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Kniest Dysplasia: New Radiographic Features in the Skeleton

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Objective: To describe skeletal findings in patients with Kniest dysplasia, focusing on osseous abnormalities that have not been characteristically associated with this disorder.
Materials and Methods: This was a retrospective study. The radiographs of four patients with known Kniest dysplasia were evaluated by three musculoskeletal radiologists.
Results: Bilateral radial head dislocations and bilateral clubfeet were seen in our series. Other characteristic findings for this dysplasia were seen in all four patients.
Conclusions: Clubfeet and radial head dislocations may be associated with Kniest dysplasia. The presence of these osseous findings in the context of multiple skeletal abnormalities suggestive of a skeletal dysplasia should indicate the possibility of Kniest dysplasia and pathognomonic features for this entity should be sought.

Introduction

Kniest dysplasia is a skeletal dysplasia with disproportionate short stature. The classically described and clinically recognized phenotype is the result of severely affected skeletal growth, with associated features of retinal detachment and deafness (1-6). The key radiographic manifestations include splaying of the long bone metaphyses with irregular punctate epiphyses and fluffiness and irregularity of growth plates; loss of normal trabecular bone pattern; flattening and squaring-off of the epiphyses of tubular bones of the hands, narrowing of joint spaces, trefoil-shaped pelvis, marked coxa vara, and platyspondyly (1-6). With growth, the long bones assume a dumbbell morphology (1,6). The histologic features in Kniest dysplasia correlate with abnormal cartilage growth, including disorganized growth plates, soft crumbly cartilage with a "Swiss-cheese" appearance, and diastase resistant intracytoplasmic inclusions in the resting chondrocytes (7). Scanning electron microscopy can demonstrate fragmentation and disintegration of collagen fibrils resulting in a web-like pattern and large open cyst-like spaces, and deficiency and disorganization of the collagen fibrils (7). At the molecular level, there is a specific amino acid deletion at the c-terminus of the type II collagen helix that disrupt the normal triple helix configuration; this deletion may result from any of several mutations in the type II collagen gene (COL2A1) (8-11). These mutations are expressed in the heterozygous state and although most cases are probably sporadic (12), although autosomal dominant transmission is known.

Kniest dysplasia has generally been classified as a type of chondrodysplasia, and because of its molecular basis, it may also be considered to be a form of collagenopathy, or more specifically, a type II collagenopathy. Besides Kniest dysplasia, other clinical entities caused by mutations in the COL2A1 gene resulting in type II collagenopathy include achondrogenesis II, hypochondrogenesis, spondyloepiphys-

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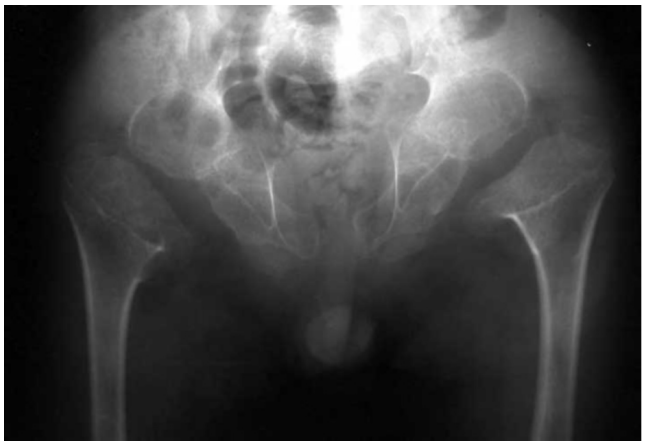

Figure 1A. Kniest dysplasia, Case 1. AP radiograph of the pelvis demonstrates absence of the capital femoral epiphyses, broadening of the metaphyses, widening of the symphysis pubis, and a narrow pelvis. While the capital femoral epiphyses are not seen, they are in actuality enlarged, but ossify late.

