Normal Variants, Congenital and Acquired Disorders

7

7.1 Introduction

Although in the differential diagnosis of fractures sustained in childhood one should be particularly aware of accidental trauma, it was found that congenital and acquired defects regularly give rise to suspicions of child abuse (see Table 7.1). Based on a combination of patient history, laboratory tests and radiological examination, it is usually possible to reach the correct diagnosis. In this chapter we discuss the most important disorders of which the radiological images could fit the criteria for child abuse.

7.2 Normal Variants

When evaluating radiographs of children, there are a number of normal variants that may cause confusion, and even lead to a false accusation of child abuse. At a very young age, subperiosteal new-bone formation around the shaft of the femur, tibia and humerus may be seen in normal, healthy neonates and infants (Fig. 7.1). This newly formed bone, which may radiologically be mistaken for a healing fracture, is most prominently present in children from 1 to 6 months old. Subperiosteal newly formed bone is usually seen bilaterally [1]; however, it may be more prominently present unilaterally [2]. Generally, the most distinct signs will disappear around the age of 8 months [3]. In physiological, subperiosteal newly formed bone, there is no obvious uptake of isotopes in a bone scan [4].

Neither should normal metaphyseal variants be mistaken for child abuse. This category comprises thickened edges of the metaphyses (collar, step off) exactly where the epiphyseal plate is attached (Fig. 7.2a–c). This collar is usually present in the proximal tibia, proximal fibula, distal femur, distal radius and distal ulna, and is regularly seen bilaterally [5]. In young children pointed metaphyseal 'spurs' can also be found, which to the untrained eye of a radiologist may look very similar to CMLs. This spur is made of cortical bone that grows under the perichondrial ring of the epiphyseal plate. Spurs may be seen in the distal femur (Figs. 7.1 and 7.2b), the lateral aspect of the distal radius, the medial aspect of the distal ulna and the metacarpals (Fig. 7.3) and metatarsals. In 25% of cases this image is seen bilaterally. Finally, the metaphysis may show medial widening, especially in the proximal tibia and the humerus (Fig. 7.4).

In 4% of children a cortical irregularity is seen on the medial side of the proximal tibia. In 25% of these children this is present in both legs [5]. This irregularity may look like a healing fracture and consequently lead to an incorrect diagnosis.

One of the most important properties of the childhood skeleton is growth. Besides the normal growth centers, accessory centers may be seen (Fig. 7.5a and b) [6], which may be interpreted erroneously as fractures, and as such lead to confusion. The sutures of the skull, where normal variants may be found (Fig. 7.6), may also lead to an erroneous diagnosis of skull fracture [7].

7.3 Osteogenesis Imperfecta

7.3.1 Introduction

Together with child abuse osteogenesis imperfecta (OI) is the most common cause for the presence of multiple fractures, often at various stages of healing,

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Table 7.1 Differential diagnosis in disease-related fractures in infancy and childhood [162, 165, 166]

Fractures	
Disorders related to collagen production	Osteogenesis imperfecta Copper deficiency Menkes syndrome Bruck syndrome
Congenital mineralisation disorders	Prematurity: metabolic bone disease of prematurity Neuromuscular disorders Vitamin-D-resistant rickets (or hypophosphatemic rickets) X-linked hypophosphatemia Liver abnormalities, such as Alagille syndrome Malabsorption Familiar osteoporosis Osteopetrosis Cole Carpenter syndrome Congenital CMV infection
Acquired mineralisation disorders	Vitamin-D-deficiency based on malnutrition: rickets Use of diuretics, glucocorticoids and methotrexate Intoxications, such as lead Cerebral paresis and spasticity
Other increased-risk disorders	Congenital pain insensitivity disorders: • Spina bifida • Congenital pain insensitivity Muscular dystrophy
Periosteal reactions	
Radiological differential diagnosis in the absence of fractures	Normal variants: • Such as: physiological thickening of the long bones (femur, tibia, humerus) in neonates and infants Congenital syphilis Osteomyelitis Septic arthritis Osteoid osteoma and other tumours Leukaemia Vitamin-C deficiency: scurvy Caffey's disease: infantile cortical hyperostosis Hurler disease: mucopolysaccharidosis type I Sickle-cell anaemia Vitamin use-related disorders • hypervitaminosis A • vitamin-E therapy Prostaglandin-E treatment Metastases of a neuroblastoma The use of intra-osseous vascular access needles

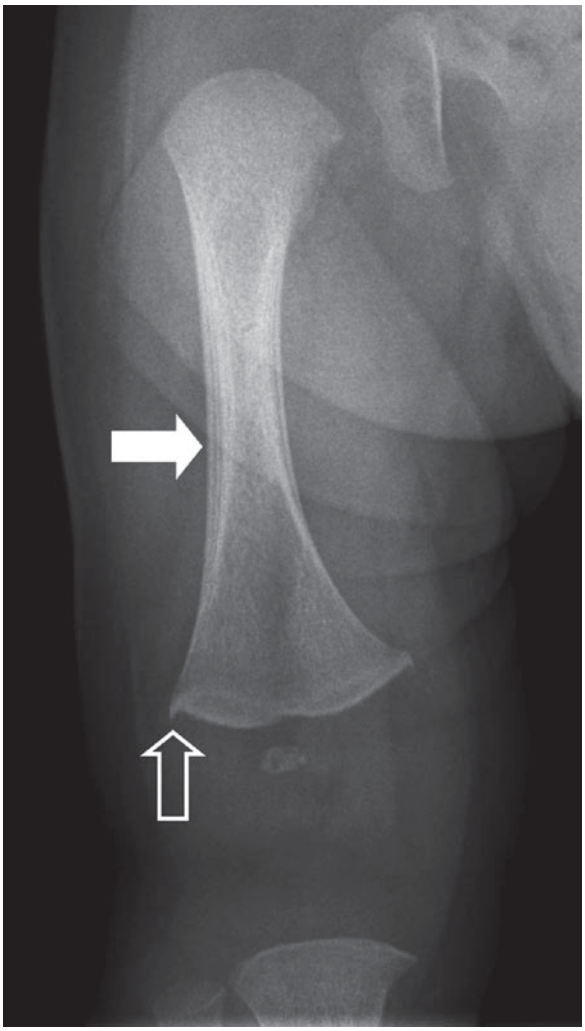


Fig. 7.1 Femur of a neonate, showing physiological subperiosteal new-bone formation (*arrow*) and metaphyseal spur (*open arrow*)

and without a plausible explanation (Fig. 7.7a and b). Hereby one should be well aware that OI is considerably less prevalent than child abuse.

7.3.2 Clinical Presentation

In OI there is a defect in the synthesis of type I collagen production. Type I collagen is an important protein in the extracellular matrix of many tissues. The disease is equally distributed between boys and girls, and is often seen in other family members, although spontaneous mutations do occur.

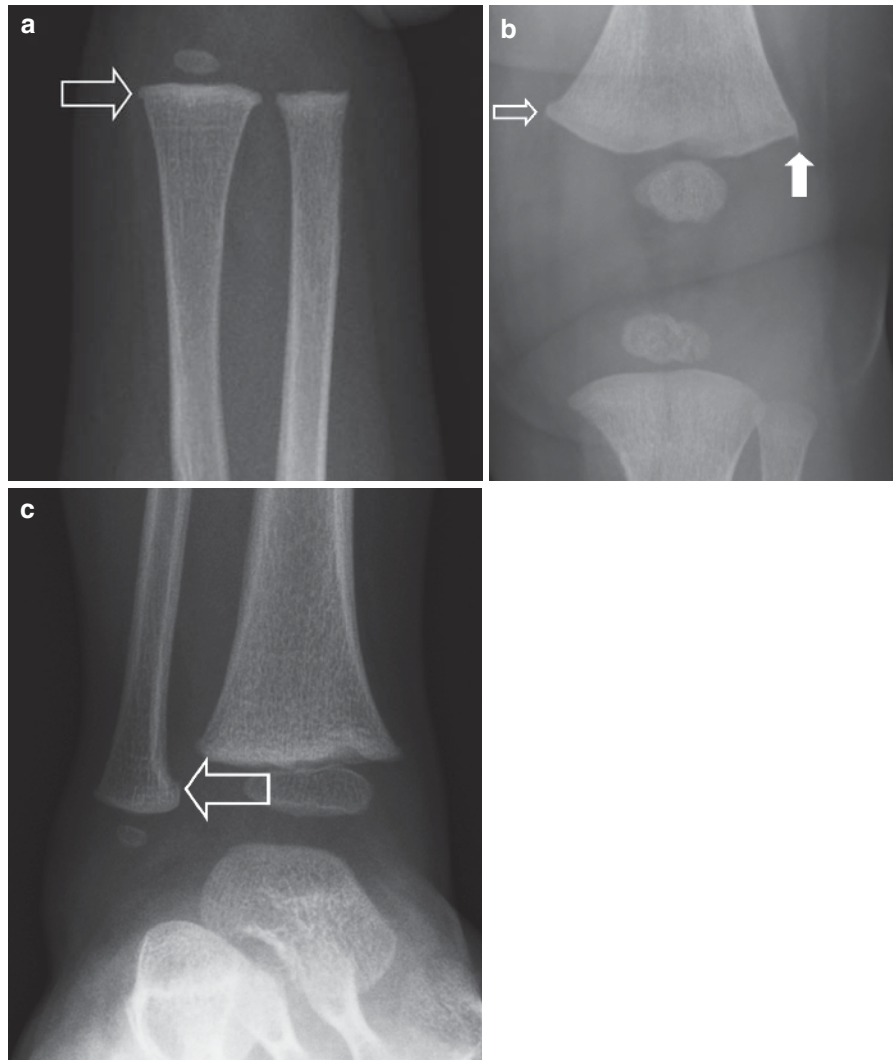


Fig. 7.2 (**a**) Physiological metaphyseal collar in the distal radius (*open arrow*). (**b**) Physiological metaphyseal collar (*open arrow*) and metaphyseal spur (*arrow*) in the distal femur metaphysis. (**c**) Physiological metaphyseal collar (*open arrow*) at the medial side of the istal fibula

In the bones, a defect in the synthesis of type I collagen will lead to osteoporosis, which makes it possible for minimal trauma to cause multiple fractures (Fig. 7.8a–c). The protein is also present in ligaments, teeth, sclera and blood vessels. Consequently, the symptoms can occur to a higher or lesser degree in all these systems. Besides the defect in the synthesis of collagen type I, two more mutations have been reported; a mutation of the CRTAP gene, which causes a mild to severe recessive rhizomal form of OI [8]. Furthermore, mutations have been reported in CRTAP together with LEPRE1, which leads to an autosomal recessive form of OI [9, 10].

Sillence et al. provide a classification in four subtypes (see Table 7.2a) [11], based on the age at which the fractures occur, other physical symptoms and the way it is inherited. The incidence figures provided are based on research in Australian children. In 2004, Rauch and Glorieux published an overview in the Lancet in which they widened the Sillence classification to seven subtypes (see Table 7.2b) [12].

In 85% of children that have OI, fractures will heal at the same speed and in the same manner as in children without OI [13]. Children with OI types I and II (80% of all patients) usually present no diagnostic problem (Figs. 7.9a and b, 7.10a and b).

Young children without OI may also have blue sclerae [14]. Consequently, in abused children there may be the erroneous impression that they have pathological bone fragility that fits OI. The presence of

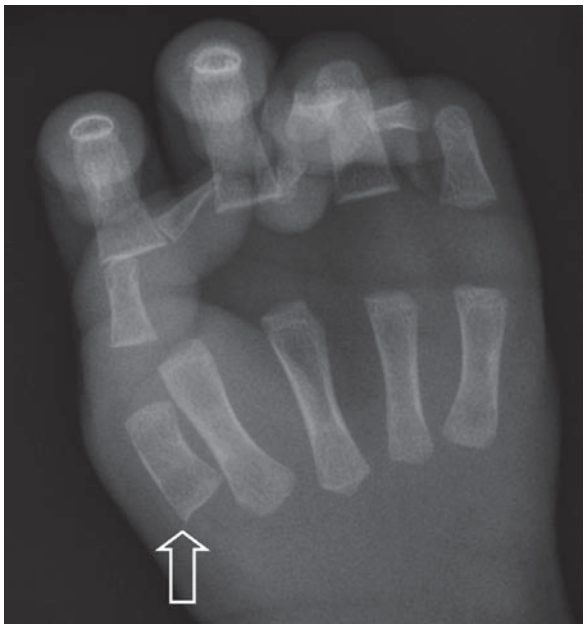


Fig. 7.3 Metaphyseal spur on the base of metacarpal 1 of the right hand (*open arrow*)

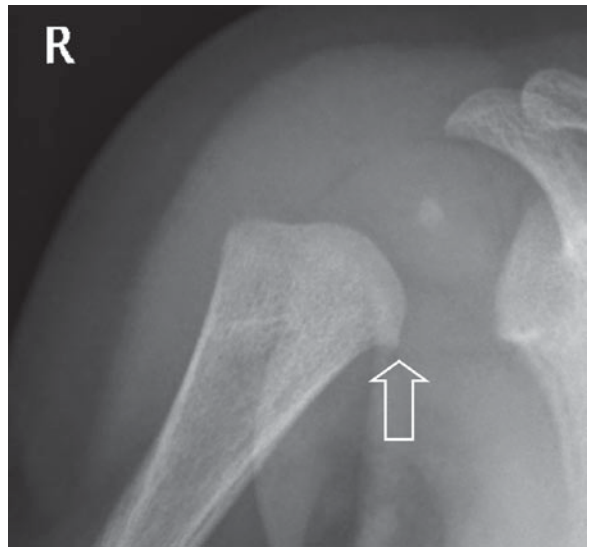


Fig. 7.4 Medial extension of the proximal metaphysis of the humerus (*open arrow*)

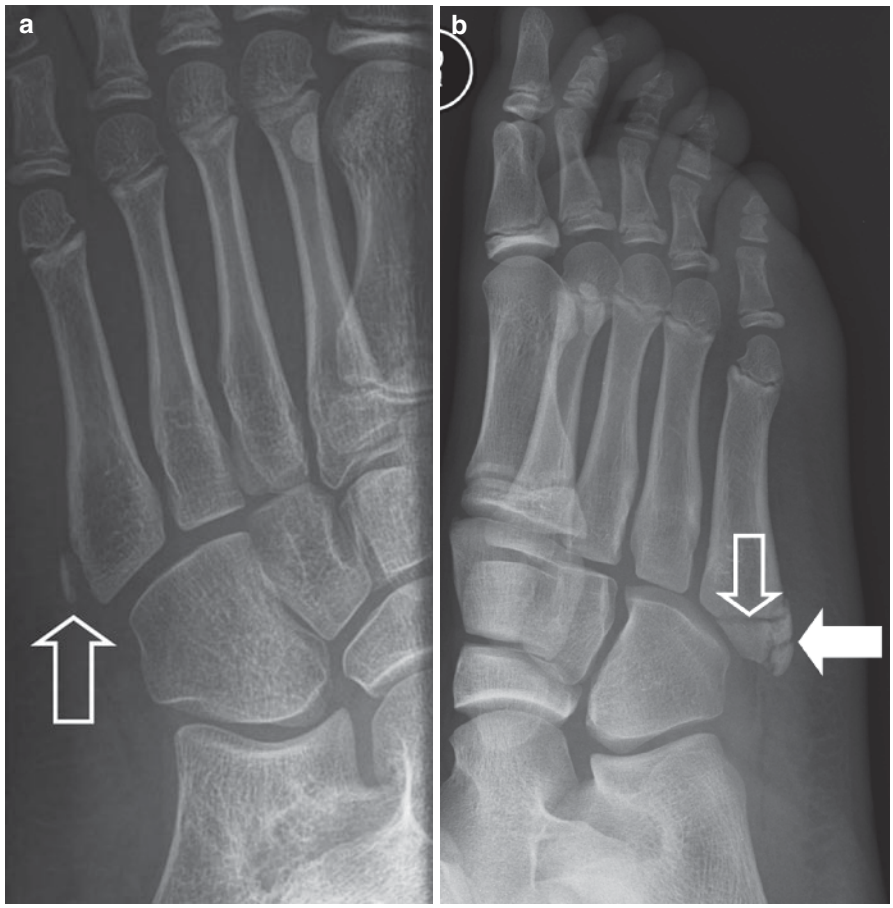


Fig. 7.5 (**a**) Accessory ossicle at the base of metatarsal 5 (*open arrow*). When one is not familiar with this phenomenon, it may be mistaken for an avulsion fracture. (**b**) Accessory ossicle at the base of metatarsal 5 (*arrow*). There is also a 'Jones fracture' visible at the base of metatarsal 5 (*open arrow*)

aberrant teeth (dentogenesis imperfecta) may either support or confirm the suspected OI. Rib fractures are frequently seen in all types, as is bowing of the lower extremities. Metaphyseal corner fractures may also be seen in children with OI [13, 15]. Astley described metaphyseal corner fractures in seven children of a group of 41 children with OI [15]. He deems it impossible that one could erroneously suspect abuse in these children, because of the other noticeable signs fitting OI. On the other hand, Albin et al. are convinced that the presence of metaphyseal defects is pathognomic for child abuse, and that for this reason it is possible to differentiate between osteogenesis imperfecta and child abuse [16].

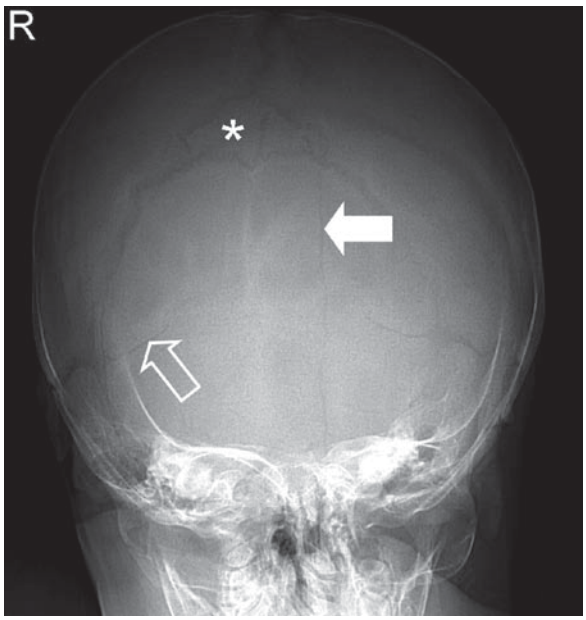


Fig. 7.6 Skull view showing multiple normal variants: suture mendosa (*open arrow*) and os inca (asterisk). There is also a sutura metopica visible (*arrow*)

7.3.3 Additional Examinations

To experienced radiologists, the diagnosis OI will generally, in view of its characteristic lesions, not present many problems. When OI is suspected, radiological examination is essential. In prenatal ultrasound it is also possible to find characteristic defects, in those cases it often concerns type II.

