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Dysspondyloenchondromatosis in the newborn

Report of four cases

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Abstract. Dysspondyloenchondromatosis is a rare form of generalised enchondromatosis with hypoplastic/dysplastic changes in the lower thoracic and upper lumbar spine. The disease presents at birth as neonatal dwarfism and is characterised later in life by marked shortening of stature, unequal length of the extremities and early development of kyphoscoliosis. We report four newborn babies – three boys and a girl – with dysspondyloenchondromatosis, who had skeletal survey performed shortly after birth. The condition can be established in the newborn, as the radiographic examination (skeletal survey) shows diagnostic radiographic findings.

Recently Freisinger et al. [1] reported three unrelated children with multiple enchondromatosis, severe segmentation anomalies of the spine and unequal limb length. The authors called the disease spondyloenchondromatosis.

The purpose of this article is to describe four children with similar abnormalities, all of whom had skeletal survey in the neonatal period of life (Table 1, Figs. 1–4).

Case reports

Case 1

A boy, the first child of healthy, normal, young Danish parents, was born at 39 weeks' gestation following an uneventful pregnancy. Caesarian section was performed because of breech position. At birth his crown-rump length was 46 cm and his weight 3045 g. Short limbs with bilateral varus curving of the distal tibia and right foot were noted clinically, the latter varus position being correctable. These deformities were thought to be the result of intrauterine constraint. No other abnormality was seen.

The laboratory examinations carried out were: serum Ca, P, alkaline phosphatase, 1,25-dihydroxy-cholecalciferol, parathyroid hormone and the metabolic screening of urine. All of these were normal.

Skeletal survey on the first day of life showed shortening of all the long tubular bones with irregular, transradiant defects in the metaphyses. There was asymmetry of the long bones of the lower extremities, with the right femur and tibia being more severely affected. The knee epiphyses were not calcified. The short tubular bones were also shortened. The changes in the spine were a combination of hypoplasia and dysplasia. There was marked lumbar platyspondyly. The cervical spine showed delayed ossification. In the lumbar region there was widening of the interpediculate distances. The acetabula were triradiate. The acetabular roofs were horizontal. The iliac outlines were irregular. The ribs were slightly widened with cupping of their anterior osseous ends. The bones of

Table 1. Dysspondyloenchondromatosis: summary of clinicae data

Case			Birth length (cm)	Birth weight (g)	Abnormal facies	Asymmetry of the lower extremities	Mental development	Hearing	Spine
no.	Age	Sex							
1	5 years	M	46	3045	?	At birth	?	?	At birth hypoplasia/dysplasia; minimal scoliosis at 9 months
2	$4^1/_2$ years	M	47.7	3500	At 20 months	At $2^1/_2$ years	Normal	Normal	At birth hypoplasia/dysplasia; scoliosis at $2^1/_2$ years
3	15 months	F	39.5	2100	At birth	At birth	Developmental delay	Probably normal	At birth hypoplasia/dysplasia; no scoliosis at 15 months
4	7 years	M	46	3650	At birth	At 5 weeks	Normal	Normal	At birth hypoplasia/dysplasia; scoliosis at $3^3/_4$ years

