The Turkish Journal of Pediatrics
1971 / Vol. 13 / No. 1 / pp. 25 - 39

Multiple Epiphyseal Dysplasia: A Report of Three Cases

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This condition is a congenital disturbance in the growth and ossification of the epiphyses and although earlier reports are available,[1] Fairbank established multiple epiphyseal dysplasia as a distinct clinical entity in a review of 26 cases in 1946.[2-3] Since the original description of this disease, variant forms have been reported and mainly through the work of Silverman it has been convincingly demonstrated that there is actually a spectrum of disease.[4] Thus in reality one should be talking of "epiphyseal dysplasia" and be alert for its various forms. According to the present classification, there are three forms of this disease; the congenita, tarda and the pseudoachondroplastic forms of multiple epiphyseal dysplasia.[5] In this report we are going to present two cases representative of the pseudoachondroplastic form and one case representing the tarda form of multiple epiphyseal dysplasia seen in Hacettepe Children's Hospital.

The disorder is heredo-familial in nature[6]. Its congenital form appears within the immediate post-natal period or is discovered in the first year of life. This is the most severe form of this disease and the affected infant has short limbs. Usually there are flexion deformities at the hips, knees and elbows. The fingers and toes are short and stubby. The head appears normal but bilateral congenital cataracts are present in 50 % of the patients. Most of the patients with this form of the disease die in the first year of life due to secondary infections.

The children affected with the pseudoachondroplastic form of multiple epiphyseal dysplasia are usually normal at birth and come to the attention of the physician by the time they reach 4 or 5 years of

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age because of a waddling gait, genu varum or genu valgum and shortness of stature. The shortness is most striking in the extremities, and the lower extremities show the greatest involvement. The head is normal and there is no disturbance of their mentality.

The third group of patients with multiple epiphyseal dysplasia, those who have the tarda form, do not usually show any symptoms during early childhood. Their slight dwarfism of the shortlimb type is usually overlooked until the ages between 5 to 14 years when complaints about joint motion, difficulty in walking and pain in the hips, knees or ankles develop. Although most cases are diagnosed in childhood and adolescence, family studies have led to the diagnosis of adults up to the age of 55 years. Many cases are diagnosed as early cases of osteoarthritis due to premature degenerative changes. The hands are typically short and stubby, with norrow nails.

Extensive laboratory examinations have failed to disclose any abnormality in the various forms of multiple epiphyseal dysplasia and radiological changes provide the only means of diagnosis and classification in this disease.[5] These will be discussed later on.

Case Reports

Case 1 : S. O. (64-43663). This thirteen and a half year old girl was seen in the hospital with complaints of short stature, deformity of the legs and abnormality in walking. She had apparently been in good health until age three, at which time she started to complain of a pain in her knees following walking and the parents noted that she had a waddling gait. She was, at various times, diagnosed as having rickets, Legg-Perthes disease and rheumatoid arthritis and was treated accordingly without any improvement in her condition. She benefitted considerably, however, from orthopedic shoes which were given to her when she was seven years old and her pains had somewhat subsided. By the time she was seen in our hospital she felt fatigued after even short walks and was unable to run.

There was no family history of a similar disturbance.

Physical examination revealed a well-developed adolescent girl who was obviously short for her age Her height was 137 cms. (normal for her age being around 160 cms.) and her span 131 cms., lower segment 70 cms. and upper/lower segments ratio 0.96. The patient had a waddling gait, genu valgum and pes planus deformities. Her fingers were short and stubby. (Figure 1).

