as a rare presentation of chronic myeloid leukemia. J Cancer Res Ther. 2018; 14(6): 1442–3. PubMed Abstract | Publisher Full Text
17. Huer TJ, Lip HT, Shamsuddin O: A rare presentation of chronic myeloid leukemia with priapism treated with corporoglandular shunting. Med J Malaysia. 2018; 73(6): 420–2. PubMed Abstract
18. Ergenc H, Varım C, Karacaer C, et al.: Chronic myeloid leukemia presented with priapism: Effective management with prompt leukapheresis. Niger J Clin Pract. 2015; 18(6): 828–30. PubMed Abstract | Publisher Full Text
19. Villegas Osorio JF, Corchuelo Mallo C, Cuevas Palomino A, et al.: Ishaemic priapism as a presentation of chronic myeloid leukemia. Arch Esp Urol. 2014; 67(8): 708–11. PubMed Abstract
20. Hintz J, Priyadarshi V, Goggi D, et al.: Pediatric priapism: a rare first manifestation of leukemia. APSR J Case Rep. 2013; 4(3): 39. PubMed Abstract | Free Full Text
21. Veļķovs D, Kuzmanovs M, Mičē D, et al.: Priapism secondary to leukemia: successful treatment with cavernous lavage plus adjuvant methoxamine. Rev Lat Med. 2014; 61(4): 297–300. PubMed Abstract | Publisher Full Text
22. Khan A, Seth T, Gupta A: Successful use of terbutaline in persistent priapism in a 12-year-old boy with chronic myeloid leukemia. Pediatr Hematol Oncol. 2009; 26(1): 70–3. PubMed Abstract | Publisher Full Text
23. Tasi I: Priapism as the first manifestation of chronic myeloid leukemia. Ann Saudi Med. 2009; 29(5): 412. PubMed Abstract | Publisher Full Text | Free Full Text
24. Castagnetti M, Saiatori L, Giona F, et al.: Conservative management of priapism secondary to leukemia. Pediatr Blood Cancer. 2008; 51(3): 420–3. PubMed Abstract | Publisher Full Text
25. Yoshida K, Kinoshita H, Taniguti H, et al.: Priapism complicated by chronic myelogenous leukemia (CML): a case report. Hinyokika Kiyo. 2007; 53(5): 323–5. PubMed Abstract
26. Alhué López M, García de Jaldón Martínez A, Pascual Regueiro D, et al.: Priapism as an initial presentation of chronic myeloid leukemia. Actas Urol Esp. 2004; 28(5): 387–9. PubMed Abstract
27. Ponniah A, Brown CT, Taylor P: Priapism secondary to leukemia: effective management with prompt leukapheresis. Int J Urol. 2004; 11(9): 809–10. PubMed Abstract | Publisher Full Text
28. Dogra PN, Kumar P, Goel R, et al.: Long duration priapism in blast crisis of chronic myeloid leukemia. J Assoc Physicians India. 2004; 52: 170. PubMed Abstract
29. Cruz Guerra NA, Ramos LC, Linares Quevedo A, et al.: Priapism secondary to chronic myeloid leukemia: value of initial treatment with cavernous lavage plus adjuvant methoxamine. Arch Esp Urol. 2002; 55(6): 320–1. PubMed Abstract
30. Murayama K, Shibuuya A, Ishii S, et al.: Embolization of the bilateral internal pudendal arteries for intractable priapism in a child with chronic myelogenous leukemia. Rinsho Ketsueki. 2001; 42(1): 1117–1. PubMed Abstract
31. Rigas B, Cabrera ME, Kliwadenko W, et al.: Priapism in a patient with chronic myeloid leukemia. Revista medica de Chile. 1998; 126(8): 978–80. PubMed Abstract
32. Ali EA, Sardar S, Yassin MA: Priapism in lymphoproliferative disorders: A systematic review. Hematol Oncol Stem Cell Ther [Internet]. 2021. Publisher Full Text
Open Peer Review

Current Peer Review Status: ✔ ✔

Version 2

Reviewer Report 14 January 2022
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✔ Ritu Gupta
Laboratory Oncology Unit, Dr B.R. Ambedkar IRCH, All India Institute of Medical Sciences (AIIMS), New Delhi, New Delhi, Delhi, India

The authors have summarized the subject adequately and I have no further comments.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Hemato-Oncology, Genomics, Single-cell sequencing, Flow cytometry

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 02 December 2021
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? Ritu Gupta
Laboratory Oncology Unit, Dr B.R. Ambedkar IRCH, All India Institute of Medical Sciences (AIIMS), New Delhi, New Delhi, Delhi, India

Priapism is an unusual complication of hematological malignancy with hyperleukocytosis and may be the presenting feature, especially in chronic leukemia as observed in this case.
The authors have described the clinical features, investigations, and management of the index case and reviewed the literature on the association of priapism with CML.