eal dysplasia congenita, Stickler arthroophthalmopathy and mild dominant spondyloarthropathy (12). This group of collagenopathies shares clinical and radiological manifestations that may be expressed as a continuous spectrum of phenotypes, ranging from perinatally lethal to very mild conditions. Biochemical studies of cartilage collagens and morphological analysis of cartilage sections suggest that the abnormalities of type II collagen structure and biosynthesis are the main pathogenetic factors in the phenotypic features of these conditions (13). Because of the wide range of clinical manifestations of type II collagenopathies and the potential that the characterization of the basic molecular defect might lead to specific genotype-phenotype correlations, we hypothesized that it would be worthwhile re-examining the range of skeletal abnormalities in Kniest dysplasia. We describe the radiographic features in four patients with Kniest dysplasia, focusing on osseous abnormalities that have not that have not been characteristically associated with this condition.

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Case 1: This newborn male presented with bilateral clubfeet that were treated with serial casting. Clinically, the patient demonstrated disproportionate short stature, hearing loss, visual impairment, and scoliosis. The diagnosis of Kniest dysplasia in this case was established by clinical and radiographic criteria. Radiographs obtained at birth showed typical absence of the capital femoral epiphyses with widening of the symphysis (Figure1). The long bones were dumbbell-shaped and the spine demonstrated a mild platyspondyly.

Case 2: As a newborn, this male presented with bilateral clubfeet and was treated with serial casting. The patient clinically demonstrated cleft palate, depressed nasal bridge,

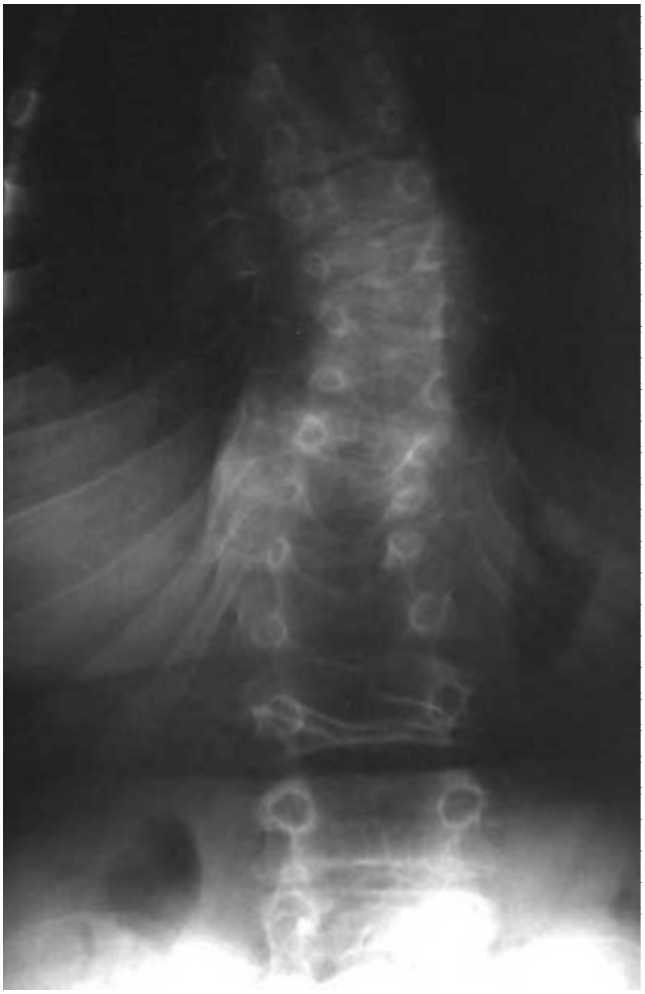

Figure 1B. Kniest dysplasia, Case 1. Frontal radiograph of the spine demonstrates mild platyspondyly and a scoliosis.

disproportionate short stature, and progressive deafness. The diagnosis of Kniest dysplasia in this case was established by clinical and radiographic criteria. Radiographic evaluation at 12 years of age demonstrated a spinal scoliosis and mild platyspondyly (Figure 2). Radiographs of the feet demonstrated persistent bilateral clubfoot deformities. Hazy calcifications adjacent to the metaphyses characteristic for Kniest dysplasia were seen. Flattening of the metatarsal epiphyses, also classic for this rare entity, were demonstrated. A frontal projection of the pelvis showed small capital femoral epiphyses with bilateral dislocations and a widened symphysis.

