Between 1990 and 1998 we saw 21 children with primary subacute haematogenous osteomyelitis. Pain, swelling and a limp had been present for two to 12 weeks with little functional impairment. Laboratory tests were non-contributory. The lesions were classified radiologically into metaphyseal, diaphyseal, epiphyseal and vertebral. There were 24 sites involved, with most (20) being in the tibia; 17 lesions were in the diaphysis, five in the metaphysis and two in the epiphysis. The diagnosis was confirmed histologically in all cases. *Staphylococcus aureus* was cultured in six patients. Healing occurred in all patients after treatment with antibiotics for six weeks and radiological improvement was seen after three to six months.

Subacute osteomyelitis develops as a result of increased host resistance and decreased bacterial virulence. The radiological features can mimic various benign or malignant bone tumours and non-pyogenic infections. Histological confirmation is necessary to avoid a delay in diagnosis.

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Primary subacute haematogenous osteomyelitis may be difficult to diagnose because the characteristic signs and symptoms of the acute form of the disease are absent. It has an insidious onset, lacks a systemic reaction and may mimic various benign and malignant conditions, resulting in delay in diagnosis and treatment. The condition has assumed importance in recent years and is becoming more common in the UK. Although osteomyelitis is frequent in Northern Nigeria and East Africa, it is only occasionally seen in the acute form.

The primary form of subacute haematogenous osteomyelitis, which occurs mainly in children, must be distinguished from subacute osteomyelitis which has been modified by inadequate or partial treatment with antibiotics, and from other forms of the condition such as chronic recurrent multifocal osteomyelitis and the SAPHO syndrome (synovitis, acne, pustulosis, hyperostosis and osteitis). In previous reports either the primary form has not been distinguished from that modified by antibiotics or both adults and children have been included.

King and Mayo described the disease as following an indolent course because of host resistance combined with low virulence of the infecting organism. Gledhill described four radiological types in long bones. Roberts et al expanded and modified the classification into six forms to include the spine, the lesions being classified as metaphyseal, diaphyseal, epiphyseal and vertebral. Their classification is based on anatomical location, morphology and the similarity of the lesions to various neoplasms.

The diaphyseal forms of subacute osteomyelitis in children have received less attention in the literature; six cases have been described in South Africa. Most other reports include mainly adult patients. The aim of this paper is to describe the spectrum of primary subacute haematogenous forms of osteomyelitis seen in children, and the difficulties in making the diagnosis. The high incidence of diaphyseal lesions and the importance of obtaining a histological diagnosis are highlighted.

**Patients and Methods**

The hospital records and radiographs of 21 children with primary subacute haematogenous osteomyelitis seen at the King Edward VIII Hospital, Durban between 1990 and 1998, were reviewed. These formed 7% of all cases of osteomyelitis treated in this period. Patients with chronic illness or immune deficiencies and those who had had previous antibiotic therapy or acute osteomyelitis were excluded. The criteria for the subacute course as previously described included symptoms which had been present for more than two weeks, mild to moderate pain of insidious onset with intermittent symptoms and little or no functional impairment, no systemic manifestations, negative blood cultures and positive findings on plain radiographs.

There were 15 boys and six girls with a mean age of 7.5 years (2 to 12). The length of symptoms ranged from two weeks to three months. Pain was the main complaint,
usually a mild ache which did not interfere with sleep. Six children remembered an episode of minor trauma. All the patients were afebrile.

The lesions were classified using the system of Roberts et al (Table I). Technetium bone scintigraphy, MRI and CT were also carried out. All patients underwent surgical exploration and biopsy. At operation, granulation tissue and a little pus were obtained from the metaphyseal lesions and small amounts of granulation tissue from those in the epiphysis. The latter were approached extra-articularly under fluoroscopy with a fine drill and a curette. Metaphyseal lesions were also curetted. Specimens of bone and granulation tissue were sent for microscopic investigations including those for tuberculosis and fungi and also for histological examination.

All the affected limbs were immobilised for four to six weeks after biopsy to allow healing and to avoid pathological fractures. Intravenous cloxacillin was given for four or five days followed by oral treatment for six weeks. All patients were assessed clinically and radiologically at intervals of about six weeks. The mean follow-up was for 2.4 years (six months to four years).

Results

Physical examination revealed minor local soft-tissue swelling in 14 patients with some tenderness. The range of movement of the adjacent joint in epiphyseal and metaphyseal lesions was normal. Twelve patients had a slight limp. Laboratory investigations revealed a haemoglobin level of 10.5 to 13.1 g%, and a white cell count of 6.3 to 12.9 ± 10^9/L with a normal differential count. The ESR ranged from 9 to 49 mm/hr (Westergren).

