International Orthopaedics (SICOT) (1992) 16: 398–402

International
Orthopaedics

Osteomyelitis and septic arthritis in sickle cell disease in the eastern province of Saudi Arabia

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Summary. *Patients with sickle cell disease are more susceptible to osteomyelitis and septic arthritis than the population at large. Seventy eight patients with these conditions were admitted to our hospital from April 1988 to March 1991. Thirty had sickle cell disease, 14 had the sickle cell trait and 34 had normal electrophoresis. The tibia, followed by the femur and humerus were the bones most commonly affected, and the knee was the joint most often involved. Salmonella was the commonest organism in osteomyelitis and septic arthritis in sickle cell disease, whereas staphylococcus was commonest in normal patients and those with the sickle cell trait. Antibiotics that cover these two organisms must be considered in patients with sickle cell disease who are suspected of having osteomyelitis or septic arthritis.*

Résumé. *Les malades atteints de drépanocytose sont plus exposés aux ostéomyélites et aux arthrites septiques que les sujets normaux. En trois ans, d'Avril 1988 à Mars 1991, 78 malades ont été admis à l'hôpital central de Qatif pour ostéomyélite et/ou arthrite septique. Ils présentaient 66 localisations osseuses et 38 articulaires. Trente malades avaient une drépanocytose homozygote, quatorze une hémoglobinose hétérozygote et les autres une électrophorèse normale de l'hémoglobine. Chez les trente malades drépanocytaires, il y avait 32 localisations osseuses et 16 atteintes articulaires. Le tibia était la localisation la plus fréquente (43.9%) suivi par le fémur (21.2%) et par l'humérus (18.2%). Le genou était l'articulation la plus souvent atteinte par l'arthrite septique (58.8%). Les salmonelles étaient les bactéries les plus fréquemment en cause chez les malades drépanocytaires (homozygotes), tandis que les staphylocoques dorés étaient plus communément retrouvés chez les malades hétérozygotes et chez les sujets normaux. Les antibiotiques efficaces à la fois vis-à-vis des salmonelles et des staphylocoques dorés doivent être utilisés chez les malades atteints de drépanocytose ou d'hémoglobinose hétérozygote chaque fois qu'existe une suspicion d'ostéomyélite et/ou d'arthrite septique.*

Introduction

Patients with sickle cell disease are known to have a greater susceptibility to severe bacterial infections than the population at large [4, 14, 15]. Among these infections are osteomyelitis and septic arthritis. In general, the commonest infecting organism in these conditions is staphylococcus aureus, but when osteomyelitis occurs in patients with sickle cell disease salmonella is more common [1, 4, 8, 12, 21]. This has been reported from different parts of the world, but two recent papers from the Eastern province of Saudi Arabia have reported otherwise [17, 18].

The present study describes the pattern of bacterial infections in our patients with osteomyelitis and septic arthritis who also have sickle cell disease.

Patients and method

A retrospective review has been carried out of all patients with a diagnosis of osteomyelitis and septic arthritis, or both, who were admitted to our hospital between April 1988 and March 1991. The records were examined for the age at onset, sex, site of involvement, type of infection, haemoglobin electrophoresis and the causative organism.

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Table 1. Numbers of Osteomyelitis and Septic Arthritis in relation to each category of patients according to the haemoglobin electrophoresis

Patient's category	Total No. of patients	No. of osteomyelitis attacks	No. of septic arthritis attacks	Total no. of attacks
HbSS	30	32	16	48
HbAS	14	10	8	18
HbAA	34	24	14	38
Total	78	66	38	104

Table 2. Anatomical sites of osteomyelitis and septic arthritis in 30 patients with sickle cell disease

Osteomyelitis (32 attacks)	No.	Septic arthritis (16 attacks)	No.
Tibia	14	Knee	7
Humerus	9	Hip	4
Femur	6	Shoulder	2
Sternum	1	Elbow	2
Radius	1	Sternoclavicular joint	1
Metacarpal	1		

The diagnosis of sickle cell disease was made on the basis of a positive sickling test and haemoglobin electrophoresis using the Super Z Electrophoresis kit (Helena Laboratories). Sickle cell trait occurs in heterozygotes in which the sickle cell gene is inherited from one parent, is usually asymptomatic and is considered to be benign, although it may become symptomatic under extreme anoxic conditions.