Case 3: As a newborn, this male showed hypoplasia of the pubic bones with a "dessert cup" shape to the pelvis, and absence of the capital femoral epiphysis (Figure 3). The pelvis resembled that seen in Morquio's dysplasia; however the latter entity would not present with abnormal findings at birth. The diagnosis of Kniest dysplasia in this case was established by clinical and radiographic criteria. Radiographs obtained at two years of age demonstrated bilateral radial head dislocations and a flattened appear-

Figure 1C. Kniest dysplasia, Case 1. Lateral radiograph of the right foot shows increased calcific density near the distal tibial epiphysis and metaphysis, characteristic for this dysplasia. The talocalcaneal angle is decreased with parallelism, consistent with clubfoot.

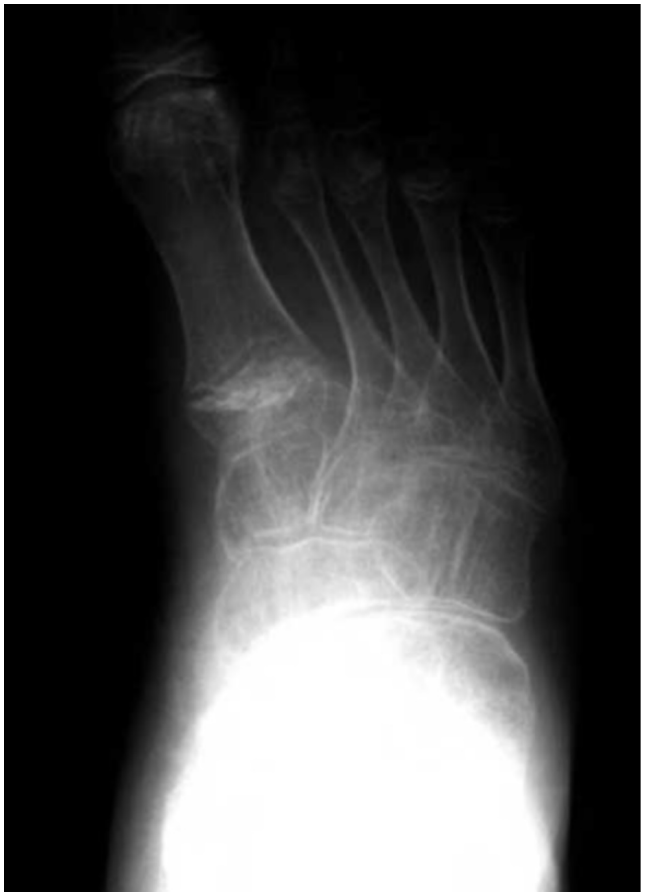

Figure 1D. Kniest dysplasia, Case 1. AP radiograph of the right foot demonstrates forefoot inversion. The metatarsal epiphyses have a flattened appearance.

ance of the metacarpal heads. Radiographs obtained at 14 years of age showed the flattened metacarpal heads and a progressively disorganized appearance to the carpal bones.

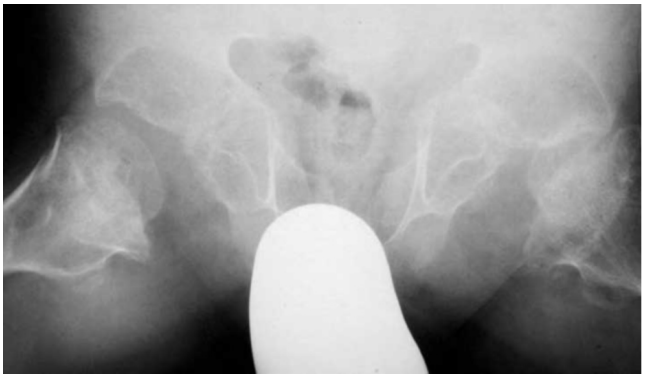

Figure 2. Kniest dysplasia, Case 2. AP radiograph of the pelvis demonstrates broad proximal femoral metaphyses with relatively small capital femoral epiphyses and bilateral hip dislocation. The pelvis has a configuration similar to that seen in Case 1.