I have a few comments/suggestions on this manuscript as detailed below:

1. The title is too long and can be abbreviated.

2. Review of hematological malignancies presenting as priapism i.e. including CLL and Acute leukemia would benefit the readers in developing insight on the conditions in which priapism could be the presenting feature. A few references include the following: Johnson et al. (2020), Ali et al. (2021) and Gogia et al. (2012).

3. The meaning of some of the sentences is not clear in several places. The authors may focus on improving the language of the paper.

References
1. James Johnson M, Hallerstrom M, Alnajjar HM, Frederick Johnson T, et al.: Which patients with ischaemic priapism require further investigation for malignancy?. Int J Impot Res. 2020; 32 (2): 195-200 PubMed Abstract | Publisher Full Text
2. Ali EA, Sardar S, Yassin MA: Priapism in lymphoproliferative disorders: A systematic review. Hematol Oncol Stem Cell Ther. 2021. PubMed Abstract | Publisher Full Text
3. Gogia A, Sharma A, Raina V, Gupta R: Priapism as an initial presentation of chronic lymphocytic leukemia. Leuk Lymphoma. 2012; 53 (8): 1638-9 PubMed Abstract | Publisher Full Text

Is the background of the case’s history and progression described in sufficient detail?
Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?
Yes

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?
Partly

Is the case presented with sufficient detail to be useful for other practitioners?
Yes

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** Hemato-Oncology, Genomics, Single-cell sequencing, Flow cytometry

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.
Author Response 03 Dec 2021

Pradana Zaky Romadhon, Airlangga University, Faculty of Medicine, Surabaya, Indonesia

Firstly, thank you for the detailed review and advice. We have simplified the title and removed unclear sentences then replaced them with more understandable ones.

*Competing Interests:* No competing interests were disclosed.

Author Response 04 Dec 2021

Pradana Zaky Romadhon, Airlangga University, Faculty of Medicine, Surabaya, Indonesia

Dear Ritu Gupta,

We already just submitted our new version of the manuscript. We also have included one of the references recommended by you in our discussion. Hope it will upgrade our manuscript quality. Thanks again.

*Competing Interests:* No competing interests were disclosed.

Reviewer Report 18 October 2021

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Wulyo Rajabto
Division of Hematology-Medical Oncology, Department of Internal Medicine, Dr. Cipto Mangunkusumo General Hospital, Faculty of Medicine, University of Indonesia, Jakarta, Indonesia

This case report emphasizes the importance of priapism as the rare clinical presentation of chronic myeloid leukemia so that as a clinician we should think if there is patient with priapism the secondary causal is chronic myeloid leukemia. The treatment of priapism consists of: 1) Local factor by urologist who performs intra cavernous aspiration 2) The systemic factor by hematologist who administers leucapheresis (mechanical and drug eg. Hydroxyurea) and TKIs such as Imatinib.

I find the title of this manuscript indeed captivating. Besides describing the priapismus phenomenon in CML, the author also showed to us a comparison study among several previously published cases known worldwide, that I think it is a very interesting plus point.

- Title: I believe it is very interesting, straightforwardly describes the case.
- Introduction: I believe it contains concise reasoning why the author brought up this case,
emphasizes the rare of similar cases, and interestingly presents one of CML emergencies.

- Case presentation: The author successfully managed to present the case elaborately along with valid data.

- Discussion: The author describes the case comprehensively, referred to similar case studies before, from the clinical course to the outcome, as mention on table 1.

Is the background of the case's history and progression described in sufficient detail?
Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?
Yes

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?
Yes

Is the case presented with sufficient detail to be useful for other practitioners?
Yes

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** CML, lymphoma, anemia

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.