Blood cultures were performed on patients with suspected osteomyelitis or septic arthritis after removing 10 ml of blood in adults or 3 ml in children. The specimen was divided; NR6A was used for aerobic and NR7A for anaerobic culture. Both bottles were incubated for 7 days at 37°C and read daily on Bactec NR660 (Becton Dickinson). Subcultures were made on blood agar, chocolate agar and MacConkey's agar incubated anaerobically for 48 h. Aspirate or pus swabs were cultured on chocolate and MacConkey's agar incubated aerobically and on blood agar anaerobically. Micro-organisms were identified by standard techniques [7] and sensitivity by the Stokes comparative method [20].

Results

During the 3 year period, 78 patients with osteomyelitis or septic arthritis were admitted. They had suffered 66 attacks of osteomyelitis and 38 of septic arthritis. Five patients had both conditions, 3 had osteomyelitis affecting 2 bones and 2 had septic arthritis of 2 joints each. Two patients had infection in multiple sites. Of these 78 patients, 30 had sickle cell disease (HbSS), 14 had the sickle cell trait (HbAS) and 34 had normal haemoglobin electrophoresis (Table 1).

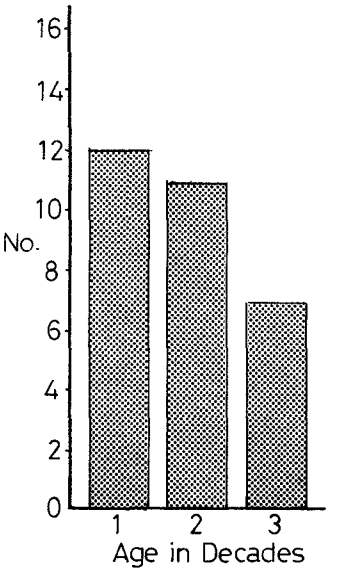

Fig. 1. The number of patients with sickle cell disease in different age groups

The 30 patients with sickle cell disease were analysed separately and comparative analysis was made of the other 2 groups. Of the 30, 18 were male and 12 female (M/F: 1.5/1). They were aged from 1 to 29 years (mean 13.4 years), and most were under 20 years (Fig. 1). Haemoglobin electrophoresis revealed HbS of 61 to 95 (mean 78.76) and HbF 5 to 35 (mean 20). These patients had had 32 attacks of osteomyelitis and 16 of septic arthritis. Two patients had both conditions, 2 had septic arthritis affecting 2 joints, and in 2 patients 2 bones were affected at the same time. In 2 multiple sites were involved including the right femur, right tibia, right humerus, both knees, right hip and right shoulder in one, and in the other the left femur, right femur, left tibia, both knees and the left hip (Fig. 2). The sites of osteomyelitis and septic arthritis are shown in Table 2.

In 32 attacks of osteomyelitis, salmonella was the causative organism in 21 (63%), staphylococcus aureus in 6 (19%), haemophilus influenzae in 1 and there was no growth in 4. In 16 attacks of septic arthritis, salmonella was responsible in 7 (44%) and staphylococcus aureus in 4 (25%) (Fig. 3).