In atypical cases, the biochemical analysis of the synthesis and structure of collagen may be used [17]. In order to differentiate with child abuse, a skin biopsy for the purpose of a fibroblast culture is not indicated. Steiner et al. concluded that based on clinical and radiological data, OI can be diagnosed in nearly all children. According to Steiner et al., biochemical

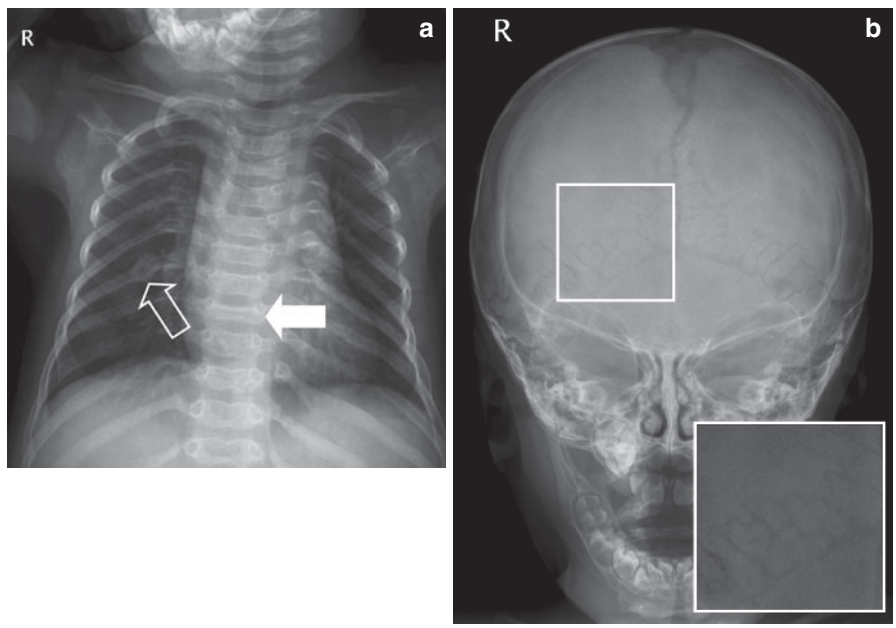


Fig. 7.7 (**a**) One-year-old boy who presented with a femur fracture after falling of the counter, in the presence of multiple witnesses. The chest radiograph shows old rib fractures (*open arrows*) and multiple collapsed vertebrae (*arrow*). (**b**) Skull view of the same patient shows multiple wormian bones (see inset). Osteogenesis perfecta was genetically

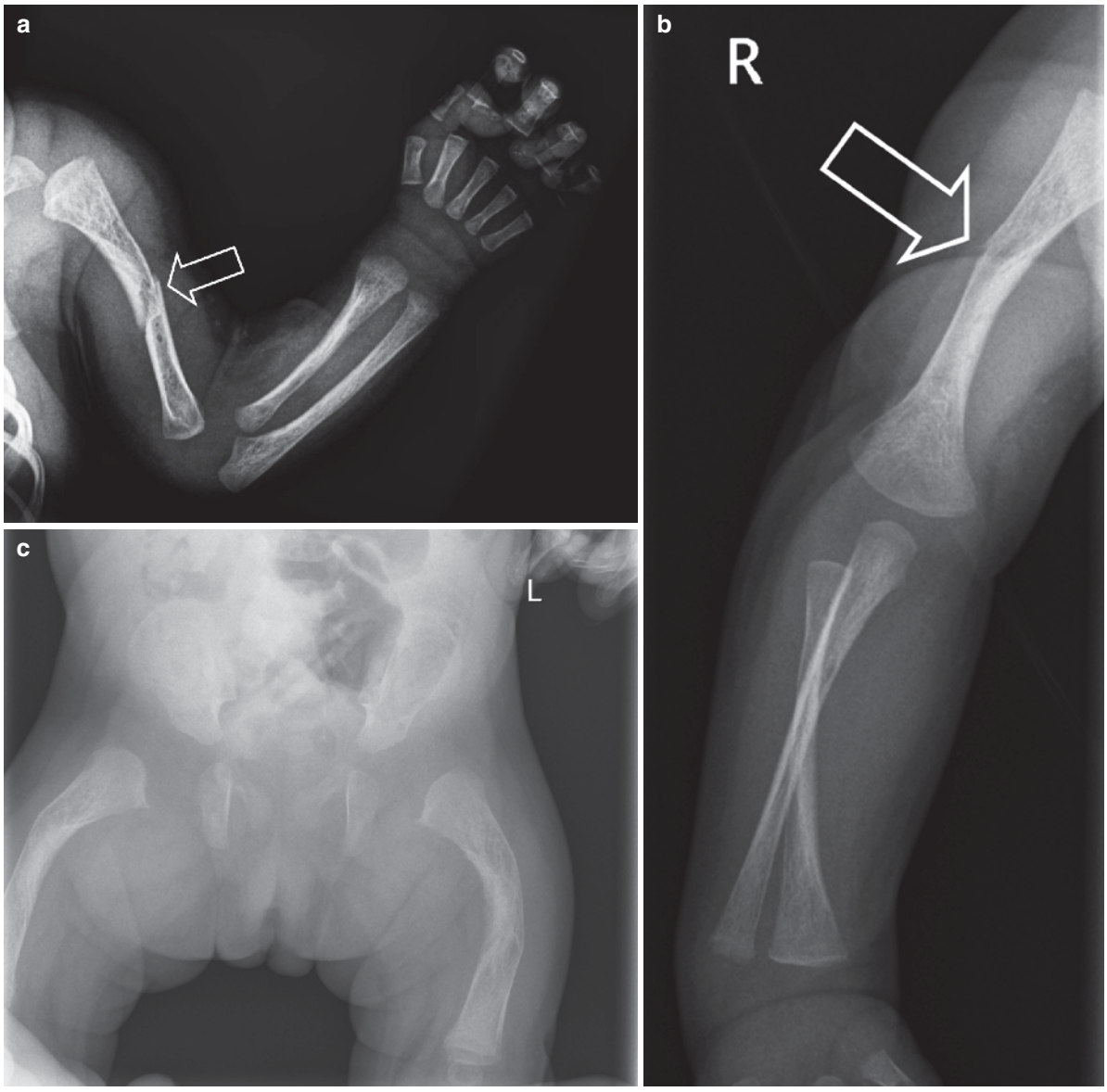


Fig. 7.8 (**a**) One-week-old girl with swollen painful left arm. Radiograph shows a fresh mid-shaft oblique humerus fracture (*open arrow*). An additional skeletal survey was made. (**b**) The right arm also shows a mid-shaft fracture of the humerus (*open arrow*), which is difficult to date. (**c**) Pelvic view shows bilateral bowing of the femurs and sclerosis, an image corresponding with healing fractures. Osteogenesis imperfect was genetically

collagen analysis should be restricted to the very rare situation in which there is continued diagnostic doubt regarding child abuse [18].

In his book 'Diagnostic Imaging of Child Abuse', Kleinman presents an scheme that may support a clinician who is confronted with a child with fractures, and the question arises whether the child has OI (Table 7.3) [19].

7.3.4 Osteogenesis Imperfecta and Child Abuse

In most cases, the differential diagnosis between OI and child abuse is based on (family) history, physical examination and radiological imaging. In most cases it concerns children with type I. The blue sclerae, the skull

Table 7.2 (**a**) Categorisation of osteogenesis imperfecta according to Sillence et al. [11]

Type	Severity	Clinical findings
I	Mild non-deforming	1:28,500 Autosomal dominant inherited – positive familial anamnesis Usually fractures occur at the age of infant/toddler. As soon as the child reaches puberty, the risk for fractures generally decreases. Radiological examination of the long bones may show normal density. Wormian bones are often absent [151]. However, radiologically the bones show characteristics of osteopenia with increases trabeculation. The cortex is thin, and the bones have a fragile aspect. Often, only few simultaneous fractures are present. Also, deformation of the bones is seldom seen, resulting in normal stature. Always blue sclerae [167]. Hearing problems may occur, usually from puberty onwards. Compared to the rest of the population, life expectancy may be slightly shorter.
II	Perinatal lethal	1:62,500 Autosomal dominant inherited – positive familial anamnesis, possibly spontaneous mutations, which can be inherited autosomal recessive as well as dominant. Severe bone abnormalities and osteopenia. Sometimes the long bones are shortened, and multiple fractures may be present, which results in abnormal stature.
III	Severely deforming	1:68,800 Progressive form. Most fractures occur before the age of 2 years. Wormian bones are always present [151]. There may a gradual increase in bone deformities. The long bones may be shortened, and there are multiple fractures present. Usually there are no blue sclerae. There may have been blue sclerae at birth, which disappeared gradually with the start of puberty [168]. Dentinogenesis imperfecta may be present. During the first decade of life there is an increased risk of death; after which life expectancy improves considerably.
IV	Moderately deforming	1–3:1,000,000 of 1:1 to 3,000,000 [169] – no reliable incidence figures available. In 30% of children fractures are found at birth. Fractures are usually seen before the age of 4 years. Radiographs of the long bones may show normal density. Wormian bones are often absent [151] No blue sclerae Mild dentinogenesis imperfecta may be present

Table 7.2 (**b**) Addition to Sillence's classificatie by Rauch and Glorieux [12]

Type	Severity	Clinical findings
V	Mildly deforming	Mild to moderate growth retardation Dislocation of the radius head, mineralised inter-osseous membranes, hyperplastic callus White sclerae No dentinogenesis imperfecta
VI	Mildly to severely deforming	Moderate growth retardation Scoliosis (Microscopic: accumulation of osteoid in bone tissue, fish-scale pattern of deformed lamellar bone) White sclerae No dentinogenesis imperfecta
VII	Mildly deforming	Mild growth retardation Shortened humerus en shortened femur, coxa vara White sclerae No dentinogenesis imperfecta

defects ('wormian' bones) and the family history will soon clarify matters. Wormian bones and occasionally blue sclerae are also present in children with type III. However, wormian bones are certainly not exclusive to OI (Table 7.4).

In type IV no blue sclerae or skull lesions are seen. Theoretically, it complicates the differentiation; however, this type occurs so rarely that only in exceptional cases it may invite mistakes. The chance that a child of less than 1 year old will be diagnosed with type IV

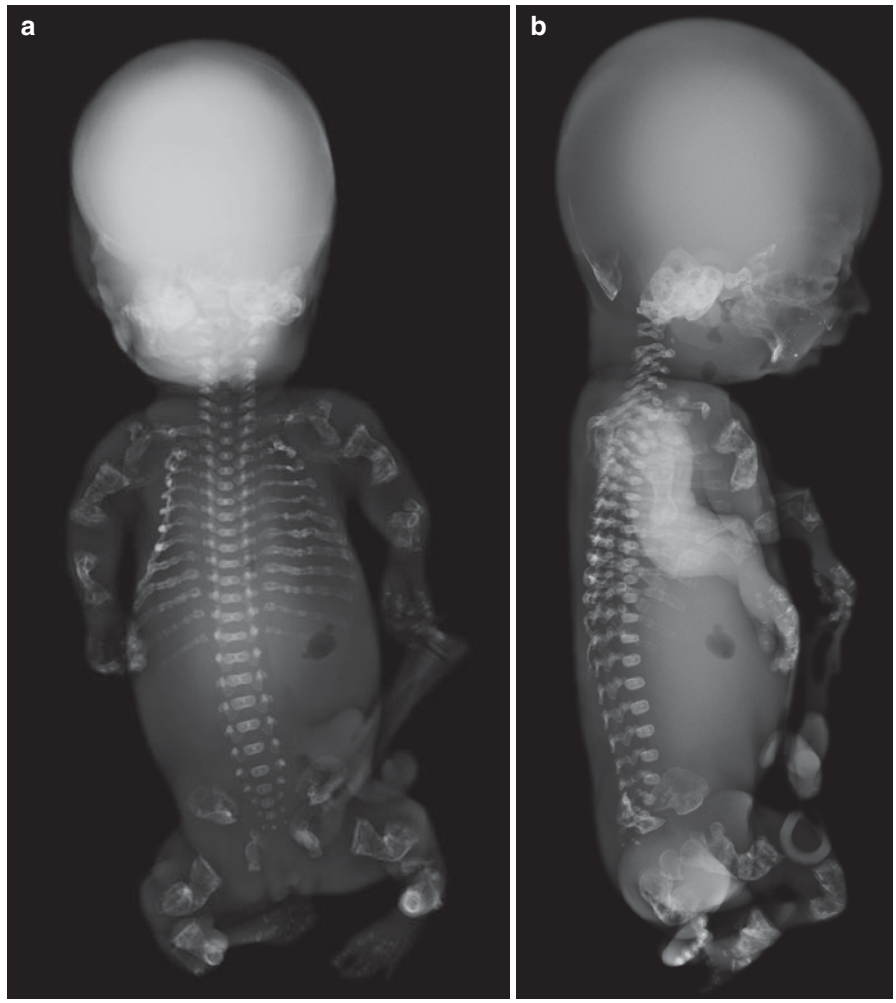


Fig. 7.9 (**a**) Stillborn female neonate whose skeleton shows innumerable healing fractures of nearly every bone. The calvaria have evidently not yet sufficiently ossified with regard to the pregnancy term. Osteogenesis imperfect type IIA was genetically confirmed. (**b**) Lateral view of the same neonate

(without a positive anamnesis, a normal skull radiograph and normal teeth) is estimated to be 3:1,000,000 [20].

One should be aware that child abuse most certainly happens in children with OI. Even if this disorder provides a plausible explanation for the fractures and bruises that correspond with the minimal trauma recorded in the anamnesis, one should still consider abuse.

Knight and Bennett describe a child with OI in whom child abuse could only be confirmed after the attending physicians had found facial abnormalities that proved that the child had been beaten [21].

7.4 Rickets

7.4.1 Introduction

Rickets is a disturbance in phosphorus-calcium processing in children, caused by a lack of vitamin D. As a result of the disturbance, the ossification of the cartilaginous tissue is too slow which leads to irregularities in the metaphyses (Fig. 7.11a and b). The clinical symptoms of rickets are presented in Table 7.5 (see also Figs. 7.12 and 7.13). Rickets can be subdivided into 11 subtypes (Table 7.6).

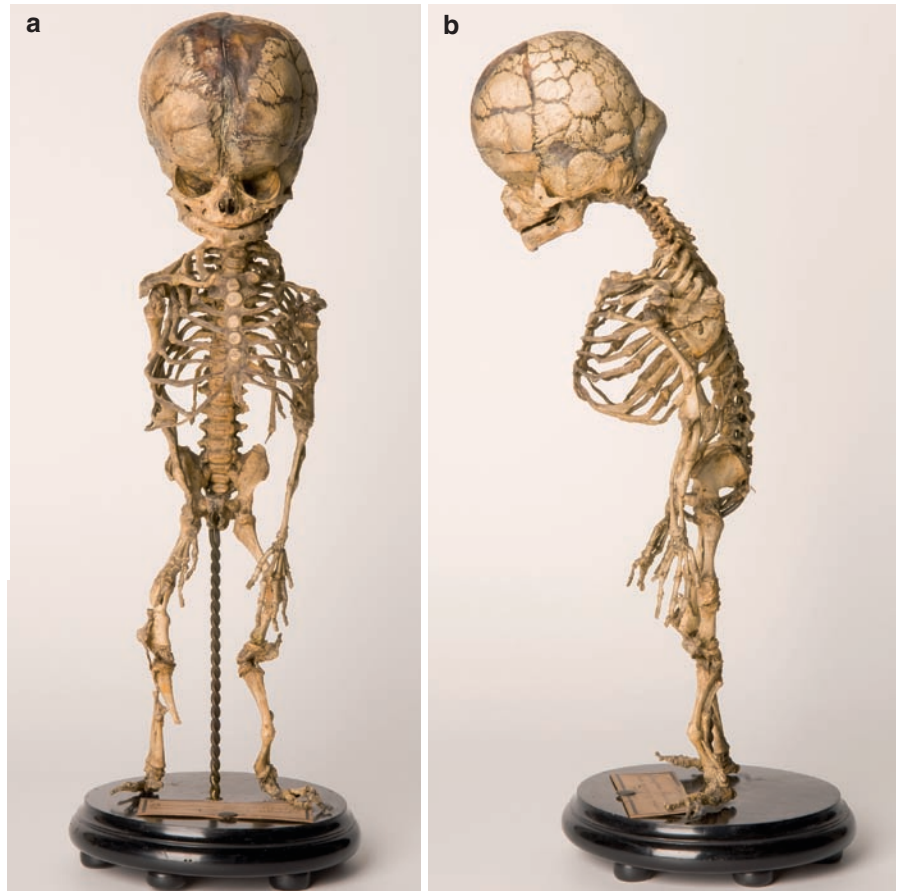


Fig. 7.10 (**a**) Specimen, dating from approximately 1850, from the Vrolik collection of the Academic Medical Centre Amsterdam. Gerardus Vrolik (1,775–1,859) described this specimen, which is considered to be one of the first reported cases of OI. A very wide sagittal suture can be seen, the ribs are fragile but intact. Both tibias show signs of healing fractures (Courtesy of R.J. Oostra, conservator of the Vrolik museum). (**b**) Lateral view of the specimen shows multiple wormian bones in the skull

7.4.2 Rickets

On a radiograph rickets can be identified by a widening and fading of the metaphyses [22]. Sometimes pseudofractures are present. As a rule, periosteal reactions and the new-bone formation are abundantly present.

