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Osteomyelitis in Children with Sickle-cell Disease

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Summary

Okoroma EO. Osteomyelitis in Children with Sickle-cell Disease. *Nigerian Journal of Paediatrics* **1986; 13:71.** A retrospective review of 59 children with sickle-cell disease and osteomyelitis seen over a 10-year period at the University of Nigeria Teaching Hospital, Enugu, has revealed multiple bone involvement in 54% of the patients. Although gram-negative organisms were more commonly isolated than gram-positive ones, *Staphylococcus aureus* was the most common single organism isolated. Initial antibiotic treatment was guided by local experience and was supplemented with blood transfusion and splinting of the affected bones, to avoid pathologic fractures.

Introduction

THE association between salmonella osteomyelitis and sickle-cell disease (SCD) was first suggested in 1925 by Carrington and Davison.[1] Several reports[2–12] then followed this observation and it was generally believed that salmonella was a more common cause of osteomyelitis in patients with SCD than any other organism. Recently however, Vichinsky and Lubin[13] stated that the staphylococcus was more common. In response to this statement, Givner, Luddy and Schnnetz[14] reported 3 patients, reviewed the literature on the subject and concluded that salmonella was clearly, the most common pathogen. Huckstep,[15] reporting from East Africa, observed that salmonella commonly caused osteomyelitis in SCD, but noted its variable incidence in different countries. In a recent review[16] of childhood osteomyelitis in 118 children, 28 of whom had sickle-cell disease, we noted that *Staphylococcus aureus* was the most common organism among patients with SCD as well as those with normal haemoglobin. Prompted by this observation and the controversy over the aetiology of osteomyelitis in SCD, we have reviewed all the cases of osteomyelitis in children with SCD seen at our institution over a 10-year period, with a view to ascertaining the common organisms causing osteomyelitis in our locality.

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Patients and Methods

A review of the medical records of all patients with homozygous sickle-cell disease seen in the paediatric department, University of Nigeria Teaching Hospital (UNTH), Enugu, from January 1974 to December 1983, was made. Diagnosis of sickle-cell disease and osteomyelitis

in each patient, was confirmed by haemoglobin electrophoresis on cellulose acetate paper and radiological examination, respectively. In addition, the duration and nature of presenting symptoms and signs, haemoglobin levels (Hgb), total and differential white blood cell counts (WBC), erythrocyte sedimentation rates (ESR), the bacteriology and the results of treatment, were noted.

Results

The medical records of 593 children with sickle-cell disease (591 with HbSS and 2 with HbSC) seen at either the paediatric outpatient clinics or wards of the UNTH during the 10-year study period, were reviewed. Of these, 59 patients had radiologically proven osteomyelitis. They were aged 8 months to 13 years (mean 4.75 years). Thirty-seven were males and 22 were females, giving a male to female ratio of 1.7:1. The Figure summarises the age and sex distribution of the patients. The highest incidence occurred between the ages of 1 and 2 years while 68% of cases occurred before the age of 5 years. Of the 59 patients, 46 (30 males and 16 females) had acute osteomyelitis while 13 (7 males and 6 females) had the chronic disease. Subsequently, the disease in 5 children (4 males and 1 female) which was initially acute, became chronic.

Symptoms and Signs

The symptoms and signs seen in the 59 patients are summarised in Table I. The duration of symptoms prior to presentation ranged from 3 days to 30 days (mean 7.5 days) in the acute disease and from 3 weeks to 1 year (mean 5.4 months) in the chronic disease. Fever was the most common symptom being present in 44 of 46 acute patients and 8 of 13 chronic patients. Draining sinuses were seen in 9 patients with chronic disease. Eight patients (5 acute and 3 chronic) had antecedent history of trauma involving the extremity that was subsequently involved by the infection.