Case 4: This 5-year-old female with a known diagnosis of Kniest dysplasia had clinically demonstrated disproportionate short stature, joint contractures, and typical facies with saddle nose and moon-shaped face. The diagnosis of Kniest dysplasia in this case was established by clinical and radiographic criteria. Hand radiographs demonstrated characteristic flattening of the metacarpal heads (Figure 4). The pelvis and spine in this patient also showed changes compatible with Kniest dysplasia. The femurs demonstrated a classic dumbbell configuration.

Discussion

Kniest dysplasia, also called metatrophic dwarfism type 2, pseudometatrophic dysplasia, and Swiss-cheese cartilage dysplasia, is a rare entity that demonstrates one or more the following clinical manifestations: flat facies, low nasal bridge, cataracts, deafness, and disproportionate short stature (1-6). Skeletal dysplasias can often be similar in clinical and radiologic appearance, however certain findings may assist in discriminating between the many forms of dysplasia. There is a specific biochemical abnormality in Kniest dysplasia, but clinical and radiographic evaluation are usually sufficient in arriving at the diagnosis (12). This entity, first described in 1952 by Kniest (2-3), consists of a type of chondrodystrophy that can be discriminated radiographically from similar entities like spondyloepiphyseal dysplasia and metatropic dysplasia, by what has been described as cloud-like calcifications adjacent to the metaphyses and vertebral body epiphyses (1,4-6). Classic metatropic dysplasia can be distinguished clinically from Kniest dysplasia because the former demonstrates normal facies and a narrow thorax, features absent from Kniest dysplasia. In addition, metatropic dysplasia demonstrates short ribs that are not seen with Kniest dysplasia. Platyspondyly is less severe in the Kniest dysplasia than spondyloepiphyseal dysplasia and metatropic dysplasia. Dumbbell-shaped femurs are not

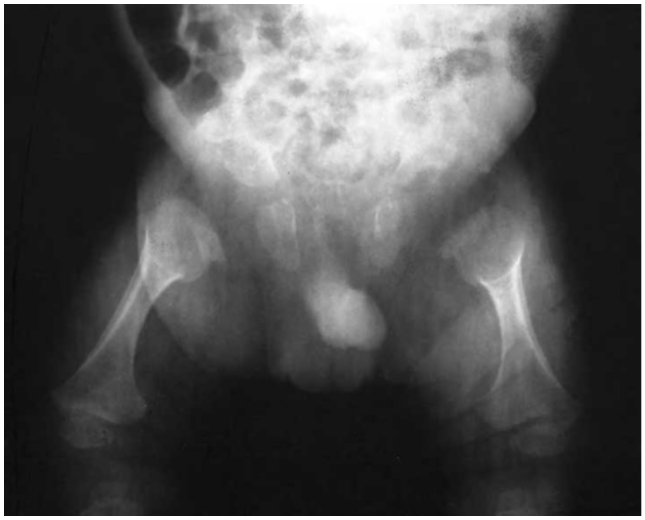

Figure 3A. Kniest dysplasia, Case 3. AP radiograph of the pelvis demonstrates dumbell shaped femurs, absence of ossified capital epiphyses, and widening of the symphysis.

