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Priapism as the initial sign in hematologic disease: Case report and literature review

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ABSTRACT

INTRODUCTION: Priapism is an uncommon sign and sometimes considered a diagnosis challenge into systemic disease; this is defined as ≥4 h continuous penile erection, without sexual stimulation. We state that this work has been reported in line with the SCARE criteria

PRESENTATION OF CASE: A Mexican 52-year-old man was brought to the emergency room with priapism of six days of evolution. His medical history reported fatigue and waxy pallor had begun a month ago, the rest of interrogation was unremarked. Hyperleukocitosis (>250,000 cells/ml) was documented on his pre-operative evaluation, the initial step was hematology consultation due to malignance suspicion, followed by corpora cavernosa drainage-irrigation and surgery penis shunts. After of procedure, we realized bone marrow aspiration, kariotype and cytogenetic analysis, histopathological and moleculars assay reported myeloid hyperplasia compatible with acute phase CML and Philadelphia translocation t(9:22)(q34;q11.2) with P210 BCR-ABL1 fusion transcriber, patient was discharged with dasatinib for maintenance phase. Actually, he has a satisfactory evolution without relapses.

DISCUSSION: The majority of reported cases shows the individual importance of hematological diseases in priapism as it is shown in the analysis of the literature of 10 years (2006–2016) that we made. It is imperative to consider the type of priapism, and the genetic and demographic patient aspects due to the early and correct approach improves the short and long term outcome of the hematological patients.

CONCLUSION: Priapism is an uncommon sign of systemic disease. In the presence of warning signs, malignancy should be considered until proven otherwise.

1. Introduction

Priapism is a condition characterized by ≥4 h continues penile erection, without sexual stimulation. There are two types of priapism: ischemic and nonischemic [1]. The most common causes of Ischemic Priapism (IP) include idiopathic (65%), hematological disorders [HD] (20%) and other causes 15% [2]. By definition, Malign Priapism (MP) appears in the frame of a solid or liquid neoplasm such as: bladder (30.6%), prostate (29.6%), recto-sigmoid (14%), kidney (6.6%) and leukemia (0.7%) [3] of this the fifty percent attributed to Chronic Myeloid Leukemia (CML). CML is an abnormal mature B cells clonal proliferation which appears with an abnormal function, and is characterized by the presence of the translocation 9:22 (BCR-ABL 1 positive [PC]). CML distribution has two periods, the first one is in the elementary age (~7 yrs) and the second varies widely in a range from 20 to 50 years old (~35 yrs) [4]. CML clinical presentation is lymphadenopathy (80%), asthenia and fatigue (60%), spleen or liver enlargement (50%), weight loss (15–20%), and bleeding (10%), hyperleukocitosis about 80%, central nervous system affection (15%) kidney (5%) and MP (≤3%).

MP diagnosis is clinic, this is based in anamnesis and physical exploration, followed by Corpora Cavernosa Blood Gas Analysis (CCBGA) and Doppler Color Ultrasound (DCU) to identify local ischemia. MP cases are a medical challenge, where the underlying disease has to be elucidated and treated. Finally, MP treatment is based on anticoagulants, fibrinolysis, puncture-aspiration and vasoactive agents injection. At the end, surgery is reserved only if conservative therapy is unsatisfactory and in special conditions which is necessary a specific treatment of the underlying disease [5–9]. We state that this work has been reported in line with the SCARE criteria [34].