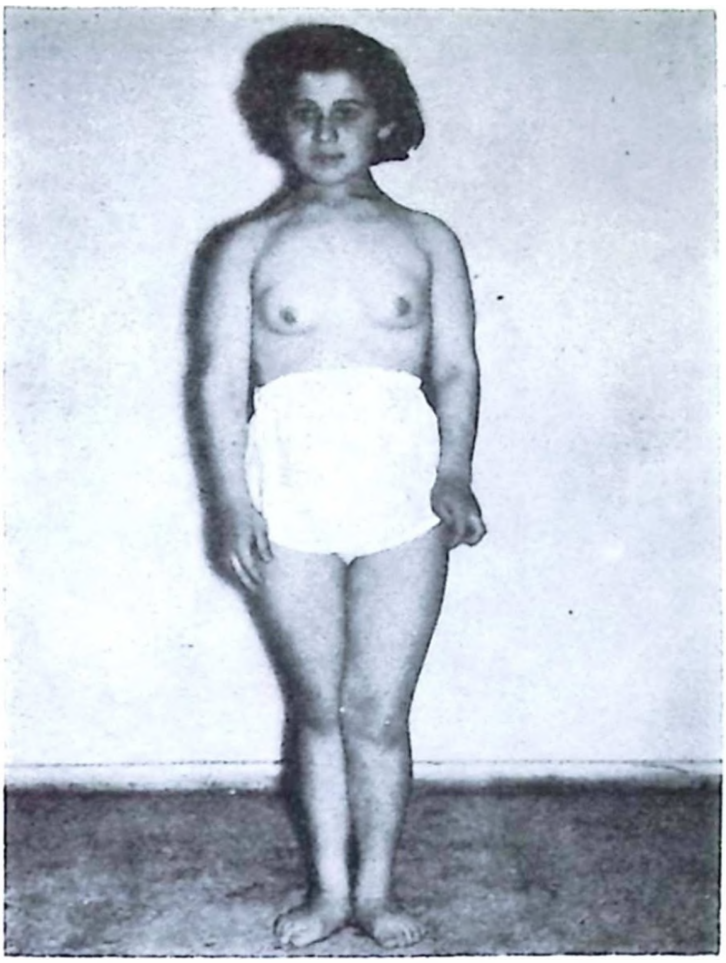
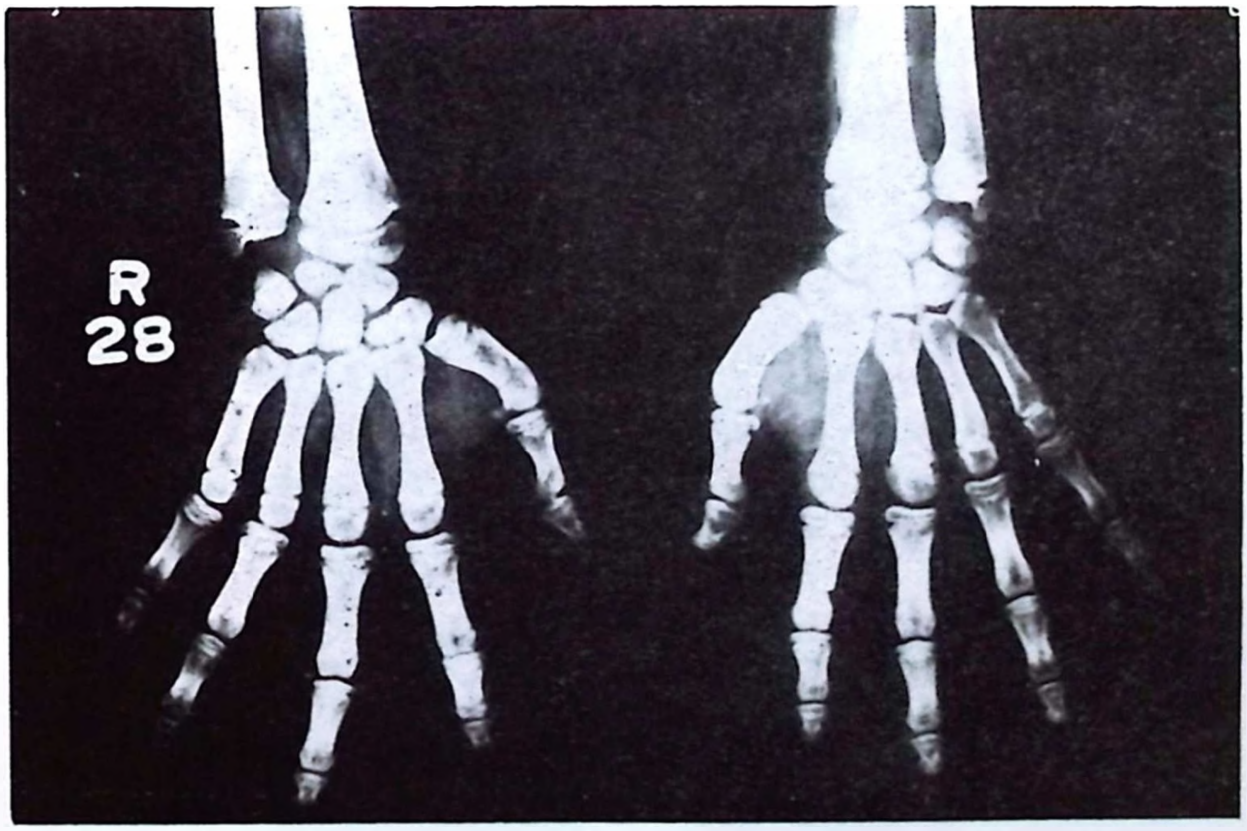


Figure 1



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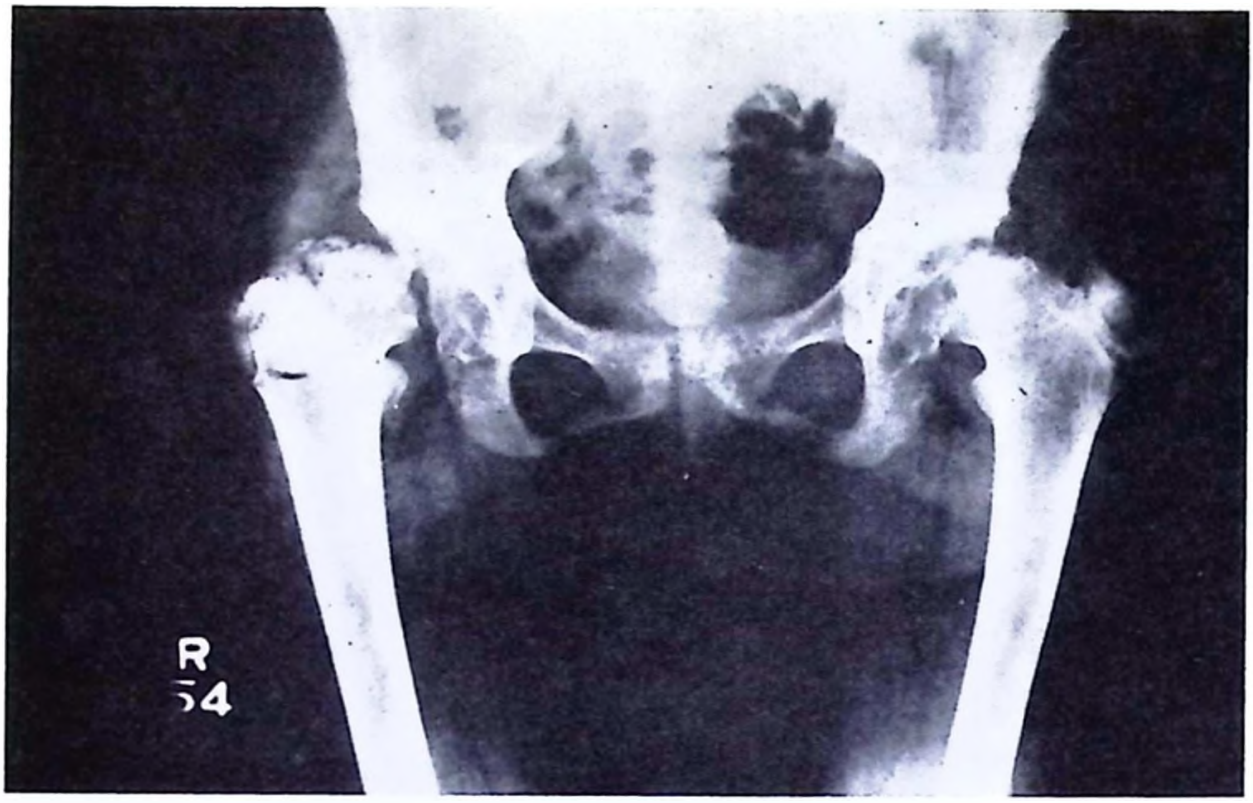