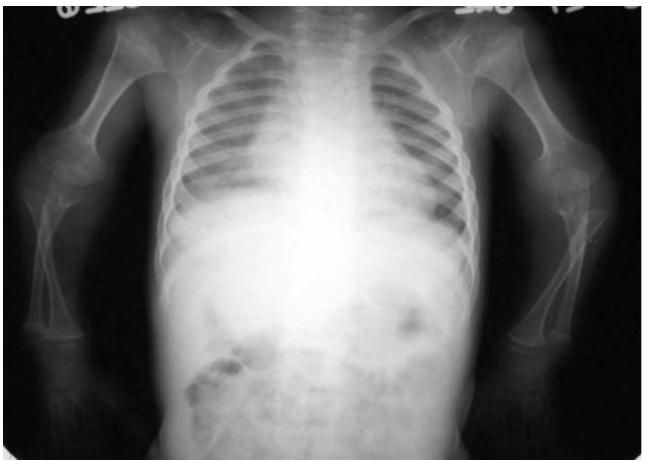

Figure 3B. Kniest dysplasia, Case 3. AP radiograph of the chest and arms demonstrates bilateral radial head dislocations. The radial head is deformed. This in conjunction with the bilaterality suggests a congenital process. Note the flattened appearance of the metacarpal epiphyses and the dumbell shaped humeri.

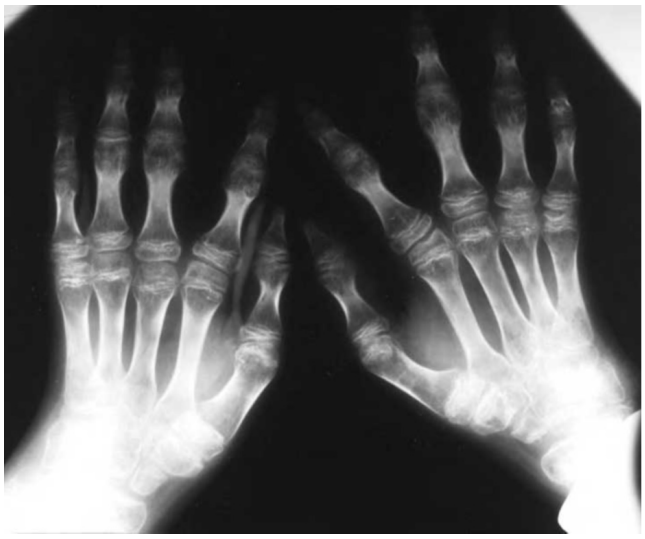

Figure 3C. Kniest dysplasia, Case 3. PA radiograph of the hands at the age of 14 years demonstrates the dramatic flattening of the metacarpal epiphyses, to the point where they appear concave in some areas. The carpus has a disorganized appearance.

a feature of spondyloepiphyseal dysplasia and may also serve to discriminate Kniest dysplasia from other forms of dysplasia. While Morquio's dysplasia in older children may bear a superficial resemblance to this Kniest dysplasia, it does not demonstrate these abnormalities at birth. Characteristic features in the hands have also been described in Kniest dysplasia, with broad ends of the bones at both poles, flattened metacarpal epiphyses, osteoporosis, and a truncation of the tuft of the first digit. Carpal centers may also appear deformed after the age of three years. However, perhaps the most highly recognized radiographic finding of this entity is the early radiographic absence of the capital femoral epiphyses. In actuality, this represents delayed ossification, the cartilaginous epiphyses may be quite large and have been dubbed "megaepiphyses" (14). They can be demonstrated by non-radiographic methods such as MR imaging (14). Narrowing of the interpedicular distance has been described in the lumbar spine, which we did not see, similar to achondroplasia (6).

Findings we observed that have not been characteristically associated with Kniest dysplasia include bilateral radial head dislocations and bilateral clubfoot deformities. The bilateral radial head dislocations demonstrated features that are typically associated with congenital posterior dislocations, where the radial head appears thinned and dome shaped with no central depression, the ulna is shortened, and the capitellum is underdeveloped (15-16). The bilaterality of these findings also suggests that they are congenital rather than acquired. Posterior congenital dislocations are more commonly associated with congenital syndromes than anterior dislocations (15-16), including nail-patella syndrome, Klippel-Feil syndrome, Silver's syndrome, Cornelia de Lange syndrome, Klinefelter's syndrome, and Larsen's syndrome. Clubfoot deformities have been associated with numerous congenital syndromes including diastrophic dysplasia, nail-patella syndrome, congenital amniotic bands, radial or ulnar ray defects, congenital radioulnar synostoses, muscular dystrophies, trisomy 13 and other chromosomal syndromes, Freeman-Sheldon syndrome, and Larsen's syndrome (17). The combination of clubfeet and radial head dislocations has been described in Larsen's syndrome and nail-patella syndrome, conditions that are easily distinguishable from Kniest dysplasia. Certain neuromuscular disorders, such as arthrogryposis, may also show this combination of findings. Flexion deformities of the joints have been noted in the Kniest dysplasia and we postulate

