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Emergency leukapheresis in chronic myeloid leukemia presenting with Priapism

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ABSTRACT

Chronic Myeloid Leukemia [CML] presenting with priapism is rare and usually caused by leukostasis due to hyperleukocytosis. Priapism is a medical emergency and requires prompt management to avoid irreversible sequel. Therapeutic leukapheresis [mechanical white cell depletion] in the management of hyperleukocytosis and leukostasis is well known. A young patient admitted to Cancer Institute at Chennai, India, with chronic myeloid leukemia and priapism is presented. Treatment of Priapism with Leukapheresis is discussed.

INTRODUCTION

Chronic Myeloid Leukemia [CML] is a chronic myeloproliferative neoplasm characterised by overproduction of myeloid cells. The condition is often diagnosed accidentally when patients present with splenomegaly and elevated white blood cell [WBC] count. Anorexia, malaise, bleeding tendencies, weight loss and enlarged spleen are the most common clinical manifestations of CML. Patients with progressive disease present with involvement of liver, lymph nodes and skin. Patients' presenting with leukostasis complications such as thromboembolic phenomenon, hearing loss or priapism is rare [1]. The clinical signs of leukostasis are related to the organ affected. Pulmonary signs are inclusive of tachypnoea, dyspnoea and hypoxia. Nervous system symptoms include mental status changes as delirium, confusion, dizziness, headache, ataxia and tinnitus. Vascular complications most often are associated with leukostasis as in priapism, myocardial ischemia, infarction, and retinal hemorhage or thrombosis.

Priapism is painful prolonged erection of penis lasting more than 4 hours and does not return to flaccid state despite absence of physical and psychological stimulation [2]. The incidence of priapism is 1.5 per 100,000 people and can either be idiopathic [64%] or secondary to haematological disorders [20%] or some medical conditions. The incidence of priapism is bimodal, initial peak occurring in children aged 5 to 10 years due to sickle cell disease and later in sexually active males aged 20 to 50 years [3,6]. Hemoglobinopathies [sickle cell disease], acute and chronic leukemia, multiple myeloma are known haematological causes of Priapism.In adult leukemic patients, the incidence of priapism is approximately 1-5%. Among them, CML accounts for 50% of all leukemic priapism [3]. The importance of prompt diagnosis and treatment of priapism is essential as erectile dysfunction can be a definite sequel of this condition [4].

Hyperleukocytosis [White blood cell (WBC) counts are more than 1,00,000 cells/cu mm] is commonly seen in various leukemias and can result in life threatening leukostasis [5]. Leukostasis leading to endothelial damage results in early mortality due to respiratory and neurological problems in these patients. The incidence of complications due to leukostasis merits rapid cytoreductive treatment. Emergency Therapeutic leukapheresis helps at reducing the number of white blood cells [5] and producing an immediate improvement in the clinical picture.

CASE REPORT

An 18 year old male was referred to Cancer Institute, Chennai, India, with complaints of body ache and bleeding per rectum for a month and history of erect, painful and swollen penis of 4 days duration. There was no history of sexual stimulation or trauma. There was no history of fever or other complaints. The patient did not report of cough or any neurological symptoms. The patient

reported history of initiation of treatment with Aspiration, Injection Phenylephrine and Detumescence with local radiation therapy before being referred to the Blood Bank for emergency leukapheresis.

Physical examination revealed that the patient was experiencing discomfort due to sustained erection of the penis. His general condition was stable and vital signs within normal limits. Generalised lymhadenopathy was absent. Pallor was present. No purpuric spots were observed on the upper and the lower limbs. Abdominal examination showed massive splenomegaly 9-10 cm below left costal margin and hepatomegaly 2-3 cm below right costal margin. Bilateral scrotal swelling was present, bilateral testis and cord structures were normal. Examination of the cardiovascular and Respiratory system revealed normal study.

Laboratory investigations showed haemoglobin [Hb] 9.6 g/dl, white blood cell [WBC] count 1,44,000/cu mm, platelet count 3,50,000/cu mm. Peripheral smear showed Leukocytosis, Granulopoiesis: Neutrophils:17%, Lymphocytes:6%, Monocytes:58%, Eosinophils:2%, Basophils:3%, Myelobasts-6%, Promyelocytes-4%, Normocytic Normochromic Anemia, and adequate platelets. Bone marrow examination was suggestive of myeloproliferative disorder. The International Normalized Ratio [INR] was reported as 1.3. Serum biochemistry results [Table 1] were unremarkable. Chest X ray was normal study. The patient was diagnosed as a case of Chronic Myeloid Leukemia [CML] Chronic Phase [CP] based on peripheral blood smear and bone marrow examination. The cytogenetic study revealed Philadelphia chromosome. Molecular study confirmed the presence of BCR-ABL transcript.

Emergency Therapeutic leukapheresis was performed on two daysafter obtaining due consent from the patient. Leukapheresis was performed with Haemonetics MCS +, a discontinuous flow blood separation system using antecubital veins as vascular access. 3.3 litres of blood were processed on Day 1 and 3.4 litres of blood processed on day 2 of the procedure. Blood flow was maintained at 30 ml/minute. The anticoagulant used was ACD. The anticoagulant to blood ratio was maintained at 1:9. With other procedure parameters remaining the same, one unit packed red cells was transfused via the opposite antecubital vein during second day of Leukapheresis. Details of Pre and post leukapheresis are as shown in [Table 2].