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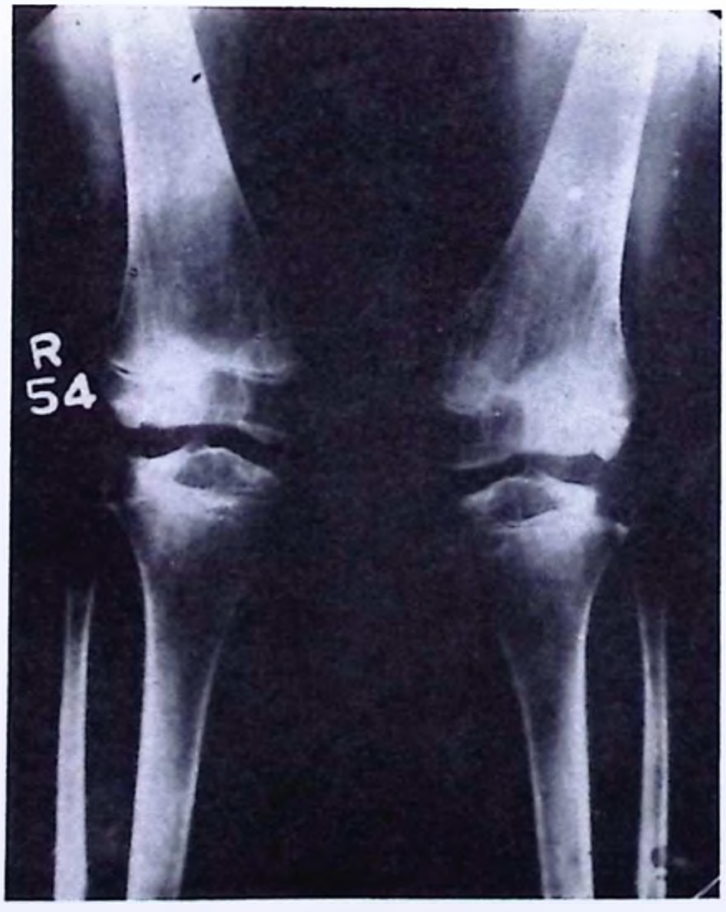

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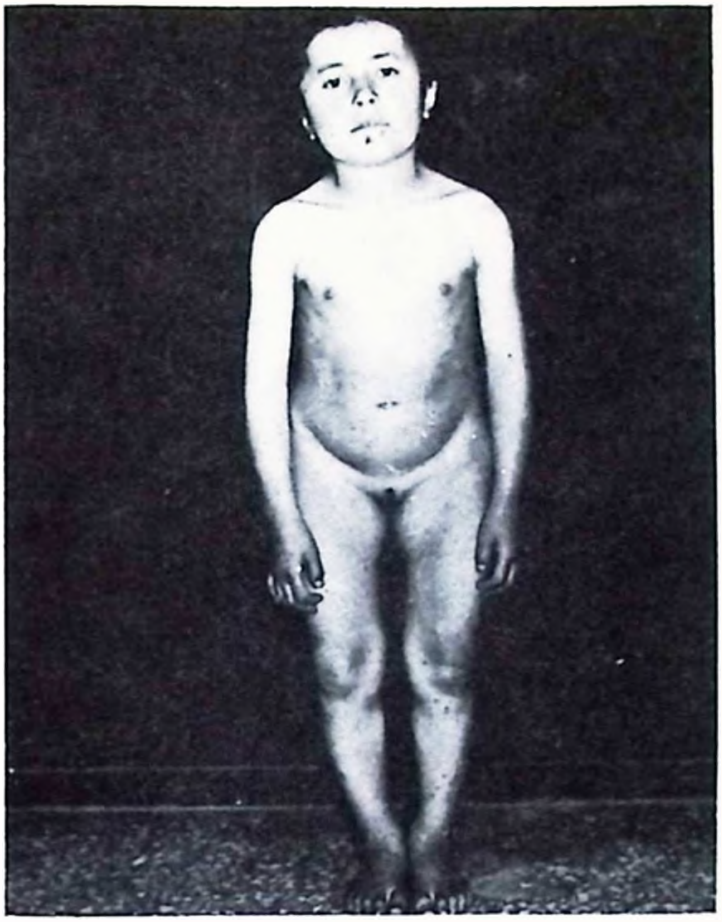