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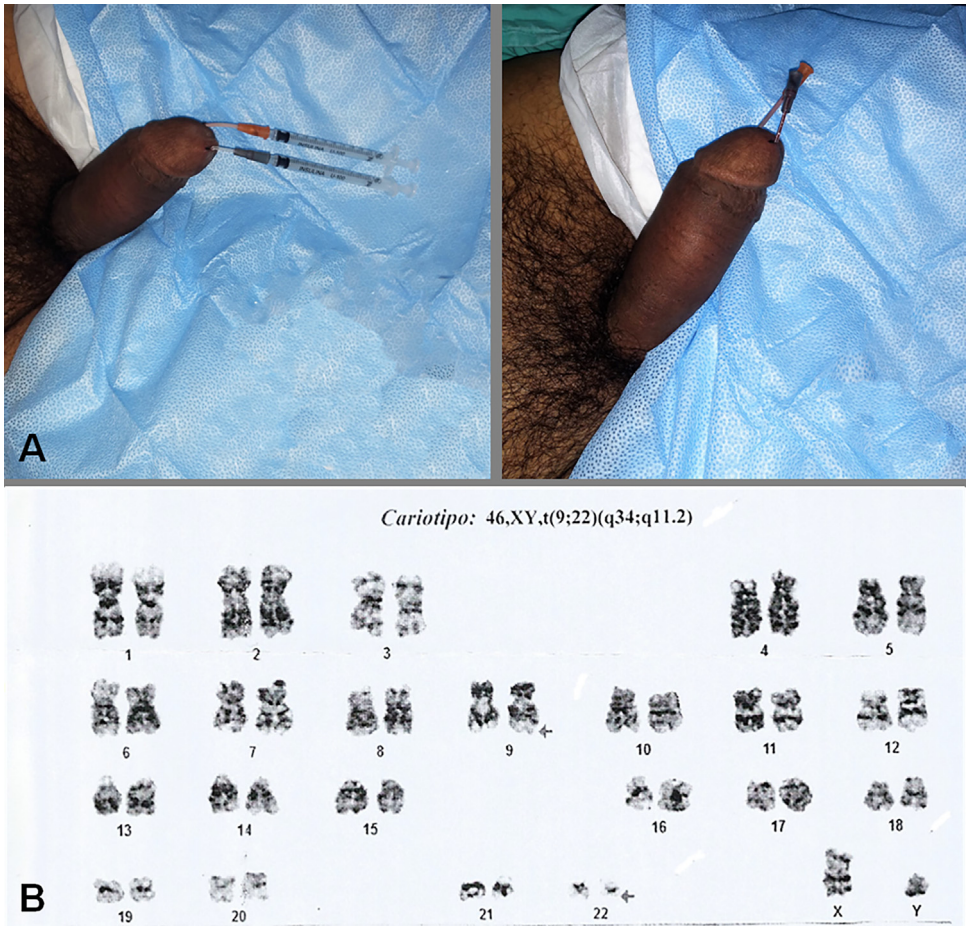


Fig. 1. A) Post-operative surgical image shows the system corpora cavernosa drainage-irrigation. B) Kariotype image display Philadelphia translocation t(9:22. [q34; q11.2]) (Full arrow).

2. Case report

A Mexican 52-year-old man without cancer history began with weight loss, generalized fatigue and pallor one month ago. He was brought to the emergency room with a painful six-day evolution priapism, gradually increased in severity and impaired ambulation. He denied swelling and fever. During physical examination ischemic priapism was observed. He denied a trauma history, drug abuse, arousal stimulation or previous similar episodes.

Preoperative analysis was taken, showed: Hemoglobin 10 gr/dl (14–16 gr/dl), white blood cells 282,000/mm^3 (7000–10,000/mm^3), platelets 368,000/mm^3 (150,000–400,000 mm^3), lactic dehydrogenase 1503 UI/L (125–220 IU/L) the studies remaining performed were normal, chest x-ray and electrocardiography without findings. The initial step was hematology consultation due to malignance suspicions. Informant consent was gotten before treatment started, treatment was started administering hyperhydratation and allopurinol. Followed by corpora cavernosa drainage-irrigation and surgery penis shunts. After of procedure, we realized bone marrow aspiration, kariotype and cytogenetic analysis, histopathological and moleculars assay report noted myeloid hyperplasia compatible with acute phase CML and Philadelphia translocation t(9:22) (q34;q11.2) with P210 BCR-ABL1 fusion transcriber (Fig. 1). The patient was discharged with dasatinib 100 mg/day by maintenance phase. and the subsequently medicals appointments was established. Currently, the leukemia is in satisfactory evolution without relapses.

3. Literature review

3.1. Etiopathogenic

About 50% of idiopathic priapism correspond to IP or Low Flow Priapism (LFP; also called veno-occlusive). There is a strong association with HD, systemic vasoactive drugs, malignancy and neurological disorders. On the other hand, non-IP or High Flow Priapism (HFP) often occurs due to a pelvic trauma and after intracavernosal injections [10,11] (see Table 1) [12].

