Case Report

A Case Report on Integrated Management of Hematological Abnormalities like Thrombocytosis and Leukocytosis in Sickle Cell Crisis Patient

Atul Desai[1,*], Kavita Desai[1], Hemshree Desai[2], Rutvij Desai[3], Chirag Desai[4], Pinky Purohit[4]

[1]Dhanvantari Clinic, Ayurveda Healthcare and Research Centre, Vyara, Gujarat, INDIA.
[2]Research Scholar, Public Health, University of Glasgow, Scotland, UNITED KINGDOM.
[3]MD, Manila Central University, Caloocan, Kalakhang Maynila, PHILIPPINES.
[4]Department of Pharmacology, ROFEL Shri G M Bilakhia College of Pharmacy, Vapi, Gujarat, INDIA.

ABSTRACT

An Indian tribal population amongst dense forest area mainly suffers from sickle cell anaemia for a long. Considering the pathogenesis and geographical limitations only symptomatic management is available as there is no cure. Diagnosis of vaso-occlusive crisis or existing complication is a critical factor in sickle cell anaemia. Increased platelets, white blood cells, and clinical manifestations demand more attention in sickle cell patients. In the current case study, a patient was presented to the site for daycare management in minimal consciousness condition with SpO_2 96% complains of left hip pain and unable to walk, joint pain, pallor, backache, and general weakness. The clinical evaluation thrombocytosis, leukocytosis, and x-ray suggested developed avascular necrosis of the hip. Considering his condition patient was started on an integrated treatment approach with T-AYU-HM Premium 300mg tablet. Regular monitoring of condition and strict adherence to treatment has lessened the financial and logistical burden of prolonged hospital stays, blood transfusion needs, and vaso-occlusive crisis sequelae. A key observation in this case study is a remarkable improvement in thrombocytosis, leukocytosis, and walking impairment in patient due to avascular necrosis. Looking at the improvement in the clinical conditions to proceed with utilising the information for better healthcare, a patient had consented for the same. The prognostic significance of platelet and white blood cells is suggestive of disease severity and progression in sickle cell anaemia patients. During the treatment, no untoward effect was reported or observed. This integrated treatment approach might become helpful in managing such kind of clinical complications in sickle cell anaemia.

Keywords: Thrombocytosis, Leukocytosis, Vaso-occlusive crisis, Avascular necrosis, Sickle cell disease.

INTRODUCTION

Vaso-occlusive crisis in sickle cell patients induces many multiple organ complications in sickle cell anemia patients and is therefore considered a prime reason behind repetitive hospitalization. Sickling is one of the main reasons apart from increased cation permeability and stickiness, distorted red blood cells, and increased red blood cell fragility. The modification in membrane stability, increased membrane oxidation, and issues brought on by dehydration are the major problems with red blood cells in sickle cell anaemia. They could become stuck in tiny blood vessels, causing excruciating agony, robbing tissues of oxygen-rich blood, and injuring organs, most notably the spleen. Inflammatory cells, platelets, and other cells interact to increase the adherence of red blood cells in addition to the sickling of the cells. It might happen in the chest, heart, lungs, belly, kidneys, and extremities, among other body organs. Because of the frequent bouts and ischemia, organ damage may result.[1]

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Address for correspondence:
Dr. Atul Desai,
Dhanvantari Clinic, Ayurveda Healthcare and Research Centre, Vyara-394650, Gujarat, INDIA.
Email id: dratuldesai@rediffmail.com

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CASE PRESENTATION

This is a case study of a sickle cell disease patient who developed avascular necrosis. His clinical presentations are thrombocytosis and leukocytosis. A remarkable outcome of integrated treatment was observed.

Mr. X is a 23-year-old sickle cell disease patient with a 51-kilogram weight. He is working as Hospital Pharmacist in hospital. Mr. X had visited the clinic once in 2021 with complaints of a sickle cell-induced painful crisis. During that visit, he presented with leukocytosis and thrombocytosis clinical features reported in laboratory investigation. But he didn't adhere to the medication order and discontinued the treatment. A year later, he was infected with COVID-19 and recovered with treatment. He was admitted to the hospital on 02/07/2022 due to complaints of fever, general weakness, and joint pain. During hospitalization, his clinical markers leukocytosis and thrombocytosis suggested his complications might progress towards severity. The laboratory details during hospitalization and previous day-care visit of a year before are mentioned in given below Table 1.