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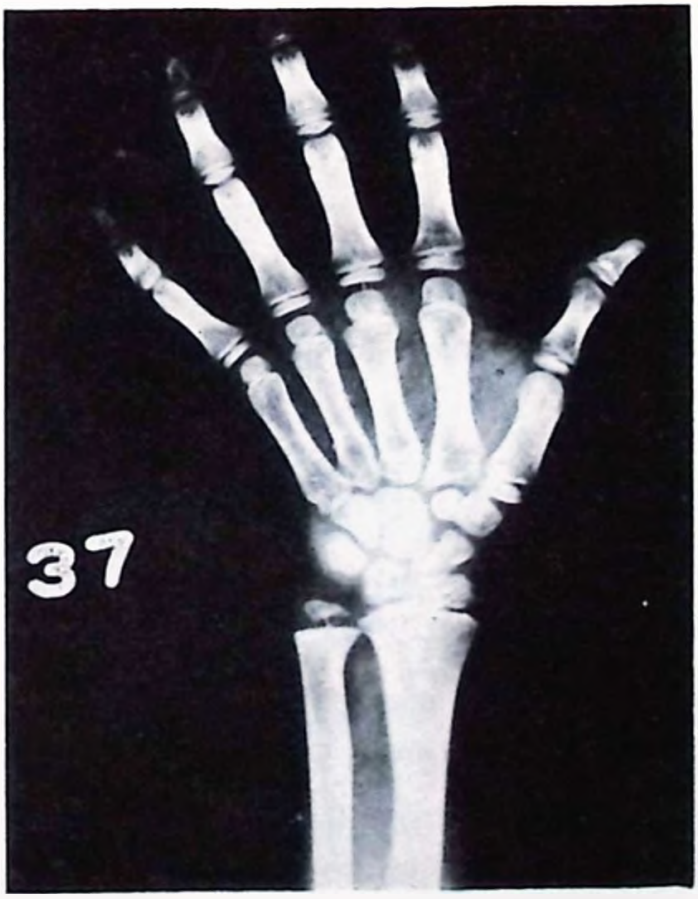

Figure 6

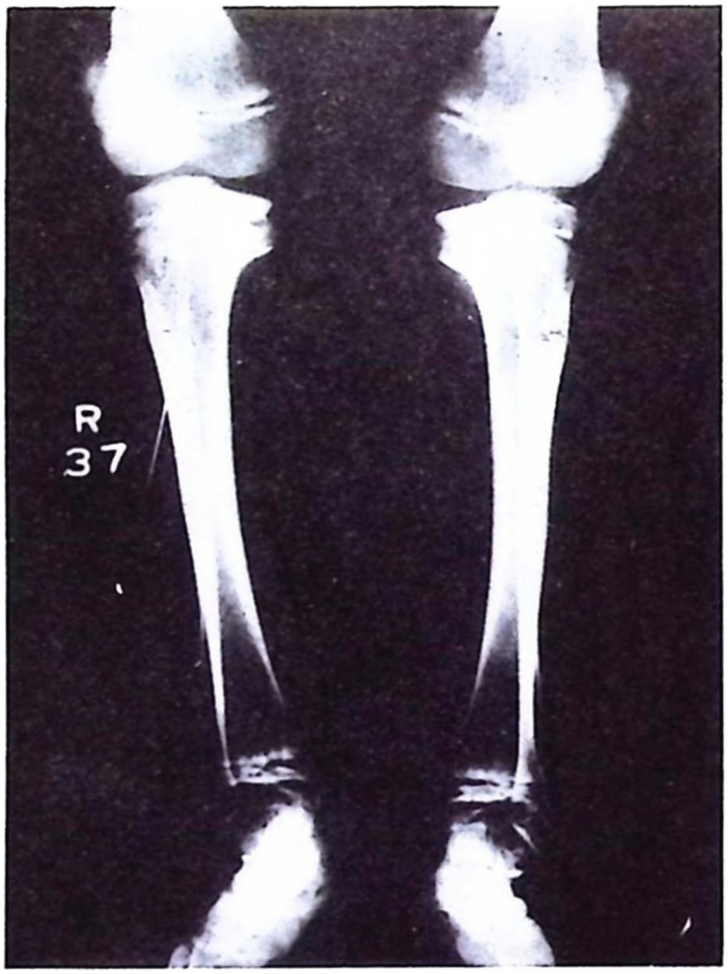

Figure 7

Blood chemistry was normal.

X-ray examinations showed the metacarpal bones and the phalanges to be short and thick. There was some irregularity of distal radial and ulnar epiphyses. (Figure 2). Epiphyseal irregularity was most pronounced in the capital femoral epiphysis. There the epiphyses revealed spotty ossification resulting in a fragmented appearance and marked deformity of the femoral heads. Degenerative changes had started in the hip joints and the right femoral head was somewhat laterally displaced in its dysplastic acetabulum. (Figure 3). In the knee joints, irregularity of the distal femoral and proximal tibial epiphyses and genu valgum deformity were present. (Figure 4).

The patient underwent corrective orthopedic surgery for her deformities and epiphysiodesis was performed on both knees.

