ORIGINAL RESEARCH PAPER

Urology

IMPORTANCE OF INTEGRATED APPROACH IN MANAGEMENT OF PRIAPISM IN HEMATOLOGICAL DISORDERS-OUR EXPERIENCES OF 15 CASES

KEY WORDS: Priapism, Haematology, Urology

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ABSTRACT

The management protocol of priapism due to haematological disorders is not well established. The study intends to evaluate different haematological disorders causing priapism, their relative incidence, associated clinical presentation, diagnostic evaluation, management & prognosis and thereby ascertain a certain management guidelines for patients of priapism secondary to hematologic disorders. The following study is a retrospective observational study conducted in our institute from January 2010 to January 2019. All the patients diagnosed with priapism were noted and the patients diagnosed to have associated haematological disorder were independently evaluated in detail. Fourteen patients (93.33%) were diagnosed to have ischemic priapism and one patient had an episode of stuttering priapism. The most highlighting aspect was 5 among the 15 patients (33.33%) presented with priapism as their first clinical manifestation of their underlying hematologic disorder. Only 2 patients were successfully managed with aspiration alone, 10 patients required a distal Winter shunt and 2 further required Al Ghorabs shunt. One patient of CML-Blast crisis (CML-BC) with priapism died before any surgical intervention because of CML-blast crisis. Priapism is a rare urological entity with definite risk of impotence of approximately 50% despite management. Collaborative efforts of Urologist and Haematologist will be essential to further advance the treatment strategies and to diagnose more and more rare cases of priapism of haematological disorders.

BACKGROUND

Priapism is defined as a persistent, purposeless, painless or painful, penile erection that continues beyond 4 hours of sexual stimulation or orgasm.[1] It is an urological emergency as delaying the treatment will lead to erectile dysfunction.[2] Priapism has an incidence of 1.5 cases per 100 000 person-years of which 20% of the cases were contributed by haematological disorders alone.[3] The management protocol of priapism due to haematological disorders is not well established. This study intends to evaluate different haematological disorders causing priapism, their relative incidence, associated clinical presentation, diagnostic evaluation, management & prognosis and thereby ascertain a certain management guidelines for patients of priapism secondary to hematologic disorders.

METHODS:

The following study is a retrospective observational study conducted in our institute from January 2010 to January 2019. Records of the patients were obtained by reviewing the details of each patient from the medical record department of the institute. The study was carried out at department of Urology in collaboration with department of Haematology. All patients presenting with priapism who were previously or newly diagnosed to have haematological disorders above 12 years of age were included in this study. Patients with incomplete records and those who did not follow up for atleast 2 years were excluded from the study.

Priapism was defined as a persistent, purposeless, painless or painful, penile erection that continues beyond 4 hours of sexual stimulation or orgasm. Stuttering priapism was defined as recurrent ischemic priapism lasting for about 3 hours or less.

All the patients diagnosed with priapism were noted and the patients diagnosed to have associated haematological disorder were independently evaluated in detail. These patients included were evaluated for associated haematological disorder, type of priapism, clinical features, general and systemic examinational findings, related haematological investigations and bone marrow aspiration (BMA) findings. The management of the underlying hematologic disorder as well as the immediate management priapism and the eventual outcome was noted. Erectile function post priapism was documented using the Erectile hardness score (EHS). Courses of the hematologic disease and potential complications within 2 years of the follow up were studied.

The above data was systematically tabulated. All the data was analysed using SPSS 16.0 software.

RESULTS:

The incidence of haematological disorder among patients diagnosed with priapism was 31.91% (15/47). Table 1 shows that priapism was seen in 15 haematological patients, out of which 11 (73.33%) were Chronic Myeloid Leukaemia (CML) cases, 3 (20%) were having sickle cell disease (SCD) and one (6.67%) was having JAK 2 + polycythaemia vera. Among the 11 patients diagnosed with CML, 9 were in their chronic phase and 2 patients presented in blast crises. Age groups ranged from 16-46 years with an average age of 26 years.

