Priapism in Chronic Myeloid Leukemia: A Rare Case

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ABSTRACT

Causes of CML not clear with an important role from gen and environment factors, such as pesticide use. Priapism in CML around 5%. The report from this case is a man 40 years old with erection complaint in 4 days, patient feel a painful and weak. Patient as a farmer. In the physical check. There is anemic palpebral conjunctiva, hepatosplenomegaly, erection. In the laboratory result, Hb 4.3, Leukocyte 354.300, peripheral blood picture suggests chronic hematological malignancy myeloid series, BMP showed chronic phase CML, cavernous sinus blood gas analysis pH 7.567 pCO2 33.7 HCO3 31.0. In the first control Hb 8.7 Leukocyte 22.500. Then, patient is aspirated and winter procedure for priapism management. Patient get transfuse PRC leukodeplected with the Hb target 10, Terbutaline tab 5 mg/12 hours, Allopurinol tab 300 mg/24 hours, hydroxyurea tab 1.500 mg/24-night hours. Giving Tyrosine Kinase inhibitor was delayed when controlling time because there is leukopenia so the blood should be monitor in two weeks routinely, then, in the second control, patient given nilotinib 1x150 mg and hydroxyurea was stopped. The conclusion is patient with priapism is clinical from leukocytosis in CML. Monitoring blood routinely is more important to assess the response to therapy, in addition, it is necessary to carry out a cytogenic and molecular evaluation.

Keywords: Chronic Myeloid Leukemia Priapism Peripheral blood

INTRODUCTION

Chronic Myeloid Leukemia (CML) is a cancer caused by the disorder in hematopoietic stem cell which sign of uncontrolled increasing from myeloid cell in the bone marrow. In the CML found proliferation from mature granulocytes (neutrophil, eosinophils, and basophil) and its precursor. This case is a myeloproliferative disease with chromosome translocation which called philadelphia chromosome (Sawyers, 1999).

Based on epidemiology, CML is generally more likely to occur at the age of 53-60 years, but the mean age is considered to be 40 years, although it can be found at a young age and it is more...
progressive. Causes of CML is not clear with a important role from gen and environment factors, such as radiation exposure and others (Rohrbacher & Hasford, 2009).

There are some risk factor that can increase a risk because of CML (Bintoro, 2019): Gender (A man has higher CML risk than a woman. But the explanation still not know yet);

1. Age
   The risk of developing CML increases with age. The age of diagnosis of CML is around 64 years. CML is rare in children and adolescents.

2. Radiation exposure
   A high radiation exposure after explosion of atom bomb in Hiroshima or after the accident of nuclear reactor in Chernobyl have related with the developing CML increasing between a survivor. Someone who exposure the radiotherapy in the cancer therapy perhaps has a CML risk.

3. Low immunity
   HIV/AIDS patients who have low immunity have a 3 times greater risk of developing leukemia than healthy people. Likewise, patients who received immunosuppressant drugs after organ transplantation had twice the risk of developing CML as normal people.

4. Ulcerative colitis or Crohn’s disease
   Some of research showed that enteritis inflammation, such as ulcerative colitis or crohn’s disease have a risk higher of suffer from CML.

5. Pesticide use
   Farmer or agricultural workers who exposure a pesticide have 40% increasing a CML risk than general population.

6. Benzene
   Have a contact with chemistry material (benzene) around years can increase a risk CML. Benzene is one of the chemistry materials in the oil and solvent which used in the rubber industry.

7. Obesity
   Canada’s research reported there is increasing twice risk of CML related with obesity. Obesity 28,5% from all the risk of CML (35,6% man and 23,0% woman).

CASE REPORT

Patient come to emergency room with erection complaint in four days SMRS. Erection occurs without sexual trigger. Drink a strong drug is denied. Erection does not subside although patient take a nap or sleep. Patient complaint the painful in the genitals.

Patients also feel weak in one weeks. Every activity he feels a weak. Weakness does not decrease if eating or sweet drink. Patient also feels weak. He denied complaints of weakness in the limbs, denied complaints of blurred vision, denied complaints of fever, and denied complaints of ringing in the ears. Complaints of shortness of breath were denied, headaches were denied.

