J. of Korean Orthop. Assoc.
Vol. 29, No. 6, November 1994

Primary subacute Osteomyelitis in Children

— A Retrospective Review —

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= **Abstract** =

In our review of 36 hematogenous osteomyelitis nine cases were subacute form. Distal tibia was the most commonly involved location(four of nine patients). According to the modified Roberts' classification cross-physeal lesions were the most common type(four of nine patients). In most of the cases the clinical findings and laboratory data were not much helpful for current diagnosis. Four patients had radiographic findings similar to those of tumors such as Ewing' s sarcoma, osteoid osteoma or bone cyst. Magnetic resonance imaging was useful in the identification of early lesions. In three patients Staphylococcus aureus was isolated by bacterial culture of biopsy specimen. In the remaining six patients diagnosis was made by histological evaluation. All patients except one were treated by curettage and antibiotics. In the other patient the disease showed a tendency of spontaneous healing without operative intervention and antibiotics. Cross-physeal lesion seemed to be a typical finding of the subacute osteomyelitis.

Key Words : Subacute osteomyelitis, Children

INTRODUCTION

Primary subacute osteomyelitis, although originally described in adults by Sir Benjamin Brodie in 1836[3], was first coined as a separate term by Harris and Kirkaldy-Willis in 1965[9]. Acute form of osteomyelitis with a short history of onset, high temperature and loss of function is readily distinguished. However, subacute osteomyelitis differs from the acute one in that it has no acute phase, usually shows only mild symptomatology, and lacks of contribution of the laboratory findings. King and Mayo[14] pointed out that any bone infection for longer than two weeks without evidence of acute illness can be classified as subacute.

Subacute osteomyelitis is essentially a problem of diagnosis, and there may be considerable diffi-

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culty in distinguishing it from tumors or tumorous conditions. Roberts and his associates[17] reported initial misdiagnosis in 90 per cent, which were most frequently misinterpreted as tumors in 50 per cent.

By the modification of Gledhill' s system[7], Roberts et al[17]. classified this disease into six radiological types based on anatomic location, morphology of the lesion, and its similarity to various neoplasms. The most commonly involved site was the distal tibial metaphysis. Ross and Cole[18] reported the most typical lesion was the metaphyseal cavity that crosses the growth plate into the epiphysis.

The current study was undertaken to help define and clarify the clinical, laboratory and radiological features of subacute osteomyelitis, and to aid in achieving earlier, and more accurate diagnosis. We also describe the outcomes of treatment along with some speculations about the natural course of this disease.

MATERIALS AND METHODS

We retrospectively reviewed 36 children with hematogenous osteomyelitis seen consecutively at the Ewha Womans University Hospital from 1987 to 1993. The patients were divided into acute, subacute, and chronic groups. The criteria for subacute course included mildness of the presenting symptoms of insidious onset, and the lack of contribution made by laboratory data. The course was generally marked by little or no functional impairment, fever, malaise, anorexia, or weight loss. Nine patients met the criteria for subacute osteomyelitis. There were four boys and five girls. The age of the patients ranged from three months to 14 years with an average age of 7.1 years. The follow-up periods ranged from six months to three years with an average of 14 months.

Of the nine lesions, four were in tibia, two in femur, one in radius, one in clavicle, and one in calcaneus. The localizations were four cross-physeal, three diaphyseal, one metaphyseal, and one metadiaphyseal.

When the nine cases were classified into six types by the modification of the system of Roberts et al[17,20]. (Fig. 1)(Table 1), type 6(cross-physeal lesion) was the most common to include four cases(Fig. 2) ; type 4(diaphyseal, simulating Ewing' s sarcoma) was also common to be present in three patients; type 1(metaphyseal, punched out) in one; and type 3(diaphyseal, simulating osteoid osteoma) in one. There was no type 2(metaphyseal with cortical erosion) or type 5(epi-

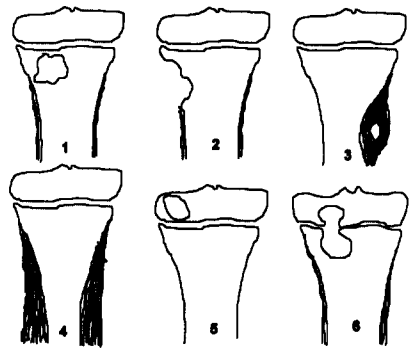

Fig. 1. Schematic presentation of 6 types by the modified Roberts' radiological classification of subacute osteomyelitis: type 1, punched-out metaphyseal lesion; type 2, eccentric metaphyseal lesion with cortical erosison; type 3, diaphyseal intracortical lesion, simulating osteoid osteoma; type 4, diaphyseal lesion with onion-peel like periosteal reaction, simulating Ewing's sarcoma; type 5, epiphyseal lesion; type 6, cross-physeal lesion.(Redrawn after Warner WCJr[20] : Subacute hematogenous osteomyelitis. In : Crenshaw AH ed. Campbell's Operative Orthopedics. 8th Ed. PP. 135-136, St. Louis, Mosby-Year Book Inc., 1992).

