BONE AND JOINT MANIFESTATIONS OF
SICKLE CELL ANAEMIA

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We investigated 57 patients with sickle cell anaemia (HbSS) and bone and joint changes. Osteonecrosis simulating a wide range of conditions was a common radiological feature, and osteomyelitis occurred in 61% of cases. Salmonella species were the commonest causative organisms, occurring in 71% of patients with osteomyelitis, although salmonella septic arthritis occurred in only two. The distinction between vaso-occlusive bone crisis and acute osteomyelitis was often difficult since the classical clinical and radiological features and laboratory findings also occurred in bone infarction, a common feature of the disease.

Sickle cell disease has been described in black and non-black people (Perrine and John 1974; Perrine et al 1978). The phenotypic frequency for the S-gene is 8 to 30% in black Americans, 10 to 45% in some black African populations and 5 to 30% in Greece, Turkey, the Mediterranean, and parts of India and South-East Asia.

The microvascular circulation of the bones is a common site for sickled cells to harbour, leading to thrombosis, infarction, and necrosis of the bone (Sherman 1959); but large-vessel obliteration can also occur (Stockman et al 1972). Bacteria commonly colonise infarcted bone following an episode of bacteraemia (Adeyokunnu and Hendrickse 1980). Patients with sickle cell anaemia have a high susceptibility to salmonella osteomyelitis (Borrett-Connor 1971; Engh et al 1971; Adeyokunnu and Hendrickse 1980). Whereas primary osteomyelitis is usually due to Staphylococcus aureus in patients with normal haemoglobin (75%) (Diggs 1967), it generally results from salmonella in sickle cell patients (70%) (Golding, Maclver and Went 1959; de Torregrosa et al 1960). The high risk of salmonella osteomyelitis in sickle cell anaemia is probably attributable to a defect in the alternative complement pathway, resulting in defective phagocytosis of the bacteria (Winkelstein and Drachman 1968; Constantopoulos et al 1973).

PATIENTS AND METHODS

We investigated 32 male and 25 female patients (mean age 15.7 years, range 10 months to 46 years) with sickle cell anaemia and bone and joint involvement. Patients were recruited mainly from referrals, either for severe bone and joint pain or for suspected osteo-articular infection.

Table 1. Clinical details in 57 patients with sickle cell anaemia

<table>
<thead>
<tr>
<th>Initial findings</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temperature &lt; 37°C</td>
<td>47</td>
</tr>
<tr>
<td>Jaundice</td>
<td>5</td>
</tr>
<tr>
<td>Splenomegaly</td>
<td>19</td>
</tr>
<tr>
<td>Cellulitis</td>
<td>7</td>
</tr>
<tr>
<td>Bone and joint pain</td>
<td>46</td>
</tr>
<tr>
<td>Deep soft tissue abscess</td>
<td>8</td>
</tr>
<tr>
<td>Flexion adduction contracture of the hip</td>
<td>3</td>
</tr>
<tr>
<td>Skin ulceration</td>
<td>2</td>
</tr>
<tr>
<td>Septic arthritis</td>
<td>4</td>
</tr>
<tr>
<td>Osteomyelitis</td>
<td>35</td>
</tr>
<tr>
<td>Joint effusion</td>
<td>8</td>
</tr>
<tr>
<td>Haemarthrosis</td>
<td>2</td>
</tr>
</tbody>
</table>

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The initial patient evaluation included a complete blood count, erythrocyte sedimentation rate (ESR), biochemical profile, urinalysis, antistreptolysin 0 titre, Widal test, and sickling test (2% sodium metabisulfate) confirmed by cellulose acetate electrophoresis (Helena. fluid was given to prevent dehydration and acidosis. In cases of suspected bone or joint infection chloramphenicol was used routinely while bacteriological culture and sensitivity tests were being done. All patients with confirmed salmonella bone infection had chloramphenicol treatment for a total of eight weeks. Surgery was done only to obtain material for bacteriological examination, for drainage of abscesses, sequestrectomy, and for treatment of late complications such as osteo-arthritis of the large joints.

