Hematological parameters in sick cell anemia patients with and without priapism

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BACKGROUND: Priapism was associated with certain hematological parameters in sickle cell anemia (SCA) patients in one report but not in another. We studied differences in haematological parameters between SCA patients with and without priapism.

PATIENTS AND METHODS: Eighteen patients with SCA who presented with acute priapism during the years 2001-2004 were compared with age- and sex-matched SCA patients without priapism with respect to hematocrit, reticulocyte count, level of irreversibly sickled cells (ISC), percentage of haemoglobin F (Hb F), total leukocyte and platelet counts.

RESULTS: SCA patients with priapism had a mean hematocrit of 0.28 L/L, which was significantly higher than the mean hematocrit value of 0.24 L/L ($P<0.05$) in patients without priapism. The mean reticulocyte count of 8% in patients with priapism was significantly lower than mean reticulocyte count of 12% ($P<0.05$) in patients without priapism. The level of ISC of 3% in patients with priapism was significantly lower than the level of 6.5% ($P<0.05$) in patients without priapism. There was no statistically significant difference in the mean levels of Hb F (7% vs. 6%). Patients with priapism had a mean leukocyte count and mean platelet count that did not significantly differ from values in patients without priapism.

CONCLUSIONS: SCA patients with priapism had a lower rate of hemolysis, resulting in a higher hematocrit and greater blood viscosity, which increased the risk of corpora cavernosal sickling and blockade. Hence, a relatively high hematocrit is a risk factor for the development priapism in patients with sickle cell anemia.

The sickle β-globin gene is widely spread throughout Africa, the Middle East, the Mediterranean, Southeast Asia and by population movement to the Caribbean, North America and Northern Europe.[1] The frequency of sickle carriers (Hb AS) is up to 20% to 25% in West Africa, including Nigeria[1,2,3] and about 10% in the Afro-Caribbean,[1] and has reached high levels in these populations because the carrier state protects against malaria.[4] Hemoglobin C carriers (Hb AC) occur with a frequency of about 6% among Nigerians and are predominantly seen in the southwestern part of the country.[3] In Nigeria, Hb SS and Hb SC are the main forms of sickle cell disease (SCD), with the former being the most prevalent, affecting up to 2% of the nation's population.[3,5]

The clinical presentation of SCD is principally due to vaso-occlusive episodes resulting from polymerization of deoxygenated hemoglobin S, leading to the characteristic change in the shape of erythrocytes to a crescent or sickle shape.[1] These sickled erythrocytes have poor deformability and tend to adhere to vascular endothelial surfaces, which leads to endo-

thelial damage and subsequent exposure of sub-endothelial structures and collagen, resulting in platelet activation and aggregation within the microvasculature.[6,7] Furthermore, recent studies suggest that sickled erythrocytes increase vascular endothelial production of adhesion molecules, which creates a situation that favors intravascular cellular adhesions, stasis and prolongation of blood flow transit time, thereby increasing the chances of sickling of erythrocytes.[8] These events finally lead to a blockade of small blood vessels, resulting in tissue infarctions, which present clinically as the characteristic painful vaso-occlusive crises that commonly affects the bones. The effect of vascular occlusion in SCD is by no means restricted to the bones. Many other organs of the body, including the central nervous system, the lungs, the penis and the kidneys are particularly afflicted and multiple organ damage may also result.[6] In addition, sickling drastically shortens the life span of red cells leading to a chronic haemolytic anemia and jaundice with the possibility of formation of bilirubin gall stones in the long run.[6]

Priapism is a genital manifestation of SCD presenting as an unwanted painful erection that occurs in male patients with sickle cell anemia. It is caused by sickling episodes and thrombosis within the channels of the corpora cavernosa, leading to stasis and protracted congestion of the penile erectile tissues.[9,10] The clinical presentation can be acute, recurrent or stuttering.[9] The engorgement in priapism typically affects the corpora cavernosa and usually spares the glans penis and corpus spongiosum, except in a minority of cases in which the corpus spongiosum is also engorged.[9] Priapism is injurious to the erectile tissues, and if severe erection persists for more than a day, partial or complete impotence may occur as a result of corpora cavernosal fibrosis.[10] Hence, patients with priapism require careful assessment and prompt and effective management. A number of changes in haematological parameters had earlier been reported as being important predisposing factors for the development of priapism in patients with SCD. Among Jamaican patients with sickle cell anemia, priapism was found to be significantly associated with low hemoglobin F (Hb F) levels and high platelet counts.[11] However, a report from the United State indicated that there were no significant differences between hematological parameters of SCD patients with and without priapism.[9] We studied the hematological parameters of Nigerian patients with sickle cell anemia (SCA) presenting with priapism in comparison to SCA patients without any history of priapism. The data was analyzed to determine any significant hematological features that might be associated with the development of priapism in Nigerian patients with SCA as seen in Maiduguri, in northeast Nigeria.

