

Case Report

Priapism as the initial manifestation of chronic myeloid leukemia, a rare presentation

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ABSTRACT

Chronic myeloid leukemia (CML) is a myeloproliferative neoplasm with a median age of diagnosis in Mexico of 40 years. The initial manifestations are varied; however, priapism is a very rare entity associated to CML. We report the case of an 18-year-old male with an 8-hour episode of ischemic priapism managed with cavernous lavage, achieving complete flaccidity of the penis. The patient was diagnosed with CML, initiating cytoreduction with hydroxycarbamide and after having molecular confirmation, we started treatment with a tyrosine kinase inhibitor. The patient was discharged in excellent conditions, without sequelae of erectile dysfunction, all this attributed to the time of evolution, the adequate management of the urological emergency and the prompt identification and treatment of the precipitating condition.

Keywords: Leukemia, Myelogenous, Chronic, BCR-ABL positive, Protein kinase inhibitors, Priapism

INTRODUCTION

Chronic myeloid leukemia (CML) is a myeloproliferative disorder of clonal origin in hematopoietic multipotent cells with uncontrolled production of mature granulocytes by reciprocal translocation between chromosomes 9 and 22 t(9; 22)(q34; q11) producing an abnormally short 22 chromosome known as the Philadelphia chromosome (Ph).¹ This generates a chimeric BCR-ABL1 gene that transcribes a BCR-ABL1 fusion protein with 3 isoforms p190, p210, p230 depending on the site where the BCR translocation occurs.² The fusion protein has tyrosine kinase activity that activates signaling pathways that favor the growth, proliferation and survival of these cells by blocking apoptosis.^{1,2} BCR-ABL1 cells are genetically unstable with a predisposition to develop genomic abnormalities with transformation to a leukemic phenotype that progresses from the stable phase, called chronic, to the accelerated and blast phases.³ Granulocytic

cell production is the predominant cellular line observed in this disease however, basophils and eosinophils may also be present.²

The incidence of CML worldwide is 2 cases per 100,000 people per year, with a mean age at diagnosis of 57 years in developed countries⁴, contrary of what is seen in Mexico where the incidence at presentation of 10 to 15 years lower has been reported, with an average of 40 years of age at diagnosis, with a slight predominance of male over woman.^{1,3} CML represents 10% of all leukemias treated in Mexico, both acute and chronic.⁵

The clinical course of CML involves 3 phases of the disease: chronic, accelerated and blast phase, defined by World Health Organization (WHO) criteria; chronic phase with <10% of blasts in both peripheral blood and bone marrow, accelerated phase of 10% -19% blasts, ≥20% basophils, platelets <100 thousand, clonal evolution with

changes in karyotype, proliferation of megakaryocytes and fibrosis. Blast phase with >20% blasts in peripheral blood or bone marrow.² The latter becoming acute leukemia where 2/3 of the cases will be myeloid and 1/3 of the lymphoid.²

The signs and symptoms seen in the chronic phase are usually attributed to the degree of anemia and splenomegaly, manifesting as fatigue, abdominal discomfort and pain in the left upper quadrant. However, less common conditions such as thrombocytopenic bleeding, episodes of thrombosis, and leukostasis have been reported. Leukostasis generates hyperviscosity and can be seen as drowsiness, confusion, dyspnea, and priapism. It usually presents with a leukocyte count greater than $100 \times 10^9/L$.^{2,3}

Priapism is defined as a penile erection that continues beyond or is not related to sexual stimulation lasting more than 4 hours.^{6,7} It is a urological emergency due to the potential loss of erectile function. It can be grouped into ischemic or low flow and nonischemic or high flow priapism.⁷ The ischemic subtype is the most prevalent in clinical practice with multiple etiologies.⁷ Among the hematological causes, it is mainly associated with leukostasis, and it is usually observed in sickle cell anemia, multiple myeloma, β -thalassemia, glucose 6-phosphate dehydrogenase deficiency, chronic lymphocytic leukemia, acute lymphoblastic leukemia and chronic myeloid leukemia.⁶ Priapism in CML has a reported incidence of 1% to 5%, being a very rare complication associated with this hematological entity.⁶