Fourteen patients (93.33%) were diagnosed to have ischemic priapism and one patient had an episode of stuttering priapism. The most highlighting aspect was 5 among the 15 patients (33.33%) presented with priapism as their first clinical manifestation of their underlying hematologic disorder (3 CML, 1 sickle cell-thalassemia, 1 JAK+ polycythaemia vera). Also 5 patients (33.33%) had atleast 2 previous episodes of priapism of which 2 patients had not sought medical attention. The common associated clinical features of CML patients presenting with priapism were weight loss, dyspnoea on exertion and low grade fever whereas those with sickle cell anaemia presented with jaundice.

Table 2 shows that CML patients with priapism had normal general examination findings except for 2 patients with blast crisis who has bilateral Axillary lymph node enlargement. All patients with CML had splenomegaly. Patients with Sickle-B-Thalassemia with priapism had WBC count in the normal range. Patient with polycythemia Vera with priapism had ruddy tongue on examination and JAK2V617F mutation.

Table 3 shows that out of 11 CML patients with priapism 10

patients were managed with chemotherapy (in the form of Hydroxyurea (HU), ALP, Imatinib, hydration) and one patient received only imatinib. Patients with sickle cell disease were managed with HU, Hydration, blood transfusion /monthly exchange transfusion surgical management for priapism. Patient with polycythemia vera was managed with adequate hydration and HU. Only 2 patients were successfully managed with aspiration alone, 10 patients required a distal Winter shunt and 2 further required Al Ghorabs shunt. One patient of CML-Blast crisis (CML-BC) with priapism died before any surgical intervention because of CML-blast crisis.

Out of 14 patients with priapism who were followed for atleast 2 years, 6 patients had EHS grade 4 and 1 had grade 3. All these patients were those who presented within 24 hours of onset of priapism and one patient with SCD had grade 4 EHS despite presenting after 4 months. (Erection Hardness Score, grade1: Penis is larger but not hard, grade 2: Hard but not hard enough for penetration, grade 3: Hard enough for penetration but not completely hard, grade 4: Completely hard and fully rigid).

DISCUSSION:

Priapism is a rare urological entity with definite risk of impotence of approximately 50% despite management.[6] Hematological disorders leading to development of priapism are Sickle Cell Anemia, Chronic Myeloid Leukemia, Chronic Lymphoblastic Leukemia And Acute Lymphoblastic Leukemia and Polycythemia Vera.[7] Lifetime prevalence of ischemic priapism in sickle cell disease is reported in the range of 2-35%.[8,9] In hematological malignancy, priapism is the result of venous obstruction due to micro emboli or thrombi as well as there is hyper viscosity of the blood caused by the increased number of circulating leukocytes in mature and immature forms.[10]Due to rarity of its occurrence as well as the small number of case reports in the literature, there is no standard treatment protocol till date.

Priapism is an unusual presentation of CML. CML is generally encountered with an elevated WBC count and/or enlarged spleen.[11] Anorexia, malaise, weight loss, sweating, abdominal fullness, bleeding episodes due to platelet dysfunction are the most common manifestations of CML.[11]Priapism as a presenting feature occurs in 1-2% of newly diagnosed CML patients.[3]

When we look at data from an Urologist's perspective among the patients diagnosed with priapism with haematological disorder, one third patient were newly diagnosed. In other words, there was a 33% chance of missing either CML, sickle cell anaemia or Polycythaemia vera if haematological investigations were overlooked which would have delayed diagnosing treatable haematological conditions. In our study the patients with priapism had associated symptoms and signs of their respective disorder at the time of presentation (Table 2 and Table 3). Thus, any clinician managing priapism in the emergency department should not neglect signs and symptoms of CML mentioned previously as they may help clinch the diagnosis.

Though priapism occurs in all age groups, two peaks in the age distribution have been noted. First, a paediatric peak, 5-10 years old, is seen in sickle cell disease especially in African patients. Second peak occurs with sexual activity age of 20-50 years old.[12]CML has been noted predominantly in the age group of 15-35 years old patients in many case reports.[3,4,6,11-14] Similar to the literature; 10 of 11 CML patients with a priapism were in the age group of 25-50 years.