At the end of the two day emergency leukapheresis procedure, the WBC count showed a 46% reduction and platelets reduced by 22%. The haemoglobin levels dropped from 9.6 g/dl pre procedure to 7.0 g/dl post leukapheresis. General condition of the patient was stable throughout and post procedure. No adverse reactions as citrate toxicity or vasovagal reactions were reported during or after the procedure. The patient experienced symptomatic relief of priapism and reported relief from body ache. Bilateral Scrotal swelling reduced on treatment with Magnesium sulphate and Glycerol dressings. The patient was on treatment with Hydroxyurea and Allopurinol. Reduction in WBC count post procedure helped initiate cytotoxic therapy. After the second day of Leukapheresis, the patient was started on Tab. Imatinib 400mg once daily. Adequate hydration was maintained by appropriate fluid and electrolyte management. The WBC counts gradually reduced over the fortnight to 6000/cu.mm at the time of discharge.

Table 1 : Pre Leukapheresis patient lab analysis report

HAEMOGLOBIN [Hb]	9.6 g/dl
TOTAL LEUKOCYTE COUNT [WBC count]	1,44,000 cells/cu mm
PLATELET	3,50,000 cells/cu mm
BLOOD UREA	41.0 mg/dl
SERUM CREATININE	0.4 mg/dl
SERUM BILIRUBIN	0.6 mg/dl
SERUM ALKALINE PHOSPHATASE	23.0 U/L
SERUM GLUTAMIC-OXALOACETIC TRANSAMINASE [SGOT]	45.0 U/L
SERUM GLUTAMIC PYRUVIC TRANSAMINASE [SGPT]	22.0 U/L
SERUM SODIUM	125.0 mmol/L
SERUM POTASIUM	3.6 mmol/L
SERUM CALCIUM	6.9 mg/dl
SERUM PHOSPHOROUS	3.7 mg/dl
SERUM CHLORIDE	101.0 mmol/L
SERUM MAGNESIUM	1.4 mg/dl
INTERNATIONAL NORMALIZED RATIO [INR]	1.3

Table 2 : Pre and post Leukapheresis blood count report

DETAILS OF PROCEDURE - LEUKAPHERESIS							
DAYS	PRE PROCEDURE COUNT			POST PROCEDURE COUNT			PRODUCT VOLUME
	Hb	WBC	PLATELET	Hb	WBC	PLATELET	
DAY 1	9.6 g/dl	1,44,000 Cells/cu mm	3,45,000 Cells/cu mm	6.0 g/dl	1,08,000 Cells/cu mm	3,45,000 Cells/cu mm	203 ml
DAY 2	6.0 g/dl	1,08,000 Cells/cu mm	3,45,000 Cells/cu mm	7.0 g/dl	77,000Cells/cu mm	2,70,000 Cells/cu mm	248 ml

DISCUSSION

The pathophysiology of Priapism in CML include (a) venous congestion of the corpora cavernosa due to massive splenomegaly causing mechanical compression of abdominal veins, (b) sludging of leukemic cells in corpora cavernosa and dorsal veins of penis, (c) local infiltration of either sacral nerves or central nervous system by leukemic cells, and (d) Hyperleukocytosis leading toleukostasis and increase in blood viscosity causing micro vascular complications [6,7]. In this case, significant Hyperleukocytosis with splenomegaly is the cause of priapism in the young individual.

Currently, there is no gold standard protocol for management of priapism in CML patients as it is a rare presentation. Traditional treatment protocols reported in literature include: local radiotherapy, with or without open surgical shunting. New treatment strategies include cytoreductive therapies with chemotherapeutic agents such as hydroxyurea and Therapeutic leukapheresis, and also early initiation of Tyrosine Kinase Inhibitors [TKIs] therapy with agents such as Imatinib and supportive treatment with adequate hydration [1,8]. American Association of Blood Banks and American society For Apheresis published guidelines stating that therapeutic leukapheresis is indicated for Hyperleukocytosis [9,10]. Therapeutic leukapheresis removes the circulating blast cells more quickly as compared to chemotherapy which would require 24 48 hours to achieve the same effect [11]. The case presented, typically underwent initiation of treatment with Aspiration, Injection Phenylephrine and detumescence with local radiation therapy before referral to the Blood Bank for emergency therapeutic leukapheresis for treatment of priapism of 4 days duration. Therapeutic leukapheresis performed on two days helped in reduction of 46% of WBC count in the patient and this helped in initiation of chemotherapy at the earliest, alleviation of symptoms, and avoiding complications such as tumour lysis syndrome, pulmonary and neurological complications due to hemodynamic variations. Moreover, the patient's general condition was stable throughout the procedure and post procedure. The patient responded to the overall treatment with immediate relief from priapism, reported no recurrence of priapism and a drastic reduction in WBC count [6000/cu mm] at the time of discharge

CONCLUSION

Priapism is a rare presentation of CML. Early diagnosis and treatment should be initiated promptly to avoid long term sequel. As emergency therapeutic leukapheresis achieves rapid detumescence, the procedure should be considered as a priority in management of leukemic patients presenting with priapism. In CML patients presenting with priapism, combined treatment protocol with local measures like aspiration, chemotherapeutic agents, TKIs , local radiation and leukapheresis helps in mitigation of complications and should be considered before elaborate surgical shunting procedures are performed.

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