East African Medical Journal Vol. 77 No 1 January 2000
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CHRONIC OSTEOMYELITIS IN PATIENTS WITH SICKLE CELL DISEASE

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ABSTRACT

Objective: **To determine the baseline pattern and audit management modalities of chronic osteomyelitis in patients with sickle cell disease.**
Design: **A retrospective study.**
Setting: **Jos University Teaching Hospital, Jos, Nigeria from August 1993 to July 1997.**
Patients: **Twenty four patients with concomitant chronic sickle cell disease.**
Interventions: **Fifteen patients had operations; eleven had sequestrectomy and curettage while four had incision and drainage. Eight patients were treated with antibiotics alone and one patient refused surgery.**
Main outcome measures: **The demographic data of patients, aetiological agents, culture and sensitivity patterns, aetiopathogenesis, treatment modalities and outcome were analysed.**
Results: **Twenty four (36.9%) out of 65 patients who had chronic osteomyelitis also had sickle cell disease. Male:female ratio was 1.2:1. The peak age incidence (37.5%) was in the first decade of life. Seventy five per cent of infections were haematogenous. The most frequently isolated organism was *Staphylococcus aureus* (58.8%) while the rest were Gram negative organisms. There was no case of *Salmonella* osteomyelitis. The most sensitive antibiotics were gentamicin and the third generation cephalosporins. Twelve patients (50%) had good results while eight (33.3%) were still undergoing treatment. Complications recorded were persistent discharging sinuses in two cases, recurrence of symptoms in one and pathological fracture with non-union in one patient.**
***Conclusion*: Though the incidence of Gram negative organisms in causation of chronic osteomyelitis in patients who have sickle cell disease is high (41.2%), *Salmonella* osteomyelitis may be related to endemicity of the organism in a given locality.**

INTRODUCTION

The manifestations of sickle cell disease in the musculoskeletal system are major causes of morbidity and disability in West and Central Africa, the Mediterranean and in the West Indies(1). The vaso-occlusive phenomenon leads to bone infarction and relapsing bone pain crisis. Also, avascular necrosis of major bone parts, for example, femoral and humeral heads result in subsequent joint degeneration. Whereas hypertrophy of bone marrow a a result of increased haemopoietic demand leads to cortical thinning and osteoporosis; this consequently predisposes the patient to pathological fractures and hand-foot syndrome (dactylitis). Furthermore, there is reduced immunity in patients who have sickle cell disease as a result of splenic hypofunction and defective opsonins(2). In the presence of infarcted bone tissue, there is an increase in the risk of osteomyelitis. The patients become susceptible to unusual organisms as was reported in the series by Ebong(3,4) in Ibadan and Givner *et al*(5) in which a preponderance of salmonella osteomyelitis was found among patients who had concomitant sickle cell disease. The morbidity of chronic osteomyelitis combined with other effects of the haemoglobinopathy decreases the quality of life. It is worth pointing out that sickle cell disease here is applied to sickle cell anaemia (haemoglobin SS), sickle cell trait (haemoglobin AS), beta-thalasaemia, haemoglobin SC, and any other condition in which the sickle cell haemoglobin is combined with other abnormal forms of haemoglobin (6).

We have retrospectively reviewed patients who had chronic osteomyelitis and sickle cell disease in Jos University Teaching Hospital over a four-year period with a view to determining the pattern and audit management modalities. This study would also furnish a baseline for further comparative and specific studies on chronic osteomyelitis in this centre.

MATERIALS AND METHODS

Twenty four patients who had sickle cell disease and presented to Jos University Teaching Hospital with concomitant chronic osteomyelitis over a four-year period from August 1993 to July 1997 were retrospectively studied. The patients were identified from the ward admission and discharge records and the operating register and the case notes obtained from the Health Record retrieval system. The information was analysed for age, sex, investigation, treatment and follow up. The diagnosis was made on the basis of both clinical and radiological findings. The sickle cell disease was confirmed by electrophoresis after routine sickling test had proved positive. Chronic osteomyelitis was diagnosed in the presence of swelling, pain, discharging sinuses, peculiarly-looking healed adherent scars and x-ray findings of sequestra, abscess cavity, irregular sclerosis and osteolytic bone changes and periosteal reaction. Wound swabs and aspirates from swollen areas were routinely sent for microscopy, culture and sensitivity. Anaerobic culture was not done on any of the patients because of lack of facilities at the study centre. Antibiotics were administered at first empirically then following culture and sensitivity results and were continued until healing or changed according to laboratory result. Sequestrectomy and curettage were offered as treatment if a mature sequestrum or abscess cavity was seen on x-ray and incision and drainage for fluctuant soft tissue abscesses. Dressing was done using hydrogen peroxide and Eusol and the frequency determined by the extent of tissue necrosis and discharge. The result was regarded as good or healing said to have occurred if after operation or a course of antibiotics, the wound remained dry and closed, and pain subsided with no further radiological sign of sequestrum or abscess.