He presented to the site on 09/07/2022 for day care management in minimal consciousness condition with SpO_2 96% complains of left hip pain and unable to walk, joint pain, pallor, backache, and general weakness. His laboratory and X-ray evaluation for detailed investigation was performed to evaluate his clinical condition. Based on physical and laboratory investigation it was confirmed that the patient had developed avascular necrosis/ osteonecrosis.

His detailed laboratory and imaging testing are mentioned in Table 2 and Figure 1 respectively. He was started on integrated treatment to manage the complications. His integrated treatment is explained in Table 3.

Table 1: Clinical history of patient.

Parameters	11/12/2021	7/2/2022	7/5/2022	7/8/2022
Hb (gm/dL)	10.4	10.4	9.1	9.3
RBC (per cmm)	4.54	4.56	4.13	4.24
WBC(per cmm)	14300	12690	9230	14190
Platelet (per cmm)	518000	426000	349000	611000
MCHC(gm/dL)	31.3	37	36.3	36.5
MCH (pg)	22.9	22.7	22	21.9
MCV(fl)	73.1	61.4	60.5	66.1
PCV (%)	33.2	28	25	25.6
Neutrophil (%)	63	81.6	72.4	69.7
Eosinophil(%)	7	0.1	0.8	0.3
Basophils(%)	0	0.2	0.1	0.4
Lyphocytes(%)	30	10.4	14.7	23.9
Monocytes(%)	0	7.7	12.2	5.7
ESR (mm/Hr)	8	-	-	-
CRP (mg/L)	33.1	-	-	-
D Dimer (ng/mL)	1510.7	-	-	-
LDH (IU/L)	453.3	-	-	-
Reticulocytes (%)	3.3	-	-	-
Total bilirubin (µmol/L)	3.57	-	-	-
Direct bilirubin (µmol/L)	1.3	-	-	-
Indirect bilirubin (µmol/L)	2.27	-	-	-

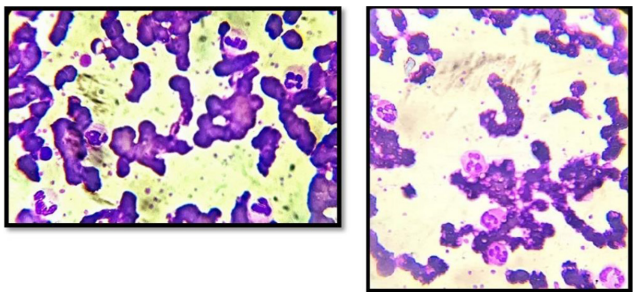

Figure 1: Imaging testing of elevated WBC and Platelets count.

DISCUSSION

Vaso-occlusive crisis consequences predominate in the sickle cell disease patient's clinical presentations. Because of intricate connections between sickled red blood corpuscles and leukocytes, platelets, endothelial cells, erythrocytes, and serum proteins. In these interactions, previous studies documented that platelets play a crucial role. Thrombocytosis, as opposed to platelet counts in emergencies, is a frequent finding in steady-state sickle cell disease. Elevated baseline platelet counts may have predictive value, although there is conflicting data linking them to disease severity or consequences.[2] Few blood parameters have been associated with the severity of sickle cell disease. The previous study states that the elevated white blood cells and platelets counts show that, patients were in an inflammatory state and experienced more episodes of pain crises even at their baseline steady state. Elevated steady-state WBC and platelet levels are indicators of increasing use of emergency rooms and may suggest maximizing therapy.[3] Patients with sickle cell disease have larger numbers of activated platelets at a steady state, and this rises during a Vaso-Occlusive Crisis (VOC).[4] Studies have shown that elevated expression of certain leukocyte adhesion molecules increases the occurrences of acute pain in sickle cell disease patients.

Table 2: Clinical Profile of Patient during treatment period at clinic.