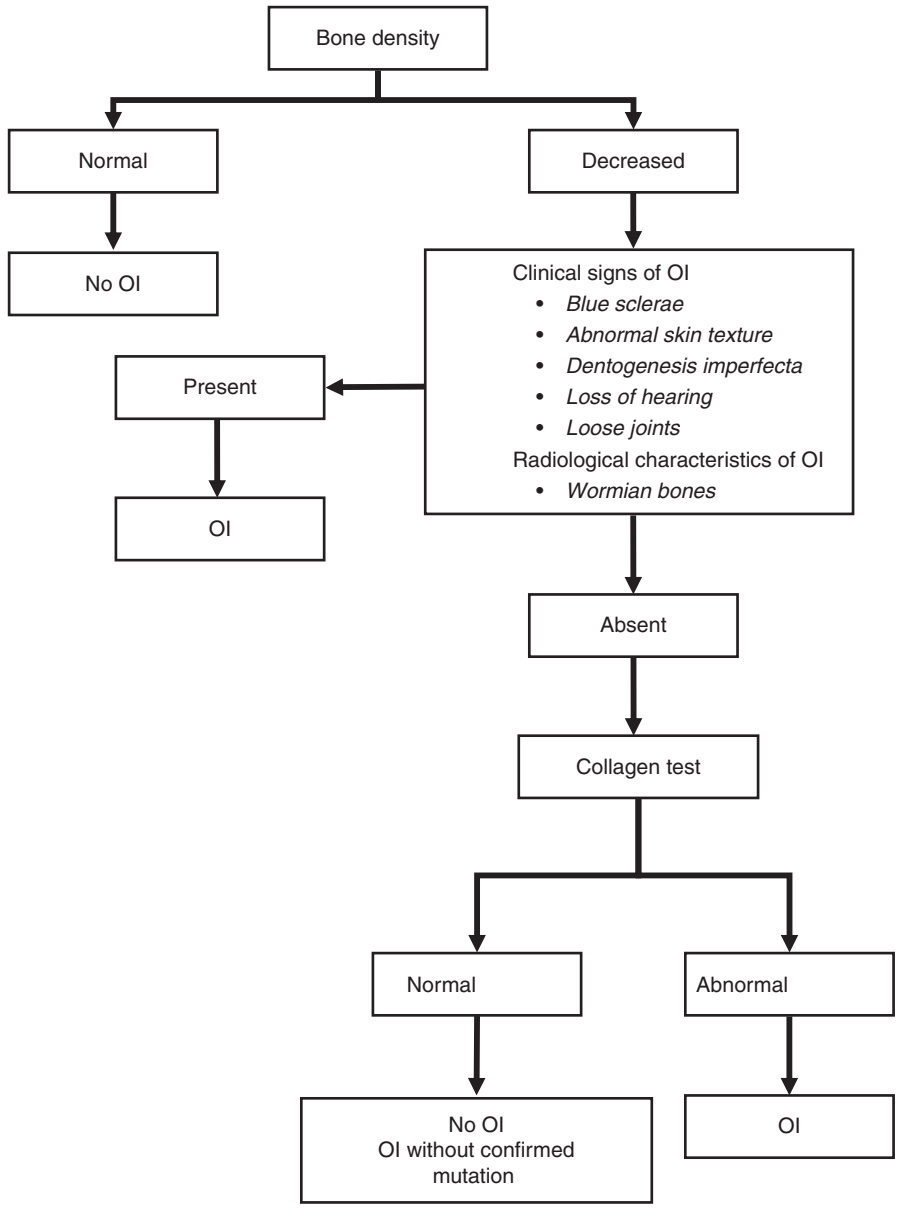
Since the radiographical lesions are symmetrically present through the whole body, in extreme cases and in the presence of fractures it will be no problem to differentiate with child abuse (Fig. 7.14). In milder cases, the metaphyseal lesions may strongly resemble CMLs (Fig. 7.15). In these cases, comprehensive laboratory tests and repeating the tests at 2-week follow-up will provide valuable information. When the disease is more protracted, bowing of the long bones may occur, in particular of the legs.

7.4.3 Vitamin-D-Deficient Rickets

From a medical point of view there is increased interest in vitamin-D-deficient rickets. One even speaks of a 'third wave' of this disease [24]. The first wave of rickets occurred during the industrial revolution in the Western world, when the smog in the cities caused a lack of sunlight. The discovery of cod-liver oil was an effective remedy for this problem. The second wave of rickets was the result of breastfeeding by women who did not get enough exposure to sunlight because their religious believes prescribed nearly full body coverage [25].

In a review article Holick established that, based on the literature, vitamin-D deficiency is present in 52% of Latin-American and African-American adolescents in Boston and in 48% of pre-adolescent white girls from Maine [26–28]. Gordon et al. examined 380 young

Table 7.3 Flow chart for diagnosing osteogenesis imperfecta (Reprinted of [19]. With permission)



infants (age 8–24 months) in Boston and found in 44 (12.1%) a vitamin-D value of ≤ 20 ng/mL. Seven of these children had a severe deficiency (≤8 ng/mL) [29].

Holick's article gives an excellent overview of vitamin-D deficiency and shows clearly that this disease, of which the medical world thought that it was extinct, is again on the rise. Holick uses as threshold value of 20 ng/mL as the lower limit of normal, and values between 20 and 30 ng/mL as being deficient. However, letters submitted to the New England Journal of Medicine refute the latter claim and the authors of the submitted letters maintain that there this is not medically supported [30, 31]. There is also a discrepancy between the recommendations of Holick and the guidelines of the American Academy of Pediatricians [32].

In 2008, Keller and Barnes wrote an article on rickets versus child abuse [33]. A large part of the text is dedicated to the epidemiology of rickets in children and mothers. It cannot be said (as described above) that it is not a growing problem. Subsequently, Keller and Barnes presented four cases of infants (age 2–4

Table 7.4 Diseases that may present with 'wormian bones'

Consistently present	Inconsistently present
Cretinism	Pyknodysostosis
Metaphyseal dysplasia, type Jansen	Sclerosteosis
Menkes syndrome[a]	Hydrocephalus
Acro-osteolysis	Osteopetrosis
Prader–Willi syndrome	Down syndrome
Cleido-cranial dysostosis	Rickets[a]
	Hypophosphatasia
	Progeria

[a] These diseases should also be included in the radiological differential diagnosis of child abuse

Table 7.5 Clinical manifestations in rickets

Pain or sensitive bones	
Skeletal deformation	
	Bowing of the long bones of the legs Pectus carinatum Ricketsian rosary Asymmetrical or deformed skull Pelvic and spinal deformities, including scoliosis and kyphosis
Increased risk for sustaining fractures	
Dental abnormalities	
Muscular spasms	
Growth disturbances, possibly resulting in stunted height	

months) with multiple fractures. All mothers presented with a decreased vitamin-D level; however, none of the children had been checked for this defect at the time when they had sustained the fractures. According to the authors none of the cases was suspect for child abuse. Furthermore, they literally posed the question: 'Would children with so many inflicted fractures not be in serious pain or be restless?' (see paragraph 9.2). The remaining part of the publication discussed the similarities between rickets and child abuse.

Considering the possible impact of this publication on future jurisprudence, it should be carefully evaluated. At the time the article was published, it was accompanied by four comments [34–37]. The main point of criticism was that it was absolutely not clear how the children that were described had been selected for this publication. Jenny, head of the American Academy of Pediatrics Section on Child Abuse, suspects frankly that the cases had been provided by lawyers [37]. Slovis and Chapman also criticised the obscure way in which the patients had been selected [35]. This greatly increases the risk for selection bias and makes correct interpretation of the data impossible. All children presented were <4 months old and consequently must have suffered from congenital rickets (in all four cases, laboratory tests that could have confirmed

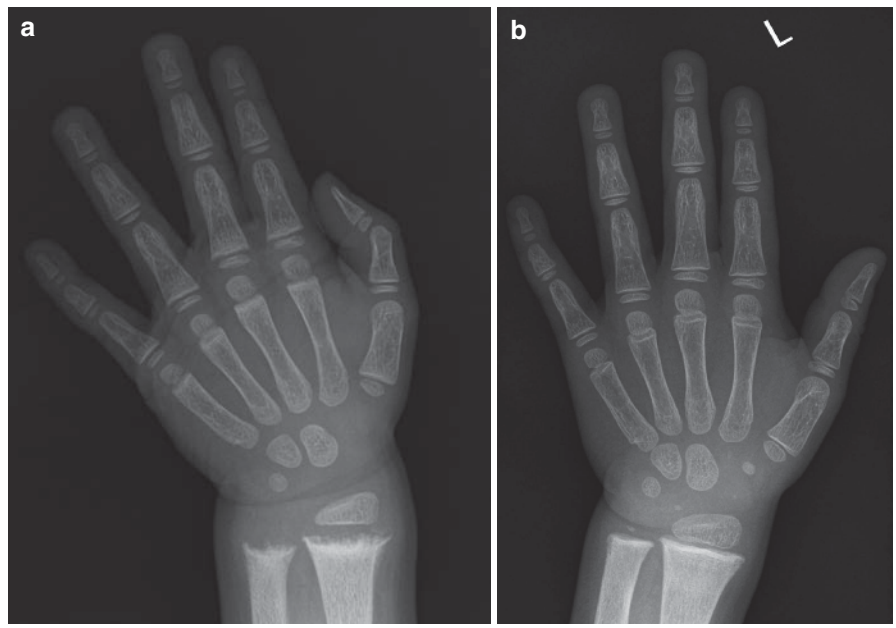


Fig. 7.11 (**a**) Two-year-old girl with rickets. The distal radius shows metaphyseal widening (splaying), concavity (cupping) and irregularities (fraying). (**b**) Two months after the therapy was initiated, the image has nearly been normalised and only a small amount of sclerosis of the distal metaphysis of the radius remains

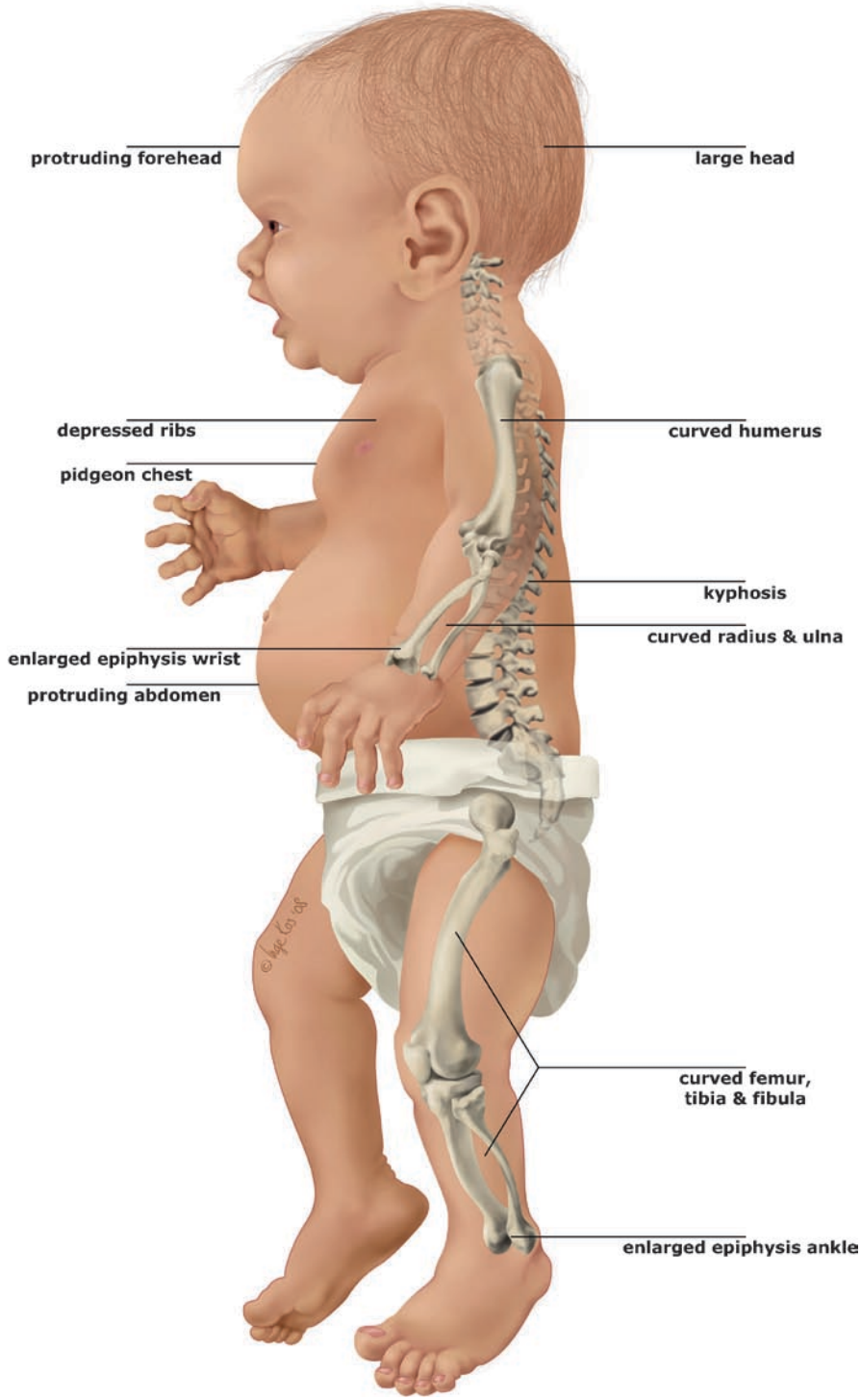


Fig. 7.12 Graphic representation of the anomalies that can be found in rickets

this fact, are absent). Indeed, in the literature one can find descriptions of children with congenital rickets, but, in a critical review of the literature cited by Keller and Barnes, the children that had been described (six of the seven children were radiologically examined) were shown to have metaphyseal lesion that corresponded with rickets [38–43]. Anyway, these peer-reviewed publications were a selection from the medical literature.

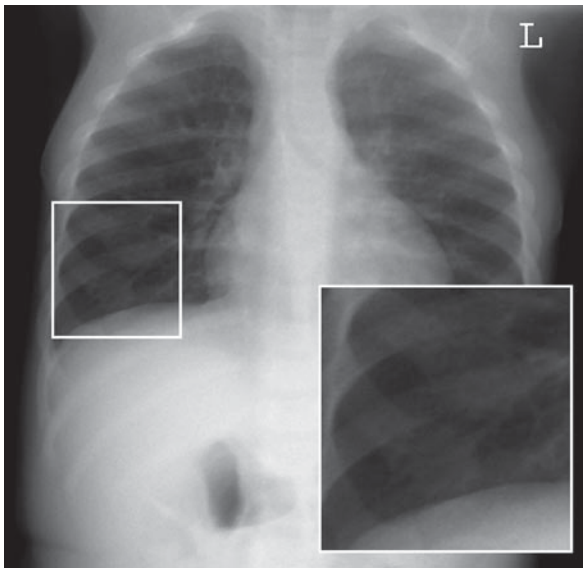


Fig. 7.13 Seventeen-month-old boy with rickets. The chest radiograph shows irregularities of the costochondral junctions (inset), resulting in the image known as ricketsian rosary

With regard to the fractures, purely on a radiological basis all one could conclude was that they were present. It was remarkable that one child showed a spinal fracture which Keller and Barnes contributed to rickets, although in the literature there are no cases to this effect (this does not exclude the possibility, but it does not make it very probable either). As earlier mentioned in this book, the diagnosis 'child abuse' is team work, and not one result that by itself is pathognomonic for the diagnosis child abuse. In the presented case, all relevant data enabling adequate evaluation are absent: social background, other signs of trauma, the presence of retinal bleeds, the dating of fractures and indications for accidental trauma. Finally, it is important to realize that, even if one assumes that these children were indeed suffering from congenital rickets, this in itself does not exclude child abuse.

Although the article of Keller and Barnes cannot withstand the critical test with regard to the description of the four cases and the link between rickets and child abuse, it

Table 7.6 Causes of rickets

Vitamine-D deficiency	Deficient diet
	Deficient endogenous synthesis
Metabolic vitamin-D disorders	Pseudovitamin-D deficiency Use of anticonvulsives Chronic kidney failure
Disorders of the gastrointestinal tract	Gastrointestinal malabsorption disorders Partial or total gastrectomy Hepatobiliary diseases Chronic pancreatic insufficiency
Acidosis	Distal tubular acidosis (classic or type I) Secondary forms of renal acidosis Ureterosigmoidostomy Medication-induced Chronic acetazolamide use Chronic salmiac use
Chronic kidney failure	
Phosphate deficiency	Low dietary phosphate contents Inherited: X-linked hypophosphatemic rickets Acquired: Sporadic hypophosphatemic osteomalacia (phosphate diabetes) Tumour-associated rickets Osteomalacia Neurofibromatosis Fibrous dysplasia

(*continued*)

Table 7.6 (continued)

Renal tubular disorders	Primary renal tubular disorders Renal tubular disorders associated with systemic metabolic abnormalities Cystinosis Glycogenosis Lowe syndrome Systemic disorders with associated renal abnormalities Congenital Wilson's disease Tyrosinemia Neurofibromatosis Acquired Multiple myeloma Nephrotic syndrome Kidney transplantation
Primary mineralisation defects	Inherited Acquired Fluor treatment Bisphosphonate treatment
Rapid bone formation, with or without relative defects in bone resorption	Postoperative hyperparathyroidism with osteitis fibrosa cystica Osteopetrosis
Defective matrix synthesis	Fibrogenesis imperfecta ossium
Others	Magnesium-dependent conditions Axial osteomalacia Parenteral nutrition Aluminium intoxication Isophosphamide treatment

will most certainly be cited in court cases. Consequently, any person involved in child abuse should be familiar with this article and the additional comments.

7.4.4 Rickets and Child Abuse

Although fractures resulting from rickets have given rise to the incorrect conclusion that they were due to child abuse, it does not mean that the presence of a vitamin-D-related disorder combined with fractures excludes child abuse [44]. Duncan and Chandry describe a little girl who presented at the age of 3 months with multiple fractures [45]. The infant was also diagnosed with rickets. When she suddenly died at the age of 5 months, child abuse was suspected. However, this could not be confirmed. Three years onwards, child abuse was confirmed in another child of that family. However, this does not proof in any way that the first child also died from child abuse.