RESULTS

Laboratory tests. Table I shows the clinical details of the patients. The mean haemoglobin level was 9.1 g/dl (range 5.9 to 12.5) with normochromic normocytic pictures. The mean white cell count was 15 200/μl (range 8 000 to 24 000). Blood films showed sickle cells in 37 patients. Target and nucleated red cells were seen in all patients.

Positive cultures were obtained in 35 patients: blood cultures were positive in 18 of 38 patients and cultures from joint fluid, abscesses, and biopsy material were positive in 23. At the onset of bone infection 28 (80%) of 35 patients were aged 10 years or younger. The infection in 25 (71%) was due to salmonella species (non-typhi salmonella in 22 and S. typhi in three), and in 10 (29%) to Staphylococcus aureus.

A total of 14 patients had joint fluid aspiration: 12 from the knee joint and two from the elbow joint. In eight patients (57%), the joint fluid was clear with an average leucocyte count of 750/μl (range 500 to 950) and a low polymorphonuclear leucocyte count. Two patients (14%) had haemarthrosis. In the remaining four patients, the joint fluid was cloudy with a mean leucocyte count of 38 000/μl (range 26 500 to 62 000), and polymorphonuclear cells averaged 93% (range 87% to 96%). Salmonella species were cultured in two of these patients and Staphylococcus aureus in the other two.

Radiographic findings. Osteonecrosis was noted in 42 (74%) patients. The metaphysis was affected in 28 (49%) patients, most commonly the proximal and distal femoral metaphysis and the metaphysis of the proximal tibia, in all age groups. Extensive infarction in the cortical wall of the diaphysis as well as the metaphysis was seen in 13 (23%) patients, 10 of whom were aged under 10 years. The cortex of the tubular bone was thickened and sclerosed, with new bone formation within the medullary canal, resulting in narrowing. The periosteum was raised in all these 13 patients (Fig. 1).

A total of 29 patients had radiological changes in the epiphyseal ossification centres of the long bones, suggestive of avascular necrosis, and often more than one bone site was affected. Table II shows the distribution of the epiphyseal lesions in these 29 patients. Necrosis of the capital epiphysis of the femur occurred bilaterally in 21 (27%) patients, (aged 11 to 42 years). The changes ranged from patchy necrosis, with preservation of the
congruity of the joint to complete fragmentation, collapse, flattening, and destruction of the hip joint (Fig. 2). In six of these patients, the changes were indistinguishable from coxa plana.

The acetabulum showed avascular changes in 15 hips, four of which showed widening and upward migration of the acetabulum simulating tuberculosis; subluxation of the hip occurred in these cases. Three patients aged 13, 14 and 17 years, respectively, had an associated flexion-adduction contracture of the hip. Avascular changes simulating osteochondritis dissecans were noted in the medial femoral condyle in two patients.

The epiphyseal ossification centre of the proximal humerus was the site of avascular necrosis in eight (14%) patients: all were children aged seven to 15 years. The necrosis affected the medial segment of the epiphysis: it was bilateral in seven patients and unilateral in one (Fig. 3). One patient, aged four years, had progressive cupping of the distal end of the tibia and avascular necrosis with partial collapse of the adjacent talus (Fig. 4). Necrosis of the tarsal navicular bone resembling Kühler’s disease occurred in two patients aged seven and 10 years respectively (Fig. 5).

Osteoporotic changes with corresponding widening of the intervertebral disc space, affecting mainly the thoracic and lumbar vertebral bodies, were noted in five patients aged nine to 27 years: all had coarse vertical trabeculation and deep central cup-like indentations (Fig. 6a). In one child aged nine years osteonecrosis and collapse of D10 vertebral body occurred (Fig. 6b).

**Outcome of treatment.** Of the 25 patients with salmonella osteomyelitis 24 had healed following an eight-week course of chloramphenicol. One patient, a boy aged 16 years, continued to have persistent infection which healed five months after saucerisation of the bone. Four patients had pronounced reticulocyte depression while on chloramphenicol and had to be transfused. All 10

![Fig. 2](image)

Bilateral avascular necrosis of the capital epiphysis of the femur in a 12-year-old girl, with the left hip resembling coxa plana.

