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Priapism and chronic myeloid leukemia in an adolescent. Rare debut presentation. A case report

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ABSTRACT

Priapism is a painful and persistent erection, with or without sexual stimulation. A rare cause of such abnormality is chronic myeloid leukemia. Few cases of priapism as an initial manifestation of this type of leukemia have been reported in adolescent patients. Here we describe the case of a 16-year-old patient who presented with priapism as the initial manifestation of chronic myeloid leukemia. No cavernosal aspiration was performed. A specific hematological treatment was started and, given the persistence of priapism, the patient required 2 corpora cavernosa shunt procedures; despite this treatment, there is a high probability of sequelae.

Keywords: *priapism; adolescent; chronic myeloid leukemia in chronic phase; case reports.*

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INTRODUCTION

Priapism is defined as a sustained erection lasting more than 4 hours, which may or may not be related to sexual stimulation.[1–3] There are 2 types of priapism, high-flow and low-flow. High-flow or non-ischemic priapism occurs when there is increased blood flow in the sinusoid arteries without affecting the venous flow. The most frequent cause is penile trauma.[1,2,4] Low-flow or ischemic priapism originates in conditions that cause low venous flow and, secondarily, there is stasis in the penile vessels. Low-flow priapism is the most common type and results in cell damage and fibrosis. The most frequent causes are blood dyscrasias, such as sickle cell anemia and chronic myeloid leukemia (CML).[1,2,4] Priapism is considered an emergency.[1–5] A poor experience in diagnosis and delayed treatment have been associated with irreversible sequelae.[5] Failure to resolve ischemic priapism within 12 hours,[4] or any type beyond 24-48 hours, has been associated with irreversible damage and poor prognosis,[5,6] with sequelae such as erectile dysfunction, penile deformities, and psychological damage, among others.[2]

CML is rare in pediatrics, accounting for 2–3% of all leukemias in children under 15 years of age,[5] while it accounts for 9% of cases in adolescents aged 15–19 years.[2,7] A slight prevalence has been described among males.[5] Only 1–5% of priapism cases are caused by some type of leukemia and, of these, half of the priapism cases are associated with CML.[1,5,8] The most common cause of priapism in children is sickle cell anemia (65%), followed by leukemias (10%), trauma (10%), idiopathic origin (10%), and medications (5%).[3,8]

Here we describe the case of a patient who presented with priapism as the initial manifestation of CML, its course, and management.

CASE REPORT

This patient was a male, 16-year-old student. He had no relevant medical history. One month before admission, he started with painful, predominantly nocturnal, prolonged erections, without sexual stimulation. He received general medical care and treatment with 5 doses of dexamethasone 4 mg (2 intravenous and 3 oral) and topical treatment with hydrocortisone/lidocaine cream, without improvement. Priapism lasted more than 5 hours, which is why he sought care at a general hospital, where he was referred to our unit 24 hours later due to the suspicion of myeloproliferative disorder.

On physical examination, he did not have jaundice or pallor. His neurological status was normal, without enlarged lymph nodes in the neck; soft, depressible abdomen; splenomegaly at 7 cm from the costal arch; hepatomegaly; Tanner genital stage IV and Tanner pubic hair stage III; testis of normal size and consistency; generalized edema in the genital area; painful erect penis, but with no color changes.

Table 1. Lab tests during the course of the condition

	Admission	10 days	21 days	Discharge	Follow-up
Hb	9.9	9.4	8.6	9.7	13.8
Htc	28	27.7	25.4	30	38
Leukocytes	542 700	208 210	4590	1470	4750
Neutrophils	243 220	142 920	3120	620	1800
Lymphocytes	27 020	7070	800	570	2270
Eosinophils	9700	7710	100	110	170
Platelets	572 000	598 000	51 000	34 000	124 000
Creatinine	1.1	0.89	0.56	0.66	0.94
LDH	1382	507	281	233	207

