BirEx JOURNAL
Budapest International Research in Exact Sciences
Medical, Biological, Argiculture, Engineering
Science and other related areas
e-ISSN : 2655-7827
p-ISSN : 2655-7835
http://www.bircu-journal.com/index.php/birex

Priapism in Patients Chronic Myeloid Leukemia

Azhari Gani[1], Muhammad Jailani[2]
[1]*Department of Internal Medicine, Faculty of Medicine, Universitas Syiah Kuala, Banda Aceh, Indonesia*
[2]*Plastic,Reconstructive and Aesthetic Surgery Division, Faculty of Medicine, Universitas Syiah Kuala, Banda Aceh, Indonesia*
azharigani@unsyiah.ac.id

Abstract: *The aims of this study are to find out the healing process of Priapism in Patients Chronic Myeloid Leukemia. This study used one case of patient which has some complaint, The patients is man with age 29 years old, The patient complained of an enlarged left stomach since 4 months and became heavy in the last 2 weeks, On vital sign examination, compos mentis awareness was found with blood pressure 110/70 mmHg, pulse 80 times per minute, respiratory rate 20 times per minute and temperature 37oC. On the visual analogue scale (VAS) examination showed a value of 4-6 (moderate pain). The result shows that CML is a hematological malignancy characterized by the Philadelphia chromosome and detected clonal expansion of hematopoietic stem cells from ABL BCR examination on chromosomes 9 and 22 which is characterized by an increase in the number of leukocytes with or without enlargement of the spleen. One of the complications of CML is priapism which occurs due to hyperleukocytosis which causes an increase in the viscosity of the blood and this is a major cause of complications of vascular obstruction. Priapism in CML is classified as low-flow (static / ischemic) caused by venocclusiveness which must be treated immediately to restore blood flow to the cavernous corpora by means of needle aspiration.*
Keywords: *priapism; patients; chronic myeloid leukemia*

I. Introduction

Chronic myeloid leukemia (CML) is a hematological malignancy that is other than hematopoietic cells, and has the characteristics of the amount of leukocyte that is very elevated in the blood. In general, leukemia is a common malignancy, but is only a small part of the overall cancer. (Appleby, 2015)

Some epidemiological data show that the prevalence of leukemia in western countries is 13 / 100,000 population / year. Leukemia constitutes 2.8% of all cancer cases, and there is not yet a single conclusion regarding the incidence of leukemia in Indonesia. The incidence of *acutemyeloidleukemia* (AML) is approximately 2-3 / 100,000 populations, and AML is more frequently found in adults (85%) than children (15%). (Sholikah, 2017)

The incidence of acute lymphoblastic leukemia (ALL) is 2-3 / 100,000 populations, and is more often found in adults (83%) than children (18%). CML is 15-20% of cases of leukemia and is the most common chronic leukemia in Indonesia, while in western countries chronic leukemia is more common in the form of chronic lymphocytic leukemia (CLL). The incidence of CML is around 1.5 / 100,000 / year and can occur in both sexes (male: female ratio 1.6: 1). Generally CML affects middle age with a peak at age 55-60 years. In children can be found in the juvenile form of CML. (Longo, 2010)

The risk of CML increases with age. The average age of diagnosis when diagnosed is 65 years, and only 10-15% are less than 50 years old. The incidence rate is in the list of 3 / 100,000 per year. In the geriatric population, the incidence over the age of 70 is about 50 / 100,000 per year. The ratio of relative risk to women in elderly is 2.8: 1. (Besa, 2014).

