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CASE REPORT

Selective rickets from localized advanced maturation—a case report

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Abstract
An unusual cause of rickets is illustrated by a patient with infantile multisystem inflammatory disease who, by age 2 years and 4 months, developed striking radiographic and clinical rickets restricted to those joints involved by the inflammatory process. The locally increased vascularity from his inflammation led to increased maturation at those sites so rapid as to override the usual enchondral calcification, thus causing a rickets pattern. Other sites, such as the proximal humeri, lacking any inflammation, showed no increased maturation rate and did not manifest local rickets. Rapid local bone maturation may cause localized rickets.

Keywords Rickets · Advanced bone age · CINCA syndrome · Prieur–Griscelli syndrome

Introduction

The well-known causes of rickets are nutritional vitamin D deficiency as well as vitamin D-derivative deficiency from liver disease or renal disease. I report a case that suggests that locally accelerated growth (and maturation), a less well known and perhaps previously unreported cause, may also lead to rickets. Advanced growth was, for example, not listed as a cause of rickets in a recent comprehensive review article on metabolic bone disease [1]. Local rapid growth may be the result of localized long-term hypervascularity. Presumably, the needs of enchondral bone growth are no longer met by the usual calcium and phosphorus in the body when skeletal growth is markedly accelerated.

We demonstrate a case in which localized markedly advanced skeletal maturation growth developed radiographic rickets limited to those sites.

Case report

The patient was a 2-year, 4-month-old male with non-consanguineous parents. He had clinical symptoms of inflammation including an evanescent erythematous maculopapular rash (seen at birth) and swollen joints with soft tissue thickening, tenderness, heat, and flexion contractures that persisted [2]. He was diagnosed with infantile-onset multisystem inflammatory disease (also known as Prieur–Griscelli syndrome and as CINCA [chronic infantile neurological cutaneous articular] syndrome). The child, reported elsewhere in another context [2, 3], had been initially radiographed at age 1 year 3 months. At that time, the patella had already begun to ossify (Fig. 1a); radiologically visible ossification of that bone usually does not occur in boys before the 4th year of life. The growth centers for distal femur and proximal tibia showed a bone age, measured by the standards of Pyle and Hoerr [4], of not more mature than 11 months, and showed normal zones of provisional calcification at metaphyses of those bones, indicating rickets was not then present at those centers (Fig. 1a). At age 2 years and 4 months, the lateral knee image (Fig. 1b) showed irregular ossification around the patella, distal femur, and proximal tibia growth centers, with absence of ossification of zones of provisional calcifications at those sites, typical for radiographic rickets. These sites had shown rapid interval growth. Within the rachitic new ossification of the femur and tibia, the previously shown growth centers seen in Fig. 1a are still visible. There were similar findings on a frontal radiograph at 2 years and 11 months (Fig. 1c), which now showed considerable periosteal reaction along the distal femur diametaphysis (either from microfractures of cortex thinned from limited physical activity or more likely from the inflammation itself). Several other inflammatory sites at joints, including distal radius and ulna, similarly showed rachitic

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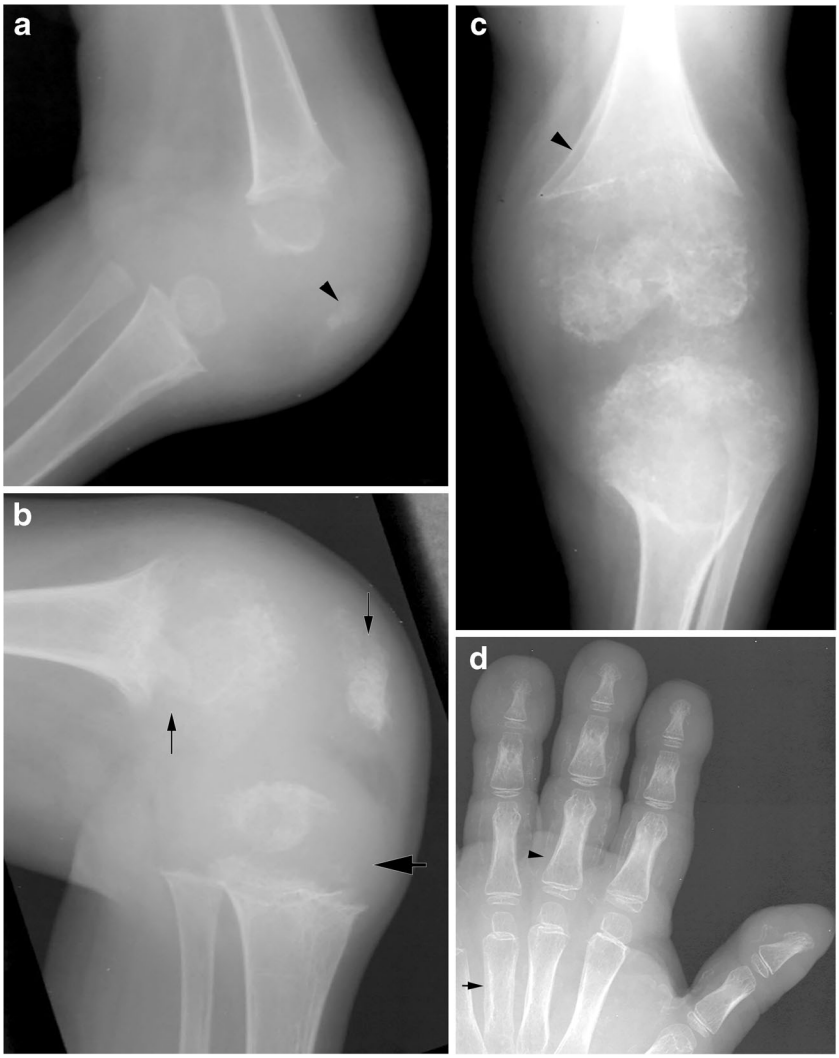