![Fig. 3](image)

Lesions of sickle cell anaemia in the epiphyseal ossification centre of the head of the humerus. Figure 3a - Early segmental sclerosis and destruction in a seven-year-old child. Figure 3b - Destruction and resorption of the medial half of the epiphysis in a nine-year-old boy.

![Fig. 4](image)

Cupping of the distal end of the shaft of the tibia with destruction of the talus in a child aged six years nine months. Note extensive necrosis and sclerosis of the distal tibial shaft with pronounced cupping of the distal end, and the extensive necrosis and partial collapse of the talus. No organism was cultured.
patients with staphylococcal osteomyelitis healed following three months on cloxacillin.

Table III gives the details of patients who had hip operations. A substantial increase in the range of hip movement was achieved in the three patients in whom soft tissue release of the hip was done for flexion-adduction contracture of the hip, although the radiological appearance of the femoral head and the frequency and severity of joint pain was not improved. Three patients (aged 11, 12 and 14 years) who had proximal femoral osteotomy for subluxation of the hip had satisfactory pain relief although deterioration of the hip

Table II. Distribution of epiphyseal lesions in 29 patients

<table>
<thead>
<tr>
<th>Number of patients*</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capital epiphysis of the hip</td>
<td>9</td>
<td>12</td>
<td>21</td>
</tr>
<tr>
<td>Distal femoral epiphysis</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Distal tibial epiphysis</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Capital epiphysis of the humerus</td>
<td>5</td>
<td>3</td>
<td>8</td>
</tr>
</tbody>
</table>

* each patient may have lesions in more than one site

Table III. Ten patients having hip operations

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age at operation (yr)</th>
<th>Hip</th>
<th>Operation</th>
<th>Follow-up (yr + mth)</th>
<th>Harris hip score</th>
<th>Final outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>17</td>
<td>L</td>
<td>Tenotomy</td>
<td>4 + 7</td>
<td>72</td>
<td>Good</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>13</td>
<td>L</td>
<td>Tenotomy</td>
<td>3</td>
<td>67</td>
<td>Fair</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>14</td>
<td>R</td>
<td>Tenotomy</td>
<td>2 + 9</td>
<td>70</td>
<td>Good</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>11</td>
<td>L</td>
<td>Proximal femoral osteotomy</td>
<td>4</td>
<td>79</td>
<td>Good</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>14</td>
<td>R</td>
<td>Proximal femoral osteotomy</td>
<td>3 + 6</td>
<td>68</td>
<td>Fair</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>12</td>
<td>L</td>
<td>Proximal femoral osteotomy</td>
<td>5</td>
<td>76</td>
<td>Good</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>29</td>
<td>L</td>
<td>THR*</td>
<td>4 + 2</td>
<td>90</td>
<td>Excellent</td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>37</td>
<td>R</td>
<td>THR*</td>
<td>5 + 4</td>
<td>87</td>
<td>Good</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>42</td>
<td>R</td>
<td>THR*</td>
<td>4 + 5</td>
<td>72</td>
<td>Good</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>L</td>
<td>THR*</td>
<td>4 + 11</td>
<td>81</td>
<td>Good</td>
</tr>
<tr>
<td>10</td>
<td>M</td>
<td>27</td>
<td>R</td>
<td>THR*</td>
<td>3</td>
<td>88</td>
<td>Good</td>
</tr>
</tbody>
</table>

* total hip replacement using Autophor 900 prosthesis

Radiographs of an eight-year-old boy who presented with pain in both feet and difficulty in walking. On the right, necrosis of the navicular and the first and third cuneiform bones is seen, and on the left, avascular necrosis of the navicular, and the second and third cuneiform bones.

Lateral radiographs of the thoracolumbar spine of a 19-year-old youth with recurrent back pain, showing generalised demineralisation and the typical fish-shaped vertebral bodies (6a); and of the thoracic spine in a nine-year-old boy, showing necrosis, collapse and resorption of D10 vertebral body (6b).
was seen radiologically in two. Five hip replacements were done in four patients. Excellent pain relief, and improvement in range of hip movement, gait and walking were obtained in all five hips giving good or excellent Harris hip scores. In the patient who had bilateral hip replacements, follow-up radiographs at four years five months revealed early bone resorption in the proximal end of the right femur without migration of the femoral component. One patient who had a total hip replacement had a postoperative haematological crisis, requiring two and a half litres of blood.