Literature has documented the incidence of priapism in sickle cell patients as 38-42% in adults[15,16] and up to 64% in the children.[17] In our study, two patients of sickle cell disease with priapism were children (12 and 15 years old respectively) and one patient was 32 years age. Majority of sickle cell patients experience 'stuttering'episodes[18] and over half of these patients have greater than ten episodes and approximately 28% have acute prolonged events.[19] In our series two out of three patients (67%) of sickle cell disease with priapism had prior 2-3 episodes of stuttering priapism and one patient (33%) had the first episode of stuttering priapism at presentation.

There have been many methods described in the literature for the management of priapism like spinal anesthesia, ice water enema, ice packs, radiotherapy[20], fibrinolytics and anticoagulants[21] but all these with limited success. For ischemic priapism, it is recommended to perform immediate aspiration and irrigation of corpora cavernosa as well as to inject alpha-adrenergic agent.[22]American Urological Association(AUA) recommended that only systemic therapy of underlying disease is not sufficient enough for the management of ischemic priapism.[23] Systemic therapies for hematological disorders with a priapism include cytoreductive chemotherapy such as high-dose HU and tyrosine kinase inhibitors (TKIs), with or without addition of leukaphresis to reduce the hyperviscosity.[24] In our series, out of 11 patients of CML presenting with priapism we have performed emergency aspiration and irrigation with systemic therapy (in the form of HU, ALP, Imatinib and hydration) in one patient. Amongst other, 7 underwent aspiration followed by Winter shunt and 2 further required Al Ghorabs shunt despite Winter shunt managed conservatively and another one patient although aspiration was done, the died because of blast crisis before further intervention.

Standard treatment for ischemic priapism in SCD involves corporal aspiration and phenylephrine injection.[25] Role of hydration, blood transfusion, and exchange transfusion has also been documented in the literature to benefit the patients with SCD.[26] HU induces HbF in patients with SCD which helps to reduce sickle cell crises.[26] In present study, patients of SCD with priapism were managed with HU, hydration, blood transfusion and exchange transfusion with aspiration or Winter shunt surgery.

We had a unique case of polycythaemia vera with priapism which hasn't been previously mentioned in literature till date and was managed by hydration, HU therapy and Winter shunt surgery. Thus of the 14 patients successfully managed, bearing 2 patients, all the others required shunt surgery. This further reinforces the importance of multimodal management among these patients as mentioned by AUA.

There is definite incidence of impotence following priapism due to hematological disorders and this impotence rate is directly proportional to the duration of priapism. Pohl et al[27] cited 35% and 60% impotence rates for patients with priapism lasting for 5 days and 10 days respectively. Out of 14 patients with priapism who were followed for atleast 2 years, 6 patients had EHS grade4 and 1 had grade 3. All these patients were those who presented within 24 hours of onset of priapism and one patient with SCD among the patients who presented beyond 24 hours had grade4 EHS. Our study thereby underlines the importance of golden hours of management of priapism in patients of hematological disorders to prevent long term sequel in young patients.

To summarize, although hematological conditions have 1-2% chances of presenting as priapism all patients already diagnosed with either CML or SCD should be made aware of importance management of priapism in early hours to preserve their potency. The management of priapism in patients of hematological disorders should involve an integrated approach as missing even a single case of hematologic disorder presenting with priapism will have disastrous implications. Urologist need to have a broader outlook in management of priapism and should consider the algorithm 1 mentioned in this study as a guide in management of priapism

CONCLUSION:

Our study is unique as we have a patient of Polycythaemia Vera with Priapism which was not reported in the past. Collaborative efforts of Urologist and Hematologist will be essential to further advance the treatment strategies and to diagnose more and more rare cases of priapism of hematological disorders.