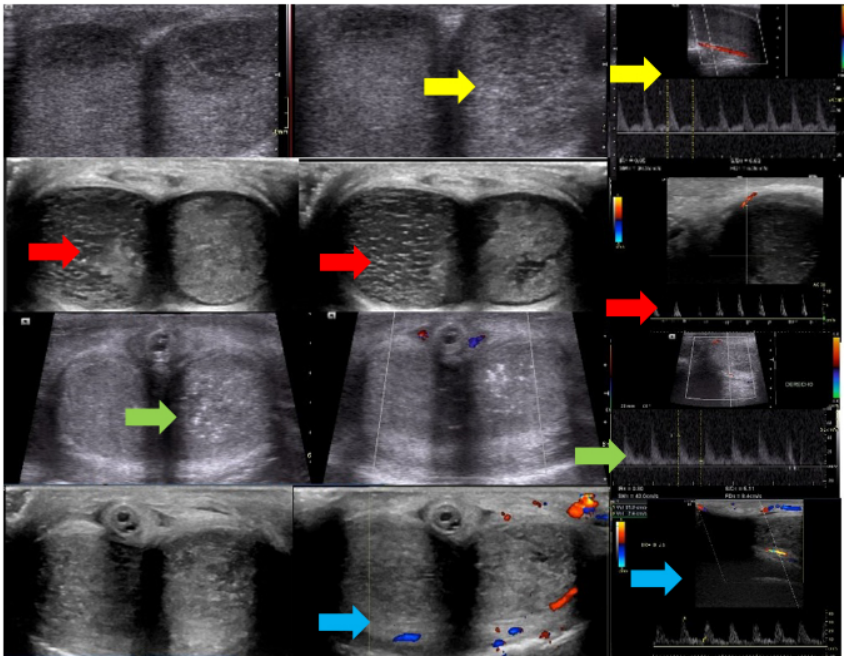
Hb: hemoglobin, grams per deciliter.
Htc: hematocrit, percentage.
Leucocytes, neutrophils, lymphocytes, eosinophils and platelets: cells/µL; creatinine: milligrams per deciliter.
LDH: lactate dehydrogenase, international units per liter.

On admission, a bone marrow aspiration and cytogenetic and lab tests were performed; the results showed normocytic normochromic anemia (hemoglobin 9.9 g/dL), leukocytosis (542 700 cells/µL), neutrophilia (243 220 cells/µL), and 572 000 platelets/µL (*Table 1*). Lactate dehydrogenase: 1382 IU/mL and hyperuricemia: 8.7 mg/dL. Acute kidney injury was reported as per the Risk, Injury, Failure, Loss, and End-stage kidney disease (RIFLE) classification.[9] Treatment was started with hyperhydration and allopurinol. A penile Doppler ultrasound was done *(Figure 1)*. Local treatment with cold compresses and systemic treatment with hydroxyurea were administered by the Service of Hematology. At no time during the course of his disease, the patient was subjected to aspiration and irrigation of corpora cavernosa.

The morphological examination of the bone marrow aspirate showed hypercellularity with predominance of myeloid series in all stages of maturation, normal erythroid and megakaryoblastic series; no blasts were observed. This supported the diagnosis of chronic phase of CML. Therefore, treatment was continued with hydroxyurea at a dose of 30 mg/kg/day. The immunophenotyping did not identify immature cells. The peripheral blood smear reported 6% of blasts. The molecular biology study of the bone marrow sample was positive for *BCR/ABL1 (Figure 2)*, karyotype 46 XY t (9:22) (q34;q11.2) *(Figure 3).*

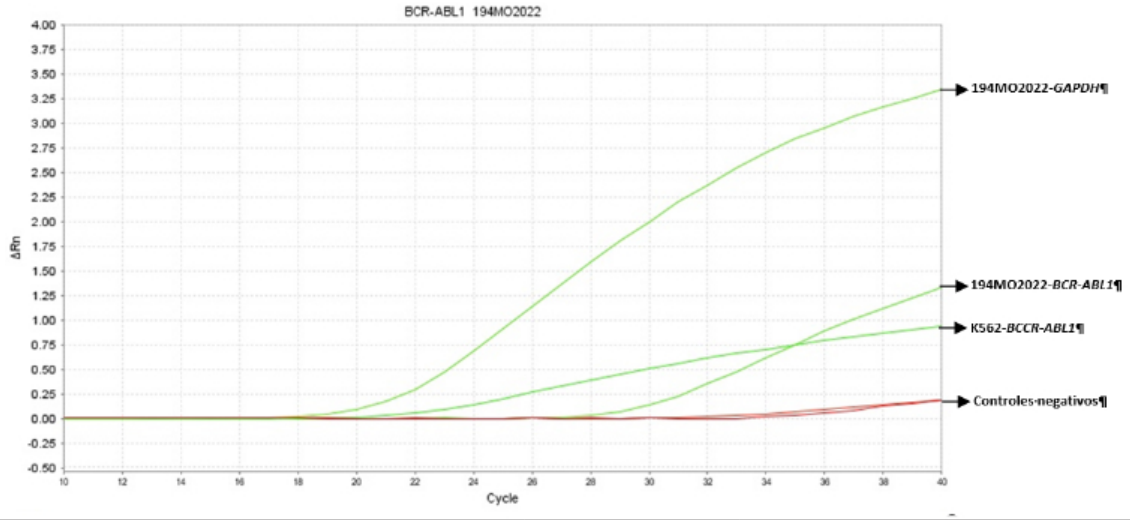
Based on clinical findings and studies, the peripheral blood smear, the bone marrow aspiration, and the cytogenetic and molecular biology studies, a diagnosis of chronic phase CML was established with certainty. Imatinib was added to the treatment at 375 mg/m^2 body surface area. Given the persistence of priapism and leukocytosis, an adjuvant treatment with