Discussion

The sickle cell gene is prevalent in the Eastern province of Saudi Arabia and is characterised by a higher level of both total and foetal haemoglobin [16]. The disease has been reported to have a wide spectrum of clinical severity, but the clinical course is usually more benign than in other countries [16]. This has been attributed to the high levels of haemoglobin F and the frequently associated thalassaemia [3, 16]. Nevertheless, sickle cell disease in

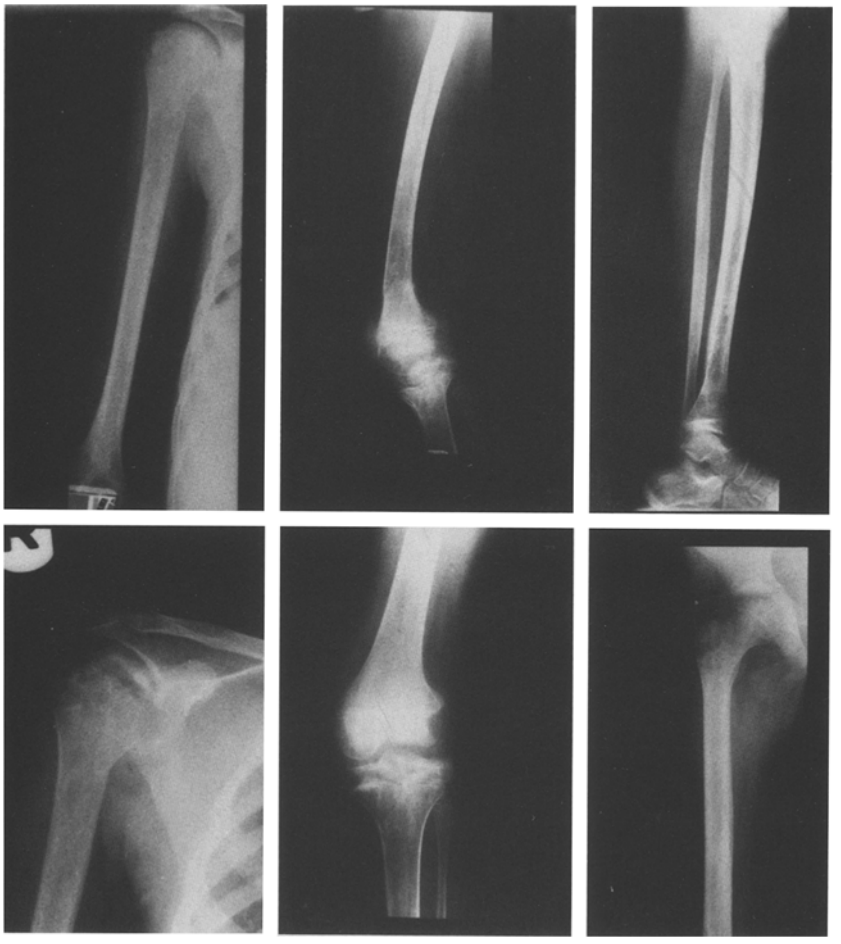

Fig. 2. Radiographs of a patient with sickle disease who had osteomyelitis and septic arthritis affecting multiple sites, including the right humerus, right femur and right knee, right tibia, right shoulder, left knee and right hip

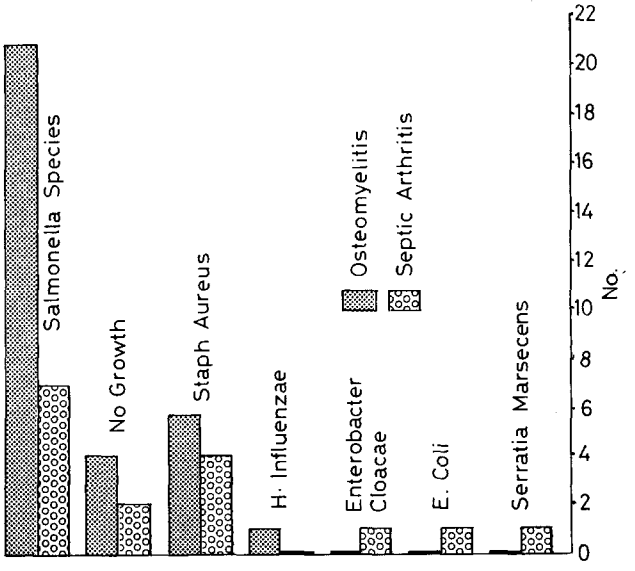

Fig. 3. Incidence of infecting organisms in patients with sickle cell disease

the Eastern province is associated with serious morbidity [18].