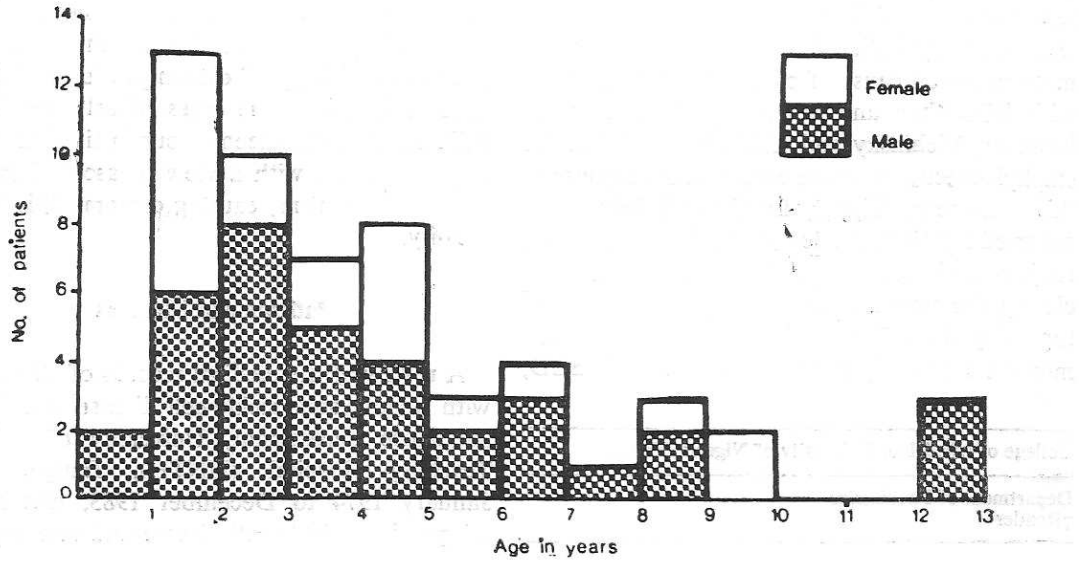

Fig. Age and sex distribution in 59 children with sickle-cell disease and osteomyelitis

TABLE I

Clinical Features in 59 Children with Sickle-cell Disease and Osteomyelitis

Feature	*Acute*	*Chronic*	*Total (%)*
Fever	44	8	52 (88)
Pain and/or irritability	38	8	46 (78)
Swelling	37	8	45 (76)
Tenderness	35	9	44 (75)
Draining sinus	–	9	9 (15)

Sites of involvement

Table II shows the distribution of the sites of involvement. Twenty-seven (46%) of the 59 patients, had single bone involvement while the remaining 32 (54%) patients (24 acute and 8 chronic) had multiple bone involvement. Two bones were involved in 12 patients, 3 bones in 9 patients, 4 bones in 3 patients and 5 or more bones in 8 patients. The long bones were more commonly involved and there was an almost equal involvement of the right and left sides of the body.

Haematology

Results of Hgb, ESR and WBC determinations at the time of presentation were available in 34 patients with acute disease and in 10 patients with chronic disease. Among the acute patients, the Hgb ranged from 3.6g/dl to 11.8g/dl (mean 6.8g/dl); the ESR from 30–145mm/hr (Westergreen method) (mean 68mm/hr) and the total WBC from 5.2 – 30.5 x 10^9/L (5,200 – 30,500/cmm) (mean 14.4. x 10^9/L; 14,400/cmm). These data are summarized in Table III. There was no definite trend in either the Hgb level or the WBC with respect to the two groups, as there was considerable overlap of values. However, the ESR was elevated in all but 2 of the 34 acute patients but in only 2 of 10 chronic patients. With clinical improvement, it became normal in those in whom it was initially elevated.