Declarations

Ethics approval and consent to participate

Although a retrospective study, ethics approval was taken from internal ethics committee and each patients gave written consent to participate

Consent for publication

Consent for publication given by all authors

Availability of data and material

All data was obtained retrospectively from Medical records department

Competing interests NONE

Funding NONE

Authors' contributions

SK and SP was responsible for the concept. Sk was responsible collection of data. All authors reviewed the results, discussion and literature

All Authors have approved the manuscripts for publications

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Importance of integrated approach in management of Priapism in Haematological Disorders-Our experiences of 15 cases

Table 1: Clinical Presentation of cases

Case No	Diagnosis	Age (yrs)	Duration since first episode of priapism	Prior history of priapism; episodes	Type of priapism	Other symptoms
1	CML-CP (ND)	30	20 hrs	No	Ischemic	-
2	CML-CP	26	3 Days	Yes, 2 episodes (NT)	Ischemic	Wt loss, Abd discomfort, DOE
3	CML-CP	25	2 Days	No	Ischemic	Fever, Abd discomfort
4	CML-CP(ND)	28	7 hrs	No	Ischemic	Abd discomfort,DOE
5	CML-CP	29	3 Months	Yes,3 episodes (NT)	Ischemic	Fever, wt loss
6.	CML-CP	46	20days	No	Ischemic	Low grade fever. Abd discomfort
7.	CML-BC	16	5 hours	No	Ischemic	Fever, weight loss
8.	Sickle-B Thalassemia	32	7days	Yes. 2 episodes	Ischemic	Intermittent body ache & joint pains , yellow discoloration of eyes
9.	Sickle-B Thalassemia	12	4months	Yes. 2 episodes	Ischemic	-Intermittent body ache & joint pains
10.	Sickle Cell Anemia(ND)	15	22hrs	No	Stuttering priapism	Intermittent body ache & joint pains , yellow discoloration of eyes
11.	Polycythemia Vera JAK2+ (ND)	33	5 days	No	Ischemic	-
12.	CML-CP (ND)	22	9 hrs	No	Ischemic	Abd discomfort,DOE
13.	CML-CP	31	5 Months	Yes,2episodes	Ischemic	Fever, wt loss
14.	CML-CP	46	18hours	No	Ischemic	Abd discomfort, DOE
15.	CML-BC	18	8 hours	No	Ischemic	Fever, weight loss

CML-Chronic Myeloid Leukemia, CP-Chronic Phase, BC-Blast Crisis, Duration - Duration of symptoms of priapism, ND-Newly Diagnosed, NT- Not treated, wt loss- weight loss, Abd discomfort- abdominal discomfort, DOE- Dyspnoea on exertion.

Table 2: Clinical Examination & Investigations of cases.

No	Diagnosis	GE	Spleen	Liver	Hb	WBC	PLT	BMA Finding	Special tests
1	CML-CP	WNL	+, 2 cms	+, 3 cms	11.2	285, ooo	462	CML-CP	98% + for FISH For BCR-ABL
2	CML-CP	P+	+,15 cms	NP	8.9	292, 000	490	CML-CP	84% + FISH For BCR-ABL
3	CML-CP	WNL	+,1 cms	NP	11.3	607, 000	320	CML-CP	100% + FISH For BCR-ABL
4	CML-CP	P+	+,15 cms	NP	7.0	441, 500	422	CML-CP	98% + FISH For BCR-ABL
5	CML-CP	P+	+,3 cms	NP	10.5	284, 500	370	CML-CP	98% + FISH For BCR-ABL
6	CML-CP	P+	+8cms	+2cm	8.7	332, 000	420	CML-CP	87% + FISH ForBCR-ABL

7	CML-BC	P+, ALN +.	+12 cms	+4cm	6.7	492, 370	401	BM-CML CP;LN Biopsy-Myeloid Sarcoma	92% FISH For BCR-ABL
8	Sickle-B Thalassemia	P+,I+	3cms	NP	8.2	11210	430	NA	HBS-67% HBA2-5.2% PD-Chronic Arterial Ischemia
9	Sickle-B Thalassemia	P+,I+	5cms	NP	10.3	8900	370	NA	HBS-62% HBA2-4.7%
10	Sickle Cell	P+,I+	NP	NP	6.7	12100	400	NA	HBS-73%
11	Polycythemia Vera JAK2+	Ruddy Tongue	+,4cm	NP	18.7	7500	43	NA	HCT-55% EPO-3.3 IU/L JAK2 V617F+
12	CML-CP	P+	+, 5 cms	NP	6.8	543, 500	413	CML-CP	98% + FISH For BCR-ABL
13	CML-CP	WNL	+,6 cms	NP	11.5	232, 700	298	CML-CP	98% + FISH For BCR-ABL
14	CML-CP	P+	+5cms	+2cm	8.7	382, 000	423	CML-CP	83% + FISH For BCR-ABL
15	CML-BC	P+, ALN +.	+7cms	NP	7.5	672, 270	418	BM-CML CP;LN Biopsy-Myeloid Sarcoma	96%+ FISH For BCR-ABL

