Original Article

Musculoskeletal Complications of Sickle Cell Disease in Enugu, Nigeria

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ABSTRACT

BACKGROUND: Sickle cell disease (SCD) is one of the most important haemoglobinopathies. It is an autosomal recessive genetic condition in which a defective form of haemoglobin, haemoglobin S (HbS) results from a single amino acid substitution. The amino acid valine replaces glutamic acid at position 6 in the beta globin gene. Musculoskeletal complications are often observed in the evolution of this disease and are common causes of morbidity and disability in these patients. The objective of this study is to describe the pattern and presentation of musculoskeletal complications in sickle cell disease at the National Orthopaedic Hospital Enugu Nigeria.

METHOD: a retrospective review of the patients with musculoskeletal complications who are genotype-confirmed sicklers who were treated in our hospital from January 1993 to December 2007 was carried out. The data collected included age, sex, complications, anatomic site, grade of disease, treatment, outcome of management and follow up. Patients with incomplete data were excluded from the study.

RESULTS: Twenty seven patients with musculoskeletal complications of SCD were treated within the study period. Two patients were excluded from the study because of incomplete data. Twenty-five patients with 44 complications were analyzed. The age range was between 7 years to 30 years with a mean age of 19.2 years. Fifty six percent of patients were males. Malleolar ulcers were the commonest complications. This was followed by avascular necrosis (AVN) of the femoral head and osteomyelitis. Septic arthritis and osteomyelitis were most common in children less than 10 years while avascular necrosis and malleolar ulcers occurred more commonly in patients more than 15 years. Majority of the malleolar ulcers were treated by split skin grafting. Seventy five percent of the femoral head avascular necrosis was treated conservatively.

CONCLUSION: Musculoskeletal complications are common causes of morbidity and disability in sickle cell disease. Malleolar ulcers were the commonest musculoskeletal complications. The predominant presentation in children below the age of 10 years is osteomyelitis and septic arthritis while AVN and malleolar ulcers occurred mostly in adolescents.

KEYWORDS: Sickle cell disease, musculoskeletal complications, pattern of presentation, Enugu.

INTRODUCTION

Sickle cell disease (SCD) is the most frequent haemoglobinopathy worldwide.[1,2] It is currently the second most common genetic disease after Down's syndrome [2].

SCD is said to affect 2-3% of the Nigerian population[3]. It affects mostly the Negroid populations in and outside Africa and also present in the Mediterranean and West Indies [4]. The first description of sickle cell disease was made in Chicago in 1910 by James B. Herrick when he identified abnormal sickle-shaped cells in an anaemic patient of Negroid extraction[5]. Hahn and Gillespie (1927)[6] showed that sickling of the erythrocytes was induced by deoxygenation and reversed by reoxygenation. Electrophoretic abnormalities of haemoglobin which is the key for diagnosis were demonstrated in 1949 by Pauling et al[7].

SCD is an autosomal recessive genetic condition in which a defective form of haemoglobin, haemoglobin S (HbS) replaces the normal haemoglobin (HbA). Ingram in 1957 identified the sequence of the defective gene. In position 6 of the beta globin gene on chromosome 11, the amino acid valine is substituted for glutamic acid which codes for a different haemoglobin called haemoglobin sickle HbS. This substitution significantly changes the solubility of the haemoglobin which ultimately leads to sickling of the red cells when exposed to acidic or hypoxic conditions.

SCD is primarily a disease of the haemopoetic system in which the skeleton bears the brunt of its complication[8]. It has been reported that musculoskeletal manifestations constitute up to 80% of indications for hospital admissions in SCD [9-13]. Two separate pathogenetic processes produce these complications, haemolysis and vaso-occlusion.

Increased destruction of deformed and inefficient sickle red cells produces haemolytic anaemia.

Vasoclusion is due to entrapment of sickled cells in the microcirculation and leads to tissue ischemia and infarction in almost all the organs.

In children dactylitis, known as hand and foot syndrome is a common presentation between the ages of 9 months and 4 years with painful tender swelling of the hands and feet[14].

It may result in premature closure of the affected

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epiphysis, leading to shortened and deformed bones.

Avascular necrosis (AVN) occurs in bones from the age of 9 years although the symptoms are more obvious and severe from the age of 11 to 15 years, the femoral head being the commonest site[15]. Other sites of avascular necrosis are the humeral head, femoral condyles, talar body, and lumbar spine.

Osteomyelitis is a common condition affecting children aged one to 10 years in developing countries and children with SCD have an equal incidence [15]. The common sites are upper and of the femur, the shafts of tibia, radius, ulna and humerus. Isolated cases have been reported in other bones, such as the pelvis[16]. The common bacterial organisms are staphylococcus, salmonella and klebsiella species[15].