Table 1. Radiological Classification(modified from Roberts et al[17,20].)

Types	Radiological Characteristics	Cases
Type 1	metaphyseal, punched out lesion	1
Type 2	metaphyseal lesion with cortical erosion	-
Type 3	intracortical lesion in diaphysis	
Type 4	diaphyseal lesion with onion-peel like periosteal reaction	3
Type 5	epiphyseal lesion	-
Type 6	cross-physeal lesion	4

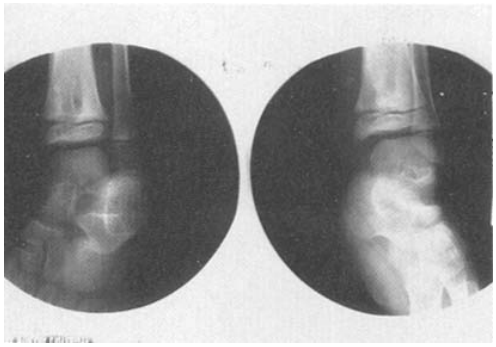

Fig. 2. Plain radiographs of a six-year-old girl with a typical cross-physeal lesion.

physeal)lesion.

In reviewing hospital records, we checked for clinical presentation and the interval between the onset of symptoms and diagnosis. We also noted fever, white blood cell count, differential count, sedimentation rates(ESR), and cultures of both blood and involved bone. The preoperative radiological studies included standard radiographs, technetium bone scans(checked in all patients), tomograms(two patients), computerized tomographic scans(two patients), and magnetic resonance imaging(four patients). In all cases we did bone biopsies for histologic examination and culture of the specimen.

All the cases except one were treated by operation that consists of fenestration. curettage and drainage. The other one was a six-year-old girl with a lesion in the proximal radial metaphysis (Fig. 3). She was initially followed-up by an orthopedic surgeon under the impression of bone tumor. No antibiotic was given before her visit to our hospital. The serial radiographs taken weekly showed a tendency of spontaneous healing. On the fifth week of observation we performed the open biopsy without curettage, that confirmed the involutional subacute osteomyelitis.

During the operative exposure we employed image intensifier control to localize the exact site of fenestration. Curettage was thoroughly performed through the fenestration until normal trabeculae were reached. Cross-physeal lesions were curetted through the metaphyseal fenestration. In these situations the granulation tissues were always confluent from the metaphysis to the epiphysis with an hourglass constriction at the perforations in the growth plate. Curettage was performed with extreme care not to injure the intact physis. The epiphyseal lesion was removed from the metaphyseal side through the small physeal opening. We did not try the drainage of it through the separate approach on the epiphyseal side. We did not remain any free fat or silastic sheet in the physis.

Antibiotics were started from the immediate postoperative period. Intravenous cephalosporins were continued for two to four weeks followed by oral cephalosporins for additional three to four weeks. In the patients with high preoperative value of the ESR, it was repeated every three other day after the operation. In these situations the intravenous antibiotics were switched to the oral antibiotics only if the ESR continues to be normal in three consecutive studies. If the initial value of the ESR was normal, we used the intravenous antibiotics for three weeks followed by oral antibiotics for another three week. The operated extremities were immobilized until adequate radiological healing was noted.

RESULTS

1. Clinical Findings

Pain was the main complaint in eight children. The other one patient was a six year-old girl already mentioned above, who had a non-tender palpable mass around her left proximal radius(Fig. 3). It was first identified by her mother three weeks before her visit to our outpatient department.

All patients except one had tender area on palpation of the limb. The tenderness varied in degree

Fig. 3-A. Plain radiographs of a six-year-old girl. A lesion in her left proximal radial metaphysis presents the intramedullary radiolucency with extensive onion-peel like periosteal reaction. The initial diagnosis was Ewing' s sarcoma.

B. Five weeks later without antibiotics, it revealed a tendency of spontaneous healing. Biopsy report confirmed an involutional subacute osteomyelitis.

C. Four months after the operation, the lesion was completely healed.

from mild to moderate, and none had severe tenderness. Swelling over the lesion varied considerably. In no instance was there the acute severe swelling. Other occasional signs were mild limping in three patients, and detectable muscle atrophy in one patient.