Patients and Methods

Hematological parameters, including hematocrit, reticulocyte count, level of irreversibly sickled cells (ISC), percentage of Hb F, and total leukocyte and platelet counts were measured in 18 patients (aged 16-42 years) with SCA (Hb SS) who presented with acute priapism at the University of Maiduguri Teaching Hospital (UMTH), northeast Nigeria, during the years 2001 to 2004. The patients presented with acute priapism with no bone pain or other features of generalized vaso-occlusive crises. Blood samples for analyses were taken at the time of presentation and before initiating any form of treatment. The mean values of these parameters were then compared with those of an equal number of age- and sex-matched sickle cell anemia patients in steady state and with no history of priapism. All the patients included in this study were registered with the hematology clinic of the UMTH, and in each case the diagnosis of SCA was established by a positive sickling test and hemoglobin electrophoresis at a pH of 8.6 on cellulose acetate paper.

The hematocrit, total leukocyte and platelet counts were determined by automation using Beckman Coulter AcT-8, and white cell count errors due to the presence of nucleated red cells were appropriately corrected using manual differential counts in all cases.[12] The reticulocyte counts were determined manually from blood films made after samples were incubated with brilliant cresyl blue; the reticulocytes were identified and counted as percentages of the total red cells enumerated under high power microscope fields as described by Dacie and Lewis.[12] The levels of irreversibly sickled cells (ISC) were manually estimated as percentages of the total red cells enumerated from blood films made with the Leishman stain and examined under high power microscope fields as described by Dacie and Lewis.[13] Percentages of Hb F were also determined manually by the modified Betke method as described by Dacie and Lewis.[14] All procedures and tests conducted on the patients in this study were conducted in accordance with local ethical codes and were carried out after informed consent was obtained in each case.

Patients with and without priapism were compared with respect to the mean values and standard deviations of the determined parameters. In this report, the mean values and standard deviations were determined manually and the statistical significance of any differences in mean values were assessed using the Student t test and a probability level of $P<0.05$ was taken as significant.

Results

The mean values and standard deviations of hematological parameters found among SCA patients with priapism and those without a history of priapism are shown in Table 1. Patients with priapism had a mean hematocrit of 0.28 L/L, which was significantly higher than the mean hematocrit value of 0.24 L/L ($P<0.05$) in patients without priapism. The mean reticulocyte count of 8% in patients with priapism was significantly lower than mean reticulocyte count of 12% ($P<0.05$) in patients without priapism. The level of ISC of 3% in patients with priapism was significantly lower than the 6.5% ($P<0.05$) in patients without priapism. However, there was no statistically significant difference in the mean levels of Hb F of 7% and 6% in patients with and without priapism, respectively. Patients with priapism had a mean leukocyte count of 11.8×10^9/L and a mean platelet count of 450×10^9/L, which did not significantly differ from the mean leukocyte count of 12.3×10^9/L and mean platelet count of 460×10^9/L in patients without priapism.

Discussion

We found a high mean total leukocyte count in SCA patients with and without priapism, but the difference between the two groups was not significant. This is in keeping with earlier studies, which showed that a modest leukocytosis is a common feature of SCA even in steady-state, which is thought to be due to a redistribution of leukocytes from a marginal pool to a pool of circulating granulocytes.[15,16] Furthermore, the mean platelet counts were high in both patient groups, but the difference in the counts between the two groups was also not significant. The finding of high platelet counts in both groups is consistent with earlier studies, which showed that thrombocytosis is common in SCD and is attributed to the background hemolytic anemia and the autosplenectomy associated with the disease.[17,18] However, the absence of a significant difference in platelet count between our patients with and without priapism is at variance with earlier reports, which suggested that SCA patients with priapism had a significantly higher platelet count as compared with SCA patients who had no history of priapism.[11] The finding of elevated mean levels of both platelet and leukocyte counts in our patients is consistent with previous studies, which showed that both thrombocytosis and leucocytosis were common in Nigerian patients with SCA.[19]