Chronic osteomyelitis is the late stage of the acute infection and may be due to delay in diagnosis or inadequate treatment. Multifocal infections are common in Africa [17-19], but spinal involvement is rare.

Leg ulcers are commonly seen amongst adolescent sicklers. They occur particularly over bony prominences e.g. the malleolus as a result of venous stasis and tissue hypoxia.

The effect of SCD on skeletal growth is variable. Retardation of growth occurs in some patients in the early years of life resulting in heights below the mean for their age. This effect is thought to result from bone infarction arising from vascular compromise[20].

However, many patients eventually have a normal growth spurt and attain average or above average height [21].

We have retrospectively reviewed the musculoskeletal complications of SCD in Enugu Nigeria. We hope this will provide useful data to healthcare professionals involved in the management of SCD patients as well as form a baseline for future comparative and analytical studies.

PATIENTS AND METHODS

A retrospective review of all the patients with musculoskeletal complications of sickle cell disease at the National Orthopaedic Hospital Enugu Nigeria from January 1993 to December 2007 was conducted after approval by the Research and Ethics committee of the Hospital. The data analyzed were patients' age, sex, musculoskeletal complications, anatomic site, treatment, outcome of treatment, and follow up.

Musculoskeletal complications were defined as problems affecting the bones, joints and/or the associated soft tissues in patients with SCD confirmed by haemoglobin electrophoresis. Patients with musculoskeletal affectations without a confirmed diagnosis of SCD as well as patients with incomplete data were excluded from the study. The diagnosis was made on the basis of clinical, radiological and microbiological findings. Radiological assessment was by means of x rays. Our hospital as yet does not have facilities for CT scan, MRI and radioisotope scan. The microbiological culture and antibiotic sensitivity of joint aspirates, wound swabs from leg ulcers and discharging sinuses were analyzed. The duration of follow up was from 22 months to 12 years with a mean follow up period of 4.5years. Data obtained were analyzed using SPSS for WINDOWS 10.

RESULTS

Demography:

During the period under review, 25 patients with 44 musculoskeletal complications were studied. They were all referred from other hospitals since our hospital being a trauma/Orthopaedic centre does not primarily treat SCD patients. Ten patients (40%) had multiple complications.

Fourteen patients (56%) were males while 11(44%) patients were females, giving a male: female ratio of 1.3:1. The age range was from 7 years to 30 years with a mean age of 19.2 years (Table 1). Three patients were below 10 years, 11 patients were in the second decade and third decade each. The peak age incidence was 16-20 years (Figure 1). All the patients were known sicklers with HbSS genotype.

Anatomical Location of musculoskeletal complications.

Forty four anatomic sites were involved the study. Five (11.4%) were located in the upper limbs, while 39 sites (88.6%) were in the lower limbs.

There was no spine affectation in our series. All the upper limb complications were osteomyelitis of either the humerus or radius and occurred mostly in patients less than 10 years.

Leg ulcers around the malleoli were the most common complication and occurred at 17 (38.6%) anatomic sites (Table 2). Most of the ulcers (70.6%) were located above the medial malleolus and 29.4% occurred around the lateral malleolus.

There were 12 cases of avascular necrosis of bone and all of which occurred in the femoral head. Osteomyelitis was found in 12 long bones; femur 4 (33.3%), humerus 3(25%), radius 2(16.7%), fibular 2(16.7%) and tibia 1(8.3%). Septic arthritis affected 3 joints (6.8%), 2 lip joints and 1 knee joint.

Infectious Complications

Septic arthritis and osteomyelitis occurred at 3 and 12 sites respectively. Analysis showed that 66.7% of septic arthritis and 75% of osteomyelitis occurred in patients less than 10 years of age (Table 3). Coliforms were isolated in all the 3 cases of septic arthritis. The bacterial isolates in osteomyelitis were Staphylococcus aureus in 8 cases (66.7%), Escherichia coli in 3 cases (25%) and Salmonella typhi in 1 case (8.3%).

All the patients with osteomyelitis had surgical debridement and sequestrectomy as well antibiotic administration. Arthrotomy with joint drainage and antibiotic administration was the treatment for septic arthritis.

Non-infectious Complications

The femoral head was the only site of AVN. Two hips (16.7%) had Ficat and Arlet stage II disease; 7 hips (58.3%) had stage III disease and 3 hips (25%) were in stage IV disease. No patient had Ficat and Arlet stage I disease. Only 1 patient less than 10 years of age had AVN. Others were in the second and third decades of life. The mean age for AVN was 19.3 years.