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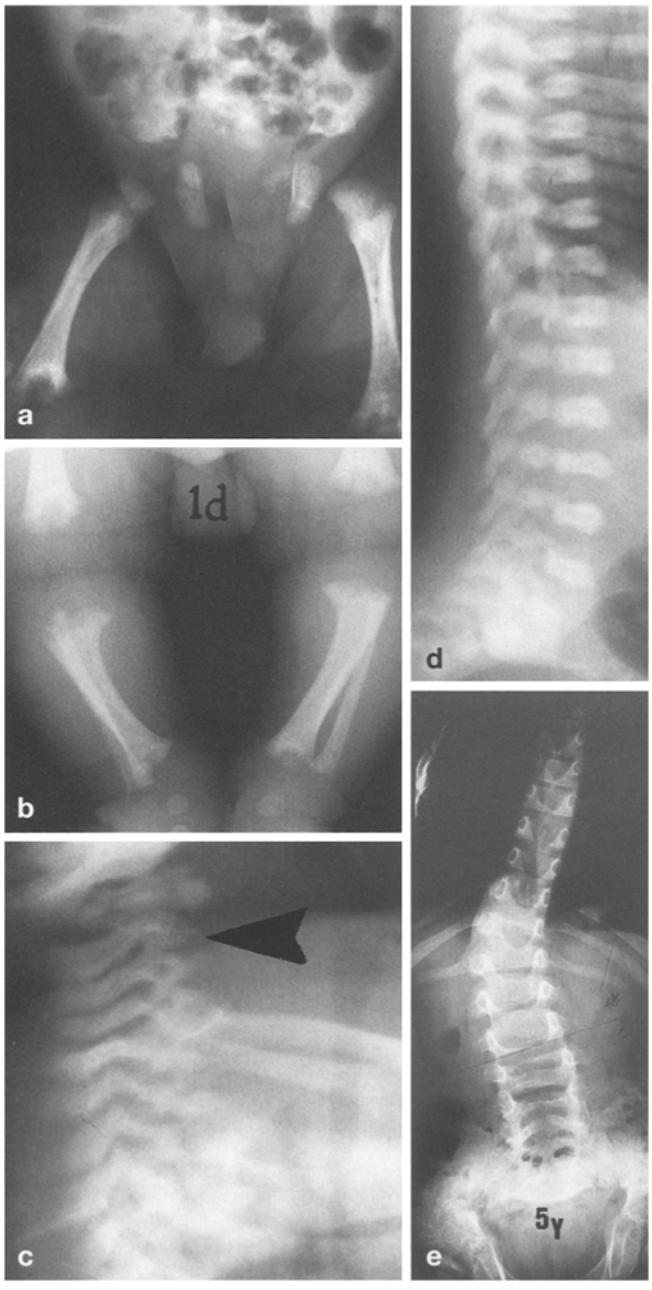

Fig. 1 a–e. *Case 1,* plain radiographs. **a–d** One day old. **a, b** Transradiant defects, characteristic of enchondromatosis. Shortened sacro-iliac notches with flattened, triradiate acetabular roofs. Irregular outlines of the iliac crests. Shortness of the right femur and tibia. The knee ossification centres are absent. **c** Delayed ossification of the cervical spine *(arrow).* **d** Platyspondyly of the lumber spine. **e** Five years old. Short segment scoliosis without obvious malsegmentation. Wide lumbar spinal canal

the cranial vault were thin and poorly mineralised. Follow-up radiograph examinations at 9 months of age showed progression of the metaphyseal changes. Minimal scoliosis was present. Further radiographs made up to the age of 5 years showed progressive scoliosis, particularly marked in the 5th year, measuring 35° on the film (Fig. 1).

Case 2

A boy, the first child of healthy, young, unrelated Caucasian New Zealand parents, was born at full term after an uneventful pregnancy and assisted breech delivery. At birth his crown-rump length was 47.4 cm, and his weight 3500 g. He was noted to have short arms and legs, a barrel-shaped chest and a short neck.

The biochemical and metabolic screening tests were normal and specifically excluded hypophosphatasia. Skeletal survey on the first day of life showed changes similar to those in case 1, the only difference being that there was no long-bone asymmetry and the pelvic changes were slightly less marked.

Hypertelorism, prominent epicanthic folds and an alternating conversion squint were noted at 20 months. At a follow-up examination at the age of $2^1/_2$ years, a short left-sided scoliosis was present with discrepancy in the leg length, the left leg being shorter (Fig. 2). A review at the age of $4^1/_2$ years commented that his spinal and leg deformities were slightly more marked. He continued to make good intellectual progress.