TABLE II

Bones involved in 69 Sicklers with Osteomyelitis*

Bone	*Right Side*	*Left Side*	*Total*
Upper Limb			
Humerus	14	13	27
Radius	13	9	22
Ulna	5	8	13
Metacarpals	5	2	7
Lower Limb			
Femur	10	10	20
Tibia	8	12	20
Fibula	4	7	11
Metatarsals	5	3	8
Calcaneus	2	1	3
Talus	1	1	2
Others			
Clavicle	1	3	4
Ribs	1	1	2
Total	69	70	139*

* Multiple bones were involved in 32 patients

Bacteriology

Cultures obtained from blood, pus or bone aspirate were recorded in 37 (63%) of the 59 patients; bacterial growth occurred in 24 of these. Cultures in 17 patients grew single organisms while the remaining 7 cultures grew multiple organisms. Table IV shows the frequency of the organisms recovered. In the 7 patients (one acute, 6 chronic) with multiple growths, *Staphylococcus aureus* and *E coli* were grown in 4, *Staphylococcus aureus* and *Klebsiella*, *Staphylococcus aureus* and *Pseudomonas*, and *Staphylococcus aureus* and *Beta-haemolytic streptococcus* were grown in one patient each. *Staphylococcus aureus* was thus, the single most commonly isolated pathogen. Among gram negative organisms, *E coli* was even more common than *Salmonellae* species, which were grown in only 3 of the patients.

TABLE III

Summary of Haematology Data in 59 Sicklers with Osteomyelitis

Group	*No of Cases*	*Mean Haemoglobin (g/dl)*	*Mean ESR (mm/hr)*	*Mean Total WBC (x10⁹/L)**
Acute	34	6.8 (3.6 - 11.8)	68 (12 - 145)	14.4 (5.2 - 30.5)+
Chronic	10	7.8 (5.4 - 10.0)	31 (6 - 130)	11.6 (7.1 - 22·5)

**Conversion*: SI units to Traditional Units
1.0 x 10⁹/L = 1000/cmm
+ Figures in parentheses = ranges

TABLE IV

Causative Organisms in 24 Sicklers† with Osteomyelitis

Organism	*Acute*	*Chronic*	*Total*
Staphylococcus aureus	9	2	11
E coli	7	2	9
Salmonella	3	-	3
Pseudomonas aeruginosa	2	1	3
Proteus	1	1	2
Klebsiella pneumoniae	1	1	2
Beta-haemolytic Streptococcus	1	-	1

+ There were multiple isolates in 7 patients

Treatment and Outcome

Patients were hospitalized initially for periods ranging from 2 weeks to 3 months. Duration of hospitalization was influenced largely by the severity of illness and number of sites involved. Those with multiple-site involvement were hospitalized for longer periods. All patients were treated initially with intravenous antibiotics which included *ampiclox,* cloxacillin, *amoxil,* ampicillin, chloramphenicol, clindamycin and *floxapen* until culture results were available when definitive antibiotic was given. In patients with negative cultures or in whom no culture was available, the initial therapy was continued if the patient showed clinical and radiological improvement; otherwise, another antibiotic was substituted. Where the drug of choice was not available, the next best antibiotic was chosen. Antibiotic therapy was usually continued until the ESR returned to normal in those in whom it was initially elevated.

Many of our patients were anaemic. Only 2 of the 34 acute patients and 2 of 10 chronic patients had a haemoglobin of 10g/dl or more. Consequently, virtually all the patients received blood transfusions as soon as it could be arranged, with those who had very low haemoglobin levels receiving multiple blood transfusions. Plaster of Paris cast for immobilization of the affected limb was applied in 17 patients, sequestrectomy and excision of bone was done in 4 patients while both procedures were carried out in 6 patients.

Pathological fracture of the affected bone was the most common complication in this study, occurring in 11 patients; it involved the femur in 5 patients, the humerus in 4 patients and both bones in 2 patients. Two patients had recurrent disease 2 years after complete healing of the initial sites. One patient was discharged against medical advice, while 5 defaulted from out-patient clinic before complete cure. There were no deaths.