Chronic Myeloid Leukemia (CML) has 3 important phases of the disease, namely chronic, accelerated and blast crisis phases. Phase chronic is characterized by the presence of the number of granulocytes and platelets almost close to normal, and in general the patient looks asymptomatic. Accelerated phases are phases in which the pain is more aggressive and painful. Symptoms of anemia include *pallor, dyspnea* and *tachycardia*. *Blemishes, epistaxis, menorrhagia,* or bleeding elsewhere due to abnormal platelet function. Rare symptoms include visual disturbances and *priapism*. (Besa, 2014)

Priapism is a prolonged penile erection (more than 4 hours) without sexual desire and is often accompanied by pain and is one of the rare complications of CML. The incidence of *priapism* in adult patients with leukemia is about 5%. *priapism* is one of the emergency emergencies in the field of urology because if it does not cause erectile dysfunction. (Tazi, 2009)

As many as 60% of cases of *priapism* are idiopathic, whose cause is not clear, while 40% of cases are associated with leukemia, sickle cell disease, pelvic tumors, pelvic infections, penile trauma, spinal *cordtrauma*, use of certain drugs (*trazodone*, alcohol, *psychotropics,* and anti-hypertension) or after *intracavernosal* injection with *vasoactive* substances, (Ervie, 2015).

II. Case

It has been examined by a 29 year old male patient with the main complaint of genital tension accompanied by pain and swelling, this has been experienced by the patient since 14 days before coming to the hospital. The patient had gone to the puskesmas but the patient was not willing to take action because the pain could still be endured and the patient was referred to the hospital. The patient complained of pubic tension and pain that was getting worse and agreed to undergo surgery.

The patient also complained about the pale that had been felt by the patient since 4 months ago and the patient had never received a transfusion. The patient also felt tired quickly when doing strenuous activities but could still do light and moderate activities such as walking. Feeling tired was not accompanied by shortness of breath and chest pain. Complaints of shortness of night during sleep, swollen legs when sitting or standing, and a history of chest pain during activity were not found. Histories of smoking with consumption of 1 pack a day.

The patient complained of an enlarged left stomach since 4 months and became heavy in the last 2 weeks. This complaint was accompanied by a feeling of fullness so that he was quickly full by eating a little without pain. Appetite was still good but was only able to eat a little. Nausea and vomiting was not felt by the patient. There is no vomiting or black bowel movement. There are no complaints of defecation and urination.

The patient has lost weight since the last 4 months by 10 kg. The patient also complained of fever fluctuating since the last 1 month. The fever was not too high and decreased without taking medication. Complaints of chills and joint pain were not complained by the patient. History of cough and cold was not complained by the patient.

The patient works as a farmer. The patient often uses fertilizers and pesticides. During this time the use of personal protective equipment such as masks and gloves when using fertilizers and pesticides. The patient is married with a sufficient daily life

On vital sign examination, compos mentis awareness was found with blood pressure 110/70 mmHg, pulse 80 times per minute, respiratory rate 20 times per minute and temperature 37oC. On the visual analogue scale (VAS) examination showed a value of 4-6 (moderate pain).

On physical examination, the patient looks pale without bleeding from the mouth and gums or from the urinary or digestive tract. On the examination of the abdomen, the spleen is palpable with a hard consistency, flat surface, with a *schuffner* size 6. On the genetalia examination, the penis is erect and swollen. The skin looks reddish, and on hard and painful touch. On palpation, there were no lymph nodes in the *cervix, clavicle, aksilar,* or *inguinal.* Other physical examinations were within normal limits.