Case 3

A girl, the fourth child of healthy, normal Caucasian Australian parents, was born at 40 weeks' gestation after an uneventful pregnancy. Ultrasound at term suggested only 34 weeks' gestation. Delivery was by caesarian section because of breech presentation. At birth, her crown-rump length was 39.5 cm and her weight 2100 g. Short limbs were noted. The baby had abnormal facies with uplifted palpebral fissures, telecanthus, epicanthus, epicanthus inversus, flat mid-face and abnormally folded ears. The maxillary alveolar ridges were hypoplastic and cleft palate was noted. There was also laryngotracheomalacia causing upper respiratory tract obstruction aggravated by glossoptosis. Tracheostomy was necessary.

Biochemical investigations and chromosome studies were all normal. Skeletal survey on the 4th day of life showed the same changes as cases 1 and 2. There was asymmetry of the lower extremities, the right being shorter. This was confirmed at follow-up examination at the age of 8 months (Fig. 3). Developmental delay was noted at follow-up examination at the age of 15 months.

Case 4

A boy, the second child of healthy, young unrelated German parents, was born at full term after an uneventful pregnancy. Caesarian section was performed because of prolonged labour. At birth his crown-rump length was 46 cm and his weight 3650 g. He was noted to have short extremities and abnormal facies. Asymmetry of the lower extremities – the left being shorter – was recognised at the age of 5 weeks.

Biochemical and metabolic screening tests were normal and specifically hypophosphatasia was excluded. Skeletal survey in the 5th week of life showed the same changes as in the other three cases (Fig. 4).

The child's motor development was slow. He sat at the age of 1 year and walked at 2 years. At the age of $3^3/_4$ years his height was 72 cm and weight 10.6 kg. His mid-face was flattened. There was hyperlordosis with scoliosis. The left lower limb was 5 cm shorter than the right. He showed some limitation in knee flexure and elbow extension. He was myopic. His mental development was normal.

Discussion

These four children presented at birth with short limb dwarfism. Lower extremity asymmetry was noted at birth in cases 1 and 3, at age 5 weeks in case 4 and at age