3.2. Pathophysiology

The physiopathology can be separated in 2 ways, as "*non-ischemic*" triggered by a trauma, which causes an irregular cavernous arterial flow and the formation of fistulas, and the most common *is* "*ischemic*" which is most commonly idiopathic-related but is also due to hematological etiologies [12]. Inside hematological causes are the hemoglobinopathies which are ahead and less common hyper-viscosity states such as leukemia, occurring during prolonged nocturnal erections, decreasing venous flow return and the mechanism of normal detumescence, is a rare syndrome characterized by multiple and recurrent episodes of ischemic priapism. In normal erection the corpus cavernosum flow facilitates the synthesis of nitric oxide (NO) and prostaglandins (PGI2), its function is to regulate the interaction between stagnant blood and the trabecular wall [13]. In ischemic priapism, hypoxia and ischemia alter the

Table 1
Principal causes of Ischemic Priapism.

Neurological Disorders	Idiopathic Drugs	Idiopathic Drugs (Continuation)	Idiopathic Drugs (Continuation)	Metastatic
Syphilis	***Anticoagulants***	***Hypnotics***	Papaverine	Penis
Stroke	Heparin	Clozapine	Prostoglandin E1	Recto-sigmoid
Brain tumors	Warfarin	Diazepam	Sildenafil	Prostate
Epilepsy	***Antihypetensives***	***Blockers***	Testosterone	Kidney
Intoxication	Dihydralazine	Tamsulosin	**Hematological Disorders**	**Metabolic Disorders**
Brain or spinal cord injuries	Labetalol	Doxazosin	Sickle cell anemia	Amyloidosis
Lumbar disk herniation or stenosis	Nifedipine	Prazosin	Leukaemia	Fabry's disease
Cauda equine syndrome	Phenoxybenzamine	***Recreational drugs***	Multiple myeloma	Diabetes
Regional or general anesthesia	Prazosin	Cocaine	Thalassaemia	Nephrotic syndrome
	Antidepressants	Etanol	Paroxysmal nocturnal haemoglobinuria	Renal failure
	Phenelzine	Marijuana	Thrombocythaemia	Haemodialysis
	Trazadone	***Drugs for intracavernous injection***	Henoch-Schonlein purpura	**Idiopathic**

Table 2
Ten years literature review previous cases with Priapism CML from 2006 to 2016.

Author(s)/Year	Priapism-CML cases	Age onset	Philadelphia chromosome	Type of priapism	Country
Pal et al. 2016 [15]	1	NIA	NIA	LF	India
Nerli et al. 2016 [16]	1	19 years old	9:22 translocation	LF	India
Alao et al. 2016 [17]	1	30 years old	9:22 translocation	LF	Nigeria
Almaeena et al. 2016 [18]	1	36 years old	NIA	LF	Saudi Arabia
Ergenc et al. 2015 [19]	1	18 years old	9:22 translocation	LF	Turkey
Shaeer et al. 2015 [20]	1	21 years old	9:22 translocation	LF	Egypt
Villegas et al. 2014 [21]	2	24 and 29 years old	Both 9:22 translocation	LF	Spain; Spain
Farhan et al. 2014 [22]	1	38 years old	9:22 translocation	LF	Saudi Arabia
Magaña et al. 2014 [23]	1	32 years old	9:22 translocation	LF	Mexico
Hazra et al. 2013 [24]	1	14 years old	NIA	LF	India
Veljković et al. 2012 [25]	1	16 years old	9:22 translocation	LF	Serbia
Paladino et al. 2011 [26]	1	16 years old	NIA	LF	Argentina
Tazi. 2009 [27]	1	30 years old	Non Karyotype Abnormality	LF	Morocco
Jamel et al. 2009 [28]	2	21 and 55 years old	Both 9:22 translocation	LF	Pakistan
Gupta et al. 2009 [29]	1	12 years old	9:22 translocation	LF	India
Htun et al. 2008 [30]	1	21 years old	9:22 translocation	LF	China
Ajape et al. 2008 [31]	2	30 and 41 years old	Both 9:22 translocation	LF	Nigeria; Nigeria
Gupta et al. 2008 [32]	1	55 years old	NIA	LF	India
Yoshida et al. 2007 [33]	1	29 years old	NIA	LF	Japan