CASE REPORT

A previously healthy 18-year-old male initiates with an involuntary erection lasting approximately 30 minutes, which spontaneously gave way. Two days after the first event, he presented a new one, unprovoked painful erection with complete penis stiffness, self-medicating himself with acetaminophen 500 mg / caffeine 50 mg / phenylephrine 5 mg without improvement, for which he arrived at the emergency department of our hospital. Upon admission with priapism of 8 hours of evolution, the Urology service was consulted who applied intracavernous phenylephrine injection without remission of the erection. The first gasometry of the corpora cavernosa showed: pH 6.8 pCO₂ 115 mmHg pO₂ 4 mmHg without improvement, so it was decided to enter the operating room for cavernous lavage with 0.9% saline solution until arterial blood was obtained, without the need to perform any other management. Intraoperative blood gases showing pH 7.27 pCO₂ 43 mmHg pO₂ 44 mmHg and at the end of the procedure pH 7.32 pCO₂ 40 mmHg pO₂ 47 mmHg.

He showed a leukocytosis of 522 thousand/uL, normochromic macrocytic anemia, hemoglobin 8.7 g/dL, MCV 100fL, HCM 32.8 and thrombocytosis, platelets 665 thousand / uL with an elevated lactic dehydrogenase of 1869 U/L. On physical examination, splenomegaly of 13

centimeters below the left costal margin stand out, which had generated abdominal discomfort of previous 3 months. Subsequently, a peripheral blood smear was performed, finding a leukoerythroblastic pattern (Figure 1) and a heterogeneous hypercellular bone marrow aspirate, with megakaryocytes per field of 2 to 3, myeloid-erythroid ratio 4:1, bands and segmented 50%, myelocytes and metamyelocytes. 23%, eosinophils 8%, red 12%, basophils 2%, lymphocytes 5% (Figure 2 A, B).

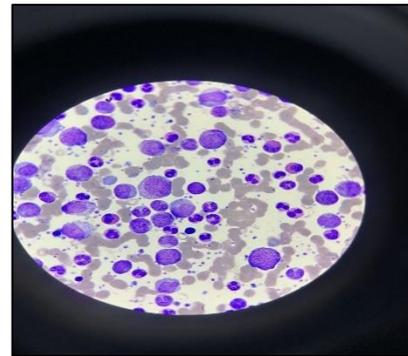


Figure 1: Peripheral blood smear with leukoerythroblastic pattern.

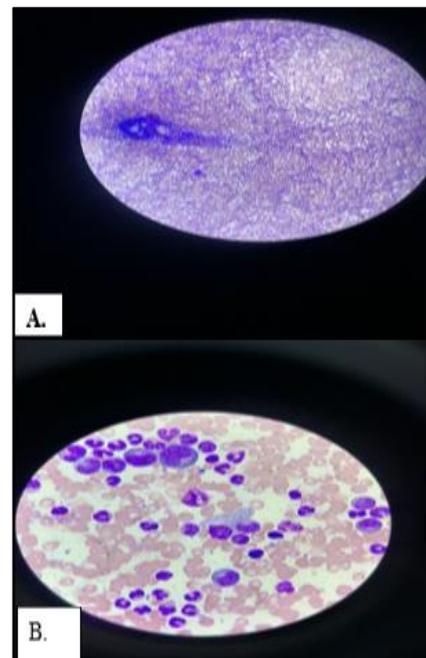


Figure 2: (A) Hypercellular bone marrow. (B) 100x magnification myeloid hyperplasia.

The iliac spine bone biopsy compatible with CML with a myeloerythroid ratio of 6:1. The bone marrow immunophenotype following the EuroFlow protocol, the screening panel for acute leukemias was carried out, finding a population of Blasts in 0.18% with the following phenotype: weak CD45 +, CD34 +, heterogeneous CD7±, MPO +, CD19-, CD79a -, CD3-, CD3cyt-. With an increase in the neutrophilic series of 92.01% and the presence of basophils in 5.02%. With a phenotypic

differentiation process of neutrophilic series within normal parameters with an increase in mature neutrophils that suggest compatibility with Chronic Myeloid Leukemia in chronic phase. A karyotype was requested finding translocation t(9; 22), we proceeded to perform real-time PCR looking for the BCR-ABL1 mutation for P210 with the result BCR-ABL1 / ABL1% (IS): 100,000 H. We decided to start treatment for cytoreduction with hydroxycarbamide at 30 mg/kg PO every 24h for 5 days and after the confirmation of the molecular diagnosis with the result of PCR. Treatment with Imatinib 400 mg PO every 24h was initiated.