Fig. 1 **a** One-year, 3-month-old boy with IOMID/CINCA including inflammation in the region of the knees. The patella (*arrowhead*) is ossified early. No radiographic changes of rickets are currently seen. From [3] with permission. **b** The same child at age 2 years and 4 months. Considerably rapid interval maturation. Rickets is strongly evident including loss of zones of provisional calcification, widened soft tissue space between epiphyses and metaphyses, and irregular margins of the metaphyses. All interval ossification of femur, tibia, and patella growth centers are rachitic, with spotty irregularity throughout (*arrowheads*). From [3] with permission. **c** The same child at 2 years and 11 months continues to show rickets and now shows considerable periosteal reaction (*arrowhead*) along distal femur diametaphysis, either due to the inflammation of his IOMID/CINCA or possibly from microfractures due to thin cortices from lack of normal physical activity. From [3] with permission. **d** The same subject at 20 years of age. Left hand. Osteoporosis, but no evidence of rickets or previous rickets. Greatly delayed bone age of about 8 years presumably reflects the lifelong severe illness. Incidental periosteal reaction (*arrow*) along at least two metacarpals. The right hand had a similar appearance. The lack of increased vascularity or maturation during childhood at these and other sites (such as the shoulders) meant that rickets had not appeared there. Other observations: puffy soft tissues and considerable calcification of blood vessels (*arrowhead*)

changes, while other sites, including proximal humerus and hand phalanges, showed no evidence of rickets (Fig. 1d). At age four and a half years, his laboratory values for parathyroid hormone, 25-hydroxyvitamin D, and 1,25-dihydroxyvitamin D were normal [2]; moreover, at ages 2 and 6 years, typical biochemical abnormalities characteristic of rickets were absent [3]. Absence of rickets on the earliest radiographs mitigates against nutritional, hepatic, or renal causes of rickets (and also against osteopetrosis). He lived only in the Cincinnati, Ohio area. He died at age 22 years.

Discussion

The many radiologic manifestations of rickets are extensively known and have been recently reviewed [5]. Each is a result of a lack of ossification of cartilage participating in enchondral growth of the growing child. Thus, zones of provision calcification remain uncalcified, associated with buildup of uncalcified growth cartilage, leading to increased distance between ossified growth epiphyses and ossified metaphyses, as well as to apparent slowed bone age because of a lack of ossification

around secondary growth centers. In general, membranous bone growth is not affected.

At local sites, increased vascularity yields increased bone growth/maturation in childhood, including vascularity from inflammatory disease such as arthritis, vascular tumors, and some vascular malformations. In our case, inflamed joints showed findings of rickets, while sites including each proximal humerus and finger phalanges did not participate in the inflammatory disease, so were spared the rickets accompanying the excessive growth/maturation.

The lack in our patient of biochemical abnormalities seen in rickets or associated hyperparathyroidism supports the impression that the rachitic changes were localized rather than systemic.

It is interesting that the *increased* growth from high vascularity might lead to *decreased* enchondral calcification at physes and their equivalents, but such seems be the case, with the explanation apparently being inadequacy of the available calcium and phosphate for matrix vesicles involved in the usual ossification of the zones of provisional ossification [6].

Advanced bone maturation/growth as a cause of rickets may have been previously unreported and so can be added to the list of reasons for development of rickets, including, as in our case, selectively involving only certain joints.

Compliance with ethical standards

Conflict of interest The author declares that he has no conflicts of interest.

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