Our SCA patients with priapism had a significantly higher mean value for the hematocrit and a lower mean reticulocyte count and ISC as compared with their counterparts who had no history of priapism. This data would suggest that the patients with priapism had a lower rate of steady-state hemolysis in comparison with their counterparts who had no history of priapism. This is supported by an earlier study, which found that the reticulocyte count and ISC are directly related to the rate of hemolysis and are important determinants of hemolysis in sickle cell anemia.[20] The higher mean hematocrit among SCA patients with priapism in this study is interpreted to correlate well with their lower mean reticulocyte count and lower mean ISC, both of which are indicative of lower rates of steady-state sickling and hemolysis.[20] These findings would suggest that SCA patients with priapism had clinically milder disease in terms of hemolysis as compared with their counterparts who had no history of priapism. This is supported by earlier studies, which showed that the rate of steady-state hemolysis and levels of ISC were significant markers of disease severity in SCA.[21,22] Variations in levels of Hb F accounts for much of the clinical heterogeneity observed in patients with SCA, and the Hb F level has emerged as an important prognostic factor as higher levels are generally associated with lower rates of sickling and hemolysis.[23] However, the observed differences in terms of rates of sickling and hemolysis

Table 1. Haematological parameters in sickle cell aaemia patients with and without priapism.

Parameters (mean±SD)	Patients with priapism (n=18)	Patients without priapism (n=18)	Statistical significance
Hematocrit (L/L)	0.28±0.02	0.24±0.03	$P<0.05$
Reticulocyte count (%)	8±1.5	12±2	$P<0.05$
Level of irreversibly sickled cells (%)	3±0.5	6.5±1	$P<0.05$
Hb F level (%)	7±1	6±1.2	$P>0.05$
Total leucocyte count (x10^9/L)	11.8±3	12.3±2.5	$P>0.05$
Platelet count (×10^9/L)	450±50	460±52	$P>0.05$

Values are mean ± standard deviation.

between our patients with and without priapism could not be explained on the basis of Hb F levels since both categories of patients had only mildly elevated levels (7% and 6%, respectively) which were not different statistically. This finding is at variance with previous reports suggesting that SCA patients with priapism had significantly lower Hb F levels as compared with patients who had no history of priapism.[11] However, our finding of mildly elevated levels of Hb F in both patient groups is consistent with previous studies that reported Hb F levels of less than 10% among Nigerian and other African patients with SCA,[5,24] which is at variance with the considerably higher levels generally seen in Middle Eastern patients.[23, 24] Therefore, certain unidentified factors other than Hb F levels may be responsible for the observed differences in the rates of sickling and hemolysis between the two categories of SCA patients in this study since many genetically determined factors influence the variability in clinical expression of SCA.[24]

Our findings suggest an association between the hematocrit and priapism. This is interpreted to be a reflection of the fact that whole blood hyperviscosity is a major contributory factor in the pathogenesis of vascular occlusion in SCA.[25] Studies have shown that the viscosity of oxygenated sickle blood was 1.5-fold that of normal at equal shear rates[26] and was increased to 10-fold that of normal blood upon deoxygenation.[26] Furthermore, a higher hematocrit in patients with SCA was found to be associated with a greater increase in whole blood viscosity, which causes a diminished blood flow and increases the tendency towards sickling, thrombus formation and vascular occlusion.[25,26,27] Therefore, our findings in this study suggest that the relatively higher hematocrit seen in SCA patients with priapism could be an important causative factor since a higher hematocrit would lead to higher blood viscosity, which increases the risk of sickling, thrombosis and vascular occlusion within the channels of the corpora cavernosa, leading to the development of priapism. In fact, earlier studies had shown that a higher hematocrit was also associated with greater risks of developing other serious complications of SCA in which vascular occlusion is an important factor, such as stroke,[21] acute chest syndrome,[28] acute multi-organ dysfunction syndrome,[29] avascular necrosis of the femoral head[30] and retinopathy,[31] all of which were thought to be related to higher blood viscosity. Although the result of this study did not find any significant differences in leukocyte and platelet counts between SCA patients with priapism and those without priapism, it should however be appreciated that blood viscosity is also affected by the number of circulating leukocytes and platelets, which can act jointly and subtly with the hematocrit to raise blood viscosity and increase the risk of vascular occlusion and priapism in SCA.[6,7,16,17] Hence, it may not be possible to precisely quantify the extent of the risk of priapism that can occur due to a higher hematocrit in patients with SCA because of the variable rheological effects of leucocytes and platelets. Nonetheless, it may be anticipated that the risk of priapism in SCA patients with a higher hematocrit would be greater if such patients also have leukocytosis and/or thrombocytosis. We conclude that a relatively high hematocrit is a risk factor for the development of priapism in patients with sickle cell anemia.

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