Case 2 : A. M. (64-35053). This eleven year old girl was brought to the hospital because of back pain. The pain would start after a long walk and would subside after some rest. She was noted to have a wadd-

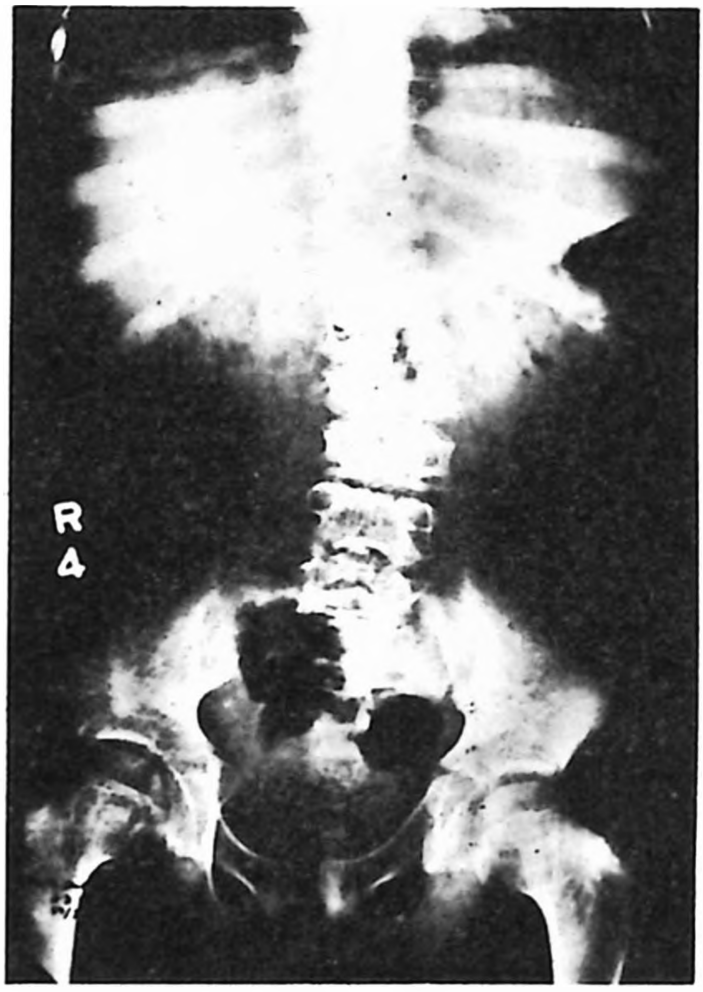

Figure 8

ling gait and to be rather small since early childhood but otherwise had unremarkable development.

A thirty year old paternal uncle (I. M.) also had a short stature and an abnormal gait.

Physical examination revealed an apparently healthy, stocky girl somewhat short for her age. Her height was 114 cms. (normal for her age being 137 cms). Her span was 119 cms., her lower segment 58 cms. and her upper/lower segments ratio was 0.96. (Figure 5).

Laboratory examinations including serum calcium, phosphorus and alkaline phoshatase were normal.

Radiological findings in this patient were as follows: There was a delayed irregular ossification of the distal radial and ulnar epiphyses; the distal phalanges were short. (Figure 6). The proximal and distal tibial epiphyses showed marked flattening and irregularity of ossification. Similar changes were also present at the distal femoral epiphysis to a

