Case study

Priapism as the first manifestation of Chronic Myeloid Leukemia: a rare occurrence

Abstract: Priapism is an involuntary, painful erection of the penis for more than 4 hours without any sexual stimulation or ejaculation. It is a urological emergency which requires urgent intervention to prevent erectile dysfunction. We report a case of a young gentleman who presented to emergency with priapism and was eventually diagnosed to have chronic myeloid leukemia (CML). The priapism resolved with proximal Sacher's shunt surgery, hydration, hydroxyurea, and tyrosine kinase inhibitors (TKI) after an early diagnosis by FISH method. The prompt in intiation of treatment is the key in managing such patients to reduce the consequences of erective dysfunction.

Key words: priapism, chronic myeloid leukemia, erectile dysfunction

Introduction:

Priapism is an involuntary, painful penile erection that persists for > 4 hours and is unrelated to sexual interest or ejaculation. It is classified into ischemic (low flow), arterial (high flow), or stuttering (recurrent or intermittent). (1, 2, 3) It is a urological emergency that requires an urgent intervention to prevent erectile dysfunction. (2) It can occur at any age, with an overall incidence of 1.5 in 1, 00,000 patients. (1) Priapism can occur due to a wide variety of causes which commonly include infection, malignancy, CNS mediated, drug-induced or hemoglobinopathies. (1) Almost 20% cases of priapism are due to an underlying hematological disorder of which chronic myeloid leukemia (CML) is one of the commonest. (1, 4, 5) Priapism as a presenting

feature of CML is very rare and occurs in only in 1-2% cases. (5) We report a case of a young gentleman who presented with priapism as a initial manifestation of CML and was managed in a multidisciplinary manner.

Case report:

A 37-year-old gentleman presented to the emergency department with the painful erection of penis unrelated to sexual stimulation, drugs or trauma. The patient had experienced a similar episode six months earlier, which had subsided spontaneously within two hours. There was a history of weight loss of around 10 kilograms in the last 3 years. There was no history of fever, loss of appetite or breathlessness or hyperviscosity symptoms. On examination, the penis was firm, erect and tender. The spleen was palpable 10 cm below left costal margin. There was no hepatomegaly or lymphadenopathy.

Initial conservative measures such as corporal aspiration using phenylephrine with cold saline and distal caverno-glandular shunt (winter shunt) were ineffective to resolve the erection. Eventually, the patient had resolution of the symptoms following proximal Sacher's open shunt between the proximal corpora spongiosum and corpora cavernosum (Figure 1). His complete blood count (CBC) showed hemoglobin of 13.2 g/dl, white blood cell (WBC) count of 2, 52,300 /mm^3 and platelet count of 3, 54,000 /mm^3. Peripheral smear showed a neutrophilic shift to the left with 7% blasts and increased eosinophil and basophils (Figure 2a). Lactate dehydrongenase, renal and liver function tests were normal. Fluorescent in situ hybridization (FISH) for BCR: ABL1 fusion on peripheral blood was positive in 97% cells confirming the diagnosis of CML (Figure 2b). Bone marrow examination was suggestive of chronic myeloid leukemia in chronic phase (Figure 2c, 2d). Conventional karyotyping did not show any additional cytogenetic abnormality. RT-PCR for BCR: ABL showed p210 transcript.

The option of leukapheresis was not considered as the patient had to be taken up for surgery due to prolonged tumescence. He was started on Imatinib 400mg once a day, besides continuing hydroxyurea and allopurinol. With the normalization of WBC counts, the hydroxyurea was tapered and stopped in the following week, while continuing Imatinib at the same dose. On the last follow-up, his hemoglobin was 10.3 g/dl, and white blood count was 5400/mm^3 with an absolute neutrophil count of 3300/mm^3 and platelet count was 2, 10,000/mm^3. Quantitative molecular analysis showed optimal response with BCR: ABL (IS) ratio of < 0.45% at 6 months from the time of diagnosi. The patient is on regular follow-up, has an active lifestyle, but able to achieve a partial erection.