RESULTS

In the four-year period under review, 65 cases of chronic osteomyelitis were treated at the Jos University Teaching Hospital. Of these, 24 (36.9%) patients had concomitant sickle cell disease. There were 13 males and eleven females giving a male: female ratio of 1.2:1.0. The incidence of chronic osteomyelitis in patients who had sickle cell disease was therefore six new cases per year.

The ages ranged from one year three months to 35 years with the peak age incidence in the first decade of life (37.5%). This was followed closely by patients in the second decade (33.3%) and 25% in the third decade of life. Only one (4.1%) patient was over 30 years.

Fourteen of the patients presented within the first six months of having symptoms. Of these, nine patients reported in the first month. One patient presented in first year and two in the second year. Four patients were seen after two years while in three patients, there were no records of duration of symptoms.

The foci of infection were found in 27 bones as shown in Table 1. The tibia was the most frequently involved bone (40%). Three patients had multiple foci of infection. Outside the long bones, the thoracolumbar spine was affected twice, the left side of mandible once, and the first left metatarsal bone once. The two cases of spinal involvement had concomitant tuberculosis.

Table 1

Anatomical sites of the lesions

Bone involved	No. of bones	%
Humerus	5	18.5
Radius	2	7.4
Femur	5	18.5
Tibia	11	40.7
Mandible	1	3.7
First metatarsal	1	3.7
Spine	2	7.4
Total	27	

Three patients had multiple bone involvement

Fifteen operations were carried out. Of these, four incisions and drainage were done, and eleven patients had sequestrectomy and curettage. One patient could not afford the cost of surgery and in eight cases, operation was not indicated and were treated with antibiotics.

In 18 (75%) patients, infection was haematogenous, but followed traumatic injury in five cases (20.8%). In one patient, chronic osteomyelitis was a result of direct extension from a chronic leg ulcer. The traumatic injuries were as a result of compound fractures from falls and road traffic accidents.

At the time of presentation, six patients (25%) were known sicklers under treatment whereas 18 (75%) were diagnosed as having sickle cell disease while under treatment. Fourteen (58.4%) of the patients had sickle cell anaemia (haemoglobin SS disease), eight (33.3%) had the sickle cell trait (haemoglobin AS) and two (8.4%) had haemoglobin SC. There was no case of beta thalasaemia.

Seventeen positive cultures were obtained from 14 patients. The cultural characteristics of the aetiological agents is shown in Table 2. *Staphylococcus aureus* was the most frequently isolated organism in 58.8% cases. Mixed infection occurred in three cases. Two patients had secondary infection of tuberculosis of the spine. There was either no growth or no record of any culture in 10 patients. No case of salmonella osteomyelitis was found.

Table 2

Culture characteristics of the aetiological organisms

Organism	No. of times cultured	%
Staphylococcus aureus	10	58.8
Pseudomonas aeruginosa	1	5.9
Klebsiella species	2	11.8
Citrobacter fruendi	1	5.9
Escherichia coli	2	11.8
Proteus species	1	5.9
Total	17 positive growths	

No growth or not done in 10 patients

The *in vitro* sensitivity pattern of the isolated organisms in shown in Table 3. Gentamicin and the

third generation cephalosporins were the most sensitive antibiotics. This was followed by erythromycin and tetracycline. Sensitivity to cloxacillin was relatively low (6.5%).