The patient was discharged after 9 days of hospitalization, with total remission of the erection, with follow-up as outpatient. Diagnosis of Chronic myeloid leukemia in chronic phase was concluded. The patient is currently in hematological and molecular remission without repercussion on sexual function.

DISCUSSION

Patients with low-flow priapism often presents with pain and a completely rigid erection. The corpus cavernosum gasometry shows acidosis, hypoxemia and hypercapnia, just as our patient showed upon admission. Tissue damage begins 4 to 6 hours after the onset of erection.⁷ A period greater than 12 hours generates thickening and trabecular edema, at 24-48 hours platelet adherence to the sinusoidal endothelium and proliferation of fibroblasts with necrosis of the smooth muscle and thrombi in the sinusoidal spaces is observed, generating fibrosis and irreversible calcification with consequent erectile dysfunction.⁶ Due to the above, the priority in the management of our patient with an 8-hour evolution with a low-flow priapism was initially the injection of phenylephrine diluted in saline solution, however, at no sign of resolution of the clinical course, surgical lavage of the corpora cavernosa was made, until obtaining well-oxygenated blood. An arterio-cavernous fistula was not necessary in our patient. The treatment should be aimed at resolving the underlying pathology, however, with a special interest on reversing the urological urgency.^{6,7} The initial treatment of ischemic priapism, with more than 4 hours of onset, is aspiration of 5 ml of blood to decompress the corpora cavernosa with subsequent intracavernous injection of phenylephrine with a concentration of 100 to 500 mcg per ml diluted in saline solution.

Injections of 1 ml of the sympathomimetic are made every 3-5 minutes until resolution is observed or for 1 hour, before deciding to escalate the treatment.⁷ If the first line of treatment fails, a bypass surgery will be performed as a second line treatment, where a fistula is created between the corpus spongiosum and the corpus cavernosum.⁷ The high-flow variant is less frequent, does not present in hematological pathologies and is associated with penile and perineal trauma and congenital anomalies.^{7,8}

The first-line treatment of CML is tyrosine kinase inhibitors (TKI), however, prior to starting these drugs, molecular presence of the BCR / ABL1 oncogene must be confirmed.⁴ Imatinib is a first generation TKI, dasatinib, nilotinib and bosutinib are second generation and only third generation ponatinib active against the T315I mutation.⁴ In our patient, we started with a first generation TKI at a standard dose, since he was a first diagnosed patient. It is appropriate to administer a short course of hydroxyurea in symptomatic patients with high leukocyte and or high platelet counts in whom the diagnostic suspicion of CML is only awaiting molecular confirmation.⁴

Once the treatment with TKI is started, three types of responses will be sought at different times, the hematological response with a decrease in cell lines to normal values and absence of splenomegaly, which will be evaluated every two weeks until it is achieved and then every 3 months afterwards. The molecular response will be followed with quantitative PCR, measuring the percentage of BCR / ABL1 expression at 3 months after the onset of the TKI, and after reaching a major molecular response (MMR) with <0.1% of BCR / ABL1, they will continue with periodic review at 6 to 12 months. A close monitoring of the molecular response is necessary for those patients in whom it is decided to interrupt treatment and continue with only with surveillance.⁴ The treatment response guidelines are classified as optimal, reaching an MMR, and must continue with the TKI. Resistance or suboptimal response where it will be considered to increase the dose of the TKI or change to a second generation one, depending on the attachment, comorbidities and characteristics of the patient.^{2,4} The cytogenetic response will be carried out 6 months after treatment, with a control per year evaluating the metaphases of the cells in the bone marrow, however; this evaluation is not very sensitive to monitor the response.⁴ The indication would be in those patients with atypical translocations where quantitative PCR fails to measure them.^{2,4} The MMR predicts 100% survival in patients with CML, since disease progression with this degree of cytoreduction is practically unusual.⁴

CONCLUSION

Priapism is unusual to account as the initial manifestation of CML, as is the age of presentation of our patient, due to this it is important to carry out an adequate diagnostic and therapeutic approach in young patients who present to the emergency department with this urological complication since the etiology could be underestimated and treatment of the disease of origin could be delayed, resulting in a poor prognosis. Ischemic priapism should be considered as a urological emergency, with special attention to resolve the erection in the shortest possible time and thus avoiding associated sequelae such as erectile dysfunction. The management of CML must initiate as soon as diagnosis is made, to avoid new episodes of priapism and disease progression. In this case, the recommendations of the

international guidelines were followed, obtaining a complete hematological and molecular response and no sexual repercussions.

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