Discussion:

The term "priapism" is from Priapus (ancient Greek god of fertility). (6) The first description of priapism was given in the year 1845. (6) Priapism is an urological emergency with an approximate risk of impotence in 50% patients. (2) The median age of presentation in a case series of 16 patients was 36 years (range: 21 to 56 years). The commonest cause was secondary to neuroleptics in 6 cases (37%), chronic myeloid leukaemia in 2 cases, sickle-cell anaemia in one case, radiotherapy in 1 case and the cause remained unknown in 6 cases (37%). (7)

The pathophysiology depends on the aetiology of priapism which can be ischemic or non-ischemic type. (8) Ischemic priapism behaves as compartment syndrome wherein there is stasis of blood within corpora leading to erect penis. Pain occurs due to tissue ischemia and muscle hypoxia. Ischemic priapism accounts for almost 95% of all cases (Table 1). (9) In ischemic priapism, it has been hypothesized that tissue hypoxia leads to changes in nitric oxide (NO) synthase, which in turn causes reduced NO production and leads to pain. (2, 9) Another hypothesis ischemic priapism is the infiltration of sacral nerves or CNS by leukemic cells. (2)

Although patients with CML is one of the most frequent haematological causes of ischemic priapism, priapism as a presenting feature in CML is rare. A high WBC count with peripheral smear showing left shift, eosinophilia and basophilia along with splenomegaly should point towards a diagnosis of CML. It may present as either chronic, accelerated or blast phase. Once suspected, the patient should be started immediately on hydration and allopurinol. Initial management is multidisciplinary with involvement of emergency medicine, haematologist, urologist, haemato-pathologist and transfusion medicine specialist. Due to high counts, it can present with symptoms of hyperviscosity (blurring of vision, respiratory discomfort or end-organ damage). (1, 2, 10)

This case highlights the importance of evaluating the causes of priapism systematically. The patient had ignored his first episode 6 months ago, which had lasted for only 2 hours and did not seek medical attention. Urgent leukapheresis is indicated in such patients whenever the facility is available and surgical intervention is not an emergency. (1, 10) Surgical approach is a therapeutic aspiration or corpora-glandular shunt surgery Proximal shunt surgery is offered for severe distal penile edema and tissue damage. Erectile dysfunction (ED) is a major complication seen in 90% cases where priapism persists for more than 24 hours. (2, 5) In case, the surgical options fail, insertion of penile prosthesis may be offered before intra-corporal fibrosis ensues American Urological Association guidelines for the management of priapism reiterates the importance of urgent surigical intervention for ischemic priapism in addition to medical management. (2)

Medical management of CML consists of hydroxyurea till WBC count normalizes along with tyrosine kinase inhibitors (TKI) like Imatinib, Dasatinib or Nilotinib. (10)

Response a monitoring is done by 3 monthly RQ-PCR for BCR: ABL as per the recommended guidelines with life long continuation of TKI. (10)

Conclusion:

Initial management of priapism is a challenge in order to prevent long term erectile dysfunction. High index of suspicion for CML and complete blood count along with peripheral smear evaluation at presentation will help rule out hematological cause for priapism. Managing the patient alongside the urologist is pivotal in the initial management of such cases.

Consent: Signed consent was obtained from the patient and kept in his medical records.

References:

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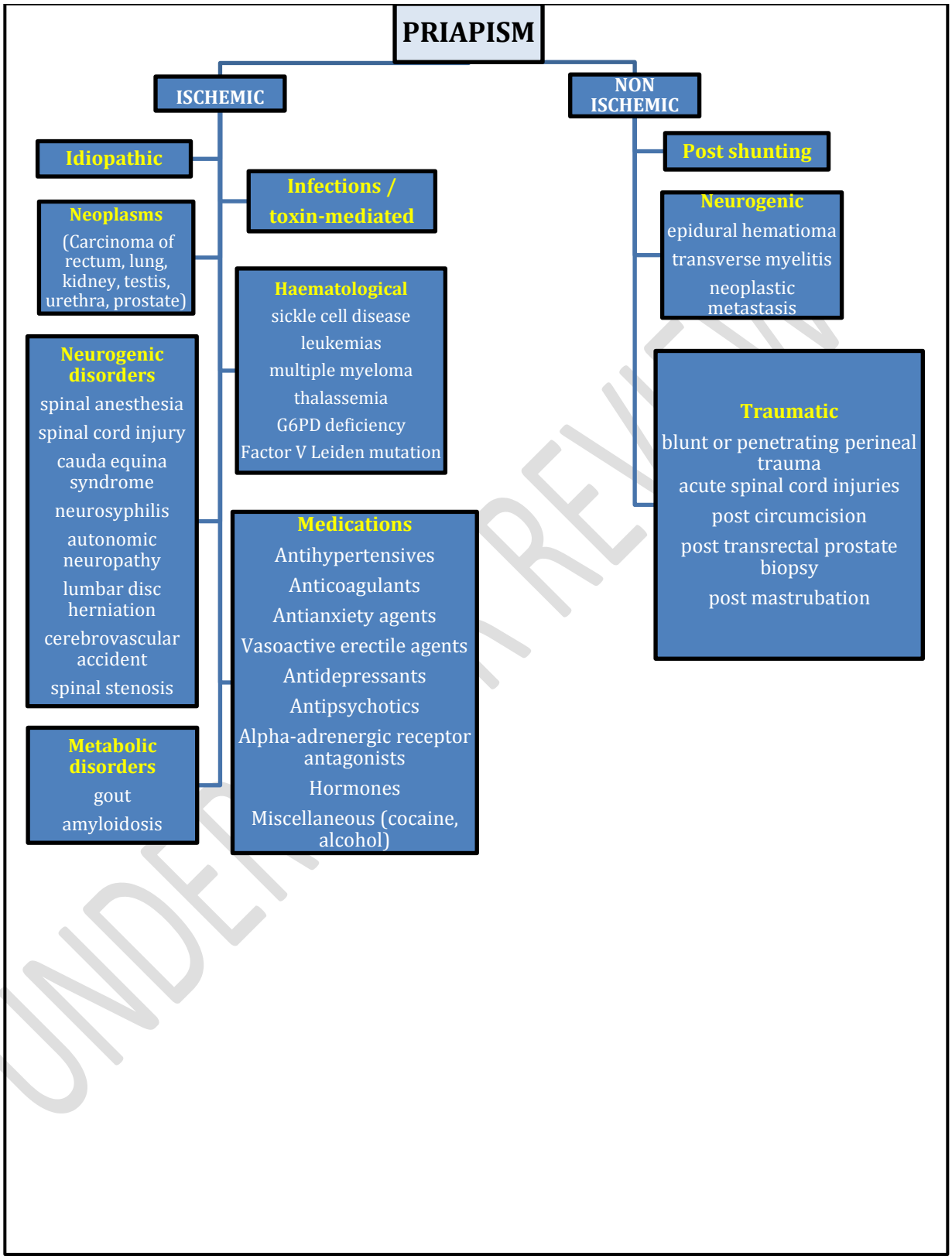
Table 1: **Causes of ischemic priapism:**


PRIAPISM
ISCHEMIC
NON ISCHEMIC
Idiopathic
Neoplasms
(Carcinoma of rectum, lung, kidney, testis, urethra, prostate)
Neurogenic disorders
spinal anesthesia
spinal cord injury
cauda equina syndrome
neurosyphilis
autonomic neuropathy
lumbar disc herniation
cerebrovascular accident
spinal stenosis
Metabolic disorders
gout
amyloidosis
Infections / toxin-mediated
Haematological
sickle cell disease
leukemias
multiple myeloma
thalassemia
G6PD deficiency
Factor V Leiden mutation
Medications
Antihypertensives
Anticoagulants
Antianxiety agents
Vasoactive erectile agents
Antidepressants
Antipsychotics
Alpha-adrenergic receptor antagonists
Hormones
Miscellaneous (cocaine, alcohol)
Post shunting
Neurogenic
epidural hematioma
transverse myelitis
neoplastic metastasis
Traumatic
blunt or penetrating perineal trauma
acute spinal cord injuries
post circumcision
post transrectal prostate biopsy
post mastrubation

Figures:

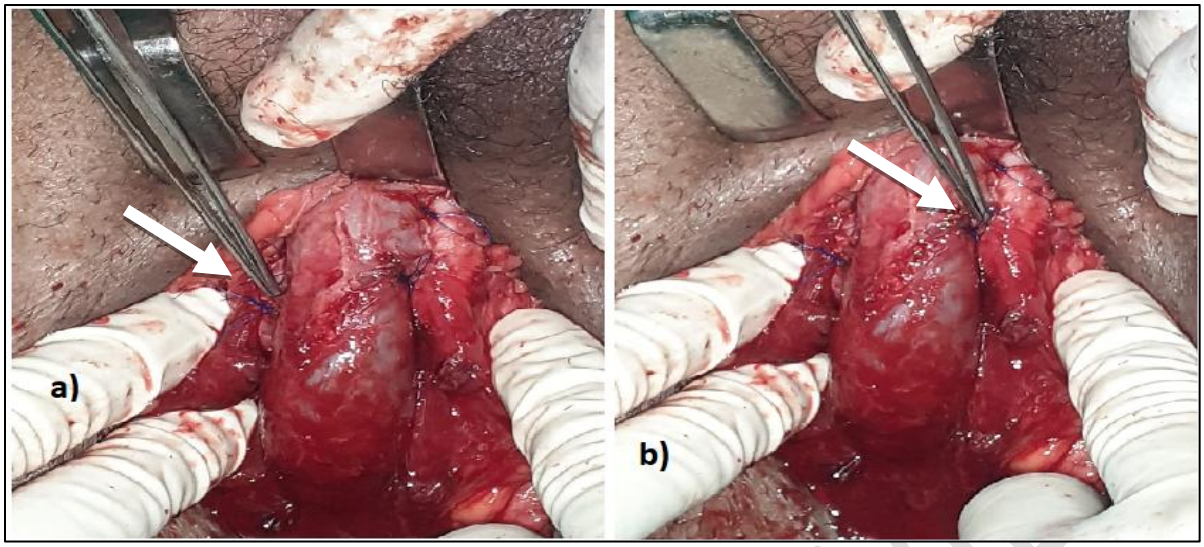


Figure 1: Intra-operative images showing a) corpora-cavernosal anastomosis on left b) corpora-cavernosal anastomosis on right

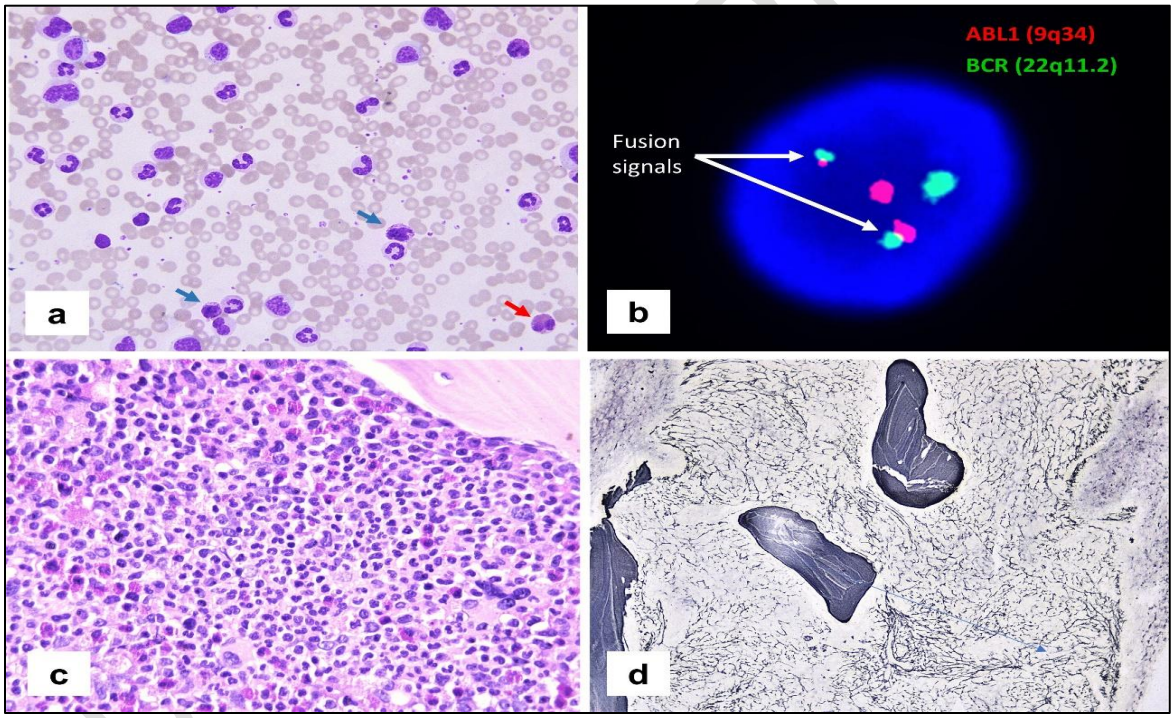


Figure 2: a) Peripheral blood film showing left shift, eosinophils (red arrow) and basophils (blue arrows); Leishman stain x 400 b) FISH for BCR-ABL1 showing two fusion signals using dual colour dual fusion probes x 1000 c) Solidly cellular trephine biopsy showing myeloid predominance with increased eosinophil precursors; Hematoxylin & Eosin stain x 400 d) Reticulin stain on the trephine biopsy showing increased fibrosis (2+) x 100

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