Parameters	7/9/2022	7/12/2022	7/19/2022	7/23/2022	7/30/2022	8/16/2022	9/24/2022
Hb (gm/dL)	7.98	7.43	7.5	7.8	8.16	9.4	9.85
RBC (per cmm)	4.09	3.85	4.08	4.24	4.37	4.45	4.69
WBC(per cmm)	14600	15690	11300	22410	17900	9870	9850
Platelet (per cmm)	712000	944000	1158000	1251000	703000	680000	520000
MCHC(gm/dL)	36.43	36.24	34.58	34.09	34.28	34.7	33.84
MCH (pg)	19.51	19.29	18.48	18.49	18.67	21.2	21
MCV(fl)	53.54	53.24	53.43	53.3	54.46	61.2	62.09
PCV (%)	21.9	20.5	21.8	22.6	23.8	27.2	29.1
Neutrophil (%)	71	50	71	60	61	58.1	59
Eosinophil(%)	6	6	6	5	6	5.1	6
Basophils(%)	0	0	0	0	0	0.05	0
Lyphocytes(%)	21	42	21	33	31	30.5	33
Monocytes(%)	2	2	2	2	2	5.8	2
ESR(mm/Hr)	44	48	65	34	21		13
CRP (mg/L)	73.7	92.3	79.3	17.2	17.5	46.04	14.6
D Dimer	5455.24	-	3409.95	-	-	-	500
LDH (IU/L)	-	-	515	225	-	-	-
Reticulocytes	5.8	-	7.8	-	5.1	3.09	4.5
Total bilirubin (µmol/L)	3.9	-	-	-	-	-	-
Direct bilirubin (µmol/L)	1.9	-	-	-	-	-	-
Indirect bilirubin (µmol/L)	2	-	-	-	-	-	-
X-RAY/CT/USG				Avascular necrosis of hip			
SpO_2 (%)	96	98	98	97	-	-	-
PR (per minute)	100	94	117	90	-	-	-
BP (mmHg)	97/64	94/63	102/66	117/70	-	--	-
Weight (in Kg)	53.4	53	51.53	53.4	-	-	-

This implies that some molecules involved in white cell adhesion may have the potential as biomarkers.[5] In the present case, some estimated blood parameters were shown in Figure 1. The elevated levels of blood parameters like WBC, platelets, and neutrophils were tried to manage by the treatment mentioned in Table 1. The main approach for managing continuous VOCs is pain management. The main components of managing VOC include, the most suitable route of analgesic administration, selecting an adequate initial dose, and repeating administration as necessary until pain is relieved.[6] The other integrated treatment to resolve this problem included antibiotics, anti-inflammatories, and multivitamins. However, hypercoagulability may be influenced by the inflammatory condition of sickle cell disease.[7] To treat this condition anticoagulant therapy was also included in the treatment. In sickle cell disease, pulmonary hypertension is a prevalent condition.[8]

The prognostic implication of elevated baseline platelet counts is debatable with no conclusive evidence of its associations with disease severity or complications. Platelet numbers correlate with clinical and laboratory indicators of disease severity. Reactive thrombocytosis must be distinguished from myeloproliferative disorder or inherited thrombocytosis syndrome. Iron deficiency also results in thrombocytosis which improves with iron repletion. In sickle cell disease, iron deficiency may be difficult to detect, as serum ferritin may be elevated due to inflammation. Reducing leukocytes through medicine is not necessary to provide the desired benefit in such cases.[9-11] The T-AYU-HM premium formulation has ingredients that serve as a source of iron and ascorbic acid which will increase the possibility of iron absorption.[12] Gradual improvement in mean corpuscular volume and eventually in thrombocytosis and leukocytosis can also be seen in Table 2.

Avascular necrosis is a major source of morbidity among sickle cell disease patients. It is normally diagnosed as an advanced condition. The history and current clinical presentation of the patient indicate thrombocyte and leukocyte counts might become an alarming signal in such conditions.[13] Along with thrombocytosis and

Table 3: Integrated Treatment.