BMA-Bone Marrow Aspiration findings, +: Present, -: absent, CP- chronic phase, BC- blast crisis-Pallor, I-Icterus, ALN-Axillary Lymph Nodes,NP-Not Palpable, NA-Not Attempted, FISH- Fluorescent-In-Situ-Hybridization for bcr-abl translocation,PD-Penile Doppler, HBS-Hemoglobin S, HBA-Hemoglobin A, HCT-Hematocrit, EPO-Erythropoietin.

Table 3:Treatment & Follow Up of cases

	Diagnosis	Medical management	Surgical treatment	Disease Course	Outcome (EHS5)
1	CML-CP	HU, ALP,Hydration Imatinib	Aspiration Winter shunt	CCyR at 6 months	Grade 4
2	CML-CP	HU, ALP, Hydration Imatinib	Aspiration Winter shunt	CCyR at 12 months; hematological relapse at 24 months	Grade 2
3	CML-CP	HU, ALP, Hydration Imatinib	Aspiration Winter shunt	Blast crisis with leukemia cutis at 3 months	Grade 1
4	CML-CP	HU, ALP, Hydration Imatinib	Aspiration Winter shunt	CCyR at 6 months	Grade 4
5	CML-CP	Imatinib	Aspiration Winter shunt	CCyR at 12 months	Grade 1
6	CML-CP	HU, ALP, Hydration,leukaphreresis Imatinib	Aspiration Winter Shunt f/b Al-Ghorab shunt	CCyR at 12 months	Grade 1
7	CML-BC	HU, ALP, Hydration Imatinib	Aspiration	Expired	
8	Sickle-B Thalassemia	HU,Hydration, blood transfusion	Aspiration	No painful crises since 6 months but priapism persisted for 2 months	Grade 1
9	Sickle-B Thalassemia	HU,Hydration, monthly exchange transfusion for 6 months	Aspiration Winter shunt	No further painful crises and priapism episode on 1 yr follow up	Grade 4
10	Sickle Cell Anemia	HU,Hydration, blood transfusion	Aspiration Winter shunt	No further painful crises and priapism episode on 2 yr follow up	Grade 4
11	Polycythemia Vera JAK2+	HU,Hydration	Aspiration Winter shunt	Control of HCT with no further priapism episodes	Grade 1
12	CML-CP	HU, ALP, Hydration Imatinib	Aspiration Winter shunt	CCyR at 6 months	Grade 4
13	CML-CP	HU, ALP, Hydration Imatinib	Aspiration Winter shunt	CCyR at 12 months	Grade 1
14	CML-CP	HU, ALP, Hydration Imatinib	Aspiration Winter Shunt f/b Al-Ghorab shunt	CCyR at 12 months	Grade 4
15	CML-BC	HU, ALP, Hydration Imatinib	Aspiration	CCyR at 12 months	Grade 3

CML-Chronic Myeloid Leukemia, CP-Chronic Phase, BC-Blast Crisis, Aspiration - Intracavernous aspirations & phenylephrine injections, Shunt - Al-Ghorab shunt, CCyR - Complete cytogenetic response, HU-HydroxyUrea, ALP-Allopurinol, HCT-Hematocrit,EHS5-Erection Hardness Score, grade 1: Penis is larger but not hard, grade 2: Hard but not hard enough for penetration, grade 3: Hard enough for penetration but not completely hard, grade 4: Completely hard and fully rigid.

EHS is analyzed at the end of follow up period i.e. after 2 years of completion of the treatment.

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