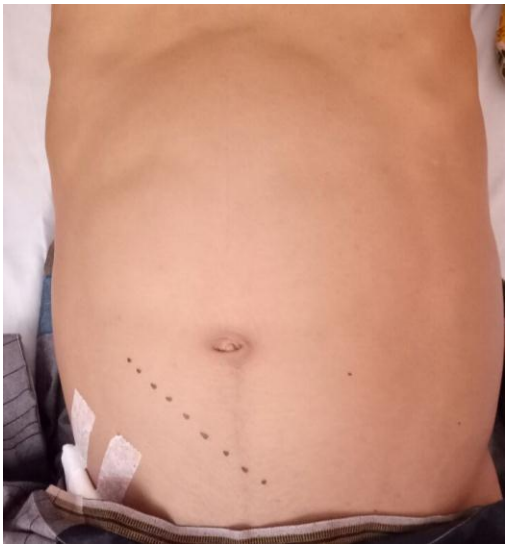

Figure 1. *Schuffner Splenomegaly 6*

Figure 2. *An Erect Patient's Penis*

On routine blood laboratory tests, Hb 6.3 g / dL, Ht 17%, erythrocytes 1.9x106 / mm3, leukocytes 544,500 / mm3, platelets 362,000 / mm3, with MCV 91 fL, MCH 34 pg, MCHC 37%. On the type of *leukocytes, eosiophils* 2%, *basophils* 4%, stem *neutrophils* 0%, segment *neutrophils* 87%, lymphocytes 2%, and *monocytes* 5%. Peripheral blood morphology has been carried out with the conclusion of the suspicion of CML, namely young leukocytes and blast cells, with an increasing number of *myelocytes* and *metamyelocytes, normochromic anisocytosis* erythrocytes and normal platelet counts and sizes. From these morphological results, bone marrow examination is recommended.

Bone marrow puncture (BMP) examination showed an increase in *granulopoitic* series, namely 74.2%, *myeloblast* 7.8%, lymphocyte series decreased by 16.7%, decreased *thrombopoysis, normal monocytes* were 4.4%, *eosinophils* 5.6%, *plasma cells* 0.3%, and no malignant cells were found. BMP results showed chronic type CML.

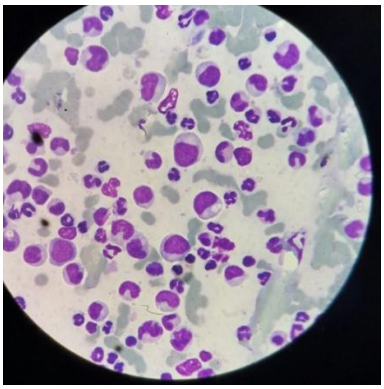

Figure 3*. Microscopic View of the BMP Examination*

On the *Break-Point Cluster Region-Abelson* (BCR ABL) qualitative test, which was carried out by taking the patient's blood, the b2a2 transcript (p210 / Major Breakpoint cluster region) was detected. ABL BCR examination in this patient showed results in accordance with CML.

Doppler ultrasound examination of the penis showed dilated dorsal veins and normal blood flow and velocity. Abdominal ultrasound examination showed the hepatic size of the right lobe was 15.4 cm and the left lobe was 10.3 cm, the parenchyma was homogeneous and there were no focal lesions, and the spleen was 25 cm in size with homogeneous parenchyma and no visible local lesions. Absent ascites and other abdominal organs in normal condition.

On a normal chest X-ray, there was no visible infiltrates in the lungs, the heart looked normal, and the *costophrenic* was sharp, the bones were intact without any signs of fracture, the soft tissue did not appear abnormal.

Based on the results of the history, physical examination, laboratory and radiological examinations, the patient was diagnosed with *priapism* and CML. The patient was admitted to the surgical urology division and resuscitation was planned by means of cavernous aspiration. After the patient and family informed consent, the action was carried out by administering local anesthetic first. Aspiration is carried out using a needle and approximately 20 cc of blood is drawn, after which the wound is closed with sterile gauze. Patients were given 2x500 mg *hydroxyurea (Citodrox)*, 1x75 mg *dabigatran (Pradaxa)*, and 2x300 mg *nilotinib (Tasigna)* given for 30 days for 1 cycle.

After 14 days of treatment, the patient was discharged without any signs of priapism and good vital signs. Laboratory examination showed Hb 6.9 g / dL, Ht 20%, *leukocytes* 361,300 / mm3, *platelets* 231,000 / mm3. On the type of leukocytes, *eosiophils* 2%, *basophils* 1%, *stem neutrophils* 0%, *segment neutrophils* 91%, *lymphocytes* 2%, and *monocytes* 4%. Patients are advised to re-control for 1 month for laboratory evaluation and treatment success.

At the first outpatient visit 1 month after being hospitalized, the patient complained that the penis was still swollen and erectile function was impaired. The patient admitted that his genitals could not be erect as before. Pain in the genitals was not complained. On physical examination, the penis was swollen with no pain, the spleen looked smaller. namely *Schuffner* 2 and the liver is not palpable. The laboratory examination showed Hb 9.0 g / dL, Ht 29%, *leukocytes* 8,300 / mm3, *platelets* 156,000 / mm3. On the type of *leukocytes*, *eosiophils* 8%, *basophils* 1%, stem *neutrophils* 0%, *segment neutrophils* 58%, *lymphocytes* 29%, and monocytes 4%.