The patient also complained of feeling full and groggy since 1 year of SMRS, but the patient ignored it and thought it was just stomach ulcers. Complaints of a full stomach and groaning have been felt heavier since 3 months of SMRS, the groaning was felt to be getting bigger, at that time the patient also complained of feeling weak and decreased appetite, because the stomach felt full and bloated. Denied complaints of nausea, denied vomiting, often belching was denied. The patient also said that during the past 3 months his weight had decreased. His initial weight was 66 kg to 54 kg.

The patient's urination is 5-7x a day, each urination is about -1 cup of star fruit, the color is clear yellow, the urine is colored like tea. The urination mixed with fresh blood was denied. The urination painful and mixed with sand is denied. The patient's bowel movements are 1x a day, soft consistency, yellow-brown color. The defecate mixed with fresh blood was denied. The defecate is black like petis is denied.
He denied a history of high blood pressure and diabetes. The patient has a known history of blood cancer (leukemia) since 1 month of SMRS, the patient just underwent a bone marrow examination on June 11, 2021 and there are no results. History of liver disease, heart disease, kidney disease was denied.

The previous disease that suffered patient is the similar disease are erection was denied, come to hospital since one month ago because Hb is decrease so he get a blood transfusion until four red blood bag, malignany was denied, allergy was denied.

In the physical check, general condition is moderate pain with awareness compus mentis, GCS: E4V5M6, blood pressure 110/60 mmHg, pulse 84x/minute, enough content and voltage, regular rhythm, respiratory rate 20x/minute, temperature 36.4°C (per axillar), visual analog scale (VAS) 2. Weight 54 kg, height 158 cm, BMI 21,6 kg/m², impress normoweight. Skin check: found paleness (+), not found hyperkeratosis in the body (-), fissura multiple (-), dry skin (-), dermatitis (-), yellow skin (-), pus (-), blood (-), butterfly rush (-), discoid (-), striae (-). Head check: not found mesocephal, black hair, white hair (-), hair loss (-), sore (-), atrofi m.temporalis (-). Face check: not found a moon face (-), malar rash (-), erythema in the face (-). Eyes check: not found a sunken eye (-/-), ptosis (-), blefaritis (-), oedem palpebra (-), found a pale conjunctiva (+/+), not found suffusion conjunctiva (-/-), icteric sclera (-/-), subconjunctiva bleeding (-/-), isochore pupil Ø (3m/3mm), found light reflex (+/+), not found cataract (-/-). Nose check: not found nostril breath (-), secret (-), epistaxis (-), olfactory dysfunction (-), septal deviation (-), nasal polip (sde), frontal sinus tenderness (-), ethmoidalis sinus (-), paranasal sinus (-). Mouth check: not found sianosis lips (-), dry lips (-), ulcer (-), sprue (-), trismus (-), hyperemic pharyngeal tonsils (-), gumboil (-), atrophic tongue papillae (-), tonsil T1-T1, hyperemic pharyngeal (-). Neck check: trachea middle, enlarged lymph nodes (-), enlarged tyroid (-), JVP (R+2) cm. Thorax check: not found normochest, symmetrical, retraction (-), thorax abdominal breathing, between ribs widening (-), aksilla lymph nodes enlargement (-). Abdomen check have schuffner 4. Extremity examination no abnormalities found.

In the supporting check found Hb 4,3 g/dl, hematocrit 11%, leukocytes 354,3 thousand/ul, platelets 254 thousand/ul, erythrocytes 1,38 million/ul, MCV 80,7/um, MCH 31,0 pg, MCHC 38,4 g/dl, eosinophils 7,00%, basophil 1,00%, neutrophils 74,00%, lymphocytes 3,00%, monocytes 1,00%.

**Electrocardiography**

![Figure 1. EKG, June 9, 2021](image)

EKG check result: sinus rhythm, frequency 100x/minute, axis normoaxis (40°), P phase 0,04 second, PR interval 0,12 second, QRS complex 0,06 second, isoelectric segment ST, T phase in the normal limit, there is no pathology Q phase, transition zone in V3, conclusion: rhythm sinus HR 100x/minute, normoaxis, ZT V3.
Thorax Photo PA

![Figure 2. Thorax photo PA, June 9, 2021](image)

In the thorax photo PA check: inspiration decrease, asymmetric, cor size and normal signs, Pulmo does not appear infiltrate in the second, pulmonary field, normal bronchovascular patterns, right left side of the costophrenicus, right left, right and left, trachea in the middle, good bone system, conclusions of cast and pulmo are not visible abnormalities.