Vitamin-deficiency can also be the result of neglect, and as such child abuse; for example, when parents/carers fail to give vitamin-D supplements. Children with a nutrition-based vitamin-D deficiency are also at risk for osteopenia (reduced bone density). Severe osteopenia (osteoporosis, see paragraph 7.7.4) may lead to in increased risk for fractures. Often it is difficult to differentiate between fractures sustained by physical violence and fractures sustained by minimal force on a weakened bone structure.

Comprehensive damage to non-weight bearing parts of the skeleton, such as clavicles, ribs, lower arms and hands, are also suspect in children with rickets. This is certainly true when radiological examination reveals signs of healing fractures [46].

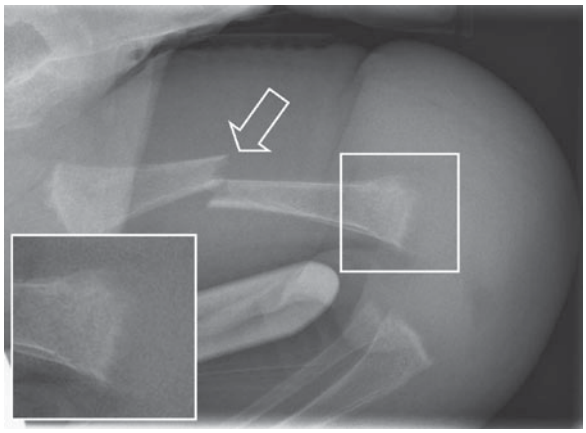


Fig. 7.14 Eight-month-old boy with a transverse mid-shaft femur fracture (*open arrow*) without evident trauma in the patient history. The distal femur metaphysis shows severe splaying, cupping and fraying, corresponding with rickets. Laboratory tests showed a vitamin-D deficiency

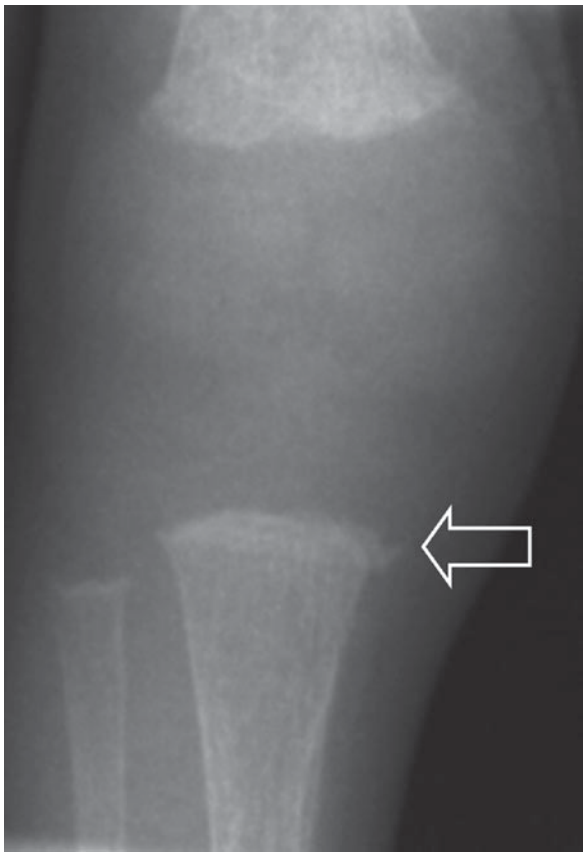


Fig. 7.15 Premature infant, born at 27 weeks' pregnancy. A radiograph at day 56 shows an irregular aspect of the proximal metaphysis of the tibia (*open arrow*). Laboratory test confirmed the diagnosis rickets. This anomaly could be interpreted as a metaphyseal corner fracture

7.5 Syndromes and Congenital disorders

7.5.1 Introduction

In the medical literature one can find case reports on suspected child abuse in skeletal abnormalities belonging to certain syndromes and congenital disorders. In this paragraph an overview is given. The overview does not claim to be complete.

7.5.2 Sickle Cell Anaemia

Sickle cell anaemia is an autosomal recessive inherited disease in which HbS is formed due to a disturbance in the production of haemoglobin. This results in sickle-shaped erythrocytes [47]. On a world-wide basis, millions of people suffer from sickle-cell disease. The disease is seen in particular in people (themselves or their ancestors) that hail from Africa, the Mediterranean countries and the Arabic peninsula, India and parts of South and Central America. Generally, the diagnosis can easily be made with a microscopic test. The symptoms of sickle-cell anaemia are due to abnormal erythrocytes that take on a sickle shape: early breakdown, which leads to anaemia. When the sickle-shaped cells occlude small vessels, it may cause pain and infection.

On a conventional radiograph, periostitis (Fig. 7.16) and radiolucencies with blurred margins are visible. These are present in bone infarcts as well as in osteomyelitis (which is more prevalent in patients with sickle-cell anaemia). After a period of time, the bone will start to show sclerosis. Since this image may resemble a healing fracture, it may cause confusion in the differential diagnosis [48]. Quite distinguishing for sickle-cell anaemia are the centrally located depression fractures of the vertebral corpora, which result in the signature H-shaped vertebrae (Fig. 7.17).

7.5.3 Alagille Syndrome

Alagille syndrome (arteriohepatic dysplasia) is an autosomal dominant disease with variable expression [49].

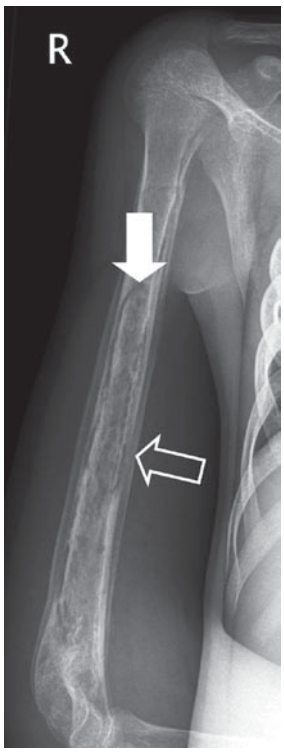


Fig. 7.16 Sixteen-year-old boy with confirmed patient history of sickle-cell anaemia presented at the emergency department with pain in the right upper arm. The radiograph shows extensive periosteal reaction (*open arrow*). Furthermore, there is an extensive anomaly in the medullary cavity, corresponding with a bone infarction (*arrow*)

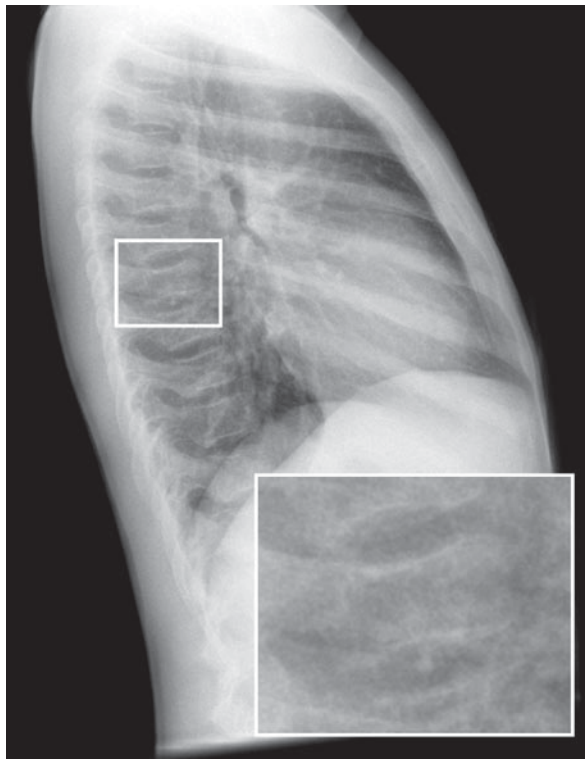


Fig. 7.17 Eleven-year-old boy with a confirmed history of sickle-cell anaemia. Routine radiograph shows the characteristic H-shaped collapsed vertebra (see inset)

In this syndrome, various organs (liver, heart, kidneys, eyes and skeleton) may be affected. Furthermore, often typical facial features are seen (prominent forehead, hypertelorism, small chin and saddle nose). Mental retardation may also be present (mostly mild to moderate). In the United Stated, the incidence is approximately 1:100,000 live-born children.

Most children with Alagilles syndrome are seen for the first time when they are not even 6 months old for a neonatal jaundices based on cholestasis (70%) or cardiac symptoms (17%). Sometimes there is a deficiency of fat-soluble vitamins (A, D, E and K). The reported skeletal defects refer to the vertebrae, the so-called 'butterfly vertebrae', and to the ribs and arms/hands (shortened radius, ulna and digital phalanges) [50]. It is also possible that post-fracture bone deformations will not spontaneously correct itself [51].

The diagnosis is made based on the earlier-mentioned complaints, complemented with genetic and (if so required) pathological examinations (liver biopsy).

7.5.4 Duchenne Muscular Dystrophy

Duchenne muscular dystrophy is a recessive X-linked inherited progressive proximal muscular dystrophy with pseudohypertrophy of the calf muscles. It is the most prevalent form of muscular dystrophy seen in childhood and has an incidence of 1:3,500 boys. Usually onset is before the age of 3, and after a period of being wheelchair dependent, the patient generally dies before the age of 21 from respiratory failure [52]. The skeletal abnormalities are characterised mainly by the development of curvature of the spine [53]. McDonald et al. report on a population of 378 patients (average age 12 years; range 1–25 years). Of this group, 79 (20.9%) had experienced a fracture [54]. In this population, no rib fractures were reported. Since it is generally possible to make a firm diagnosis, the differential diagnosis should present no problems in these children.

7.5.5 Congenital Pseudarthrosis

Congenital pseudarthrosis of the tibia is a relatively rare defect, associated with neurofibromatosis type 1 (NF1). Fifty-five percent of patients with congenital pseudarthrosis also have NF1 [55]. Congenital pseudarthrosis is the result of segmental mesodermal dysplastic bone development. Although the defect is linked to neurofibromatosis, no neurofibromas are visible near the pseudarthrosis. In 99% of cases the defect is unilateral [55]. Because of segmental bone weakness, there is progressive anterolateral bowing of the tibia (often also fibula), which may finally break. Congenital pseudarthrosis of other bones is found to a lesser degree.

In case there is a fracture, it will happen in the first 2 years of life. After the fracture has been sustained, no spontaneous healing takes place, which results in a real pseudarthrosis. Treatment of the fracture is protracted, difficult and sometimes even without success, which will lead to amputation.

Crawford distinguishes four radiological types [56]. Typical anterolateral bowing is always present:

- Type I: Medullary cavity is normal.
- Type II: Medullary cavity is narrowed and there is cortical thickening.
- Type III: Presence of cysts, sometimes with a fracture.
- Type IV: Actual pseudarthrosis. After the fracture, a pseudarthrotic image develops in which the fracture ends may assume an osteolytic-like configuration.

Type II can simulate child abuse when the patents have not sought medical help, because the image can be interpreted as a healing fracture that has been badly reduced (Fig. 7.18a and b).

Type IV may be interpreted as pseudarthrosis due to non-immobilisation of the fracture in a neglected child (Fig. 7.18c).

7.5.6 Caffey's Disease

Caffey's disease (infantile cortical hyperostosis) is a little understood inflammatory disease which manifests itself by a gross periosteal reaction during infancy [57]. It mainly involves the long bones (often asymmetrically). However, the disease may also manifest itself in different locations, such as: the mandibles, ribs, scapulas and clavicles. Spine, phalanges and pelvis are hardly ever affected. Its autosomal dominant inheritance is reported to have variable expression [58]. Caffey's disease is self-limiting and by the age of 3 the clinical and radiological abnormalities have disappeared.

The patients have swollen and painful extremities, are irritable and show a sub(febrile) temperature. ESR and alkaline phosphates are often elevated. Conventional radiographs show extensive subperiosteal new-bone formation in the affected bones. In the extremities, the epiphyses and metaphyses are usually spared (Fig. 7.19a and b). As a result of subperiosteal haemorrhages, extensive subperiosteal new-bone formation can also be found in non-accidental injuries. Consequently, Caffey's disease can simulate child abuse and vice versa [59]. However, in child abuse fractures are a regular feature and the periosteal reaction is predominantly metaphyseal, contrary to the images in Caffey's disease.

Other disorders associated with pronounced periosteal reactions, and as such may cause differential diagnostic problems, are: hypervitaminosis A, prostaglandin-E1 medication in children with duct-dependent cardiac defects, leukaemia, syphilis, some storage-diseases (I-cell disease, mucolipidosis type II, GM gangliosidosis type I), vitamin-C deficiency and hypertrophic osteoarthopathy. These diseases can be differentiated from Caffey's disease on the basis of clinical, clinical-chemical and radiological results.

7.5.7 Menkes' Syndrome

Menkes' syndrome is a progressive neurodegenerative disease based on a congenital, X-linked recessive defect in copper metabolism [60]. Copper is required for enzymes essential to the formation of bone, nerve tissue and other structures.

The disease is seen nearly exclusively in boys. Yet, there are a few case reports on girls with this syndrome [61, 62]. The incidence is not well known. In Australia, Danks estimates it at 1:40,000 live births [63]. Over the period 1976–1987, Tonnesen et al. estimated the incidence in Denmark, France, The Netherlands, The United Kingdom and Germany to be 1:298,000 live births [64]. On the other hand, Gu et al. found a much lower incidence in Japan, 1:4.9 million boys [65].

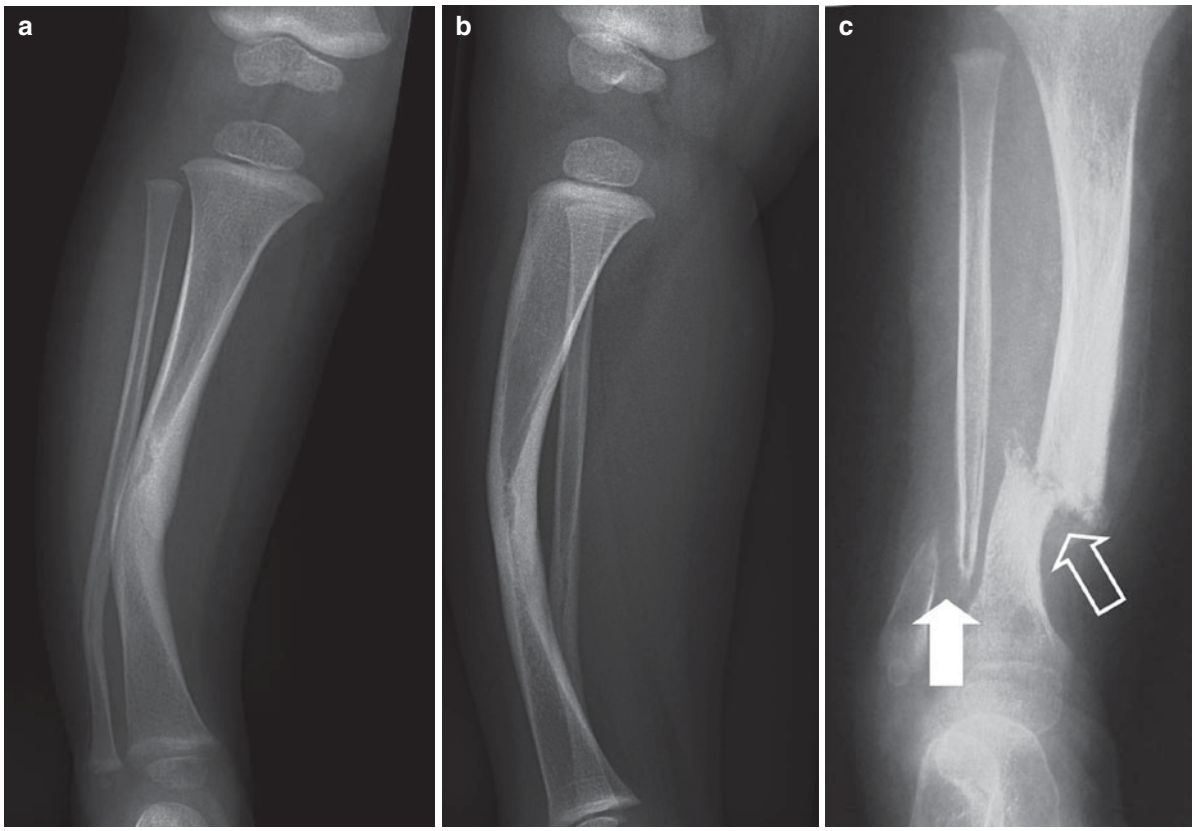


Fig. 7.18 (**a**) Congenital pseudarthrosis of the tibia, Crawford type II. Antero-posterior view of the lower leg. Anterolateral bowing with thickening of the cortical bone and narrowing of the medullary cavity. (**b**) Lateral view of the lower leg. (**c**) Crawford type IV with typical pseudarthrosis of the tibia (*open arrow*) and osteolytic-like pseudarthrosis of the fibula (*arrow*)

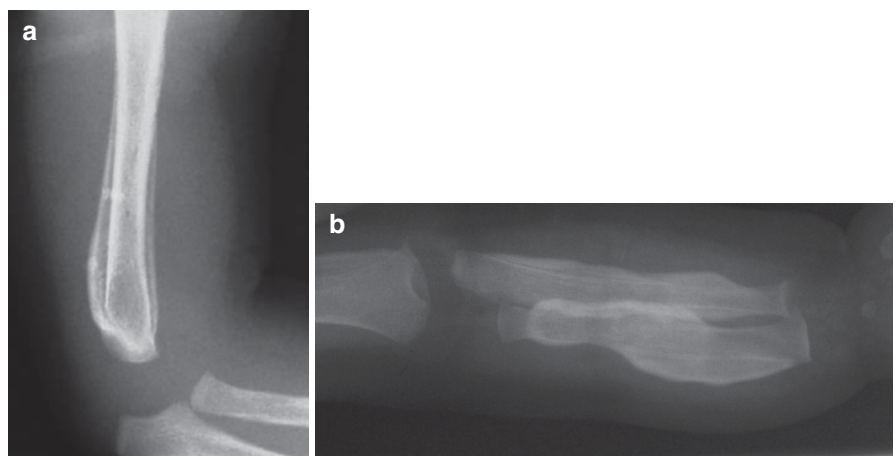


Fig. 7.19 (**a**) Two-month-old girl with Caffey's disease. Clinical presentation showed painful, slightly swollen limbs. Radiographs showed extreme periosteal reaction of the distal humerus without fractures. (**b**) Extreme periosteal reaction of along nearly the complete radius and ulna without fractures. After a year the girl was symptom-free and the bone anomalies had all but disappeared

Onset of the disease occurs in the first weeks to months after birth. Initially, development progresses normally, after which there is a delay with loss of the earlier acquired skills. Hypotonia and convulsions may also be present, as is 'failure to thrive' [66]. The prognosis is poor: generally, the children will die before the age of 4, although sporadically there has been the odd child that survived longer, even past the age of 21 [66].