None of the children was systemically ill. Oral temperatures in all patients were normal and their activities were limited only by local signs and symptoms. The interval between the onset and hospitalization varied from one week to nine months, with an average of 11 weeks. Two patients had a known recent illness. One was an inguinal lymphadenitis in a seven-year-old boy. He subsequently developed the type 1 subacute osteomyelitis in the proximal femoral metaphysis. The other was the distal radius fracture in a six-year-old girl. She subsequently developed a type 4 lesion in the ipsilateral proximal radius.

2. Laboratory Data

The full blood count was essentially normal in all patients, the white cell was less than 10,000, and their differential counting was also normal. The ESR was above 30 in four patients, and 20 or less in five patients. The blood culture was negative in all cases. Cultures of biopsied material failed to grow bacteria in six instances. The others grew Staphylococcus aureus in three patients.

3. Radiological Studies.

Standard radiographs over the suspected lesion were taken in the routine anteroposterior and lateral planes. The initial suspicion of infection was made in only three patients. Typical findings of cross-physeal lesions were helpful for diagnosis. We met such a case in one occasion(Fig. 2). In four cases bone tumors were the first differential diagnosis made by the radiologists; they were Ewing' s sarcomas in two instances, bone cyst in one, and osteoid osteoma in one. In two patients who had early lesion, there was no identifiable lesion in the initial plain radiographs.

For the special radiographic studies, technetium

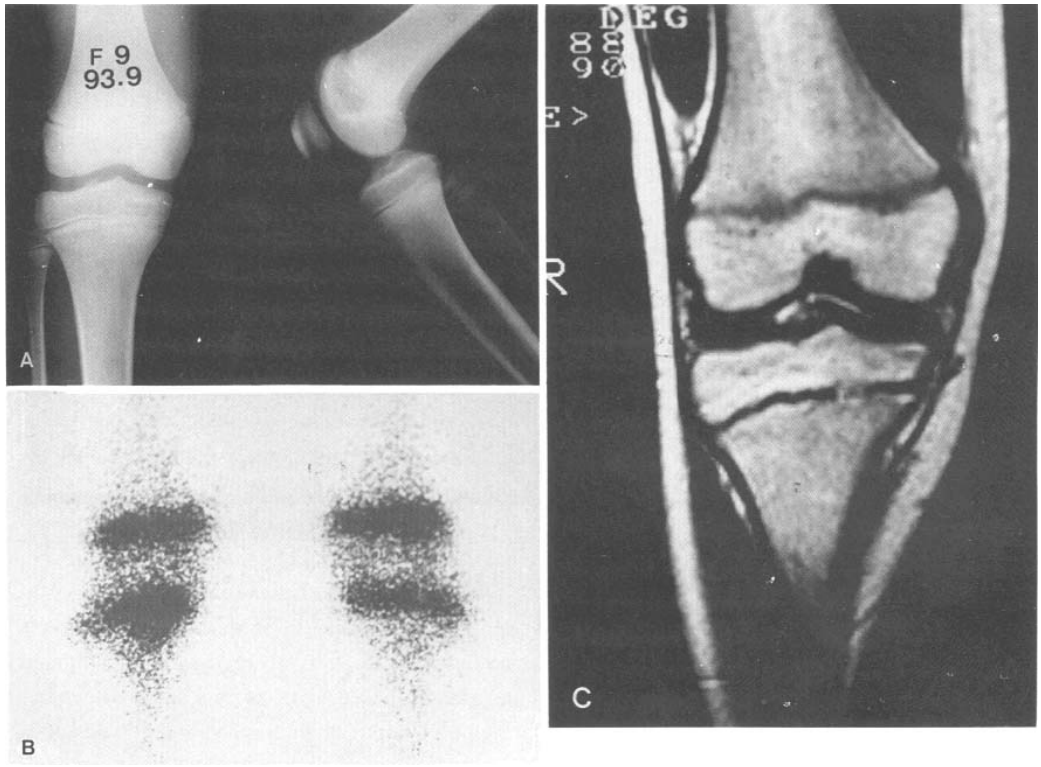

Fig. 4-A. A case of 14 year old girl. Intermittent mild pain with minimal tenderness on the medial aspect of the proximal tibia was the only clinical finding. There was no identifiable abnormality in the plain radiographs.
B. Technetium bone scan revealed hot uptake on the tender point.
C. Magnetic resonance imaging defines a small lesion over the physis with tissue reaction in the surrounding metaphysis

bone scan was the next step in the diagnostic work-up. A hot uptake in the suspected area was noted in all cases. Tomograms and computerized tomographic scans, done in two patients respectively, were not more informative than the standard radiographs. Magnetic resonance imaging, performed in four patients, were very useful in identifying the early lesions in which the plain films were negative and the bone scan showed hot uptake(Fig. 4). It was also valuable in identifying the anatomic extent of lesion with the reactive zone and in differentiating the content of lesion.