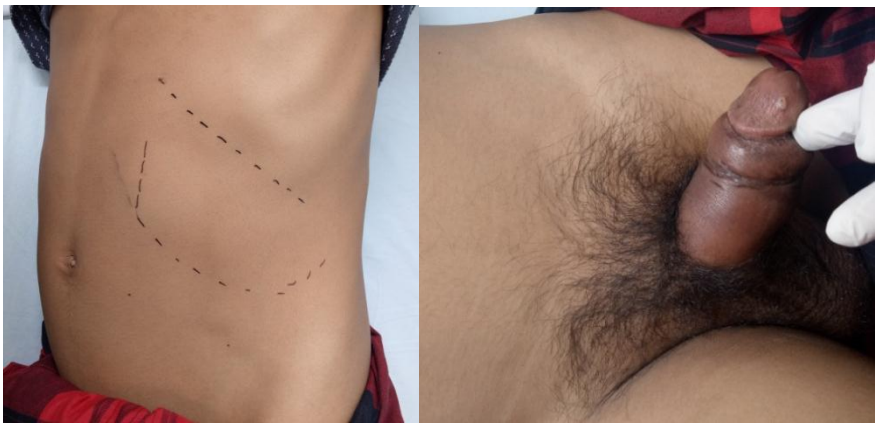

Figure 4. *Schuffner 2 Splenomegaly at 1 Month Post-treatment*

At the second visit after 2 months after treatment at the polyclinic, the patient still complained of genital swelling and could not get an erection. On physical examination, the penis appeared swollen without pain. Abdominal examination, the spleen was felt with a Schuffner 1 size, solid consistency, flat surface and no pain. Other physical and laboratory examinations are within normal limits.

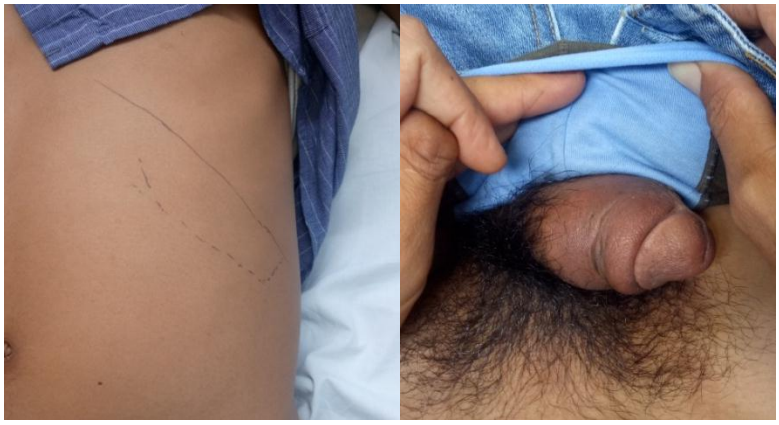

Figure 5. *Schuffner's Splenomegaly 1 and Penis 2 Months Post-treatment*

III. Discussion

CML is a *haematological* malignancy characterized by the Philadelphia chromosome and detected clonal expansion of *hematopoytic* stem cells from BCR ABL examination on chromosomes 9 and 22. This disease is generally caught accidentally in patients when performing blood tests with white blood cells that are increased with or without enlargement. lien. The most common manifestations of CML are anorexia, malaise, weight loss, sweating, bleeding in platelet dysfunction, feeling full and pain in the abdomen due to the enlargement of the spleen. (Ocheni, 2015)

The general diagnosis of MCL is *hematologically* determined by the presence of *leukocytosis* and immature *cellmyeloid* in peripheral blood. On a chronic basis, the number of leukocytes found is more than 50,000 / dL of blood, many myeloid cells in the peripheral blood smear, ranging from blast cells to *neutrophils*. Some patients also show *basophilia, eosinophilia, thrombocytosis* with *anisocytocystrombocyte*, usually a platelet count of more than 1,000,000 / dL. (8)

In the laboratory examination of the patient, there was an increase in the number of leukocytes on routine blood tests, namely 544,500 / mm3 leukocytes with a platelet count of 362,000 / mm3. On the type of leukocytes, the increase in segment *neutrophils* was 87%. Increase in *myelocyte* and *metamyelocyte* series. This is in accordance with the criteria of CML and is recommended for BMP and BCR ABL.