Table 3

In-vitro sensitivity pattern of isolated organisms to antibiotics

Antibiotic	No. times positive	%
Erythromycin	6	13.0
Gentamicin	8	17.4
Cloxacilin	3	6.5
Cephalosporins	11	23.9
-Cefuroxime		
-Cefriazone		
-Cefutaxime		
-Ceftazidine		
Chloramphenicol	1	2.2
Streptomycin	4	8.7
Tetracycline	5	10.7
Ampicillin	2	4.3
Kanamycin	2	4.3
Septrin	2	4.3
Clindamycin	2	4.3
Total	46	
Not recorded	3	

Table 4

Duration of follow up

Duration of follow up (in months)	No. of patients	%
0-6	9	37.5
7-12	3	12.5
13-18	1	4.2
19-24	1	4.2
25-30	5	20.8
31-36	1	4.2
>36	4	16.7
Total	24	

The duration of follow up of the patients is shown in Table 4. Of the 12 patients who were followed up for one year or less, eight were still under treatment. Twelve patients were found to have no recurrence of symptoms and were considered to have good results. We recorded complications of persistent discharging sinuses in two cases, recurrence of symptoms in one and pathological fracture with non-union in one patient. No death was recorded in the period of study.

DISCUSSION

It was observed that 36.9% of sixty five patients treated for chronic osteomyelitis during the study period had concomitant sickle cell disease. This high figure is not surprising, as osteomyelitis is known to be common in sicklers(7-10). The vaso-occlusive crisis that results in frequent bone infarction, coupled with reduced immunity, contributed to the high incidence. Bone tissue is usually resistant to infection and only gets overcome by organisms of high virulence, in the presence of foreign body and when there is decreased host resistance(7).

Our finding of a preponderance of chronic osteomyelitis in the younger age group in this study conforms with the known fact that it is usually a disease of children(1-10). The oldest patient was aged 35 years. This could be accounted for by the low life expectancy in sickle cell anaemia. In sickle cell trait, with normal life expectancy, absence of older patients is explained by the relative less susceptibility of adult bones to infection(7). In addition, the study period was a time of severe economic depression in Nigeria when hunger and malnutrition were prevalent. This could have contributed to reduced host immunity in the more vulnerable age group. Haematogenous spread of infection which was observed in 75% of the patients in this series is directly related to reduced host immunity(1,7,9,10).

There were 27 bones affected in twenty four patients. Only three patients had double bone involvement. This finding contrasts with previously held view that chronic osteomyelitis usually involves multiple bones in patients who have sickle cell disease(2,5,6,10).

Staphylococcus aureus was the leading causative organism accounting for 58.8% of the cases with positive culture. There was no case of salmonella osteomyelitis even though the remaining 41.2% were caused by gram negative organisms. Givner *et al.* (5) in a pulled study involved 84 patients with sickle cell disease isolated salmonella in 74% and *Staphylococcus* in ten per cent of the positive cultures(2).

In a study of children in Ibadan, Nigeria, Ebong found a preponderance of salmonella osteomyelitis which he attributed to endemicity of the organism in the environment(2,3). Another study in Enugu, Nigeria, found the most frequent aetiological agent of osteomyelitis among sicklers to be *Staphylococcus aureus* in 50% of 18 patients(2). These studies were carried out in the southern part of Nigeria with different climatic condition from Jos, which is situated in the savannah zone. Even though enteric fever is not a rarity in this environment, absence of salmonella osteomyelitis among sicklers would require a much larger series to elucidate. In the general population, *Staphylococcus* accounts for upto 80% of chronic osteomyelitis(9).

We note that there was high sensitivity to gentamicin and the cephalosporins in 41.3% of isolates with relatively low sensitivity to cloxacillin (6.5%). The tendency to abuse cloxacillin in self medication in this locality is enhanced by easy procurement, cheapness and the oral route of administration. The laws restricting acquisition of drugs via prescription is not strictly enforced. The cephalosporins and gentamicin are less likely to be

abused because of parenteral administration and high cost.

In conclusion, we observe that the pattern of chronic osteomyelitis in patients who have sickle cell disease vary according to prevailing circumstances. The peculiarity of a given locality needs to be determined by regular audit. In this environment, the incidence of Gram negative osteomyelitis is high. This, coupled with low sensitivity to cloxacillin makes gentamicin, cephalosporins and erythromycin the initial choice of antibiotic treatment. The changing pattern of sensitivity can only be determined by periodic review.

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