The symptoms resolved within three to four weeks after treatment had commenced. Leg length and angular deformity were assessed clinically and radiologically. Clinical examination showed no leg-length discrepancy and there was no radiographic evidence of growth disturbance. There were 24 lesions in 21 patients. The sites were in the tibia (20), femur (three) and ulna (one) (Table I). All patients had unifocal lesions except one in whom both tibiae and the ulna were involved (see Fig. 5). There were two type-Ib lesions (Fig. 1), three type-II (Fig. 2), three type-III (Figs 3 and 4), 14 type-IV (Fig. 5) and two type-V (Figs 6 and 8). There were no type-Ia or type-VI lesions in this group. Metaphyseal lesions did not show radiological extension into the epiphysis and those in the epiphysis did not penetrate the articular surface or extend into the metaphysis. There were no pathological fractures.

Table I. Characteristics of primary subacute haematogenous osteomyelitis in 21 patients

<table>
<thead>
<tr>
<th>Type</th>
<th>Classification (Roberts et al)</th>
<th>Differential diagnosis</th>
<th>Number of cases</th>
<th>Sites</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Metaphyseal (no cortical erosion)</td>
<td>(a) Solitary localised punched-out zone of radiolucency</td>
<td>Eosinophil granuloma</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(b) Localised radiolucent zone with sclerotic margin (Brodie's abscess)</td>
<td>Osteoid osteoma</td>
<td>2</td>
</tr>
<tr>
<td>II</td>
<td>Metaphyseal (cortical erosion)</td>
<td>Large radiolucent zone</td>
<td>Osteosarcoma</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Eosinophilic granuloma</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Tuberculosis</td>
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<td></td>
<td></td>
<td></td>
<td>Fungal infection</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>Diaphyseal (cortical)</td>
<td>Localised cortical and periosteal reaction</td>
<td>Osteoid osteoma</td>
<td>3</td>
</tr>
<tr>
<td>IV</td>
<td>Diaphyseal (periosteal)</td>
<td>Periosteal reaction</td>
<td>Ewing's sarcoma</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Linear (single) or laminated (multiple)</td>
<td>Round-cell tumours</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Leukaemia</td>
<td></td>
</tr>
<tr>
<td>V</td>
<td>Epiphyseal</td>
<td>Radiolucent defect in epiphysis with fine sclerotic margin</td>
<td>Chondroblastoma</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Tuberculosis</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Osteosarcoma</td>
<td></td>
</tr>
<tr>
<td>VI</td>
<td>Vertebral</td>
<td>Destructive process involving vertebral body</td>
<td>Tuberculosis</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Fungal infection</td>
<td></td>
</tr>
</tbody>
</table>

Fig. 1
Radiograph showing a well-defined radiolucent lesion in the metaphysis of the distal femur surrounded by dense sclerosis (Brodie's abscess; type-Ib lesion).
Technetium bone scans were positive in all cases, and helped to identify the two other sites in the patient with multifocal lesions.

MRI showed replacement of normal fatty marrow with a high signal intensity on T2-weighted images in two patients with diaphyseal type-IV lesions (Fig. 7). CT helped to localise the extent of an epiphyseal lesion in the femoral head (Fig. 8). In patients with epiphyseal lesions there was no evidence of disturbance of the articular surface at follow-up (Fig. 6b). Radiological healing was seen at three to six months. Residual sclerosis was observed in metaphyseal lesions (Fig. 2b); all epiphyseal (Fig. 6b) and diaphyseal infections (Fig. 4b) healed completely.

No extension of metaphyseal lesions into the epiphysis was found at operation. Epiphyseal lesions were also
confined to the epiphysis and did involve the articular surface. In the cortical lesions granulation tissue was found in a nidus surrounded by reactive thickened cortex. The nidus was curetted. In the periosteal lesions a rectangular core of bone consisting of periosteum, cortex and medullary contents was removed with an osteotome. The cortex and periosteum were slightly thickened; no pus was found but there was granulation tissue within the cancellous bone.

Culture of granulation tissue and of medullary curettings was positive for *Staphylococcus aureus* in only six patients. The histological features of chronic pyogenic infection characterised by inflammatory cells, plasma cells and polymorphonuclear leukocytes were seen in all specimens.

Discussion

Primary subacute haematogenous osteomyelitis remains uncommon, but the incidence is increasing in the UK compared with that of the acute form. Some authors have reported a change in the clinical characteristics and epidemiology of osteomyelitis in recent years. Subacute osteomyelitis develops when there is an altered host-pathogen relationship as a result of increased host resistance and decreased bacterial virulence. The acute process may also be masked by antibiotics administered early in the clinical course. True primary subacute haematogenous osteomyelitis occurs mainly in children without a history of previous antibiotic treatment.
Differences in the virulence of strains of staphylococci have been identified and variations in host susceptibility demonstrated. The clinical course in subacute osteomyelitis has an insidious onset with mild symptoms. An occasional history of minor trauma has been noted in this and other series and may be regarded as a predisposing factor.