DISCUSSION

In our series osteonecrosis was common; necrosis of the tarsal bones has not been described previously. Shaub et al (1975) reported 'tibialalar slant', and attributed this to retarded growth in the lateral segment of the tibial epiphyseal cartilage, possibly because of occlusion of the arterioles supplying the lateral segment of the proliferative cartilage. We have not seen this lesion in our patients, although one patient had cupping of the distal tibial articular surface, due to necrosis of the central portion of the epiphysis and early fusion with the shaft (see Fig. 4). One patient had thickening of the skull vault but we did not see the 'sun ray' appearance described by others (Reynolds 1966; Diggis 1967).

We saw necrosis and collapse of the vertebral body with dorsal kyphosis in only one patient. To our knowledge necrosis of a vertebral body has previously been recorded only in adults (Legant and Ball 1948). The most common spinal lesions were coarse vertical trabeculation and characteristic deep central cup-like indentation, as reported by Reynolds (1966) and Langundoye (1970).

It is noteworthy that salmonella species was cultured in a child who presented with bilateral hand and foot swelling and tenderness: most other workers suggest that this condition is caused by aseptic infarction of the marrow, cortical bone, periosteum and peri-articular tissues (Haggard and Schneider 1961; Watson et al 1963; Pearson and Diamond 1971).

In vaso-occlusive crises, treatment by anti-inflammatory analgesics, oxygen, and intravenous fluid proved to be effective. Blood transfusion was needed only when the haemoglobin fell below 6.5 g/dl, and should be used with caution, because of the risk of iron overload and haemochromatosis (Forget 1985).

In our series, osteomyelitis was most frequent in the younger age group, confirming earlier work (Smith 1953; Saphra and Winter 1957; Hendrickse and Collard 1960; Adeyokunnu and Hendrickse 1980). The finding of only two patients with salmonella septic arthritis confirms the rarity of this condition in sickle cell anaemia (Black, Kunz and Swartz 1960; Engh et al 1971; Dich, Nelson and Haltanin 1975; Givner, Luddy and Schwartz 1981; Molyneux and French 1982).

Sickle cell osteomyelitis can be differentiated from vaso-occlusion by the presence of positive cultures or multiple, often symmetrical, bone involvement, a florid involucrum, and longitudinal fissuring of the cortex (Engh et al 1971). Patients presenting with pyrexia, bone and joint pain, leucocytosis, and radiological bone lesions should be treated immediately with antibiotics after specimens for bacteriology have been obtained.

Because of widespread bone infection major surgery for osteomyelitis was not indicated. For septic arthritis, early diagnosis, decompression of the joint by arthroplasty, and antibiotics proved to be effective. Joint damage resulting from severe avascular necrosis may lead to haemarthrosis, but this is uncommon in sickle cell anaemia (our findings, Patel (1973) and Alavi et al (1976)). Joint effusion, which is non-inflammatory and rare in the absence of crisis (Schumacher, Andrew and McLaughlin 1973), occurred only during vaso-occlusive crises and subsided within 14 days on rest and analgesics.

Treatment of the early stages of avascular necrosis of lower limb joints includes a regime of non-weight-bearing. Proximal femoral osteotomy with or without soft tissue release is indicated if the femoral head is subluxed with or without coxa plana. Pain was relieved in all three patients so treated but progression of avascular changes occurred in two. In later stages of avascular necrosis of the femoral head total hip replacement should be done if there is severe and persistent pain (Eppe and Castro 1978; Hanker and Amstutz 1988).

Prophylactic cloxacillin (Hanker and Amstutz 1988) has been successful in replacement operations, but a postoperative haematological crisis requiring transfusion was recorded in one of our patients. Hip replacement arthroplasty in sickle cell anaemia may be complicated by infection, loosening of prostheses, and fractures at the level of the femoral stem (Eppe and Castro 1978; Bishop et al 1988; Hanger and Amstutz 1988), and hence careful pre-operative assessment is necessary. In our patients with necrosis of the humeral head surgical treatment was not necessary, but Chung, Alavi and Russell (1978) have reported good early results with shoulder replacement.

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