Examination of bone marrow in MCML patients revealed a very significant myeloid cell hyperplasia. The *granulopoitic* series increases by a proportion of 74.2% and can form a highly visible cluster on the biopsy specimen. In addition, the presence of *erythroid hypoplasia* is caused by increased *ratiomyeloid* and *erythroids*.

The occurrence of CML is related to the translocation of chromosomes 9 and 22 which produces the Philadelphia chromosome (Chromosome Ph). The translocation of chromosomes 9 and 22 causes a fusion between BCR and ABL agents which then becomes the BCR-ABL *genfusion* which codes for several fusion proteins that have high *tyrosinkinase* activity. BCR-ABL fusion has a size varies, depending on the type of BCR break *pointgen*. (Yu Kp, 1985)

Patients were given 2x500 mg of *hydroxyurea (Citodrox)*, 1x75 mg *dabigatran (Pradaxa)*, and 2x300 mg *nilotinib (Tasigna)* given for 30 days for 1 cycle and it was recommended to re-control for once a month. The purpose of giving *hydroxyurea* is to reduce the incidence of *vasocclusion* in veins. *Nilitinib* is a *tyrosine kinase* inhibitor (TKI) class that is used to enhance treatment in chronic phase CML or in conditions of resistance / intolerance to *imatinib*. (Ware, 2009)

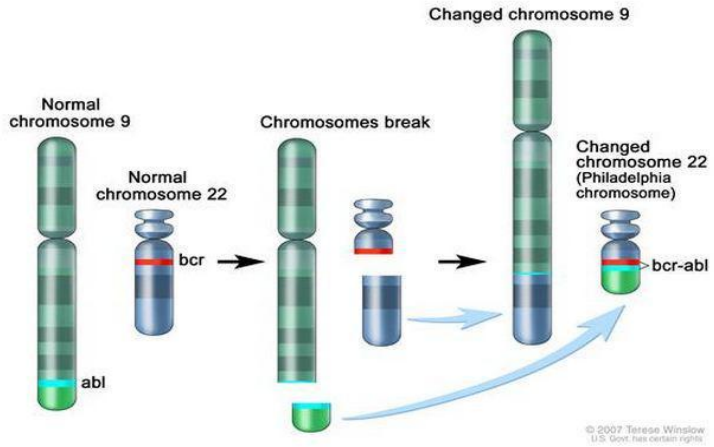

***Figure 6**. Philadelphia chromosome*

On physical examination, the spleen size decreased every month, *Schuffner* 6 spleen size at admission and reduced to *Schuffne*r 2 at the first visit to the clinic and *Schuffner* 1 at the second visit.

In the laboratory examination, the number of leukocytes was 544,500 / mm3 at admission and after 14 days of treatment the leukocytes fell to 361,300 / mm3. At the first visit to the polyclinic after 1 month of treatment, the leukocytes were 8,300 / mm3.

Priapism is a penis that experiences prolonged infections (more than 4 hours) without the presence of sexual desires. *Priapism* can occur at any age. In children it is usually caused by hematological disorders, while in adults (sexually active age) 20-50 years many are caused by other causes, for example the use of certain drugs. (Change, 2003)

The patient had *priapism* for 14 days and a cavernous aspiration procedure was performed which drained 20 cc of blood. After the procedure, complaints began to decrease and the penis was no longer erect but looked swollen. After 1 and 2 months after the procedure, the patient was still unable to maintain an erection and the penis was visibly swollen.

Priapism can occur due to: (1) disruption of the outflow mechanism (veno-occlusion) so that blood cannot get out of the erectile tissue, or (2) an increase in the inflow of arteriolar blood flow that enters the erectile tissue. Therefore, *hemodynamically*, *priapism* is divided into (1) *venoclusive* or low flow type *priapism* and (2) arteriolar or high flow type *priapism*. The two types can be distinguished by observing the clinical, laboratory, and color *doppller* ultrasound imaging examination and *arteriography*.