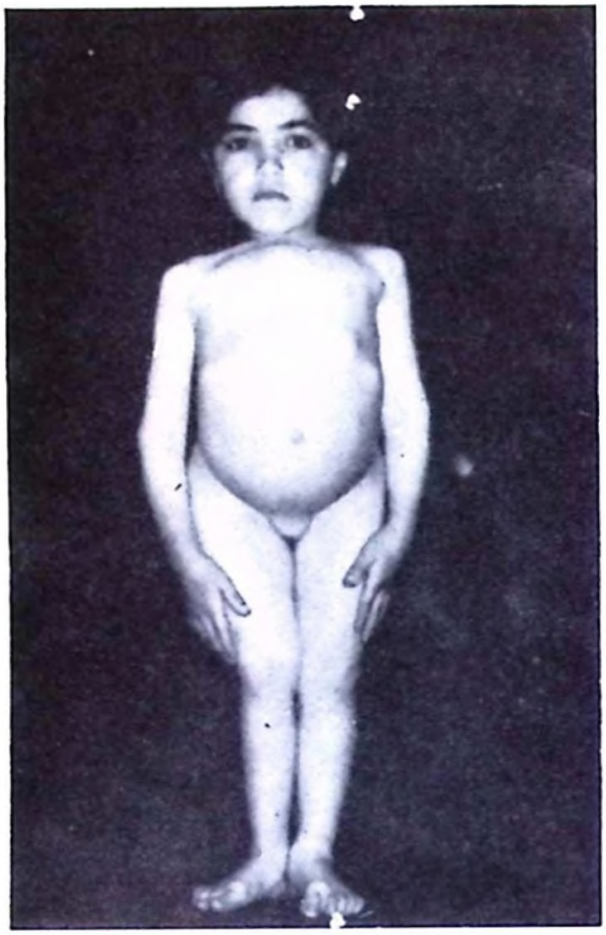

Figure 9 a

Figure 9 b

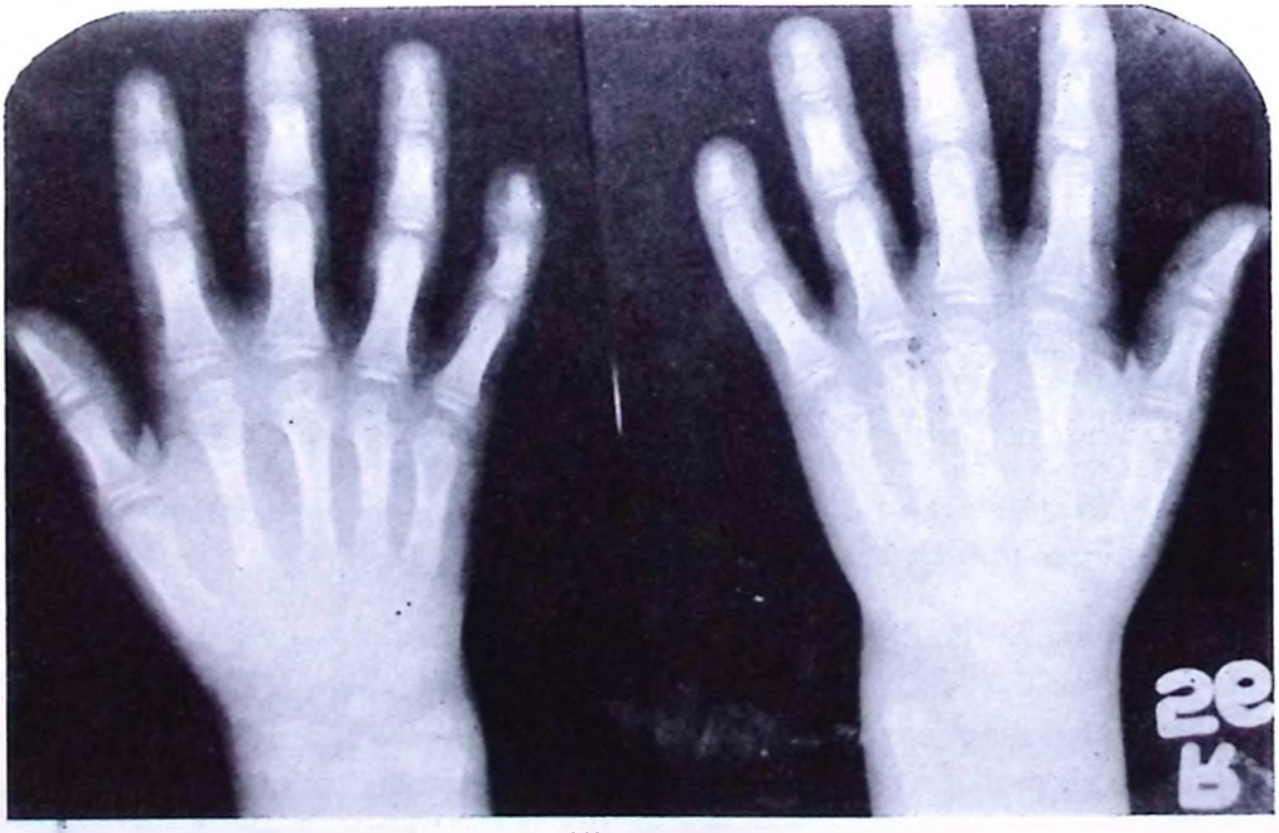

Figure 10

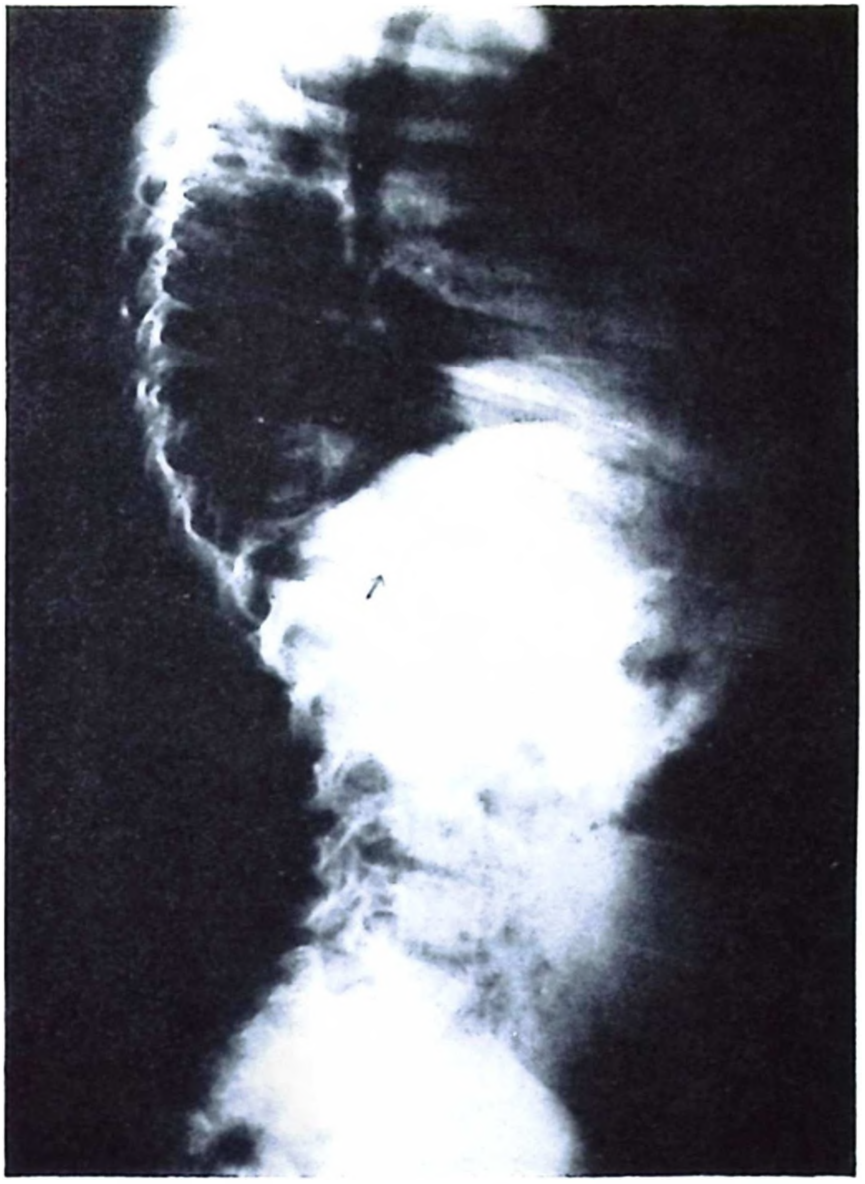

Figure 11

lesser extent. (Figure 7). Vertebral bodies revealed irregular ossification of their epiphyseal plates. They showed a tendency to flattening. A lumbar scoliotic curvature was present. Slight flattening of femoral heads and protrusio acetabui were observed. (Figure 8).