CML: Chronic Myeloid Leukemia; NIA: No Information Available; LF: Low Flow.

synthesis of NO and PGI2, causing homeostatic imbalance, facilitating platelet aggregation and increasing adhesion of white blood cells, leading to thrombus formation and tissue damage, venous thrombosis with persistent vascular block that leads to pain at 4 h, platelets adhere to the basement membrane of sinusoidal spaces and proliferation of fibroblasts, the glycopenia of HD also alter the smooth muscle [8,13]. Ischemia of 32 h duration, causes endothelial and trabecular destruction, with subsequent irreversible fibrosis and calcification, leading to erectile dysfunction [8]. The molecular mechanisms that may lead to HD priapism are: adenosine deaminase deficiency leading to excessive levels of adenosine causing priapism and opiorphin to the via ornithine decarboxylase [8,10]. Finally hyperviscosity by excess leukemic cells are added to the corpora cavernosa and dorsal veins of the penis, decreased flow and stagnation of the blood, resulting in LFP. Another contributing factor in the venous congestion of the corpora cavernosa is the mechanical pressure on the abdominal veins by the splenomegaly [8].

3.3. Diagnosis

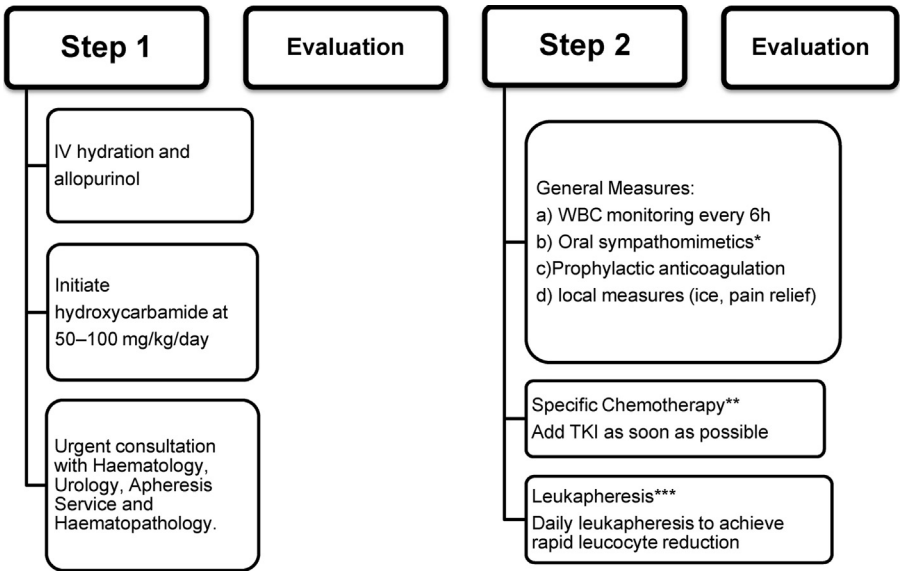
Medical history diagnosis and directed interrogation are the initial step by determine the priapism etiology. The initial exploration has to look early signs of ischemia (pain, paleness, paresthesias, color changes and function loss) The presence of extra-urological signs and symptoms (splenomegaly, adenomegaly and weight loss) must suggest malignancy [8,10,12]. Some signs (e.g. Piesis Sign) can differentiate flow features, however they are rare findings, and commonly viewed in pediatric patients with HFP [12].

CCBGA must be performed to differentiate IP to non-IP. The normal arterial blood analysis has similar values than HFP (pO_2 >90 mmHg, pCO_2 < 40 mmHg, pH 7.4) furthermore, LFP (pO_2 < 30 mmHg, CO_2 > 60 mmHg, pH > 7.25) show abnormal levels. The use of magnetic resonance is limited, it can predict smooth muscle viability and erectile function restoration post-event. Finally, elected pudenda arteriogram can be diagnostic and therapeutic, it should be reserved for the management of arterial priapism when embolization is required [14].