4. Biopsy & Histological Findings

The most common gross finding was a fairly dense granulation tissue, which was in some cases surrounded by a reactive bone. The granulation tissue in the crossphyseal lesion was usually in an hour-glass shape with its constricted portion located in the growth plate. Purulent material was infrequent. Histologically, it was an osteomyelitis with rich plasma cells, lymphocyte, neutrophils, and histiocytes(Fig. 5). Focal marrow fibrosis was an occasional finding.

5. Response to Treatment

All cases healed at our recent follow-up. Symptoms disappeared rapidly after the treatment. Radiological healing was usually obtained within three months. There was no evidence of identifi-

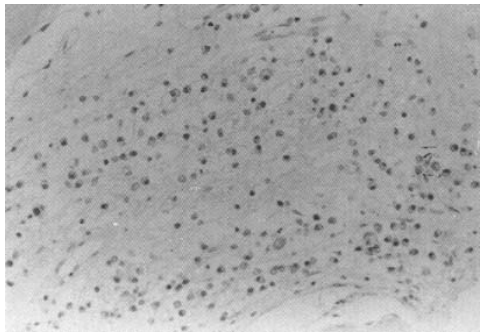

Fig. 5. Typical histologic finding of subacute osteomyelitis shows rich plasma cells, lymphocytes, neutrophils and occasional histiocytes

able growth disturbance in the cross-physeal lesions until the last follow-up.

In the six-year-old girl mentioned above with a lesion in the proximal radial metaphysis(Fig. 3). we initially waited until five weeks without the administration of antibiotics. The first impression of her plain radiographs was the Ewing' s sarcoma. However, as the operation delayed for a few weeks, we found a tendency of spontaneous healing. After five weeks of observation it showed definite healing with remaining a small intramedullary radiolucent lesion. The ESR, which was initially 33, was dropped to 14 at the time of operation. In this situation we decided a biopsy, which confirmed the typical findings of the involutional subacute osteomyelitis. The biopsy site healed two months after the biopsy.

DISCUSSION

As the previous reports pointed out, the primary subacute osteomyelitis is not an uncommon disease to be 25 per cent of hematogenous osteomyelitis in our series. Jones et al[12]. reported the incidence as 35 per cent, which showed an increasing tendency in their recent study. Basically, it has the same pathogenic organism, mainly Staphylococcus aureus, as in the acute disease. However, the subacute osteomyelitis should be regarded as a separate entity, because the clinical presentations in the symptomatology, laboratory and radiological findings as well as the natural course seem to be quite different from the acute one. We agree with Gledhill' s hypothesis that subacute osteomyelitis develops because of an altered host-pathogen relationship[7].

The subacute osteomyelitis has an insidious onset with mild symptoms. We agree with Lindenbaum and Alexander[16] that the patient history is helpful only in determining the chronicity of the problem; it does not necessarily aid in the diagnosis of infection. Laboratory data and radiographic findings frequently do not support the diagnosis of infection. Definite diagnosis can be made by culture of the bone and/or by the histological appearance.

We have found, as have others[5,13,16], that the radiological appearance of subacute osteomyelitis is often highly suggestive of benign or malignant neoplasm. Indeed, four patients had a delayed or incorrect initial diagnosis as Ewing' s sarcoma, osteoid osteoma, or bone cyst. In the series of Cabanella et al[5]., among the 23 patients in whom subacute or chronic osteomyelitis simulated bone tumors, the most common initial diagnosis was Ewing' s sarcoma followed by osteogenic sarcoma.

Plain films were inadequate to find the early lesion in three patients. Technetium bone scan showed 100 per cent sensitivity, and was useful in detection of the early lesions that had negative finding in their plain films. Magnetic resonance imaging was also useful in identifying the lesions that showed negative plain x-ray finding but hot uptake in the bone scan.

Misdiagnosis as Ewing' s sarcoma at the early stage is understandable. The literature contains numerous statements describing the similarities, both clinically and radiographically[10]. In both conditions pain and swelling are characteristic features. Fever and elevated ESR are also common to

both. Either lesion may show reactive periosteal new bone formation with destructive changes on the radiographs.