Seventy five percent of patients with AVN of the femoral head were treated conservatively with weight relief and skin traction. Girdlestone excision arthroplasty was done in 2 patients (16.7%) and intertrochanteric realignment osteotomy was done in one patient (8.3%). Malleolar ulcers were seen in patients between 16 and 25 years of age. There was a positive bacterial culture in 58.8% of ulcers. Staphylococcus was the most frequently isolated organism in 70% of cases.

Majority of patients with leg ulcers (70.6%) were treated by split skin grafting. Three patients (17.6%) were treated conservatively with elevation, wound dressing and antibiotics. Fascial flap cover was done in two patients. The duration of follow up was from 22 months to 12 years with a mean follow up period of 4.5years. One patient died during follow up.

Table 1: Demographic parameters of patients with musculoskeletal complications.

Parameters	No	%
Male	14	56
Female	11	44
Male: Female Ratio	1.3:1	
Age Range (Years).	7-30years	
Mean age	19.2years	
Age (Years)		
6-10	3	12
11-15	1	4
16-20	10	40
21-25	9	36
26-30	2	8
Genotype		
HbSS	22	100

Fig 1: Age Distribution

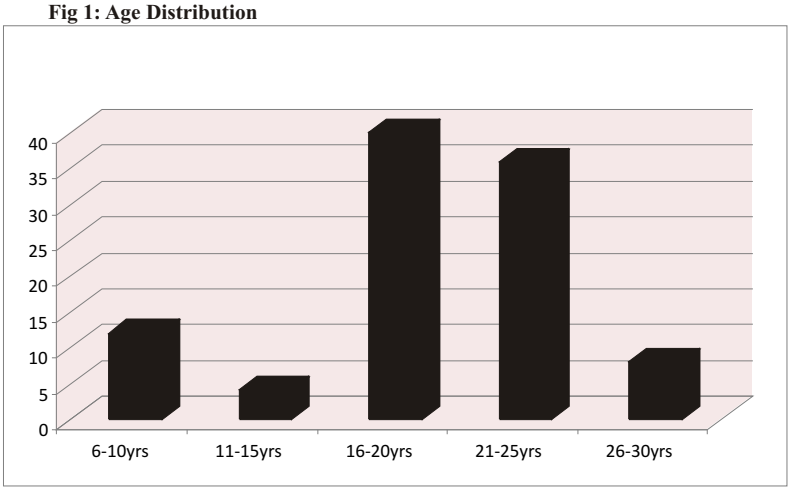

Table 2: Distribution of Musculoskeletal Complications

Disorder	Frequency	%
Leg Ulcer	17	38.6
Avascular necrosis	12	27.3
Septic arthritis	3	6.8
Osteomyelitis	12	27.3
TOTAL	**44**	**100%**

Table 3: Distribution by age of presentations

Age /Disorder	AVN	Ulcer	Septic Arthritis	Osteomyelitis	Total
6-10	1	-	2	9	12
11-15	2	-	-	-	2
16-20	4	7	1	1	13
21-25	3	10	-	2	15
21-30	2	-	-		2
Total	**12**	**17**	**3**	**12**	**44**

DISCUSSIONS

We studied 25 patients with 44 musculoskeletal complications of SCD. Ten patients (40%) had multiple complications. This is higher than the 28% reported by Balogun et al [22].

In our series, the oldest patient was 30 years. This may be explained by the significantly reduced life expectancy of SCD patients as reported by previous authors [23, 24]. We also observed that only 12% of our patients were below the age of 10years while 44% were in the second decade and third decade of life each. This age distribution is in contrast to the reports by Balogun et al[22] and Nwadiaro et al[25] in which the peak age incidence was in the first decade of life.

The poor life expectancy in sub Saharan African SCD patients has been attributed to factors like the absence of hydroxyurea therapy which may improve the survival,[26] the low educational background, poor life style and limited access to medical facilities [27]. The slight male preponderance in this study is similar to findings in previous studies [11-13, 25]. All our patients had HbSS genotype. There were no cases of HbSC or Beta thalasaemia. This finding that HbSS is the commonest variant of SCD amongst Nigerians has been reported earlier [12,22].

Malleolar ulcers were the commonest musculoskeletal complications seen in our study constituting 38.6% of all the complications with a mean age incidence of 20.9 years. This frequency is higher than the 25% by Sawhney et al [28], 22% by Bahebeck et al, [29] and 10.7% by Balogun et al [22].