Figure 1. Penile Doppler ultrasound



The initial ultrasound observed heterogeneous echogenicity of the corpora cavernosa with increased arterial resistance of the dorsal artery of the penis and no evidence of vascularity on color Doppler of the cavernous artery or corpora cavernosa (yellow arrow).
On day 10, the echotexture was observed to have changed at the expense of bilateral echogenic thrombosis, mainly on the left of the corpora cavernosa, without evidence of color Doppler signal, with diastolic inversion to the spectral color Doppler signal of the dorsal artery of the penis (red arrow).
On day 15, the echogenic images after the shunt procedure did not evidence a vascular pattern with the color Doppler; changes were observed in the echotexture of the corpora cavernosa, with permeability of the veins and dorsal artery of the penis and diastolic widening of the arterial range (green arrow).
On day 23, heterogeneous changes were observed in the echogenicity of the corpora cavernosa, without evidence of a vascular pattern in the color Doppler during the Valsalva maneuver, identifying peripheral vascular and Foley catheter in the penile urethra, where permeability of the cavernous artery with high resistance spectrum was noted (blue arrow).

Figure 2. Real-time reverse transcriptase polymerase chain reaction (RT-PCR) where the BCR/ABL1 gene was identified.



Sample	Gene	Ct	
194-BM-2022	*BCR-ABL1*	27.4	Positive for BCRL-ABL1
K562 cell line	*BCR-ABL1*	20.6	Positive for BCRL-ABL1
194-BM-2022	*GAPDH*	19.1	Intact RNA
K562 cell line	*GAPDH*	13.4	Intact RNA

Interpretation: Ct values below 32 are considered positive for BCRL-ABL1.
GAPDH is the internal control: Ct values below 20 are required to consider that the quality of RNA is adequate.
194BM2022: corresponds to sample.
GAPDH: glyceraldehyde-3-phosphate dehydrogenase is used as an expression control gene in real time PCR assays. Ct: cycle threshold is the number of cycles in which the signal exceeds an estimated threshold to determine its expression.
RNA: ribonucleic acid. BM: bone marrow.
BCR-ABL1: gene fusion between the B-cell receptor and ABL proto-oncogene 1, non-receptor tyrosine kinase; it is a chromosomal aberration involving the fusion of these 2 genes.
K562 cell line: erythroleukemia cell line derived from a patient with chronic myeloid leukemia having a blast crisis. RT qPCR: real-time reverse transcriptase polymerase chain reaction, a type of PCR that is used to quantitatively determine the RNA of a certain gene by comparison with a continually expressed gene.

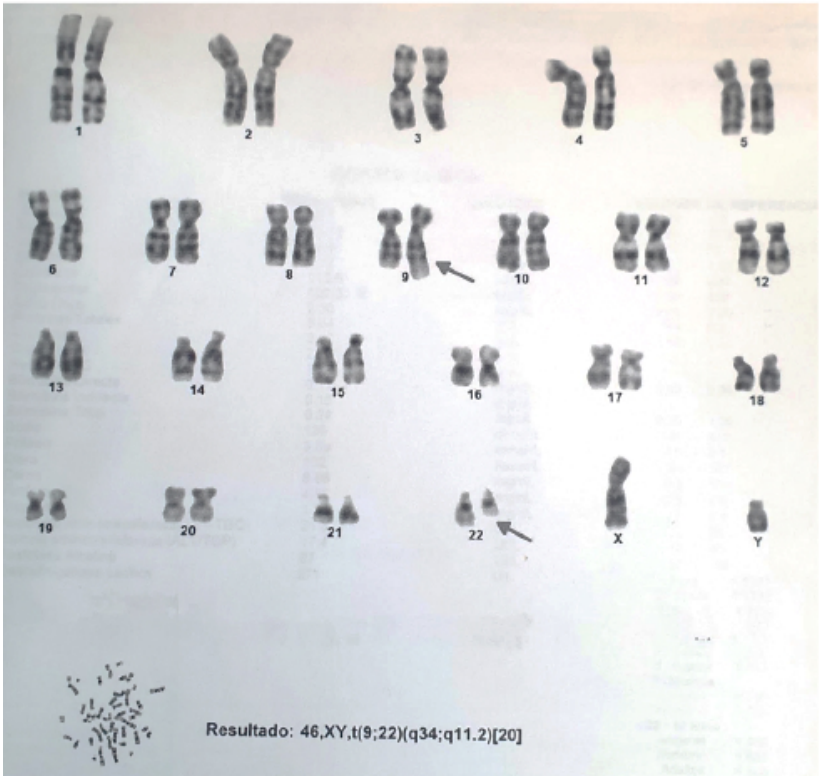
5 doses of cytarabine at 40 mg/m^2 body surface area was added.