Discussion

From this study, a definite clinical pattern of osteomyelitis in SCD has become apparent. It is a common disease; our 10% incidence agrees with other published reports[6 17] of 10 - 12%. Most of the patients in the present series were young children with 68% being aged 5 years or less, a proportion similar to that reported by other workers.[6 9] It would appear that first attacks of osteomyelitis are rare after the age of 10 years in patients with SCD. There was only a slight male predominance of 1.7:1 among our patients unlike in patients with normal haemoglobin genotype where male to female ratio has been reported to range from 2 to 4:1.[5 9] The reason for this almost equal involvement among the sexes is not clear but may reflect the fact that SCD, being transmitted by a simple autosomal recessive gene, affects both sexes equally and consequently, they have the same predisposing factor(s) to the development of osteomyelitis.

The difficulty in distinguishing patients with osteomyelitis from those with thrombotic or vaso-occlusive crises has been highlighted by some authors.[18 19] In places where adequate diagnostic facilities such as radioactive scanning exist, differentiation can be easier. However, in most developing countries like ours, with large populations of sicklers, such facilities are often not available. One therefore, has to rely on careful clinical examination and the natural history of certain symptoms and signs such as fever, tenderness and swelling, which tend to be more severe and persist longer in patients with osteomyelitis than in those with thrombotic crises.

One of the most distinctive features of osteomyelitis in the patient with SCD is multiple bone involvement. This has been reported previously [4 6 9 20 21] and was confirmed by the present study in which 54% of the patients had multiple bone involvement. Some authors [4 6 21] believed this feature was peculiar to salmonella osteomyelitis but Eng *et al*[9] and Barrett-Connor[20] have suggested that it was more a feature of sickle-cell disease than that of the causative organism. We share this view since only 3 patients in this study had salmonella infections. In fact, the girl with the largest number of involved bones had pseudomonas infection. It is pertinent to note that many of these infections start with one bone and then spread quickly to involve other bones. Early institution of appropriate therapy may therefore, prevent multiple bone involvement. The generally low haemoglobin levels in many sicklers may also be a contributing factor. In our previous report,[16] we noted that 2 of the 3 children with normal haemoglobin genotype, who had multiple bone osteomyelitis, were very anaemic. This underscores our rationale for giving blood transfusion to these patients as soon as possible.

Positive bacterial culture was obtained in 24 of 37 patients. Amongst the remaining 13 that had no growth, 8 had had prior antibiotic treatment. *Staphylococcus aureus* was the most common organism in this study. Among the gram negative organisms, *E coli* was the most common. This contrasts with reports from other countries.[4–11] Even in Nigeria, there is still some controversy over the most common pathogen. While reports from Ibadan [21–23] have shown salmonella to be the most common infecting organism, reports from Enugu [16] and Benin (Scott-Emuakpor, unpublished data) and the present study indicate *Staphylococcus aureus*. We believe however, like Huckstep, [15] that there is an environmental influence on the incidence of salmonella osteomyelitis in sicklers. It is perhaps pertinent to point out that many of the reports on which the conclusion that salmonella is the most common organism has been based, were either case reports [4–11] involving small numbers of patients, or studies of salmonella osteomyelitis [21 22] in children, many of whom were sicklers; none has therefore, been a truly comparative study. Our study is perhaps, the largest series to date, on osteomyelitis in children with SCD. We may therefore, conclude like Nwangemi [24] and Diggs, [25] that salmonella and *Staph aureus* are both common causative

organisms with local factors probably influencing which of the two would predominate in a particular environment. Consequently, initial antibiotic therapy should be guided by local experience; if necessary, definitive antibiotic therapy can then be substituted when culture results become available.