At biopsy the gross appearance of Ewing' s sarcoma often presents the most difficult diagnostic problem. Because it usually lacks stroma, there may be a central accumulation of soft, white creamy fluid, grossly resembling purulence. Microscopically, there may be areas of hemorrhage and necrosis, producing reactive inflammatory response that simulate infection.

Localization of the lesions in subacute osteomyelitis is different from that of the acute disease. Acute hematogenous osteomyelitis is usually found in the metaphysis, whereas the subacute form shows divesity. It can be found in the metaphysis[7,9,13,17], diaphysis[11], epiphysis[1,8], and crossphysis[4,13,14,15,16,18].

Brailsford[2] concluded in 1938 that the epiphyseal plate formed an effective barrier against infection. However, in a recent review Kandel and Mankin[13] reported that in three of their nine patients with staphylococcal subacute osteomyelitis the infectious process extended across the epiphyseal plate and into the epiphyseal nucleus. In our series, four of the nine cases were of the cross-physeal location. The reported prevalence of perforation of the growth plate varies from nil[17] to the consideration that it is a usual feature[14].We agree with King and Mayo[14], Kandel and Mankin[13], Kozlowski[15], Bogoch et al[4]., and Ross and Cole[18] that metaphysal cavities extending across the growth plate are a common feature of subacute osteomyelitis, whereas such extensions are rarely seen in lesions such as simple bone cyst, aneurysmal bone cyst, fibrous cortical defect, chondroblastoma or chondromyxoid fibroma.

The mechanism of the cross-physeal spread is not yet determined. It may involve vessels or canals that cross the growth plate[6,19]. Through our observations in the early detected cases, we speculate that the reactive sclerosis formed in the relatively early phase of this disease might play a role. This reactive bone, a defence mechanism against the spread of pathogen, is usually not found in the early phase of the acute form of osteomyelitis. The reactive sclerosis is typically formed toward the metadiaphysis with its opening into the growth plate. The increased pressure by the formation of purulent discharge in metaphysis, which is protected to spread toward the diaphysis by the wall of reactive bone, might be evacuated through vessels or canals in the physis into the epiphysis.

Curettage followed by antibiotics for six to eight weeks was effective in the most of our cases. The results published in the literature are also uniformly good[7,14,17]. Ross and Cole[18] reported that 87 per cent of the metaphyseal, epiphyseal, and crossphyseal lesions were cured with only antibiotics and immobilization. They suggested that surgery is indicated only for the cases that looks like "aggressive" and need for the biopsy; and antibiotics may be sufficient treatment for children with cavities typical of subacute osteomyelitis. Our single case of a six-year-old girl with a proximal radial lesion showed a tendency of spontaneous healing in a short period of five weeks even without antibiotics.

Kandel and Mankin[13] and Bogoch et a[14]. reported that longitudinal and epiphyseal growths were usually normal at their late review, even in patients who had perforation of the growth plate when first seen. However, through our short-term follow-up we can not tell if the cross-physeal lesion is really benign without any possible growth disturbance.

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= 국문 초록 =

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원발성 아급성 골수염은 뚜렷치 않은 임상 증상과 검사 소견, 간혹 종양과 구별이 어려운 방사선 사진 소견 등 급성 골수염과 많은 차이점이 있다. 저자는 1987년 부터 1993년 사이에 치험한 36례의 소아 혈행성 골수염 중 아급성 유형에 속하는 9례를 분석하였다. 가장 흔히 침범한 골은 경골로 4례가 이에 속하였다. 방사선 사진 상의 유형은 골간단에서 시작된 병소가 골성장판을 뚫고 골단으로 퍼진 모양이 4례로 가장 많았으며, 이 모양은 아급성 골수염의 전형적인 진행 형태로 생각되었다. 진단에 동원된 정보 중, 병력, 임상 증상, 임상 병리 검사는 기여도가 극히 낮았다. 단순 방사선 사진은 4례가 골종양으로 판독되었으며, 유잉 육종, 유골 골종, 골 낭종과 유사하였다. 골주사와 자기 공명 영상 촬영은 조기 진단에 도움을 주었다. 병원균은 생검 조직의 세균 배양으로 3례에서 검출되었으며, 모두 포도상 구균이었다. 세균 배양이 음성인 6례의 진단은 병리 소견으로 가능하였다. 치료는 8례에서 발견 즉시 골소파술을 하였으며, 1례는 5주 간의 관찰 후 조직 생검 만을 시행하였다. 수술 후 약 6주간 항생제를 투여하였다. 최종 추시 시 전례가 완치되었고, 5주 간 항생제를 투여하지 않고 관찰하였던 1례는 병변이 스스로 소멸되는 경향을 보였다.