Laboratory data, apart from a slightly raised ESR, do not support a diagnosis of infection and the radiological presentation may be suggestive of a benign or malignant neoplasm.

Roberts et al. modified Gledhill’s classification into six types (Table I) including four basic forms of the disease occurring in the long bones and spine, defined as metaphyseal, diaphyseal, epiphyseal and vertebral. The vertebral form is usually seen in adults. Some authors have reported the presence of subacute osteomyelitis in other sites, such as the calcaneum, pelvis, clavicle and metatarsal bones.

Metaphyseal lesions are the most common and occur mainly in the tibia. Type 1a is a punched-out localised zone of lucency and can mimic forms of histiocytosis especially an eosinophilic granuloma. Type 1b resembles a typical Brodie’s abscess with dense sclerotic margins and may be mistaken for an osteoid osteoma. Type-II cavities erode the metaphyseal cortex and may resemble osteosarcoma; they may cross the growth plate, but no disturbance of growth has been reported. Lesions similar to type II have been reported in cystic tuberculosis and also in fungal infection.

There have been several recent reports of the epiphyseal form of the condition (type V) which, however, remains rare. The lesions appear as a central lucency, with a faint sclerotic margin and may resemble a chondroblastoma. They usually occur within the epiphysis in children less than six years old and do not cross the epiphyseal plate. Similar lesions have been reported in tuberculosis.

Subacute diaphyseal osteomyelitis has received less attention in the literature than the other forms. Most reports mainly involve adults. There are two types, cortical (type III) and periosteal (type IV). In this study the commonest site was the diaphysis, usually of the tibia. Similar findings have been reported by Hoffman et al. from South Africa. This is at variance with previously reported studies on the distribution of subacute osteomyelitis in which the lesions were mainly in the metaphysis.

In this series the cortical form (type III) consisted radiologically of a localised cortical and periosteal reaction with a small central lucency resembling an osteoid osteoma. Diaphyseal osteomyelitis, characterised by a linear periosteal reaction (type IV), was the commonest subtype. This was single (eight cases) or finely laminated (four cases) with only a slight increase in the density of the medullary canal on plain radiographs. There was bilateral symmetrical tibial involvement in one patient (Fig. 5b), which has not been previously reported. Unlike other studies, the diaphyseal lesions showed a less aggressive periosteal reaction. According to Harris and Kirkaldy-Willis, diaphyseal involvement indicated diffuse local involvement, starting in the metaphysis. Cole described diaphyseal forms as aggressive, destructive lesions with the formation of ‘onion-skin’ or ‘sunburst’ subperiosteal new bone. King and Mayo also described lesions with a considerable amount of layered periosteal reaction. The radiological picture in type IV is indistinguishable from that of round-cell
tumours of bone especially Ewing’s sarcoma, and also from leukaemia. This differential diagnosis has been emphasised. Primary subacute osteomyelitis commonly involves a single bone, and Cole emphasised that it is distinct from chronic multifocal osteomyelitis of which the recurrent type and the SAPHO syndrome are the forms which it may resemble. These conditions are usually recurrent and may be associated with skin infections. Although multifocal lesions were seen in this and other studies, the lesions resolved with treatment, and were not recurrent or associated with skin changes.

The recommended treatment for subacute osteomyelitis with a lucent lesion or nidus has been curettage, biopsy and culture followed by immobilisation and antibiotics. In diaphyseal lesions with skin changes, treatment, and were not recurrent or associated with skin changes.

The recommended treatment for subacute osteomyelitis with a lucent lesion or nidus has been curettage, biopsy and culture followed by immobilisation and antibiotics. In diaphyseal lesions with skin changes, resolution of growth or compromise of joint function were found. Similarly, as observed previously, epiphyseal lesions were confined to the epiphysis with no connection with the metaphysis or the joint margin. Only Ross and Cole have reported arrest of growth in a child with metaphyseal and epiphyseal lesions in the proximal femur.

True primary subacute haematogenous osteomyelitis represents a favourable host-pathogen response and the diaphyseal form appears to be more commonly seen in children in South Africa. It is important to re-emphasise that it is a clinical entity which is distinct from the acute form and from those types in which the clinical presentation has been modified by the administration of antibiotics. These lesions are frequently confused with a variety of benign and malignant bone tumours and non-pyogenic infections.

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References