A striking feature is the hair anomaly, and not just of the scalp, but also of the lashes and eyebrows. In light-skinned people, the hair is often without colour and sometimes silver or steel-grey in colour. In black-haired ethnical groups, the hair may be blonde or brown in colour. It is sparsely present and fuzzy or stubbly to the touch. It is crinkly and breaks easily. It resembles glass wool. Consequently, Menkes' syndrome is also known as 'kinky hair disease' or 'steely hair disease'.

Besides the hair anomaly, the children often have growth problems, anterior rib defects (flaring) and 'wormian bones' on radiographs. Due to the disturbances in bone metabolism, which causes osteoporosis, there is a risk for fractures. Moreover, metaphyseal defects and periosteal reactions may be found. On radiographs, this set of anomalies is indistinguishable from fractures resulting from child abuse. However, the anamnesis, combined with the above-mentioned symptoms should make it possible to differentiate between disease and child abuse.

Jankov describes a neonate with a rapidly progressing fatal syndrome. The boy died on day 27. He has been seen because of an acute presentation with severe intra-abdominal bleeding, haemorrhagic shock and multiple fractures. The physicians made the diagnosis at autopsy, which was confirmed by copper accumulation in the fibroblast culture [67].

Grünebaum et al. described four children with copper deficiency who did not have Menkes' syndrome [68]. All four showed 'sickle-shaped metaphyseal spurs', two children showed fractures of these spurs'. This case report seems to indicate that the metaphyseal defects in Menkes' syndrome may be the result of copper deficiency.

7.5.8 Pain Insensitivity in Spina Bifida

In spina bifida there may be insensitivity to pain in the lower extremities. When there is incomplete paralysis, an effort will be made to have children with this disorder walk with devices such as splints. As a result, abnormal stress on the joints may lead to damage of the epiphyseal plate and the metaphysis, possibly resulting in a fracture. Moreover, patients with a severe form of spina bifida will develop immobilization-related osteoporosis. The combination of osteoporosis and pain insensitivity may lead to fractures that are only noticed at a later stage (Fig. 7.20).

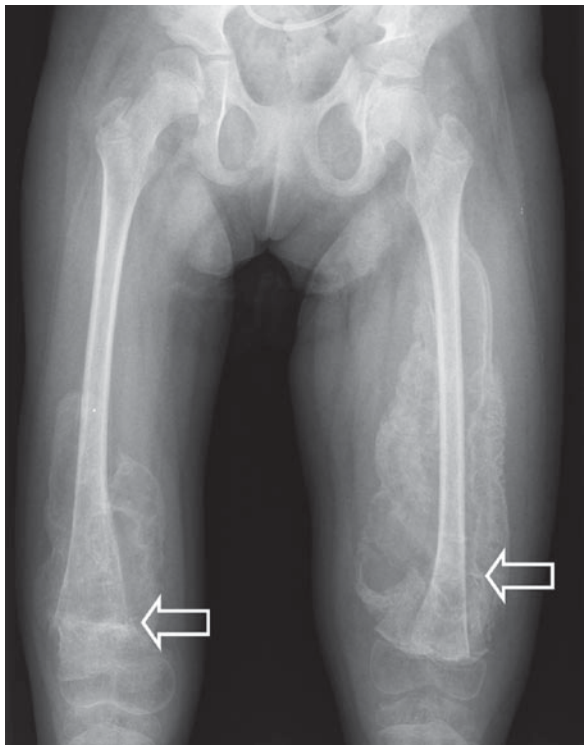


Fig. 7.20 Six and a half-year-old girl with spina bifida showed bilateral swollen knees at physical examination. Radiographs revealed bilateral distal metaphyseal femur fractures (*open arrows*) with extensive new-bone formation. Based on the anamnesis, child abuse was excluded

7.5.9 Congenital Pain Insensitivity

Congenital pain insensitivity is an autosomal recessive disease. Children with this disease have normal intelligence. The only aberrant neurological finding is their insensitivity to pain, which may lead to a plethora of unaccounted for injuries (Fig. 7.21). Especially in young children, repeated damage to the growing skeleton will not be noticed. This may cause defects to metaphyses and epiphyses. A meticulous neurological examination and careful anamnesis will make it possible to differentiate with child abuse [69, 70].

7.6 Skeletal Dysplasias

7.6.1 Introduction

Skeletal dysplasias are a heterogeneous group of disorders characterised by anomalies in bone and cartilage

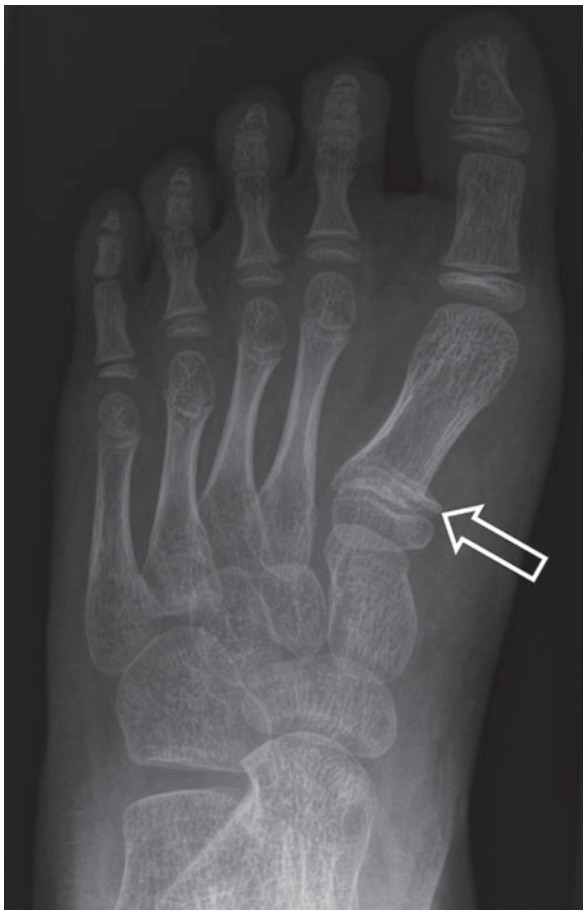


Fig. 7.21 Six-year-old girl with inherited sensitive-autonomous neuropathy (a serious defect in pain sensitivity) with a swollen left foot. A radiograph of the foot showed a torus fracture of metatarsal I (*open arrow*)

development and growth. Although the prevalence of skeletal dysplasias (350:1,000,000) is many times higher than that of bone tumours (20:1,000,000), trainee radiologists generally pay little attention to these disorders [71]. The resulting lack of knowledge may result in the unjust allocation of a radiological finding such as a metaphyseal spur in Jeune's 'asphyxiating thoracic dysplasia' (Fig. 7.22a and b, MIM %208500) to child abuse.

7.6.2 Metaphyseal Chondroplasia Type Schmid

Metaphyseal chondroplasia type Schmid is a rare autosomal dominant inherited skeletal dysplasia, characterised by irregular margins of the metaphyses (Fig. 7.23, MIM #156500) [72, 73]. The metaphyseal defects cause bowing and shortening of the extremities during growth. The metaphyseal defects are very similar to rickets (see Sect. 7.4) and may be confused with metaphyseal corner fractures.

7.6.3 Spondylometaphyseal Dysplasia 'Corner Fracture Type'

Spondylometaphyseal dysplasia 'corner fracture type' (Sutcliffe type) is a rare skeletal dysplasia characterised by short stature and an aberrant, waddling gait (MIM %184255) [74, 75]. Often the diagnosis is not made until the age of 2–3 years, when an increasingly abnormal gait pattern is noticed.

From a radiological point of view, the most important anomalies are, as already indicated by its name, vertebral and metaphyseal anomalies, the latter having irregular margins. The metaphyses show triangular fragments, which may lead to the incorrect diagnosis 'metaphyseal corner fractures' when one is not familiar with this dysplasia (Fig. 7.24a–c).

7.7 Metabolic Disorders

7.7.1 Introduction

In the medical literature case reports can be found regarding suspected child abuse in skeletal abnormalities compatible with metabolic disorders. In this paragraph an overview is presented. The overview does not claim to be complete.

7.7.2 Osteopetrosis

The term osteopetrosis relates to a group of anomalies in which osteoclastic activity is suppressed, resulting in increased bone density (sclerosis) and ultimately in abnormal bone modelling [76].

From the point of view of a differential diagnosis concerning child abuse, it is important that infantile osteopetrosis is mentioned. In this disorder, the metaphyses may show a translucent area and have an irregular aspect

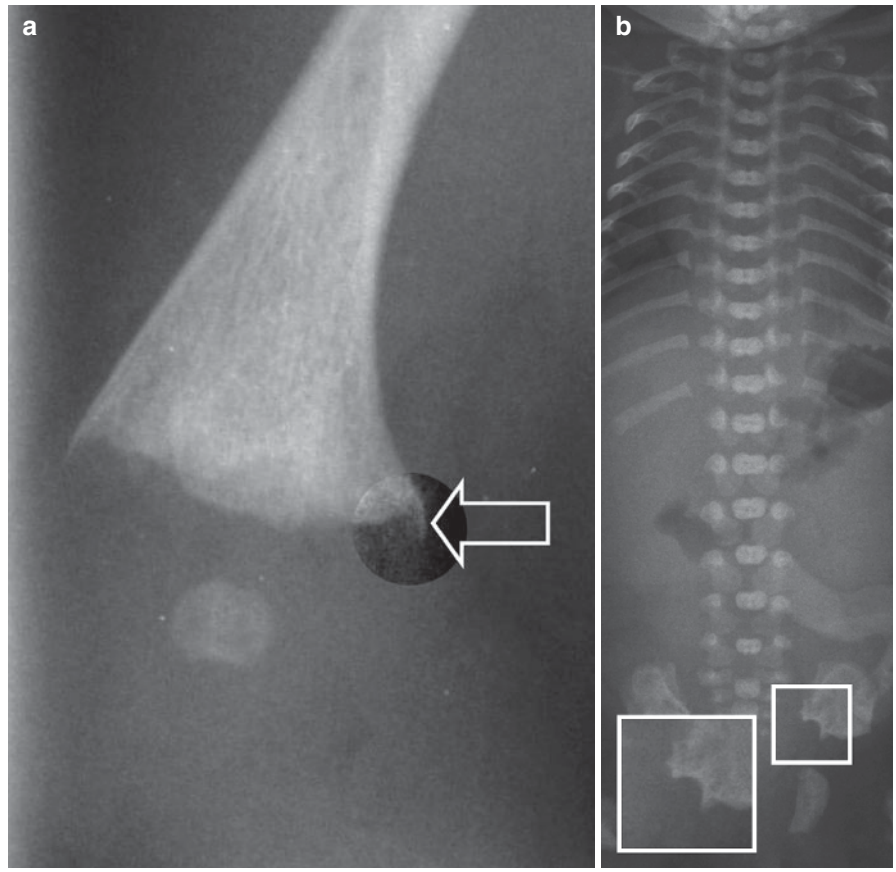


Fig. 7.22 (**a**) Neonate with a narrow chest. Radiographs of the knee showed a metaphyseal spur which may be confused with a metaphyseal corner fracture (*open arrow*). (**b**) Image of another patient with the same clinical presentation. Radiographs of spine and pelvis show a narrow chest and relatively short ribs. The pelvis shows spurs of the ileum (see inset). Based on o.a. the radiological examination, the diagnosis Jeune's asphyxiating thoracic dysplasia could be made

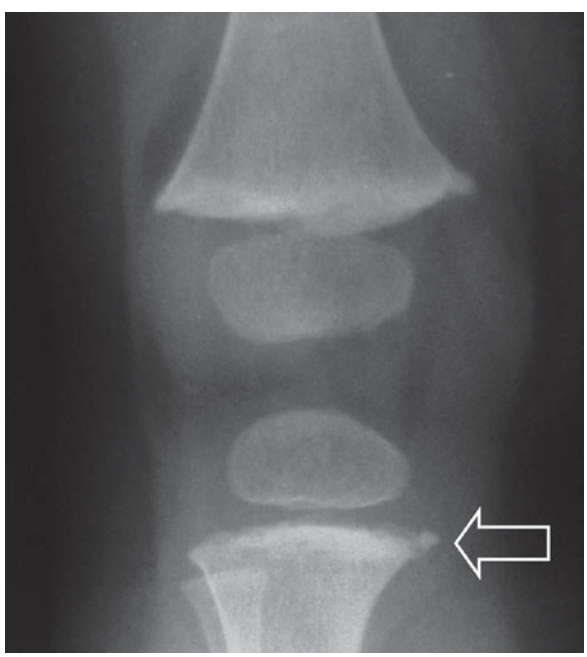


Fig. 7.23 Two-year old child with metaphyseal chondrodysplasia type Schmid. The irregularities of the proximal metaphysis of the tibia have a strong resemblance to metaphyseal corner fractures (*open arrow*)

(Figs. 7.25 and 7.26a and b). The presence of generalised skeletal sclerosis and metaphyseal undertubulation makes it possible to come to the correct diagnosis.

7.7.3 Osteoporosis

The World Health Organisation defines osteoporosis as a systemic disease characterised by low bone mass and micro-architectural regression of bone tissue, resulting in increased fragility of the skeleton and risk for fractures. Childhood osteoporosis may result from o.a. chronic disease, malnutrition, immobilisation and genetic defects (Table 7.7) [77, 78].

A specific form of childhood osteoporosis is idiopathic osteoporosis, a self-limiting primary osteoporosis of unknown origin, seen mainly in children in their second decade of life (Fig. 7.27a and b) [79]. The diagnosis of childhood osteoporosis is not always straightforward, since the commonly used techniques are validated for adults [80]. In osteoporosis the most frequently seen fractures are vertebral and metaphyseal.

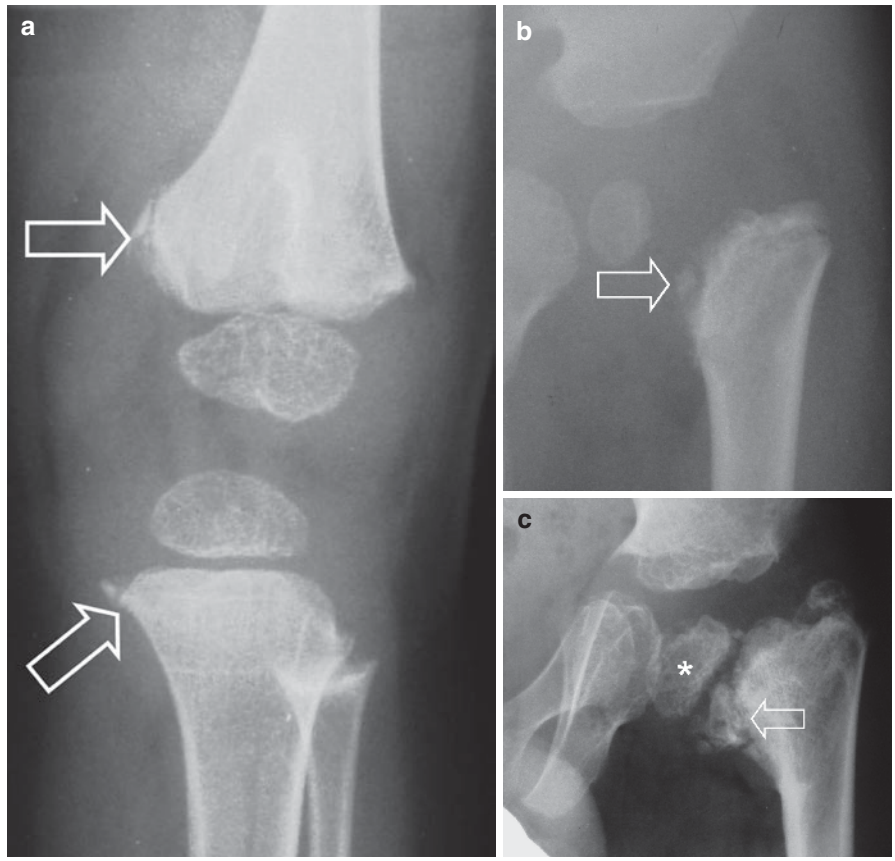


Fig. 7.24 (**a**) Two-year-old child with spondylometaphyseal dysplasia, corner fracture type. The distal femur metaphysis as well as the proximal tibia metaphysis show anomalies that strongly resemble metaphyseal corner fractures (*open arrows*). (**b**) Hip radiograph of the same patient shows an anomalous aspect of the proximal metaphysis of the femur (*open arrow*). (**c**) Radiological image of the left hip at 13 years of age shows besides an irregular metaphysis (*open arrow*) with strong developmental retardation also deformation of the femoral head (asterisk)

In children with multiple fractures osteoporosis should be excluded.

7.7.4 Dysostosis Multiplex Congenita

Dysostosis multiplex congenita is a group of storage diseases of complex proteins that have a large number of aspects in common. These include: mucopolysaccharidosis (such as Hurler disease and Hunter disease), gangliosidosis and mucolipidosis.

Clinical manifestation depends on the degree of storage and the organs in which the metabolite is stored. When storage occurs in the brain, progressive mental retardation will be the primary symptom. Other clinical symptoms are: typically course facial features, opaque corneas and organomegaly. Radiological lesion are: incomplete modelling of the long bones, epiphyseal dysplasia, broad ribs, abnormal configuration of the corpora vertebrae, in particular at the thoracolumbar transition (so-called 'vertebral beaking' or 'hook-shaped vertebra'; Fig. 7.28). Periosteal reaction may be very pronounced in GM1 gangliosidosis and mucolipidosis II (I-cell disease) [81].

Suspected dysostis multiplex congenita is usually based on clinical and radiological anomalies and is confirmed by biochemical analysis of urine and blood for abnormal metabolites. However, the younger the child, the more difficult it is to make the diagnosis, since at a young age the clinical presentation has not yet fully developed, and consequently the radiographs may appear to be normal.