Case 3 : S. K. (65-13354). This eleven year old girl was hospitalised with complaints of difficulty in walking and a waddling gait. The patient first started walking at the age three of and ever since had been getting tired easily and complaining of pains in the legs and hips following walking. Six other siblings were normal and there was no history of any similarly affected person in the family.

Physical examination revealed a mentally alert child with multiple deformities, i.e. short trunk with the arms appearing relatively

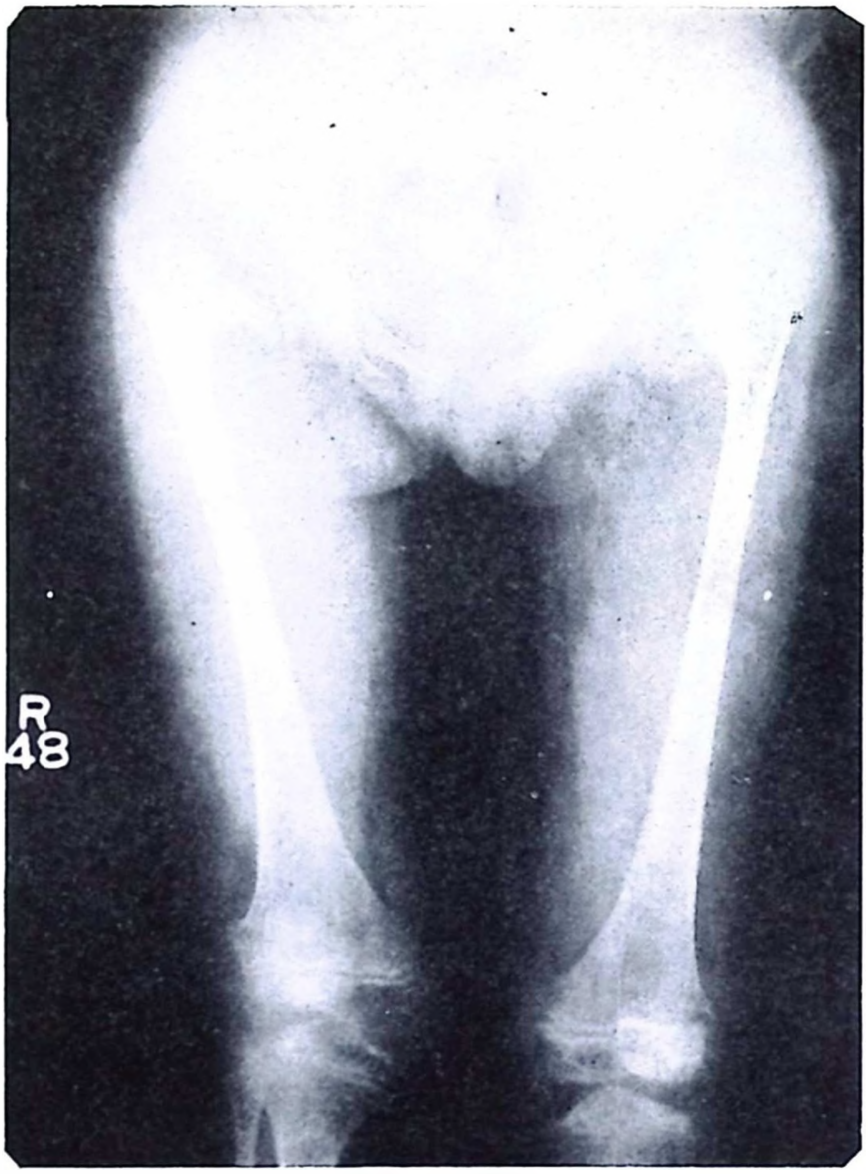

Figure 12

long, a marked increase in lumbar lordosis and genu valgum. Her height was 97 cms. (normal for her age 137 cms.). (Figures 9a, 9b).

Laboratory tests failed to reveal any abnormality.

X-ray examination of the hands showed the epiphyseal ossification centers of the radius and ulna as well as the phalanges to be small and irregular. (Figure 10). The vertebral plates were very irregular and some revealed deep notches resulting from disc intrusion resembling Schmorl's nodes (arrow on Figure 11). Anterior and lateral wedging of the dorsal vertebra was present leading to a slight right dorsal scoliosis and kyphosis. True vertebra plana was absent. The irregularity of ossification was most pronounced in the femoral head and in the epiphyses on both sides of the knee joints. Marked coxa vara and genu valgum deformities were also present. (Figure 12).

Discussion

Multiple epiphyseal dysplasia is a disorder of the skeleton, transmitted by the autosomal dominant mode of inheritance with a wide variation both in degree of skeletal manifestation and at the time of onset. It consists essentially of irregularity in the form and structure of the developing epiphyses.[5-6] In the most severe form of the disease the irregularity of epiphyseal ossification is present at birth and radiographically manifests itself with marked stipling in the same. This form of the disease has been called *multiple epiphyseal dysplasia congenita* or *dysplasia epiphysealis punctata.* There are many reports of autopsied cases of this form of the disease (Tisdall,[7] Harris,[8] Bateman,[9] Hassler,[10] Coughlin,[11] and Silverman[4]). The common pathological finding in these reports was the presence of patchy mucoid degeneration and cystic spaces in cartilaginous epiphyses. There were circumscribed, polymorphous deposits of calcium in this cartilage. The primary defect leading to these changes probably appeared to be an inadequate vascular invasion of the epiphysis.