Date	Parenteral	Ayurvedic Treatment	Allopathic Treatment
11/12/2021 (Past visit detail)		Tab T-AYU-HM Premium 300mg BD. Tab ACUPEN 300mg BD.	Tab Eupod 200, Tab Zerodol P, Tab Myconit –D,
09/07/2022 (Date of admission)	i.v. Dolo 100 mL	Tab T-AYU-HM Premium 300mg BD. Tab ACUTAC 300mg BD.	Tab B-folcin Plus, Tab Levocet 10, Tab Rabemint –DSR, Tab Zifi 200, Tab Acemol SP,
12/07/2022	i.v. LMH i.v. Dexa	Tab T-AYU-HM Premium 300mg BD.	
14/07/2022		Tab T-AYU-HM Premium 300mg BD. Tab ACUTAC 300mg BD.	Tab Zerodol P, Tab B-folcin Plus, Cap Razol-D, Tab Levoflox 500,
19/07/2022		Tab T-AYU-HM Premium 300mg BD	Tab Diclozone, Tab Wysolone 10, Tab Propranolol 20mg, Tab Rabemint –DSR, Tab Zybend 400,
23/07/2022		T-AYU-HM Premium tablet 300 mg BD	Tab Zerodol P, Tab Wysolone 10 Cap Folvite active, Tab Rabemint –DSR, Tab Azithral 500 tablet,
30/07/2022		T-AYU-HM Premium tablet 300 mg BD	
24/09/2022		T-AYU-HM Premium tablet 300mg BD	

Dolo 100 mL (Paracetamol 1000mg/100mL), Azithral 500 (azithromycin 500mg), Rabemint –DSR (rabeprazole sodium and domperidone), Folvite active ((L-methyl folate, methylcobalamin and pyridoxal-5 phospate), Wysolone 10 (prednisolone 10mg), Eupod 200 (cefpodoxime 200mg), Zerodol P (Aceclophenac 100mg and Paracetamol 325mg), Zybend 400 (albendazole 400mg), Diclozone (diclofenac sodium, Paracetamol, chlorzoxazone), Zifi 200 tablet (cefixime 200mg), Acemol SP (Aceclofenac, Paracetamol and Serratiopeptidase), Myconit –D (Vitamin-D_3, methylcobalamin, folic acid, pyridoxine HCl and alpha lipoic acid), B-folcin Plus (riboflavin, folic acid, niacinamide, lactic acid bacillus spores), Levoflox 500 tablet (levofloxacin 500mg), Razol-D (rabeprazole sodium and domperidone), Levocet 10 (levocetrizine 10mg).

leukocytosis, parameters like D-Dimer and C-reactive protein also indicate cellular lysis progressed with inflammation in the patient. Because the change in the cellular membrane of the red blood corpuscle causes hemolysis and overtime a period it may lead to tissue or organ damage. It is already established in sickle cell anaemia, greater red blood corpuscle deformability is linked to osteonecrosis.[14] whereas constant iron depletion is also considered a major reason for bone resorption and osteoporosis.[15] With time patient's haemoglobin and red blood corpuscles level improvised suggesting the patient didn't experience any hemolysis-mediated complications. Gradually the inflammatory markers like ESR, C-reactive protein and LDH improvised with integrated treatment in a patient also suggest clinical improvement in the patient.

In the sickle cell, Adenosine Diphosphate (ADP) helps to activate platelets. It is unknown where the extra ADP in sickle cell disease comes from, but it could be erythrocyte-derived and released through hemolysis. Another possibility is that it comes from platelets and is released as a result of thrombin stimulating the platelets.[16] Even Monocytosis observed in the clinical profile is also considered a reason for activating Platelets. Because Monocytosis is common among sickle cell disease patients.[17] Preventing cellular lysis in sickle cells possibly prevents such activation of platelets and further complications.

CONCLUSION

Integrated treatment found effective in managing the patient of sickle cell disease having developed complication of avascular necrosis. The key observation was thrombocytosis, leukocytosis, iron depletion, and medication non-adherence are observational laboratory parameter suggesting development of sickle cell complications in patient. Implementation of Integrated treatment produced remarkable improvement in patient clinical and laboratory profile. The role of T-AYU-HM Premium tablets along with integrated treatment in preventing cellular lysis, boost iron stores, sustain oxygen supply, and prevent Vaso-occlusion became critical approach in management of complications of sickle cell patient. Patient recovered without any untoward

effect reporting during entire treatment period suggest there were no any adverse effect observed or reported. Improvement in walking, reducing painful episodes, and overall treatment cost definitely makes a difference in sickle cell complications management.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

RBC: Red Blood Corpuscles; **ESR:** Eyrthrocyte Sedimentation Rate; **VOC:** Vaso-occlusive crisis; **LDH:** Lactate Dehydrogenase.

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