In patients with dysostosis multiplex, an injury may unjustly be suspected based on the periosteal reaction in GM1 gangliosidosis and mucolipidosis II (I-cell disease) [59]. Also, when observed cursory, the spinal anomalies may be considered spinal fractures after non-incidental injuries. The clinical presentation and the radiological anomalies in the remaining skeleton are usually sufficient to reach the correct diagnosis.

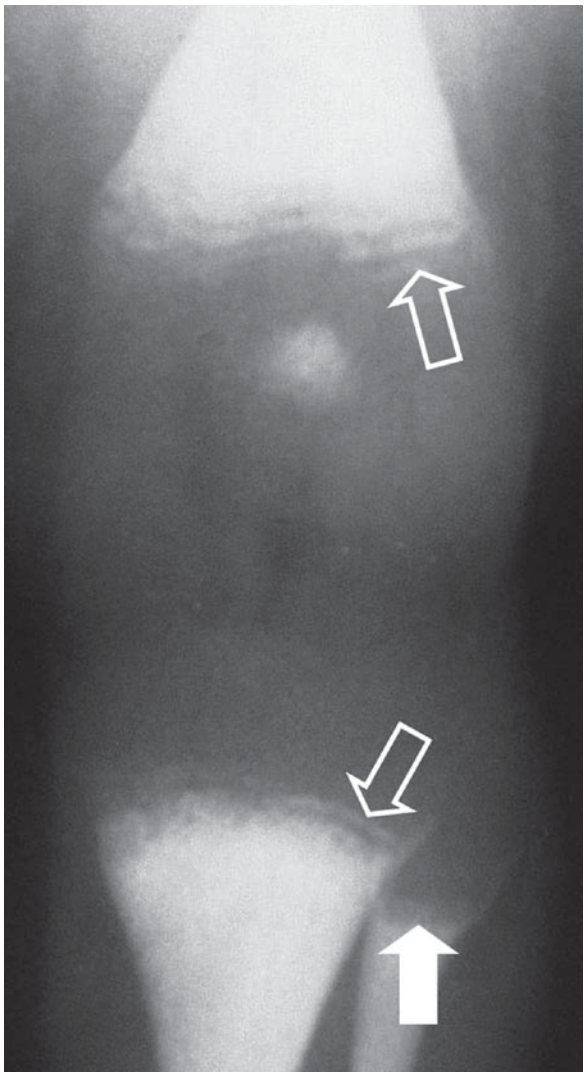


Fig. 7.25 Neonate with osteopetrosis. The distal femur and proximal tibia show irregular metaphyses (*open arrow*). In particular in the proximal metaphysis, the image could be confused with a bucket-handle fracture (metaphyseal corner fracture). The proximal fibula also shows an anomalous aspect

7.7.5 Hypophosphatasia

Hypophosphatasia is a rare disorder caused by a mutation of the gene coding for the enzyme alkaline phosphatase. The prevalence is estimated to be 1:100,000 [82]. There are six categories, depending on age: the perinatal (fatal), benign perinatal, infantile, child and adult forms and odontohypophosphatasia [82]. In the latter category only dental anomalies are present.

In young children decreased mineralisation of the cranium is seen with wide sutures, which later progresses to craniosynostosis, a noticeable bowing of the long bones, sometimes even angular (kyphomelia), fractures and pseudo-fractures and irregular metaphyseal ossification defects (Fig. 7.29a and b) [81]. Due to its heterogenic presentation, it may initially be difficult to diagnose, and the fractures, bowing and metaphyseal irregularities may even be reminiscent of non-accidental injury.

Moulin et al. describe a 9-year-old girl and her sister who frequently sustained fractures after trivial injuries. They had normal growth, normal sclerae, no rickets and only minor dental abnormalities. In the end, hypophosphatasia appeared to be the cause [83]. A clinical presentation of this kind may also look like non-accidental injuries within the home.

Ultimately, the diagnosis is made by DNA sequencing, measuring serum alkaline phosphatase activity, and proving an increased concentration of phosphoethanolamine and calcium in urine and pyridoxal 5'-phosphate and calcium in blood. By DNA sequencing, approximately 95% of mutations in severe hypophosphatasia (perinatal and infantile forms) can be found [82].

7.8 Infectious Diseases

7.8.1 Introduction

In the medical literature case reports can be found regarding suspected child abuse in skeletal anomalies compatible with infectious diseases. In this paragraph an overview is presented of the disorders. The overview does not claim to be complete.

7.8.2 Osteomyelitis

Osteomyelitis in childhood is a relatively rare diagnosis, with an estimated prevalence of 1:10,000 children under 12 years of age [84]. Since the course of the illness is often slow, it is often not diagnose until it reaches a well-advanced stage.

In osteomyelitis, metaphyseal abnormalities and periosteal reactions may be found (Fig. 7.30), which

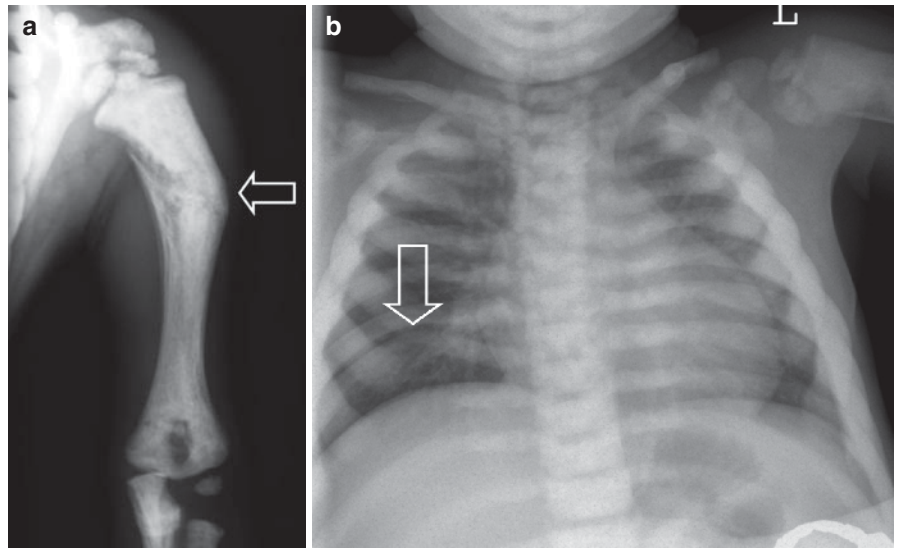


Fig. 7.26 (**a**) Three-year -old boy showing a healing humerus fracture (*open arrow*). The skeleton shows diffusely increased density. The diagnosis osteopetrosis was made based also on the radiological examination. (**b**) Chest radiograph of the same patient shows an anomalous alignment of the 8th rib on the right (*open arrow*), corresponding with a healed fracture

Table 7.7 Causes of osteoporosis in childhood

Chronic diseases	Immobilisation Anorexia nervosa Asthma Coeliac disease Neuromuscular diseases Chronic kidney failure Cystic fibrosis Diabetes mellitus Epilepsy Human immunodeficiency virus infection Inflammatory bowel disease Malignancies Organ transplantation Rheumatic diseases Sickle-cell disease Thalassemia Turner syndrome
Endocrinopathies	Cushing's syndrome (hypercortisolemia) Growth hormone deficiency Hyperthyroidism Hyperparathyroidism Hyperprolactinemia Hypopituitarism Hypothyroidism Gonadal steroids deficiency/ hypogonadism
Medication use	Anticonvulsive drugs Corticosteroids Cyclosporine A Heparin Lithium Methotrexate Various chemotherapeutics

can resemble metaphyseal and other fractures, and as such result in an incorrect diagnosis of child abuse.

Taylor et al. described a 7-month-old infant that had sustained a fracture of the left proximal humerus, without a clear explanation. Initially, child abuse was suspected [85]. However, follow-up examination showed that the radiological anomalies looked more like a pathological fracture. Biopsy showed an *S. aureus* infection.

In a meningococcal septicaemia, the epiphyseal plate may be affected. Initially, this will not show up in the radiological examination. The possible results will not be visible until a few years later: the epiphyseal plate will show central premature closure, which leads to a characteristic deformation (Fig. 7.31). However, this deformation may also be the result of an experienced trauma. In these cases, the anamnesis is conclusive.

Especially the slow progression of the clinical presentation may present the clinician with a diagnostic dilemma.

7.8.3 Chronic Relapsing Multifocal Osteomyelitis

Chronic relapsing multifocal osteomyelitis is a disease that affects the metaphyses of the long bones, in

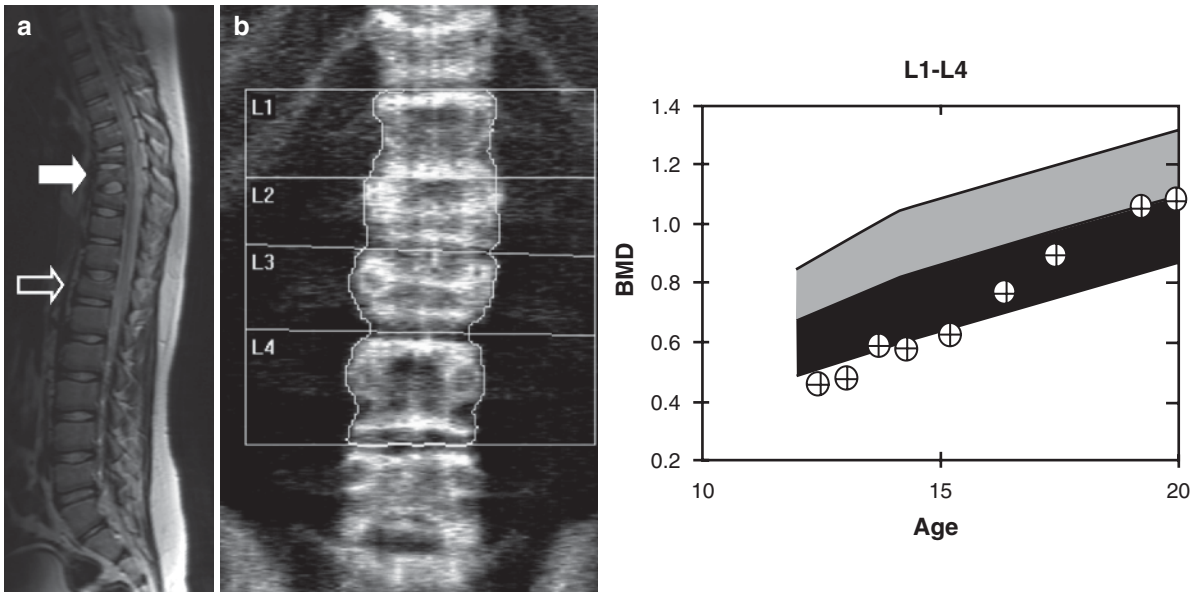


Fig. 7.27 (**a**) Twelve-year-old boy with idiopathic osteoporosis. The MRI of the spine shows collapsed vertebrae at the level Th7–9 (*arrow*) and Th12 (*open arrow*). (**b**) DXA scan of this patient, presenting the values of 12–20 years of age, shows normalisation of bone-mineral density

particular in older children [86]. Spine, pelvis and shoulder girdle are also involved, but to a lesser degree (Fig. 7.32a and b).

The presentation of the patient will depend on the location of the inflammation. Systemic symptoms such as weight loss and fever are seldom seen [87]. Because of the lack of systemic symptoms, the periosteal reaction seen during the healing process may present a source of diagnostic dilemmas. The anamnesis has a pivotal role in the diagnosis.

7.8.4 Congenital Syphilis

Over the past few years, and particularly in the United States, physicians have seen an increase in the incidence of syphilis in women of reproductive age. This may lead to an increase of congenital syphilis [69, 88]. In the differential diagnosis serological tests are often conclusive.

Solomon and Rosen described a series of 112 children with serologically confirmed congenital syphilis [89]. In these children, the bones most frequently affected were: tibia, femur and ulna (Fig. 7.33). The most prevalent abnormalities on the radiographs are metaphyseal osteomyelitis and periosteal reactions. Pathological fractures of the metaphysis and periosteal new-bone formation may mimic skeletal lesions seen in child abuse, and the image may even resemble lesions at various stages of healing. In the patient group of Solomon and Rosen, 31% of children had bone lesions corresponding with trauma, as described by Caffey [90].

7.9 Oncological Diseases

7.9.1 Introduction

Oncological diseases in childhood are relatively rare (168:1,000,000 children in the United Stated over the period 2001–2005). It is often forgotten that they occur significantly less frequent than skeletal dysplasias. Because they are so rare, they may present a diagnostic problem [91]. Due to centralised treatment, which has an advantageous effect on the therapeutic result [92], radiologists not specialised in paediatric oncology will

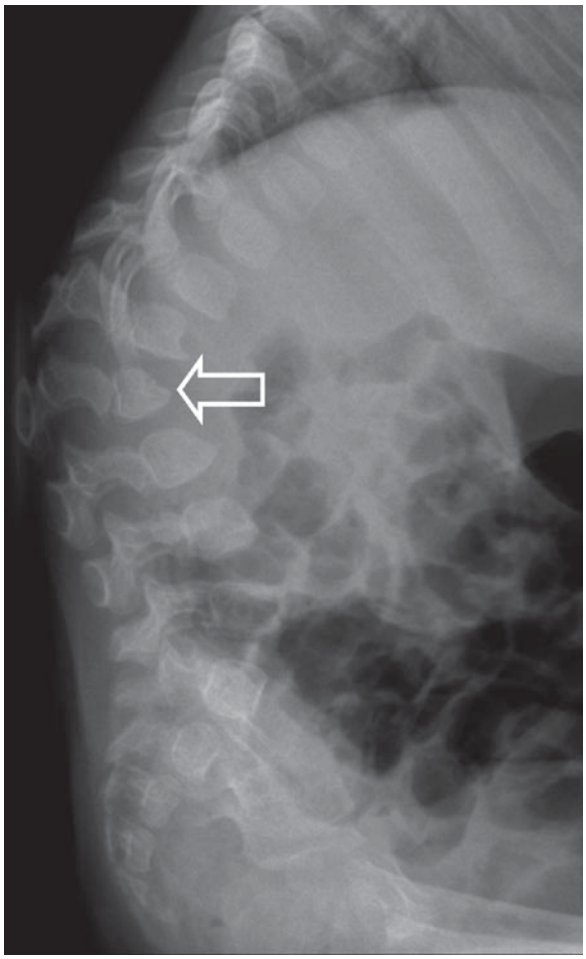


Fig. 7.28 Seven-month-old boy with mucopolysaccharidosis Hurler type. At several levels the lumbar spine shows considerably increased kyphosis and anterior beaking of the vertebral corpora

generally have limited knowledge of this topic, which may lead to problems when interpreting examinations.

7.9.2 Malignancies

7.9.2.1 Leukaemia

Leukaemia is the most prevalent oncological disease in childhood, with an estimated incidence of 50:1,000,000 in the Western world. In over 75% of cases it is acute lymphatic leukaemia (ALL). The clinical symptoms are generally due to decreased blood production: anorexia, pallor, fever, joint pain, haematomas and lymphadenopathy [93]. Generally, complaints will have been present for some weeks before the diagnosis is made.

Due to joint complaints, patients are regularly first referred to an orthopaedic surgeon, which is often followed by radiological examination. The latter may show osteopenia, metaphyseal radiolucencies, periosteal reactions, osteosclerosis, pathological fractures of a combination of the above (Figs. 7.34 and 7.35) [59, 94]. When adequate clinical information is absent, the radiological manifestations may be hard to interpret. On the whole, when ALL is suspected, the diagnosis will be simple and fast.

7.9.2.2 Ewing Sarcoma

Ewing sarcomas are predominantly seen in the second decade of life, and at that age will not present any diagnostic dilemmas. However, they may also present at a younger age and then, due to their radiological manifestation, they may cause confusion. Radiologically, the Ewing sarcoma is an aggressive tumour that may show an erosive aspect as well as an abundant periosteal reaction (onion skin aspect) (Fig. 7.36) [95]. The periosteal reaction in particular may cause confusion when incorrectly interpreted as a old fracture.

7.9.3 Benign Diseases

7.9.3.1 Osteoid Osteoma

An osteoid osteoma is a small benign neoplasm, which is predominantly seen in the cortical bone of the long bones [96]. The disorder is usually seen in boys and 50% of patients with this disorder are between 10 and 20 years old.

Over 50% of osteoid osteomas are located in the femur or tibia, mainly diaphyseal or diametaphyseal. The classical presentation is pain, mainly at night, which reacts well to acetylsalicyl acid. Pain complaints are related to hypervascularisation of the osteoid osteoma, and prostaglandines probably have an important role, which would explain the adequate reaction to acetylsalicyl acid (prostaglandin synthetase inhibitor).