3.4. Treatment

There are several ways of treatment which begin into conservative measures to complex surgical techniques. Control pain with penile anesthesia or systemic analgesia is considerate a key measure to decrease the adrenergic response, and decreasing patient's distress. Nevertheless, anesthesia sometimes does not relieve ischemic pain, so is necessary perform hard interventions doing use of local nerve block or even sedation drugs [14]. Mild invasive measures can helps patients while surgery is available, aspiration-irrigation can be an initial invasive measure; followed by intracorporal sympathomimetics drugs (phenylephrine, etilephrine, epinephrine and norepinephrine) alone or mixed with

Table 3
Therapeutic steps in malignant priapism.



*Oral sympathomimetics, such as etilferine, phenylephrine, metaraminol and terbutaline, are superior to placebo if administered within a short timeframe (<4 h) after onset of priapism. This's complement treatment while other measures are being.
**Tyrosine kinase inhibitors (TKIs) such as imatinib, dasatinib and nilotinib, are being commenced immediately the diagnosis of CML is confirmed.
***Leukapheresis may be used as a complement to systemic chemotherapy.
WBC: With Blood Cell.

aspiration-irrigation, both are considered an effective measures [10].

Surgery is reserved only if conservative therapy was unsatisfactory. Several surgical options may be considered depending of patient's particular setting and evolution time [14]. Surgery penis shunts (distal-shunt) has a higher performance, this can be done easily and has minimal complications compared with the proximal-shunts. On the other hand, surgical prosthesis implantation are the last rung and should be considered in patients with refractory or recurrent priapism associated with erectile dysfunction [10,14]. The main step is establishing specific treatment of the underlying disease, as well as early hematological consultation [10,15] (Table 3).

4. Discussion

Priapism is an uncommon sign into systemic disease. The iatrogenic cause is secondary to overuse of erectile dysfunction medications. In the United States IP is the most common presentation of priapism, with an incidence of up to 5.34 per 100,000 men per year.

Hematological diseases in children can develop priapism. In the present case, our patient was diagnosed with CML and secondary hyperleukostasis. This underlay mechanism lead to corpora cavernosa venous congestion by neoplastic cells and viscosity blood increasing, although HD are uncommon causes of priapism, we must think in all of them as a possible etiology.

There are several case reports that show the individual importance of CML and priapism, we made a literature analysis (ScienceDirect, Medline and Pubmed) from 2006 to 2016 using the keywords: "*priapism*; *leukemia*; *chronic myeloid leukemia*; *priapismo*; *leucemia mieloide crónica*" looking for a 9;22 translocation and priapism type flow (Table 2).

Malignancy red flags (weight loss, generalized fatigue and pallor) must be considered to underlying disease diagnosis. In our case, preoperative evaluation detected lymphocytic line affectation, so our initial suspicion was lymphoproliferative disorder. In regard to acute phase diagnostic, it should be oriented to detect ischemia through CCBGA and DCU with the purpose of make an early intervention (Table 3).

Finally, the treatment should be multidisciplinary with medical oncologists, surgeons, urologists, radiologists, nursing and psychology. The early and correct diagnosis approximation improves at short and long term the outcome of the hematological patients. The acute phase treatment is lead to avoid local and systemic complications, which the patient stabilization and early consultation of internal medicine or hematology plays a predominant role. During chronic phase follow-up, continuous check-up and illness remission are the treatment of the underlying disease which improve the functional prognosis and consequently the survival. In conclusion, the present article exemplifies the importance of priapism in adult patients with hematological disease, with prompt diagnosis and standardized treatment, patients may have a good prognosis for life and function.

Patient perspective

– "*Currently, I'm satisfied with my treatment, I hope to continue improving as I have been doing it so far.*"

Conflicts of interest

None.

Funding

None.

Ethical approval

Ethical approval has been exempted by the institution, since it is not considered a risky investigation for the patient or for the researchers.

Consent

The informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editorial-in Chief of this journal on request.

Authors contribution

All authors contributed to this work, commented on the manuscript at all stages and finally approved the final version to be published.

Becerra-Pedraza Luis Cuitláhuac: conceived and supervised study design, data collections, data analysis, writing.

Jiménez-Martínez Luis Enrique: study design, data collections, data analysis, writing.

Peña-Morfin Iran: study design, data collections, data analysis, writing.

Nava-Esquivel Rogelio: study design, data collections, data analysis, writing.

Villegas-Martínez Juan Alfredo: performing the surgery and surgical image collections.

Guarantor

Luis Cuitlahuac Becerra Pedraza.

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