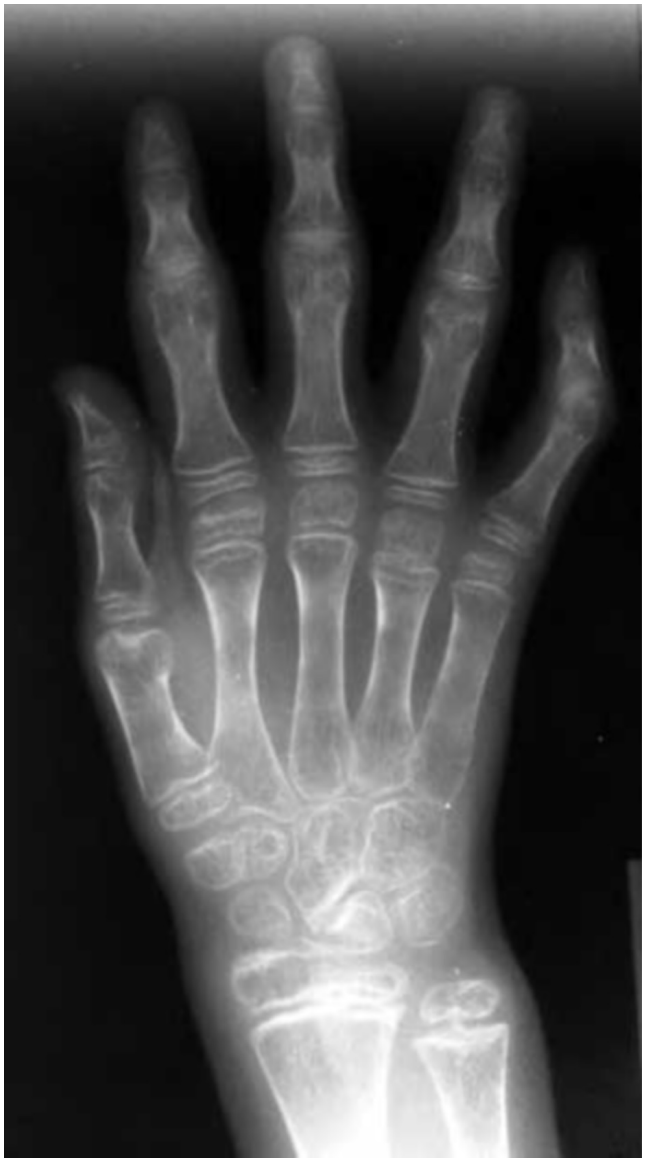

Figure 4. Kniest dysplasia, Case 4. PA radiograph of the right hand at the age of 5 years demonstrates similar findings to Case 3; however, the carpus has a more organized appearance, because, with age, the carpal centers have become progressively more disorganized in size and shape.

that the bilateral clubfoot deformities and the bilateral radial head dislocations may occur on the basis of muscular imbalance and contracture deformities, similar to clubfoot deformity and dislocations seen in arthrogryposis. Coincidental occurrence of idiopathic congenital clubfoot in these cases of Kniest dysplasia seems unlikely, but cannot be entirely excluded as a possibility (18).

In summary, bilateral clubfoot deformities and bilateral radial head dislocations are described in patients with Kniest dysplasia, findings not characteristically associated with this rare entity. The ultimate diagnosis of Kniest dysplasia rests on the presence of pathognomonic skeletal manifestations in the hands, spine, long bones, and pelvis, or in laboratory demonstration of specific molecular abnormalities.

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