Bone and joint complications are among the most common sequelae and 80% of the patients suffer from such complications which can produce serious disability. The commonest organism causing osteomyelitis and septic arthritis is in general the staphylococcus aureus, but in patients with sickle cell disease salmonella has been reported frequently [1, 4, 8, 12, 21]. This was first recorded in 1925 [5], but the association between the two diseases was not recognised until 1951 [10]. Since then, reports from different parts of the world have confirmed this association, including an earlier paper from the Eastern province of Saudi Arabia [2]. On the other hand, the staphylococcus aureus was found to be the commonest causative organism in sickle cell haemoglobinopathy with osteomyelitis and septic arthritis in two reports from this province [17, 18]. Contrary to this, we have found that salmonella is more common in both complications; the reason for this difference is not known. Patients with sickle cell trait (HbAS) do not have more risk of salmonella osteomyelitis

Table 3. Causative organisms of osteomyelitis

Type of organism	Normal patients (HbAA) (24 attacks)[a]	Sickle cell patients (HbSS) (32 attacks)	Sickle cell trait (HbAS) (10 attacks)
No Growth	3	4	2
Salmonella	–	21	–
Staph Aureus	19	6	6
H. Influenza	–	1	–
B-hemolytic streptococci	4	–	–
Pseudomonas	1	–	1
Proteus mirabilis	3	–	1
E. Coli	1	–	–
Providencia staurtii	1	–	–
Staph Epidermidis	–	–	1
Anaerobic streptococci	–	–	–

[a] In 5 patients more than one organism were isolated from pus culture and sensitivity

Table 4. Causative organisms of septic arthritis

Causative organism	Normal patients (HbAA) (14 attacks)	Sickle cell patients (HbSS) (16 attacks)	Sickle cell trait (HbAS) (8 attacks)
No Growth	4	2	1
Salmonella	–	7	–
Staph Aureus	9	4	5
E. Coli	–	1	–
Enterobacter cloacae	–	1	–
Brucella	1	–	–
Klebsiella	–	–	2
Serratia	–	1	–

Table 5. Sensitivity pattern of salmonella isolated from sickle cell disease patients with osteomyelitis and/or septic arthritis at our hospital

Antibiotic	Ampi-cillin	Chlor-amphenicol	Cotrimox-azone	Ceftri-axone	Cefer-oxime	Genta-mycin	Ceftiz-oxime	Norflox-ocin
Salmonella sensitivity (%)	24	100	80	100	85	100	100	89

than normal individuals. Fourteen of our patients with the sickle cell trait suffered 10 attacks of osteomyelitis and 8 of septic arthritis in which staphylococcus aureus was the commonest organism, which is similar to patients with normal haemoglobin electrophoresis (Tables 3 and 4).

The reason for the high susceptibility of patients with sickle cell disease to salmonella is not known, but several factors have been incriminated, including hyposplenism and a defective complement system which hinders phagocytosis of salmonella [9, 13, 19]. Impaired function of macrophages as a result of phagocytosis of the breakdown products of red blood cells reduces the capacity of these cells to ingest and kill salmonella [11].

In order to prevent the crippling sequelae of osteomyelitis and septic arthritis, early and intensive treatment is essential; antibiotics must be started without waiting for the result of cultures, which can sometimes be negative. Our results indicate the need for antibiotics effective against both salmonella and staphylococcus aureus, and not just against the staphylococcus as has been suggested by others [17]. A combination of anti-staphylococcal penicillin with chloramphenicol or a third generation cephalosporin, such as ceftriaxone or ceftizoxime, should be given initially and continued until the microbiological results are available (Table 5).

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