There was a predilection for the medial malleolus (70.6%) which is in keeping with reports by Sawhney et. al.[28] The malleolar ulcers are usually due to venous stasis, tissue hypoxia and subsequent devascularization of the affected area. The preponderance of malleolar ulcers in the older patients may result over the years of life from chronic anaemia and progressive ischemia at the affected sites. There may be a history of trivial trauma which was observed in 49% of cases in our study. Staphylococcus aureus was the most frequently isolated organism from the wound cultures. Other organisms were Escherichia coli (20%) and Pseudomonas species (10%). Most of the leg ulcers were treated by split skin grafting (70.6%). Others were treated either conservatively (17.6%) or with fascial flap (11.8%). We noted a recurrence in 4 cases (23.5%). Three patients with chronic leg ulcers developed osteomyelitis from where the same organism as that isolated from the ulcers were cultured. One patient with septic arthritis of the hip had a chronic malleolar ulcer and the same pathogen was identified from the two sites.

We therefore postulate that chronic malleolar ulcer may be a predisposing factor for bone and joint infectious in SCD. However, randomized controlled studies are needed to establish this fact. We recommend early closure of leg ulcers with split skin graft in order to prevent this possible sequela.

Bone and joint infectious are serious complications of sickle cell disease and important causes of morbidity and hospitalization. Osteomyelitis accounted for 27.3% of complications in our study. This figure is higher than the 18% reported by Bahebeck et al, [29] but comparable to the 29% and 30% in the studies by Mujiyawa et.al[30] and Balogun et al [22] respectively.
Only long bones were affected and the femur was the commonest site. Seventy five per cent of these patients were less than 10 years. The oldest patient was 25years. The preponderance of osteomyelitis in the younger age group in this study conforms to the known fact that it is usually a disease of children.[22, 25] Staphylococcus aureus was the leading causative organism accounting for 66.7% of the cases. This was followed by Escherichia coli (25%) and Salmonella typhi (8.3%). Only 3 patients (25%) had double bone involvement. This is in contrast with a previously held view that chronic osteomyelitis usually involves multiple bones in patients with SCD [18, 19, 30-32.] All the patients with chronic osteomyelitis were treated with surgical debridement, sequestrectomy and antibiotics administration for 6-8 weeks. Recurrence was noted in 16.7% while pathological fracture occurred in one patient.

Septic arthritis like osteomyelitis is known to occur more commonly in the younger age group. In our series, septic arthritis occurred in 6.8% of our patients, majority of who were less than 10 years. These findings are in tandem with studies by Acurio et al [10] and Bahebeck et al [29]. Infections occurred only in the hip joint and coliforms were the isolated organisms. We did not observe any correlation with low socio economic status or poor sanitary living conditions in these patients. All the patients had arthrotomy with joint irrigation and antibiotics administration for a period of 6 to 8 weeks without any adverse sequelae.

We recommend arthrotomy and joint irrigation and not joint aspiration as the surgical treatment of septic arthritis. Antibiotics administration should be for a period not less than 6 weeks to ensure complete eradication.

Sickle cell disease is the commonest cause of AVN in Nigeria [30, 33]. The prevalence rate of AVN complicating SCD is reported as 3-19% [11, 30]. The higher rate in our study of 27.3% and the high incidence (83.3%) of late stages of the disease (Ficat and Arlet III and IV) maybe due to late presentation by our patients. Majority of the

patients presented first to traditional bone setters and faith healers before presenting to our centre. There is therefore need for awareness campaigns for SCD patients, the primary care givers and the society in general on the need to seek appropriate care early. We also believe that the provision of modern diagnostic facilities such as magnetic resonance imaging (MRI) at affordable costs would help to identify the early stages of this disease and thereby reduce the morbidity associated with advanced diseases.

The mean age for femoral head AVN in our study was 19.3 years. Akinyoola et al[34] in their study reported a mean age of 23.7 years while Gheldere et al[35] recorded 12 years as the mean age. With the increasing awareness of this disease, better quality of healthcare and consequent increase in life expectancy of SCD patients, the mean age for development AVN is expected to increase. Majority of our patients (75%) were treated conservatively with either skin traction or weight relief with bilateral axillary crutches with satisfactory results. Only two patients with stage IV disease were treated with Girdlestone excision arthroplasty while one patient with stage III disease was treated with intertrochanteric osteotomy. None of our patients had a total joint replacement. We therefore support the opinion that conservative treatment be preferred over arthroplasty in these patients because of the known poor results of the surgery [36, 37,] the high rate of associated peri-operative complications [36,38] and finally the poor life expectancy of these patients.

CONCLUSION

This study has shown that malleolar ulcers are the commonest musculoskeletal complication of sickle cell disease in our environment. The predominant presentation in children below the age of 10 years is osteomyelitis and septic arthritis while AVN and malleolar ulcers occurred mostly in adolescents.

Chronic malleolar ulcers maybe a predisposing factor to bone and joint infections in SCD however, randomized controlled studies maybe needed to confirm this finding. There is need for more efforts to improve the quality of life and life expectancy of patients with SCD in developing countries.

These efforts should be in form of awareness campaigns and improved social and medical services.

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