If the infant with this severe form of the disease does not succumb to superimposed infections and die, as most of them do, the stippling disappears with time and the epiphyses ossify, though somewhat irregularly. Several cases of this type have been followed over the years (Raap,[1] Swoboda,[13] Paul,[14] Selakovich[15] and Burckhardt[16]), the longest follow-up being 19 years by Weber[17]. Irregularity of the capital femoral epiphysis leading to hip degeneration and scoliosis were almost invariably the resulting deformities.

Silverman, in review of this subject, studied the evolution of epiphyseal dysplasia punctata.[4] He noted the disappearance of stippling and subsequent development of malformed epiphyses. He followed three cases from infancy to adolescence with numerous studies and noted that in a rough way the amount of calcification tended to parallel the severity of the disease and subsequent deformity. He observed that the calcifications were mainly localized in the subarticular area of the epiphysis. This resulted in deformity of the articular portion of the epiphysis whereas the growth plate (physis) remained relatively normal although some restriction of longitudinal growth did occur. The resemblance of these follow-up cases to those of dysplasia epiphysealis tarda which came to the attention of the physician toward the later years of the patients, has prompted Silverman to conclude "that these two diseases are different stages of the same disease which, in general, tends to be more severe in the form discovered in infancy."

The two other milder forms of this disease, the pseudoachondroplastic and the tarda form apparently are caused by a milder genetic expressivity and are present, with a less striking clinical picture and radiological changes. One can speculate, of course, that the epiphyses of patients in these two latter groups were not entirely normal since birth, and only when the anatomical abnormality became severe enough to produce clinical symptoms did we become aware of them. This may very well be true but there are no documented case reports to prove this point.

Here again the difference between the two forms is essentially matters of degree and the time of onset. The pseudoachondroplastic form is the more severe of the two and these children develop an abnormal gait and joint pains in early childhood, whereas those with the tarda usually have a symptom-free childhood. Patients in both groups otherwise have a similar clinical picture: a stunted child with apeculiar gait, deformities of the spine and the knees and with stubby fingers. Radiographic examinations are the only means of differential diagnosis.

In the pseudoachondroplastic form of multiple epiphyseal dysplasia X-rays of the long bones show the epiphyseal nuclei to be irregular and fragmented. The changes are more striking in the lower extremities than in the upper extremities and the femoral heads display the greatest involvement. This is probably because of the addition of the stress of weight bearing on the poorly formed hypoplastic epiphysis. The capital femoral epiphysis shows marked fragmentation and the findings are very similar to those seen in Legg Pertes disease. The long bones are all shorter and thicker than normal but this is not as striking as in true achondroplasia. There is slight flaring of the metaphyseal segments. The metacarpals and metatarsals are short and brachydactylia may be seen. The vertebrae show defects in the anterior, inferior and superior aspects at the site of the annular epiphyseal ring. Scoliosis may be present. The skull, ribs and illiac bones are normal.

In multiple epiphyseal dysplasia tarda the radiological findings are again the reflection of faulty development of the epiphyses and are usually much milder. The femoral heads are somewhat flat and pseudoachondroplastic form. Later on findings of degenerative osteoarthritis develop in the hip joints. The other epiphyses of the long bones are somewhat small, shallow and irregular in outline. The knees and

ankles are more severely involved than the wrists and elbows. In the hands the phalanges and the metacarpals are short and their epiphyses are irregular. The vertebrae almost always show pathological changes: The vertebral plates are irregular. There is some tendency to flattening. The intervertebral spaces may be reduced and Schmorl's nodes may be present. Anterior and sometimes lateral wedging resulting in scoliosis are also observed.

When applied the above radiological criteria two of our three cases (Cases 1 and 3) were seen to be representative of the pseudoachondroplastic form of multiple epiphyseal dysplasia whereas the third child was apparently a case of multiple epiphyseal dysplasia tarda.

Although the familial aspects of this condition were not emphasized by Fairbank,[2] later reports strongly suggested the hereditary and familial nature of the disease. Weinberg, Frankel, Makin and Vas[18] reported the most extensive series in the literature. In their report 45 cases of multiple epiphyseal dysplasia in six generations of one family were presented. Genetically this family provides a typical example of simple dominant inheritance with an extensive pedigree.

Many laboratory examinations on patients with various forms of epiphyseal dysplasia have failed to reveal any constant abnormality.[5]

The only treatment is palliative orthopedic surgical correction for the various deformities.

Three diseases merit consideration in the differential diagnosis of multiple epiphyseal dysplasia : Spondylo - epiphyseal dyplasia (Morquio's disease), achondroplasia and Legg - Perthes disease. The loss of vertebral height which may be observed in epiphyseal dysplasia involves only the anterior or the lateral portion of vertebrae and wedging results but true platyspondylia (uniform loss of vertebral height) is absent. In Morquio's Disease platyspondylia is always present.

In the pseudoachondroplastic form of the disease there is some flaring of the metaphyses but the shortness and thickness of the long bones are never as striking as in achondroplasia. The characteristic cranial and pelvic changes of achondroplasia are also absent. We have pointed out that the changes in the hip joints in this form may resemble Legg - Perthes disease. These changes in the femoral head have a dynamic nature on serial films in Legg - Perthes disease (Fragmentation - repair - deformity), whereas in the entity under discussion they are more or less static. In addition, the normal appearance of the other epiphyses in Legg - Perthes disease helps us in establishing the correct diagnosis.

Summary

Three cases of multiple epiphyseal dysplasia are presented. Two of them show marked fragmentation and deformity of the capital femoral epiphyses in addition to the other findings and thereby qualify to be classified as representing the pseudoachondroplastic form of this disease. The third patient with the tarda form of this dysplasia presents milder changes in the epiphyses, and displays characteristic findings in the vertebrae.

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