Ischemic type *priapism* is characterized by ischemia or anoxia in the cavernous smooth muscle. The longer the erection, the more severe the ischemia, and after 3-4 hours, the erection is very painful. After 12 hours of erection, there will be interstitial edema and damage to the cavernous sinusoid endothelium. *Muscle crosis* plain *cavernosa* occurs after 24-48 hours. After more than 48 hours there is blood clotting in the cavernous and endothelial destruction occurs so that the *trabecular* tissues lose their elasticity. If untreated, detachment (the size of the penis that returns to shrinking) occurs after 2-4 weeks and the smooth muscle that experiences *ecrosis* is replaced by fibrous tissue so that it loses the ability to maintain a maximum erection. arterial reconstruction in erectile dysfunction. The prognosis is better than the ischemic type and the erection can return to normal. (Farhan, 2015).

There are 5 *pathophysiological* mechanisms of *priapism* in CML, namely: (1) venous congestion of the *corpora cavernosa* that occurs due to mechanical pressure from the enlargement of the spleen in the abdominal veins, (2) deposits of leukemia cells in the *corpora cavernosa* and dorsal penile veins, (3) local infiltration *laukemic cells* in the sacral nerves, (4) leukemic infiltration of the central nerve, and (5) *hyperleukocytosis* which causes increased viscosity of the blood and is a major cause of complications of vascular obstruction. (Farhan, 2015).

Table 1. The Difference between Low Flow and High Flow in the *Pathophysiology* of *Priapism*

Parameter	Low flow (static / ischemic)- Veno Occlusive	High flow (nonischemic) -Arteriel
Onset	While sleeping	After trauma
Pain	At first, it becomes very painful at first	Mild to moderate
Penis tension	Very tense	Not Too Tense
Cavernous blood		
• Color	Black	Red
• pO2	<30 mmHg	>50 mmHg
• pCO2	>80 mmHg	<50 mmHg
• pH	<7,25	>7,5
Color Doppler	No Flow	There are streams and *fistulas Arteriovena malformations*
Arteriography	Whole blood vessels	

Hyperleukocystosis in CML causes the formation of leukocyte aggregations which will result in the formation of thrombus in small blood vessels which will lead to vascular obstruction. In this patient, *hyperleukocytosis* causes *leukostasis* and *microthrombus* in the *cavernosal* circulation which is the basis for *priapism*. (Ergenc, 2015).

In principle, the pyriapism is the immediate return of blood flow to the cavernous corpora which is achieved both medically and operatively. Prior to aggressive action, the patient is asked to perform the exercise by jumping in the hope of diversion of blood flow from the *gluteal cavernosakeotot*. Applying compresses of water to a cold to penis or enema may stimulate sympathetic activity thereby improving cavernous blood flow. In addition to providing good hydration and regional anesthetics may help in some cases. If the above measures do not work it may require aspiration, irrigation, or surgery. (Ergenc, 2015)

Aspiration of cavernous blood is indicated in non-ischemic *priapism* or *pismusischemic* men. Severe *pismusischemic* men who have occurred for several days do not respond to intra-cavernous aspiration and irrigation of the drug so surgery is required. Aspiracid is done using a scalp vein needle 21 as much as 10-20ml of *intracavernous* blood, then instillation of 10-20 μg of epinephrine or 100-200 μg of *phenylephrine* dissolved in 1ml of physiological saline every 5 minutes until the penis deteriorates. If done before 24 hours after the attack, almost all cases can heal this way. In addition to these drugs, strep *tokinase* instillation can also be used in men who have lasted 14 days of *priapism* who have previously failed α-adrenergic instillation.

IV. Conclusion

CML is a *hematological* malignancy characterized by the Philadelphia chromosome and detected *clonal* expansion of hematopoietic stem cells from ABL BCR examination on chromosomes 9 and 22 which is characterized by an increase in the number of leukocytes with or without enlargement of the spleen. One of the complications of CML is *priapism* which occurs due to *hyperleukocytosis* which causes an increase in the viscosity of the blood and this is a major cause of complications of vascular obstruction.