After 10 days of hospitalization, given the persistence of priapism and ultrasound findings, an Ebbehoj shunt of the distal corpora cavernosa was performed. After 24 hours, due to the presence of extreme bleeding from the glans, the shunt was closed and the condition was managed with transfusions (*Figure 1*).

At 21 days of hospitalization, normal leukocyte levels were observed and treatment with hydroxyurea and cytarabine was discontinued. The patient showed improvement of erection without achieving remission. A Doppler ultrasound and a second Ebbehoj shunt with drainage of penile hematoma and extraction of 150 mL of clotting mold in the corpora cavernosa were performed, achieving a definitive resolution of priapism (*Figure 1).*

Given the resolution of priapism, normalized blood count levels, and remission of kidney failure, the patient was discharged from the hospital after 31 days, with specific treatment with imatinib. He continued with follow-up as an outpatient. At present, 10 months after diagnosis and treatment initiation, the patient has controlled his hematologic disease, but has erectile dysfunction as a sequela.

Figure 3. Bone marrow karyotype



DISCUSSION

Priapism is an unusual symptom with a frequency of 1–5 cases per 100,000 inhabitants per year, hence the importance of reporting cases.[1] Only a few reviews have identified priapism as a clinical manifestation of CML. Bintoro, in a 20-year review, identified 10 cases of pediatric patients with priapism secondary to CML; 3 younger than 10 years and 7 adolescents.[1] Leukocytosis and splenomegaly were the initial manifestations in 8 of the 10 cases.[1] Kurosawa reported that the most frequent symptoms observed in patients with CML were asthenia (45–60%), left flank pain due to splenomegaly (20–30%), weight loss (15–20%), and bleeding (10%).[10] Our patient had leukocytosis and splenomegaly, but no non-specific symptoms or bleeding were reported at the time of diagnosis. In Kurosawa's series, only 2.8% of patients with hyperleukocytosis developed priapism.[10]

Only 1–5% of priapism cases are related to leukemia.[1] Cases of CML with priapism require a multidisciplinary approach,[11,12] considering the combination of systemic chemotherapy with hydroxyurea and tyrosine kinase inhibitors, leukapheresis, intracavernous therapy, and, ultimately, shunts to drain the blood accumulated in the corpora cavernosa.[4,11,13] In various publications, the aspiration of the corpora cavernosa has been described as the initial treatment of choice for this type of priapism; however, it requires experienced staff, who are not always available.[4,11–13]

Kurosawa's review reported that all patients were initially treated with cytoreductive therapy immediately after diagnosis, although medication varies according to the treating physician's criteria.[5] Our patient was started on treatment with hydroxyurea and imatinib but did not achieve remission of priapism; so 2 cycles of cytarabine were added, still without achieving remission. Then the patient underwent 2 surgical procedures to resolve priapism.

It has been described in the bibliography that the longer the duration of priapism, the greater the possibility of developing sequelae.[8] Regarding treatment with leukapheresis, there is no consensus about its benefits, and it has only been studied in small case series.[12] It is recommended only when hyperleukocytosis

causes symptoms and should be reserved for emergencies,[5] always in conjunction with a cytoreductive systemic management.

According to some series, despite cytoreductive treatment, leukapheresis and local management with aspiration and irrigation of the corpora cavernosa —which is the recommended initial treatment— 50–90% of patients may develop erectile dysfunction.[5,8,13]

Given the rarity of this diagnosis and the paucity of data, current treatment recommendations for priapism in leukemia are derived from adult studies and clinical practice guidelines.[7] Treatments vary and there are no standardized treatment recommendations for pediatric patients.[3]

To conclude, priapism as an initial manifestation in CML is rare. Given the unusual nature of these cases, there is no consensus on their management. The reports may help to collect data for future pediatric therapeutic guidelines. Although the most frequent initial manifestations of CML are asthenia, adynamia, and hemorrhage, we must be alert to uncommon manifestations, such as priapism. A timely diagnosis and specific treatment may prevent the impact in the quality of life of pediatric patients, who, like adult patients, require optimal erectile function for their relationship life. ■

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