Peripheral blood picture

![Figure 3. Peripheral blood picture](image)

In the peripheral blood picture: eritrocyte in the figure of normochrome, normocyte, eritroblast cell (+); total leukocyte increase, eosinophilia, basophilia in the maturation, myeloblast (+); Platelet there is an impression of the amount within normal limits, macrotrombocytes, clumping (+) in several fields of view. Conclusion the picture of the peripheral blood leads to the malignancy of the chronic hematology of the Myeloid series. Suggestion: BMP.

![Figure 4. BMP result, June 12, 2021](image)
BMP result, erythropoietic system: activity was decrease, maturase normal, granulopoietic system: activity was increase, myeloblast 9.8%, promielocytes 6.8%, thrombopoietic system: activity was normal, megakaryocytes > 2 lobus easy founded, Lymphopoietic system: decreased activity, normal maturase, conclusions in the picture of the bone marrow indicate chronic myelocytic leukemia (cml) chronic phase. During treatment, the patient gets a leukodeplected PRC transfusion with a target HB10, Terbutaline tab 5 mg/12 hours, Allopurinol tab 300 mg/24 hours, hydroxyurea tab 1.500 mg/24 hours night.

Based on clinical and supporting data, the patient's diagnosis after internal TS consultation is obtained by priapism, leukstasis, anemia with leukocytosis EC malignancy hematology (CML DD CLL). Currently obtained Goldman Score 0, with ACCP 7. medium risk. Acc Raber Sub HOM. After the TS Anesthesia consultation, a moderate general condition was obtained. A = Airway Clear, Open the mouth of 3 fingers, free neck motion, B = rr20x/minute, SDV +/+, ST -/- SPO2 99% with nasal canul 3LPM, C = TD = 116/82, HR 75x/minute, Ctr <2 seconds. In principle, agreed to take anesthesia with the status of hope Iie, Advis IV Line, Inform Concen, Fasting, Post Operation Moving Work. In TS Cardio consultation, compensated cordis. Mild risk tolerance. No acc Raber. For his reconciliation BTK.

In the controlling, patient have done routinely blood monitoring since June 10, 2021 – June 18, 2021 with the increase hemoglobin 11.4 g/dl, hematocrit 32%, leukocyte decrease 229.9 thousand/ul,
thrombocyte 315 thousand/ul, erythrocyte 3.72 million/ul, MCV 87.1/um, MCHC 35.2 g/dl, eosinophil 5.00%, basophil 0%, neutrophil 41.00%, lymphocyte 47.00%. In the laboratory result, Hb 4.3, Leukocyte 354,300, peripheral blood picture suggests chronic hematological malignancy myeloid series, BMP showed chronic phase CML, cavernous sinus blood gas analysis pH 7.567 pCO2 33.7 HC03 31.0. In the first control Hb 8.7 Leukocyte 3000, BCR ABL detected. In the second control, leucocyte 22,500.

Assessment priapism post aspiration and winter procedure, CML chronic fase with BCR ABL was detected. Allopurinol therapy tab 300 mg/24 hours, hydroxyurea tab 1.000 mg/24 hours night, tablets plus blood 1 tab/24 hours. Planning with control in two weeks, routine blood checks during control. During second control, patient was given nilotinib 1x50 mg and hydroxyurea was discontinued.

RESULTS AND DISCUSSIONS
In this case, the report from this case is a man 40 years old with priapism in Chronic Myeloid Leukemia (CML). This is based on patient’s anamnesis complaint suddenly erection. In the physical check obtained that anemic conjunctiva and hepatosplenomegaly. Meanwhile, in the supporting check obtained that Hb 4.3, Leukocyte 354,300. In the peripheral blood picture leads to malignancy of chronic hematology myeloid series, BMP obtained CML with BCR ABL was detected.

Patients obtained leukocytosis, with leukocyte total 354,300. Leukocytosis itself means an increase in the leukocytes total more than 11 x 10^9/uL. Leukocytes that range from 50,000-100,000/mm^3 in the absence of hematological abnormalities is called a leukemoid reaction. Leukocytosis itself means an increase in the number of leukocytes more than 11 x 10^9/uL. Leukocytosis that ranges from 50,000-100,000/mm^3 in the absence of hematological abnormalities is called a leukemoid reaction (Saultz & Garzon, 2016; Sudoyo, 2009).