On radiographs a cortical osteoid osteoma is visible as a small radiolucent focus (nidus) in a considerably widened sclerotic cortex, which is the result of a protracted periosteal reaction, often with a multi-layered

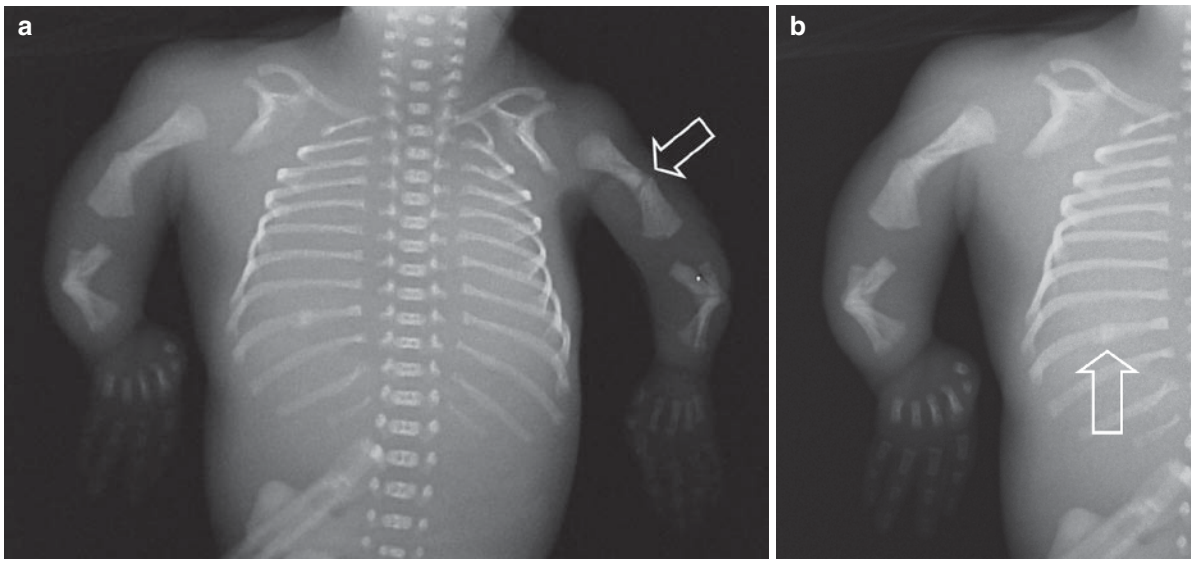


Fig. 7.29 (**a**) Neonate with hypophosphatasia, lethal perinatal variant. Bilateral angular bowing 'kyphomelia' of radius and ulna, and to a lesser extent of both humeri with (pseudo) fractures (*open arrow*). (**b**) Detail view of the chest shows a healing mid-posterior rib fracture (*open arrow*)

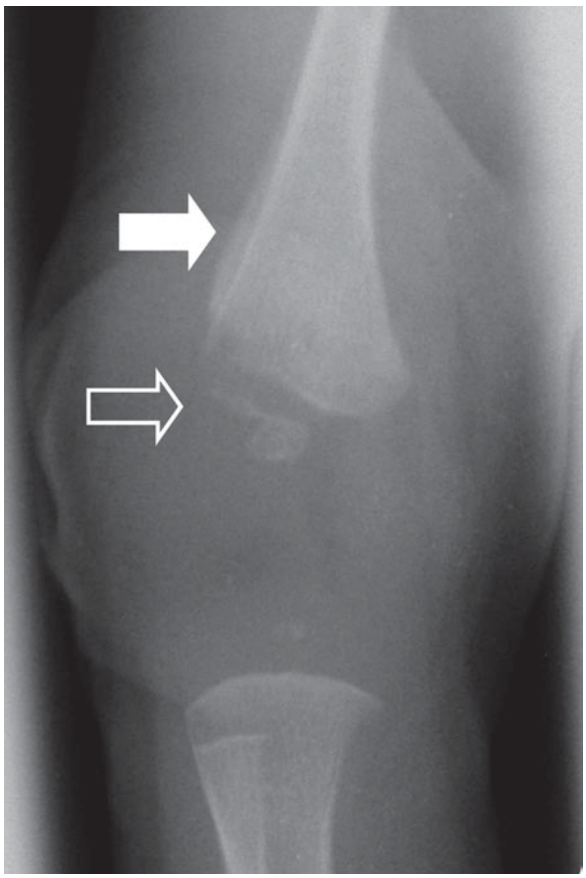


Fig. 7.30 Neonatal osteomyelitis of the distal femur. There is a periosteal metaphyseal reaction visible (*arrow*). Furthermore, there may be a metaphyseal corner fracture (*open arrow*)

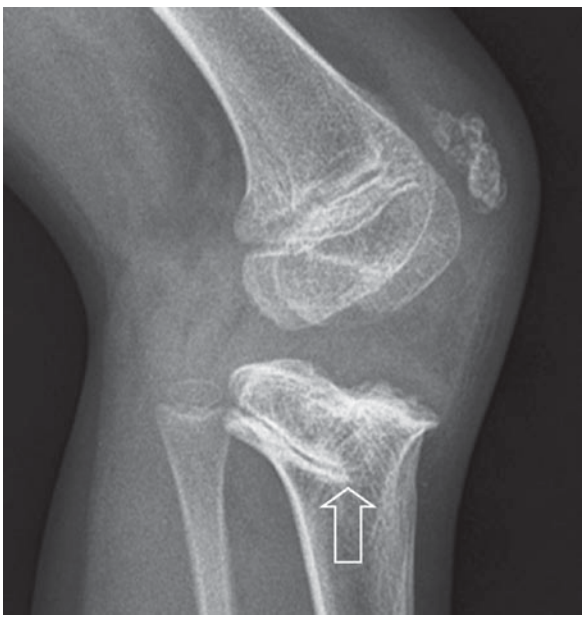


Fig. 7.31 Eight-year-old boy, who suffered meningococcal septicemia at the age of 18 months. This resulted in premature partial closing of the epiphyseal plate (*open arrow*), resulting in joint deformation

aspect. This may mimic a healing fracture (Fig. 7.37a and b). However, it is seldom confused with non-accidental injuries, since the pattern of complaints is fairly typical and the age of the average patient usually leads to a reliable anamnesis.

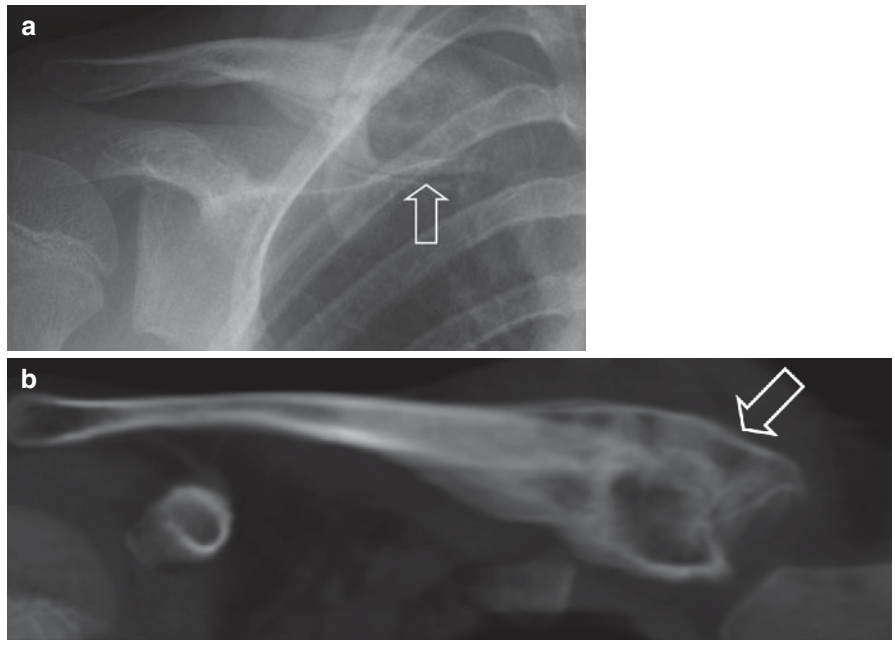


Fig. 7.32 (**a**) Eight-year-old girl with swelling of the proximal clavicle (*open arrow*). Later, a sacral focus was found in keeping with the diagnosis chronic recurrent multifocal osteomyelitis. (**b**) CT of the clavicle (coronary reconstruction) clearly shows the sclerotic abnormality in the proximal clavicle

A small percentage of osteoid osteomas is not found in cortical bone, but in trabecular bone or subperiosteum, and then predominantly periarticularly. In this manifestation of osteoid osteoma, the sclerotic reaction is far less pronounced and no confusion with non-accidental injury is possible.

7.9.3.2 Osteoblastoma

Like the osteoid osteoma, an osteoblastoma is a benign bone tumour. Age and clinical presentation are also very similar; on average the patient is 24 years old (range: 1–69 years) and at presentation pain is the dominant complaint [97]. The tumour favours boys (M:F = 2:1). Locations of preference are the long bones, posterior aspect of the vertebrae and the mandible. Conventional radiographs will show a radiolucent lesion, mostly >2 cm in diameter, without any reactive sclerosis or periosteal reactions worth mentioning.

Because of their histological similarities, an osteoblastoma is also called a 'giant osteoid osteoma'. However, the typical favourable response to acetylsalicyl acid is absent, as is excessive periosteal new-bone formation. In a periosteal osteoblastoma there may be at the most a visible periosteal reaction; however, most osteoblastomas are located medullary or cortically.

7.10 Medication-Related Abnormalities

7.10.1 Introduction

When evaluating the radiological examination of children, the clinical history is generally known. However, the radiologist should also take the use of medication into consideration. Several medications may influence bone development and growth. These medications have not always been prescribed by physicians, and accordingly some cannot be recorded in the medical dossier.

7.10.2 Corticosteriods

In childhood there are a number of indications for the use of corticosteroids, such as asthma, juvenile rheumatoid arthritis, inflammatory bowel disease (IBD) and organ transplantations. Corticosteroid use may lead to disturbances in bone mineralisation. Protracted use may cause osteoporosis [99]. The primary mechanism of corticosteroid-induced osteoporosis is decreased bone formation. Even in childhood this may result in insufficiency fractures (Fig. 7.38).

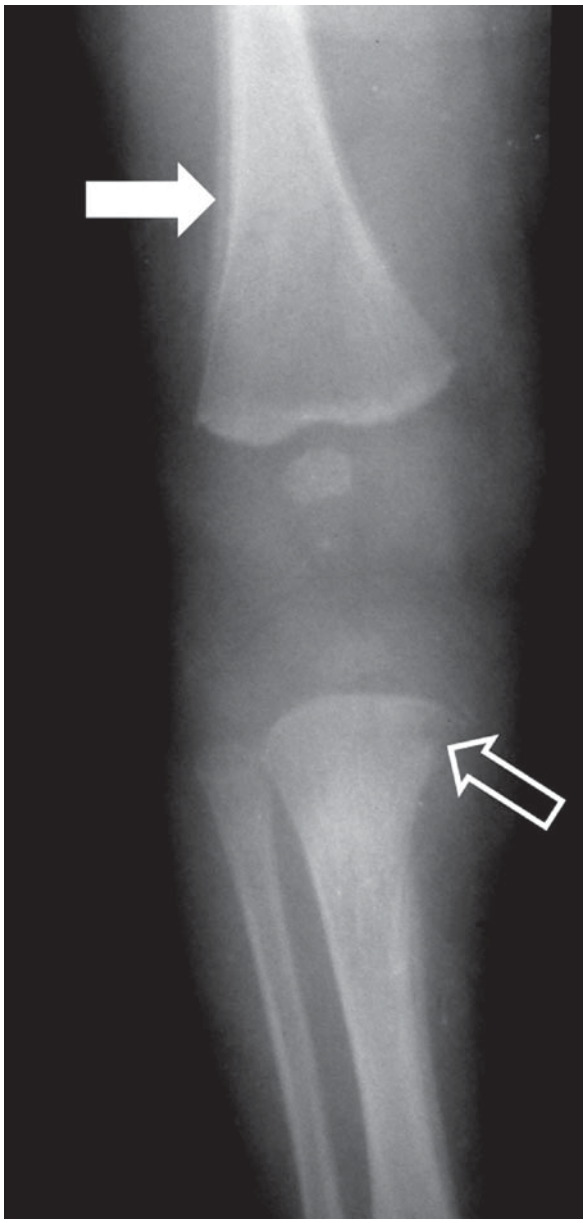


Fig. 7.33 Neonate with congenital syphilis. A radiograph of the knee shows a metaphyseal periosteal reaction in the distal femoral metaphysis (*arrow*). In the proximal tibia metaphysis a cortical radiolucency is visible, known as Wimberger sign (*open arrow*)

7.10.3 Methotrexate

Methotrexate-induced lesions are characterised by osteopenia (in particular in the lower extremities), dense metaphyseal banding, growth retardation and metaphyseal fractures that may strongly resemble

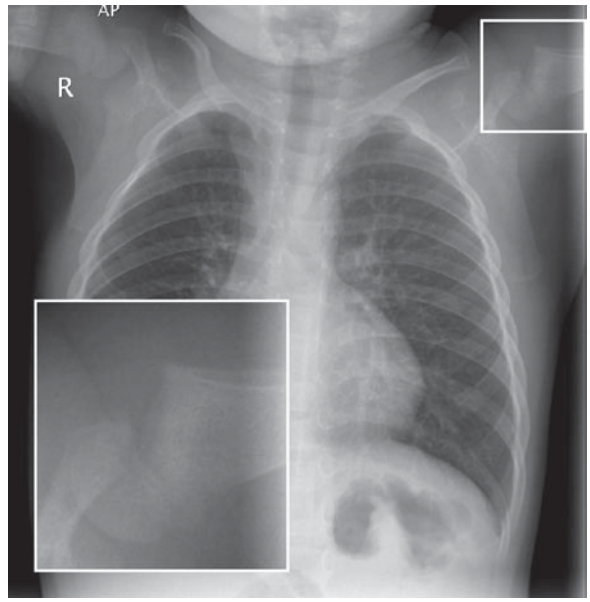


Fig. 7.34 Nearly 2-year-old boy with B-cell leukaemia. At the edge of the chest radiograph a periosteal reaction of the proximal humerus is visible (see inset)

CMLs [100]. However, these lesions only occur after protracted use in relatively high doses [101].

7.10.4 Hypervitaminosis A

Children with hypervitaminosis A may present with a great variety of clinical complaints such as: anorexia, pruritis, lip fissures, stiff joints and bone pain, multiple nodular soft tissue swelling, alopecia and hepatosplenomegaly [102]. From a radiological point of view it manifests as the result of hypercalcaemia, in particular by periostitis, in which the ulna is most frequently affected [103]. This periostitis, which in severe cases is palpable, may suggest an experienced trauma. In these cases the anamnesis should provide the answer. Hereby one should be aware that vitamin A, and products in which it is present in a relatively high dose, is generally freely obtainable. Consequently parents/carers may inadvertently give their child an overdose [104–106]. But also administered in a medical setting, for example as adjuvant therapy in children with neuroblastoma or vitamin-A deficiency, hypervitaminosis A has been reported in exceptional cases [107, 108]. In the literature there is one case that reports on an iatrogenic overdose in an

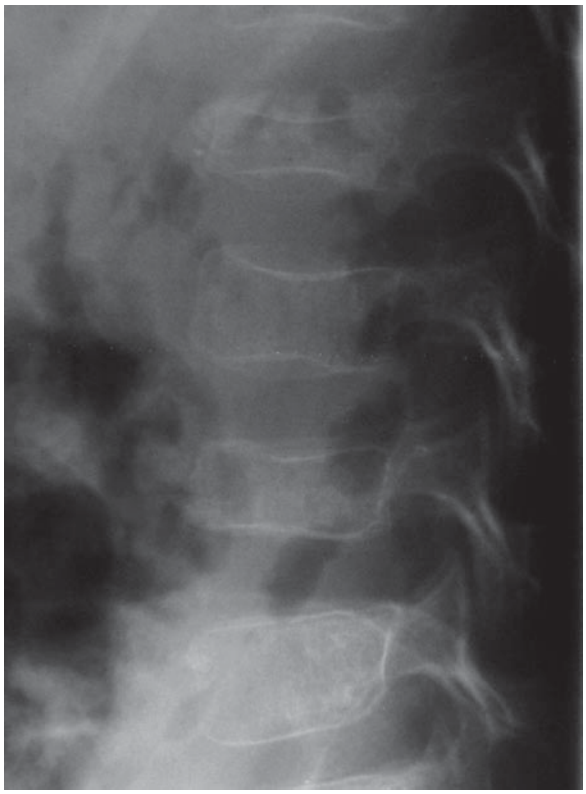


Fig. 7.35 Five-year-old boy with collapse of the spinal corpora in leukaemia

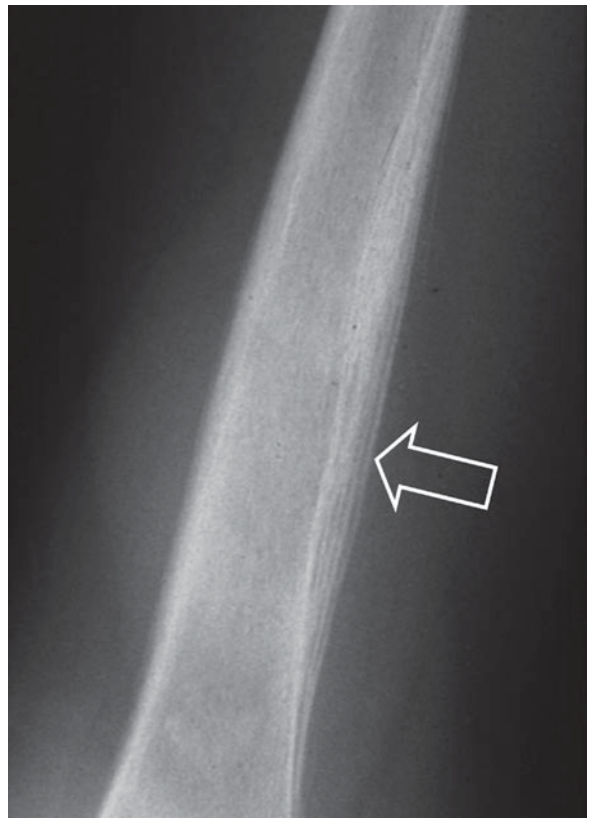


Fig. 7.36 'Onion peeling' in a Ewing sarcoma (*open arrow*). Especially when this is the only visible aspect of the tumour, there may be confusion with a healing fracture

autistic child. His parents put him on a special 'autism diet' that contained extremely high doses of vitamin A: 100,000 IU/day for 3 months, followed by 3 months of 150,000 IU/day (the recommended dose of vitamin A is 1,200–1,600 IU/day) [109, 110].

When these cases present, determining blood values may clarify matters, although this may also provide a false-negative result [111].

7.10.5 Prostaglandines

Prostaglandines are used in neonates with duct-dependent congenital heart disease to bridge the time to operation [112]. Treatment with prostaglandins may cause periosteal reactions in the long bones (Fig. 7.39) [113]. Generally it takes 30–40 days for these changes to present, although it has been reported that at as early as 9 days treatment was initiated [114]. The periosteal changes may be sufficiently pronounced that the manifestation may resemble Caffey's disease (see paragraph 7.5.6); however, in prostaglandine treatment the mandible is spared.

7.10.6 Bisphosphonates

Bisphosphonates are derivatives of pyrophosphate and binds to bone surface. In bone resorption the osteoclasts absorb the bisphosphonates. Depending on the presence of nitrogen atoms, the osteoclasts are inhibited. When no nitrogen atoms are present (clodronate and etidronate), there will be interference with the energy supply of the osteoclast, leading to apoptosis [115]. In the more potent nitrogen-containing bisphosphonates (alendronate, ibandronate and residronate) inhibition of the essential proteins in the osteoclasts is seen, which will also result in apoptosis [116].