Priapism in CML is classified as low-flow (static / ischemic) caused by *venocclusiveness* which must be treated immediately to restore blood flow to the cavernous corpora by means of needle aspiration.

References

Appleby N, Burke E, Curran T, Neary E, Medicine Y, Marrow B. (2015). Chronic Myeloid Leukaemia : Molecular Abnormalities and Treatment Options. Res Gate;6:45–51.

Besa E, Krishnan K.(2014). Chronic Myelogenous Leukemia. Medscape;1–9.

Chang M-W, Tang C, Chang S. (2015). Priapism--a rare presentation in chronic myeloid leukemia: case report and review of the literature. Chang Gung Med J [Internet]. 2003;26(4):288–92. Available from: http://www.ncbi.nlm.nih.gov/pubmed/12846529

Ergenc H, Varım C, Karacaer C, Çekdemir D. (2015). Chronic myeloid leukemia presented with priapism : Effective management with prompt leukapheresis. Niger J Clin Pract. 2015;18(6):–7.

Ervie M, Boongaling DC, Mortel SRC, Deala RP. (2015). Priapism as a Rare Presentation of Chronic Myelogenous Leukemia;53(4):1–5.

Farhan S, Anjum F, Fs A, Ka A. Chronic Myeloid Leukemia Presenting with Priapism. Leukemia;3(1):1–5.

Hochhaus A, Saglio G, Hughes TP, Larson RA, Kim D-W, Issaragrisil S, et al. (2016). Long-term benefits and risks of frontline nilotinib vs imatinib for chronic myeloid leukemia in chronic phase: 5-year update of the randomized ENEST nd trial. Leukemia [Internet].;30(5):1044–54. Available from: http://www.nature.com/doifinder/10.1038/leu.2016.5

Longo DL.(2010). Harrison's Hematology and Oncology. 17th ed. Harrison's Hematology and Oncology. New York: McGraw Hill.

Minckler MR, Conser E, Figueroa JJ, Scott AJ, Gaither J, Amini R, et al. (2017).Case Report The Semantics of Priapism and the First Sign of Chronic Myeloid Leukemia.

Hindawi.;x:1–3.
Ocheni S, Ibegbulam O, Olusina D, Oyekunle A, Durosinmi M. (2010). Chronic Myeloid Leukaemia Presenting as Priapism: A Report of 2 Cases and Review of Literature. J Coll Med;15(2):5–10.
Reksodiputro H, Tadjoedin H, Supandiman I, Acang N, Kar AS, I MB, et al. (2015). Epidemiology Study and Mutation Profile of Patients with Chronic Myeloid Leukemia (CML) in Indonesia. J Blood Disord Transfus;6(3):1–13.
Sholikah TA. (2017). Fusion Gene BCR-ABL : from Etiopathogenesis to The Management of Chronic Myeloid Leukemia. J Kedokt dan Kesehat Indones;8(1):29–37.
Tazi L. (2009). Priapism as the first manifestation of chronic myeloid leukemia. Vol. 29, Annals of Saudi Medicine. p. 412.
Wahyudi SS, Soetojo. Priapismus [Internet]. p. 1–18. Available from: https://www.google.co.id/url?sa=t&rct=j&q=&esrc=s&source=web&cd=10&ved=0ahUKEwiko9SkKTXAhWJP48KHcdIBZ8QFghrMAk&url=http%3A%2F%2Fjournal.unair.ac.id%2Fdownloadfullpapersurologid6cd788b89full.pdf&usg=AOvVaw2zkKRuBH8CyDTOpz9yaUfp
Yu KP, Hwang WS, Lee WC, Lin JS, Her Twu B. (1985). Priapism in Patients with Chronic Myelodi Leukemia: Report of Two Cases. J Med Sci1.;6(1):87–92.
Ware RE, Aygun B. Advances in the use of hydroxyurea. Hematology [Internet]. 2009;2009(1):62–9. Available from: http://www.asheducationbook.org/cgi/doi/10.1182/asheducation-2009.1.62