In the CML meets Philadelphia chromosome (Ph1 chr) is a reciprocal translocation 9,22 (t9;22). Philadelphia chromosome is a abnormal chromosome 22 that caused by partial translocation genetic materials in the long sleeve (q) chromosome 22 to chromosome 9, and translocation reciprocal in the part chromosome 9, include oncogene ABL, to breakpoint cluster region, BCR is a point of separation where the break of a chromosome is specifically found on chromosome 22 (Saultz & Garzon, 2016). The most of oncogene ABL in the long sleeve of chromosome 9 have juxtaposition with oncogene BCR in the long sleeve of chromosome 22. Breaking point of ABL is between exon 1 and 2. Breaking point of BCR is one of the two points in the group region of main breaking point (M-BCR) of CML or some cases ALL Ph+. This fusion gene will transcribe chimeric RNA to form chimeric protein (210 kd protein). The emergence of this new protein will affect signal transduction, especially through tyrosine kinase to the cell nucleus, resulting in an excess of proliferative impulses in myeloid cells and decreased apoptosis. This causes proliferation in the myeloid series (Sudoyo, 2009). The patient was also tested for ABL BCR with detectable results.

Priapism is a prolonged erection of the penis (more than 4 hours) without sexual desire and accompanied by pain. Priapism is an emergency in the field of urology because if it is not treated quickly and appropriately it can cause erection dysfunction (Shaeer, Shaeer, AbdelRahman, El-Haddad, & Selim, 2015; Varm, Karacaer, Çekdemir, & Ergenc, 2015).

Most of the 60% priapism case is a idiopathic with no clear cause, meanwhile 40% of cases are associated with leukemia, sickle cell disease, pelvic tumors, pelvic infections, penile trauma, spinal cord trauma, use of certain drugs (trazodone, alcohol, psychotropics, alcohol, and antihypertensive) or after intracavernous injection with a vasoactive agent. The incidence of priapism in adult patients with leukemia is about 5% (Basuki, 2007; M, DC, SRC, & RP, 2015; Shaeer et al., 2015).

Priapism can occur because: (1) disruption of outflow mechanism (veno-oclusion) so that the blood cannot drop out from erectile system, or (2) there is an increase of in the inflow arterial blood into the erectile system. Therefore hemodynamic, priapism can be divided into (1) priapism in type veno oclusion or low flow and (2) priapism in type arterial or high flow. Both of those type can be
distinguished with the attention to clinical, laboratory, and color doppler ultrasound imaging checkup and arteriography. Anamnesia and conscientious check can be showed priapism etiology. In the local check obtained that penile shaft tension without being followed by tension on the glans penis. Doppler ultrasound can detect cavernous artery pulsations and analysis of blood gases taken intracavernous can distinguish ischemic or non-ischemic priapism (Basuki, 2007; Shaeer et al., 2015).

The patient had an ischemic priapism, which was characterized by ischemia or anoxia in cavernous smooth muscle. At the time of aspiration, the blood was black color, but the AGD showed incompletely compensated metabolic alkalosis leading to non-ischemic priapism (Basuki, 2007; Shaeer et al., 2015).

The mechanism of priapism in CML is thought to be caused by hyperleukocytosis and leukocyte aggregation in the sinusoids of the corpora cavernosa, resulting in sinusoidal swelling and penile erection. Blockage of the emissary and dorsal veins results in cessation of venous return. Another possible causes include mechanical pressure on the abdomimal veins by an enlarged spleen resulting in venous congestion in the corpora cavernosa (López & Martínez, 2004). Hyperleukocytosis in CML causes the formation of leukocyte aggregation which will result in the formation of thrombus in small blood vessels which will cause vascular obstruction. In these patients, hyperleukocytosis causes leukocytosis and microthrombi in the cavernous circulation which is the basis for priapism (Breyer & McAninch, 2008).

In this patient, emergency management of priapism was carried out, namely aspiration of the corpus cavernosum and the winter procedure. Management of chronic phase CML is given hydroxyurea to suppress leukocytosis. Hydroxyurea can reduce the white blood cells to normal in a few days or weeks and reduce spleen size, but does not reduce the percentage of cells with the Philadelphia chromosome and does not prevent blastic crises (Bintoro, 2019; López & Martínez, 2004; M et al., 2015). To avoid tumor lysis syndrome, the recommended fluid requirement is 2.5–3L per day taking into account the performance of the heart and kidneys. Sodium bicarbonate is administered maintaining a urine pH of 6.4–6.8 to optimize uric acid clearance. Allopurinol may be administered to increase the risk of xanthine accumulation in renal failure, and should be limited to patients presenting with symptoms of hyperuricemia (Andreas Hochhaus & Kantarjian, 2013).