Bisphosphonates have been developed for therapeutic use in postmenopausal women. Due to their optimal

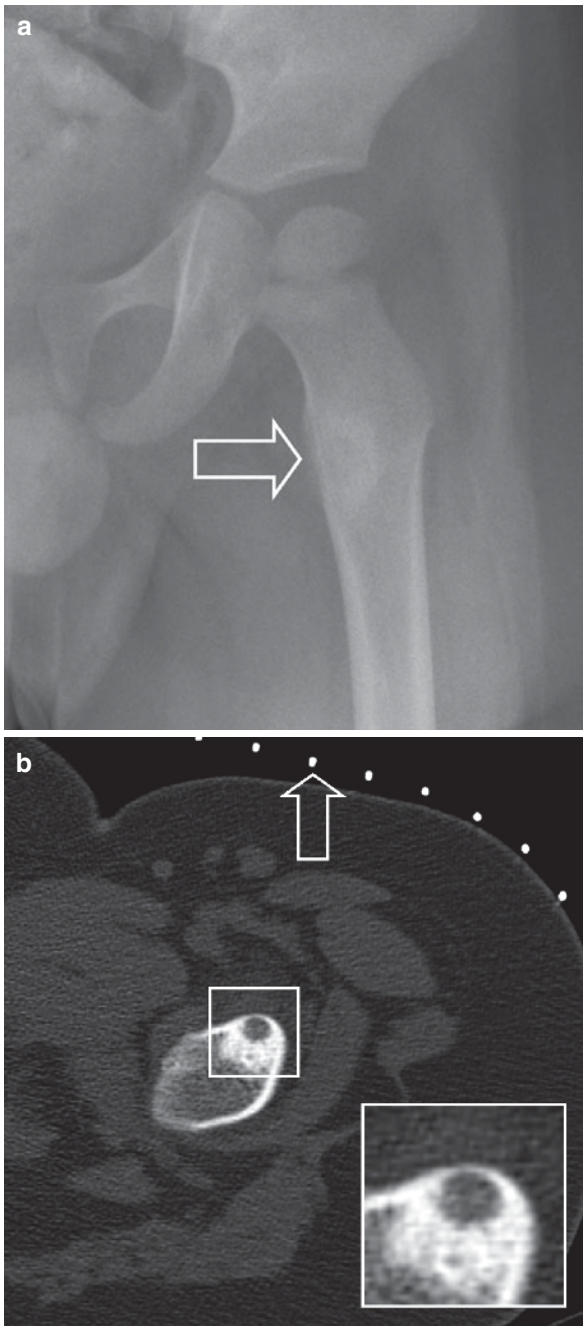


Fig. 7.37 (**a**) Ten-month-old boy with pain in the left leg. A radiograph of the femur shows cortical sclerosis (*open arrow*). Centrally a radiolucency can be seen. (**b**) A CT of the femur during radiofrequency ablation (see markers on the skin – open arrow) shows a cortical radiolucency with a central nidus (see inset)

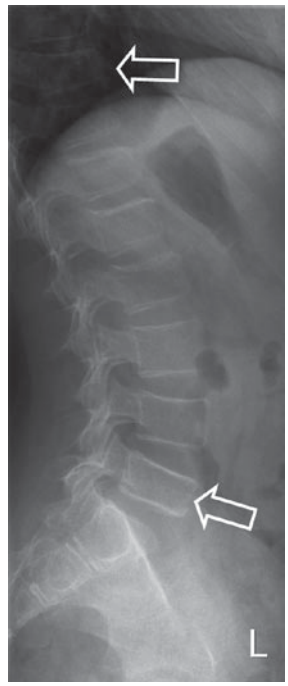


Fig. 7.38 Ten-year-old girl with IBD, for which she was treated with prednisone. As a consequence of the therapy corticosteroid-induced osteoporosis developed, which resulted in multiple vertebral fractures (*open arrows*)

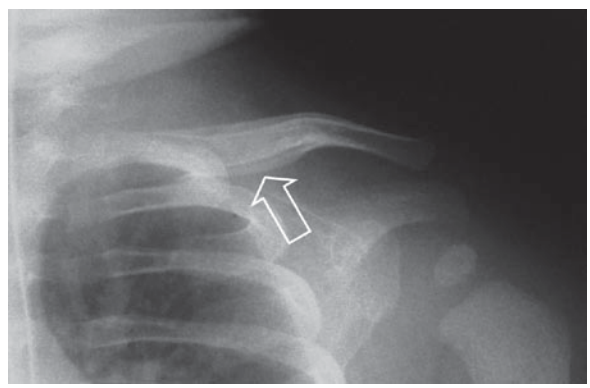


Fig. 7.39 Baby with duct-dependent cor vitium, treated with prostaglandins. There is a clearly visible reaction visible around the clavicle (*open arrow*)

effect in ideal circumstances (efficacy) and their minimal side effects, they are at the moment the medication of choice [117]. However, paediatric medicine can also accommodate treatment with bisphosphonates, such as in: osteogenesis imperfecta, fibrous dysplasia, idiopathic osteoporosis, juvenile idiopathic arthritis and in some children with tumours [118–122]. In children these medications are often administered intravenously, resulting in the characteristic image of successive growth-retardation lines corresponding with the number of treatments

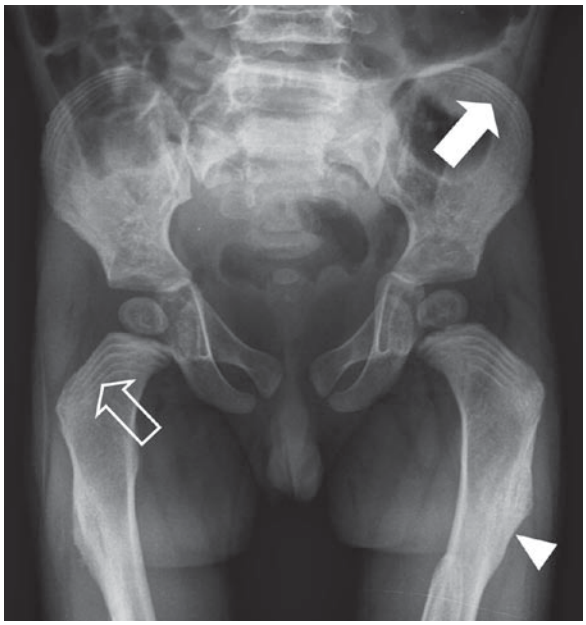


Fig. 7.40 Patient from Fig. 7.7 a year after treatment with intravenous pamidronate (a bisphosphate). The pelvic film shows sclerotic bands in both proximal femurs (*open arrow*) and near the iliac crest (*arrow*). Every sclerotic band equals an intravenous treatment. Healing retardation of the left femoral fracture is also visible (*arrow point*)

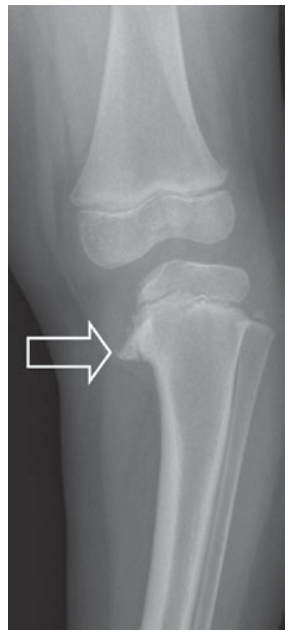


Fig. 7.41 Four-year-old girl with genu vara. Radiological examination shows a strong deviant aspect of the proximal metaphysis of the tibia (*open arrow*). Since this girl is well over 2 years old, this should not cause a diagnostic dilemma

(Fig. 7.40). When a radiologist is not familiar with this image, he/she may consider failure to thrive. However, in day-to-day practice this should not be a problem.

7.11 Other Disorders

7.11.1 Blount's Disease

Blount's disease is a deformity on the medial side of the proximal metaphysis of the tibia accompanied by tibia vara. In the more serious cases the metaphysis of the distal femur is also affected, but to a lesser degree. Generally it is assumed that this is a subclinical compression injury. It is more frequently seen in young children with preexisting tibia vara, in which case the medial side is already overloaded [123]. The compression leads to growth defects at the medial side of the tibia, increasing the tibia vara. A variant at adolescent age has also been reported, and was associated with obesity [124, 125]. The disease may present at both ages, bilateral as well as unilateral.

The radiological image shows a deformity of the medial metaphysis of the tibia with irregular margins; the metaphysis has been displaced downwards; the pointed end of the metaphysis is directed downwards (Fig. 7.41). This may cause fragmentation of the metaphysis. This image could be interpreted incorrectly as a metaphyseal avulsion fracture in a non-accidental injury; however, the fact that these children are much older and have been known to have bow-legs for some time should be sufficient to reject this erroneous diagnosis.

7.11.2 Epilepsy

Patients that are affected by epilepsy and/or spasticity are at increased risk for fractures. The literature provides several reason: accidental trauma during epileptic seizure (e.g. as result of a fall), non-epilepsy-related accidental trauma, the seizure itself, decreased bone density due to inactivity and anticonvulsant drugs, increased muscular tone with contractures and decreased muscle mass [126–136].

In children, epilepsy is one of the most prevalent neurological anomalies [131]. It may occur isolated, but is often seen combined with spasticity. The fracture rate

in epileptic patients is three times that for the general population [135, 136]. The fractures are mostly fall-related and associated with an epileptic seizure. This risk increases in the presence of more risk-increasing factors such as spasticity and decreased bone density.

Sheth et al. report four mechanisms that apply to epilepsy-related fractures: the seizure itself or a fall related to the seizure, accidental trauma not related to the seizure, and a pathological fracture resulting from decreased bone density [135]. In newly diagnosed patients, the incidence of seizure-related fractures was very low, 5% [126].

Fractures caused by the seizure itself are rare. Schnadower et al. describe bilateral femur fractures in an adolescent with primary vitamin-D deficiency due to a hypocalcaemic seizure [133]. Presedo et al. pose that 2% of all fractures in spastic children may be the result of a seizure, but refrain from reporting whether it concerns a fracture by the seizure itself or a fracture due to seizure-related trauma (fall) [130].

In children with normal bone density (no anti-epileptica or inactivity osteopenia), no fractures of the extremities due to notably increased muscle tone during a seizure are known.

The prevalence of fractures in spastic children with an average age of 10 years is 6%, of which 45% has no identifiable cause, 32% is due to trauma, and 11% is caused by medical proceedings or physiotherapy [130]. It usually concerns the lower extremities (82%). The main risk factors are: immobility, osteoporosis and the use of anti-epileptica.

Lingam et al. described 5 spastic patients (10–19 years old) with five femur fractures and one cruris fracture without identifiable causal incident [129]. In this case the authors maintain it was a combination of inactivity osteoporosis, increased muscle tone with contractures and decreased muscle mass.

Anti-epileptica, such as phenobarbital, phenytoin, primidone, valproate, carbamazepine and oxacarbazepine cause decreased bone density [127, 131, 134]. Babayigit demonstrated this in 68 children who had been on anti-epileptica for over a year [127]. Sheth et al. found a pathological fracture due to reduced bone density in 15% of fractures in epileptic children [135].

There are no comprehensive studies known on fractures in spasticity and/or epilepsy in the age group up to 2 years old.

In conclusion, one may pose that patients with epilepsy and/or spasticity are at higher risk of fractures, especially of the lower extremities, in relatively minor trauma and sometimes even without identifiable cause. Of course this does not imply that there are no non-accidental injuries in this patient group. In each patient that presents with a fracture, this subject must be open for discussion.

After all, intentional or unintentional negligence in the medical treatment or care in these often institutionalised, fragile patients can also be considered non-accidental injury. Fractures in epileptic children of less than 2 years old without comorbidity should not just be ascribed to epilepsy and as such are suspect for child abuse.

7.11.3 Vitamine-C Deficiency

Infants are protected from congenital vitamine-C deficiency (scurvy) by vitamin-C storage in utero. They deplete this storage when after birth they receive vitamine-C-deficient artificial nutrition [137]. When postpartum there is total vitamin-C deprivation, it will still take at least 5 months before the supply has been depleted. Since severe vitamin-C deficiency in pregnant women results in early abortion, congenital vitamin-C deficiency is unknown [138].

Vitamin C is, amongst others, a catalyst in collagen formation. A disturbance in collagen formation results in many of the symptoms seen in vitamin-C deficiency: disturbance in wound healing, increased fragility of the capillary walls and osteoporosis.

Scurvy is hardly ever seen in children, especially in the Western industrialised world [138]. The last case report of a child in a Western industrialised country dates from 2001 and was a 15-month-old child that had been given deficient nutrition from the 4th months of life onwards (cow milk and oat meal). It showed all the classical symptoms of a vitamin-C deficiency [139]. In the nineties there were three case reports from France (1993), Italy (1992) and Spain (1991) [140–142]. In non-Western and non- or less industrialised countries, case reports and announcements on epidemics still surface regularly [143–150].

Even in the early stages, the radiological images are rather characteristic: limited density and irregularity of the epiphyseal lines, ‘ringed’ epiphyses (Wimberger rings) and slight osteoporosis (Fig. 7.42). At a later stage, examination may show swelling of the ends of the long bones, in particular the distal ends of the femur. These swellings are due to subperiosteal

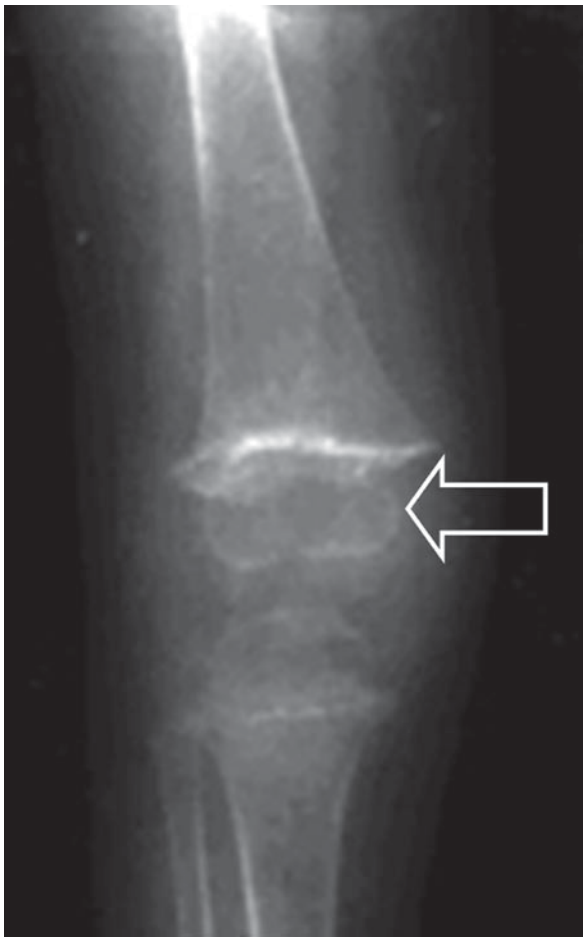


Fig. 7.42 Child with vitamin-C deficiency (scurvy). The radiograph shows an evident osteopenia with the characteristically exempt edge of the epiphysis (Wimberger ring – *open arrow*)

haemorrhages that will only in time be visible on radiographs. Externally, a shiny, livid (blue-black) skin will be visible at the location of the swelling.

If the child has already has incisors (at 7 months usually the incisors of the mandible), haemorrhagic areas will be found at their base. The gums are swollen. In adults, teeth may fall out when the deficiency has been present for a protracted period, which will reduce the state of the gums even further.

7.12 'Temporary Brittle-Bone Disease'?

In 1993, Patterson et al. described 39 children who presented with a set of symptoms that they considered to be a variant of osteogenesis imperfecta [151]. They called it 'temporary brittle-bone disease' (TBBD). As the name already implies, it supposedly was a temporary disease in which the presence of fractures is limited to the first year of life. The affected children would be susceptible to sustaining fractures after minor trauma for just a short period of time. The disorder heals spontaneously, without any visible pathology. Patterson et al. suspected that these symptoms were due to a temporary, self-limiting period of copper deficiency; although no evident proof was found in the limited study into serum copper contents.

Usually the disorder will starts with a period of vomiting, followed by diarrhoea, anaemia, hepatomegaly, incidences of respiratory arrest, neutropenia and oedema. The most common radiological findings were metaphyseal corner fractures, rib fractures, diaphyseal fractures and periosteal reactions along the long bones, anomalies at the costochondral junction and retarded bone age. Only 31% of children had a radiologically visible osteopenia.

It did not take long before doubt arose regarding the existence of TBBD, since children with confirmed copper deficiency hardly ever show fractures [152–154]. Not just the medical world criticised Patterson, also the legal world issued its comments [155–158]. One of the children in the series that Patterson described had sustained injuries as a result of child abuse. The authors did not report this in their article. This lead to concern that a full investigation into injuries in children would (no longer) take place, since the medical world could assume that one single disease could completely explain the anomalies.

In 2001, it was proclaimed in a court case in the United Kingdom that the testimony of an expert witness in the field of TBBD was not only inadmissible, but also that the scientific foundation was found to be inadequate. According to the judge, the study of the expert witness in question, doctor Patterson, was subjective, unreliable, unscientific and unproven [159, 160]. In 2004, the General Medical Council (GMC) retracted the qualifications of Patterson as pathologist. According to the GMC, he had failed as expert witness in two court cases in which the parents were accused of child abuse [161].

In 2005, the Society for Pediatric Radiology and the European Society for Paediatric Radiology jointly published an article [162]. Both societies maintain there is no scientific basis at all on which TBBD can be accepted a disease entity. Only a limited number of medical professionals believe, based on speculations, that TBBD exists. Moreover, they use conflicting ideas regarding the disorder and its origin. A few of the causes they put forward are:

- Bone or collagen pathology [151]
- Copper deficiency [151]
- Decreased in utero activity in children with reduced bone density [163, 164]

In his article, Mendelson concludes that there is no scientific foundation at all for the above-mentioned hypotheses as cause of TBBD. Consequently, this diagnosis should no longer be made [162].

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