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References

1. Carrington GL and Davison WC. Multiple osteomyelitis due to bacillus paratyphosus B: Demonstration of bacillus in fresh blood preparation. *Bull Johns Hopkins Hospital* 1925; **36:** 428–30.
2. Hodges FJ and Holt JF. Editorial comment. Year Book of Radiology. Hodges FJ and Holt JF, eds. Chicago: Year Book Publishers Inc., 1951: 89.
3. Smith WS. Sickle cell anemia and salmonella osteomyelitis. *Ohio State Med J* 1953; **49:** 692–5.
4. Hughes JG and Carroll DS. Salmonella osteomyeiitis complicating sickle cell disease. *Pediatrics* 1957; **19:** 184–90.
5. Silver HK, Simon JL and Clement DH. Salmonella osteomyelitis and abnormal hemoglobin disease. *Pediatrics* 1957; **20:** 439–47.
6. Hook EW, Campbell CG, Weens HS and Cooper GR. Salmonella osteomyelitis in patients with sickle cell anemia. *N Engl J Med* 1957; **257:** 403–7
7. Torregrosa MV, Dapena RB, Hernandez H and Ortiz A. Association of salmonella-caused osteomyelitis and sickle-cell disease. *JAMA* 1960; **174:** 354–6.
8. Widen AL and Cardon L. Salmonella typhimurium osteomyelitis with sickle cell hemoglobin C disease: A review and case report. *Ann Intern Med* 1961; **54:** 510–21.
9. Eng CA, Hughes JL, Abrams RC and Bowerman JW. Osteomyelitis in the patient with sickle cell disease. *J Bone Jt Surg* 1971; **53A:** 1–15.
10. Nelson JD. Sickle cell disease and bacterial bone and joint infection. *N Engl J Med* 1975; **292:** 534–5.
11. Al-awamy B, Wilson WA, Esmail SM and Abu-nawarig M. Sickle cell hemoglobinopathy and salmonella osteomyelitis in the Eastern provinces of Saudi Arabia. *Trop Geogr Med* 1982; **34:** 51–4.
12. Jenkins T. Osteomyelitis in a child with sickle cell anemia. *Cent Afr J Med* 1962; **8:** 212–6.
13. Vichinsky EP and Lubin BH. Sickle cell anemia and related hemoglobinopathies. *Pediat Clin North Am* 1980; **27:** 429–47.
14. Givner LB, Luddy RE and Schnnetz AD. Etiology of osteomyelitis in patients with major sickle hemoglobinopathies. *J Pediat* 1981; **99:** 411–3.
15. Huckstep RL. Bone changes in sickle cell disease. *J Bone Jt Surg* 1970; **52B:** 396.
16. Okoroma EO and Agbo DC. Childhood osteomyelitis-A 5-year analysis of 118 cases in Nigerian children. *Clin Pediat* 1984; **23:** 548–52.
17. Kaine WN. Morbidity of homozygous sickle cell anemia in Nigerian children. *J Trop Pediat* 1983; **29:** 104–11.
18. Wethers DL and Grover R. Pitfalls in diagnosis of osteomyelitis in children with sickle cell disease. *Clin Pediat* 1983; **22:** 614–8.
19. Worrall VT and Butera V. Sickle cell dactylitis. *J Bone Jt Surg* 1976; **58A:** 1161–3.
20. Barrett-Connor E. Bacterial infection and sickle cell anemia. *Medicine* 1971; **50:** 97–112.
21. Hendrickse RG and Collard P. Salmonella osteitis in Nigerian children. *Lancet* 1960; **1:** 80–2.
22. Adeyokunnu AA and Hendrickse RG. Salmonella osteomyelitis in childhood. *Arch Dis Child* 1980; **55:** 175–84.
23. Tindimwebwa G, Adeyokunnu AA and Effiong CE. Acute haematogenous osteomyelitis in childhood. *Nig J Pediat* 1983; **10:** 93–7.
24. Nwangemi PM. Pattern of the complications of sickle cell anemia at Kenyatta National Hospital. *E Afr Med J* 1979; **56:** 151–7.
25. Diggs LW. Anatomic lesions in sickle cell disease. In: Sickle cell disease: diagnosis, management, education and research. Abramson H, Berthes JF and Wethers DL, eds. St Louis: CV Mosby Company, 1973: 184–229.

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