This patient needs to be monitored to see the response to therapy according to the 2017 ESMO guideline, including: (A. Hochhaus et al., 2017).

1. Hematological Response

Hematologic response can be determined after 4 weeks of treatment by performing a complete blood count and peripheral blood smear every 2 weeks from the start of treatment. Complete Hematologic Response (CHR) if hematologically the leukocyte count < 10 x 109/L with a normal leukocyte count, platelet count < 10 x 109/L, basophils < 5%, no young cells and promyelocytes are found in the blood edge, and without symptoms and signs of disease.

2. Cytogenetic Response

Cytogenetic response is a therapeutic response to determine Philadelphia chromosome residuals by karyotyping at least 20 metaphases of bone marrow leukocyte cells taken by bone marrow aspiration. Cytogenetic examination was performed after 6 months of treatment. Cytogenetic responses are divided into 5 responses as follows:

a. Complete Cytogenetic Response (Complete CyR), if there is no Ph chromosome from 20 metaphases by "chromosome banding analysis" method or no Ph chromosome by the FISH (Fluorescence in situ hybridization) method.

b. Partial Cytogenetic Response (Partial CyR), if the Ph chromosome 1%-35% is still obtained from 20 metaphases.

c. Minor Cytogenetic Response (Minor CyR), if the Ph chromosome > 36%-65% is still obtained from 20 metaphases.

d. Minimal Cytogenetic Response (Minimal CyR), if 66%-95% Ph chromosomes are still obtained from 20 metaphases.
e. No Cytogenetic Response (NoCyR), if the Ph chromosome > 95% is still obtained from 20 metaphases.

3. Molecular Response

Molecular response is a benchmark to determine treatment response molecularly by measuring the number of ABL BCR transcripts by quantitative PCR (RT-PCR) examination. This test is performed by taking blood on a buffycoat to measure the BCR-ABL transcript, which is expressed as BCR-ABL with the International Scale (IS). Monitoring should be done every 3 months until the MMR is reached. This molecular assay is the most sensitive monitoring technique, thus detecting signs of drug resistance early.

a. Complete Molecular Response (CMR), if the concentration of the BCR-ABL transcript cannot be detected by the RQ-PCR method.

b. Major Molecular Response (MMR), if BCR-ABL < 0.1% (IS) or if there is a 3-log decrease in BCRABL1mRNA, equivalent to 109 leukemia cells.

c. Deep Molecular Response 4, if BCR-ABL1 0.01% IS or BCR-ABL is not detected at least 10,000 ABL or 24,000 GUS transcripts.

d. Deep Molecular Response 4.5, if BCR-ABL1 0.0032% IS or BCR-ABL is not detected at least 32,000 ABL or 77,000 GUS transcripts.

e. Early Molecular Response (EMR), if BCR-ABL< 10% (IS) in therapy three month with imatinib (Harrington, 2017). Failure to achieve RMD is associated with a lower risk of progression and survival. Patients who received imatinib 400 mg, nilotinib 2 x 300 mg or nilotinib 2 x 400 mg with dose discontinuation 5 consecutive days had a greater risk of RMD failure testing 15 of 16 studies that showed RMD achievement was also associated with longer OS and PFS. RMD is also associated with possible increased MMR and deep molecular responses such as MR 4.5 (BCR-ABL 0.0032%, decrease 4.5 log) (A. Hochhaus et al., 2017; Hughes et al., 2014; Yeung & Mauro, 2014).

Monitoring response to therapy To assess the effect of treatment, complete blood counts and peripheral blood smears are performed every 2 weeks, until a complete hematological response is achieved, then every 3 months (Network, 2018).

CONCLUSION

In this case, hyperleukocytosis causes leukocytosis and microthrombus in the circulating cavernosa that form the basis of priapism. In this patient, the emergency management of priapism was carried out, namely aspiration of the corpus cavernosum and the winter procedure. Management of chronic phase CML is given hydroxyurea to suppress leukocytosis. Routine blood monitoring is very important to assess the response to therapy in assessing the effect of treatment which is carried out every 2 weeks until a complete hematological response is achieved which is then every 3 months.

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