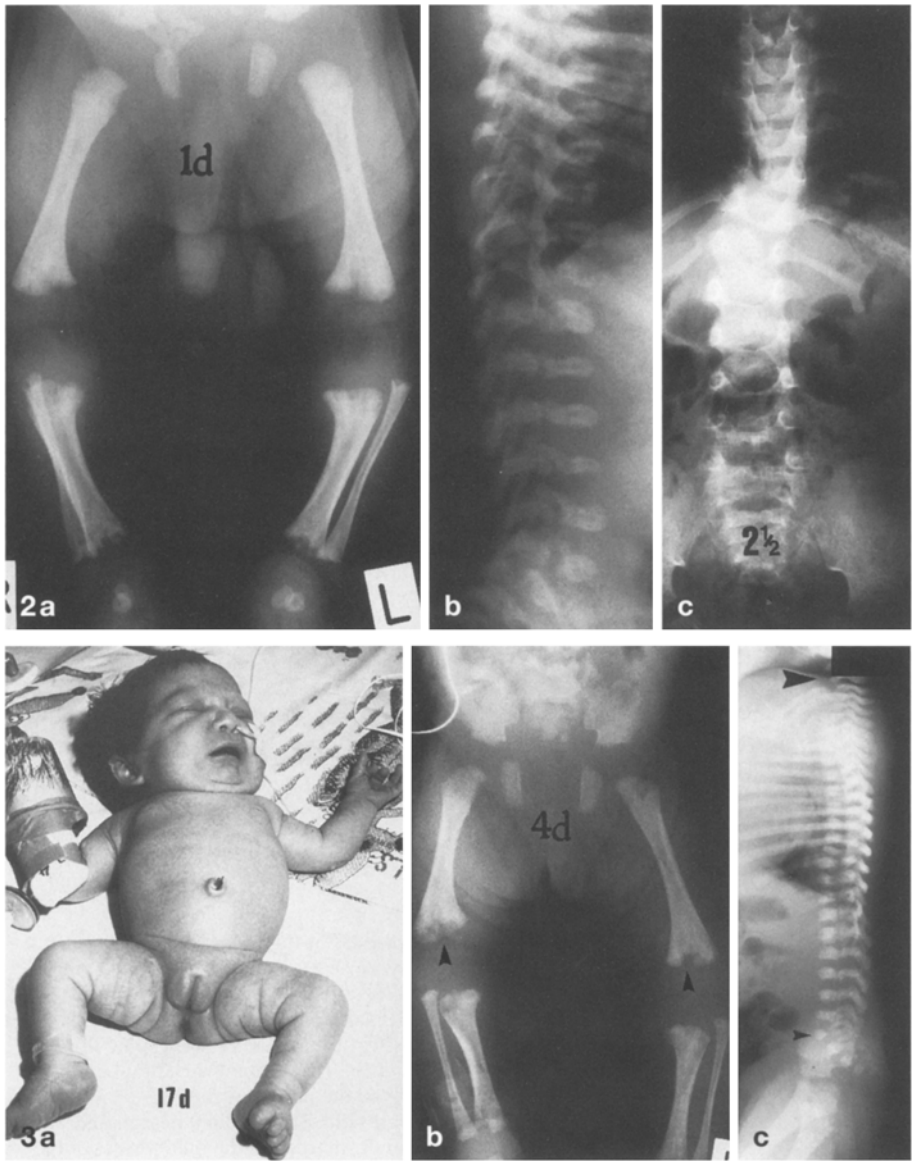

Fig. 2 a–c. *Case 2,* plain radiographs.
a, b One day old.
a Transradiant metaphyseal defects, characteristic of enchondromatosis.
b Platyspondyly of the lumbar spine.
c Two and a half years old. Short segment scoliosis without obvious malsegmentation. Wide lumbar spinal canal

Fig. 3 a–c. *Case 3.*
a Seventeen days old. Photograph of the patient shows shortening of the extremities and abnormal facies.
b, c Four days old. Plain radiographs.
b Transradiant metaphyseal defects characteristic of enchondromatosis *(arrows).*
c Delayed ossification of the cervical spine *(large arrow).* Hypoplasia of the lumbar spine and S1 vertebral body *(small arrow)*

$2^1/_2$ years in case 2. Abnormal facies were recognised in cases 3 and 4 at birth and in case 2 at 20 months.

All the children had radiographic signs of enchondromatosis with distinctive appearance of the vertebrae, including delayed ossification of the cervical vertebrae, the remainder of the spine being hypoplastic/dysplastic. The vertebral bodies were rectangular and slightly irregular in outline, and there was platyspondyly of the lumbar spine in cases 1, 2 and 4. Lumbar platyspondyly was less well marked in case 3. Initially none of the children showed scoliosis but at follow-up it was documented by the age of 9 months in case 1, $2^1/_2$ years in case 2 and $3^3/_4$ years in case 4. No scoliosis was present in case 3 at the age of 15 months. Metaphyseal bone changes were less marked in the short tubular bones.

There is no doubt that these children were similar to those described by Freisinger et al. [1], who named this condition dysspondyloenchondromatosis. Similar cases have been reported previously by Mainzer et al. [2], Spranger et al. [3], Lerman-Sagie et al. [4] and Azouz [5]. Freisinger et al. [1] and Azouz [5] report the vertebral changes was malsegmentation with hemivertebrae, but they do not specify the type, whether "classical hemivertebrae" or hypoplastic unilateral hemivertebrae [6]. Hypoplastic unilateral hemivertebrae – unlike classical hemivertebrae – have both halves of their corresponding neural arch. The first case of Mainzer et al. [2], the first case of Spranger et al. [3] and the third case of Freisinger et al. [1] certainly showed malsegmentation of the vertebral bodies with preservation of the neural arches. In the second case of Freisinger et al. [1] no radiograph of the spine was presented. Their first case, and that of Azouz [5], showed severe malsegmentation changes but it is not possible, on the evidence of the reproduced radiographs, to confirm or reject the presence of "classical hemivertebrae" without the corresponding neural arch. The case of Lerman-Sagie et al. [4] showed scoliosis without obvious malsegmentation but hypoplastic/dysplastic lower thoracic and lumbar

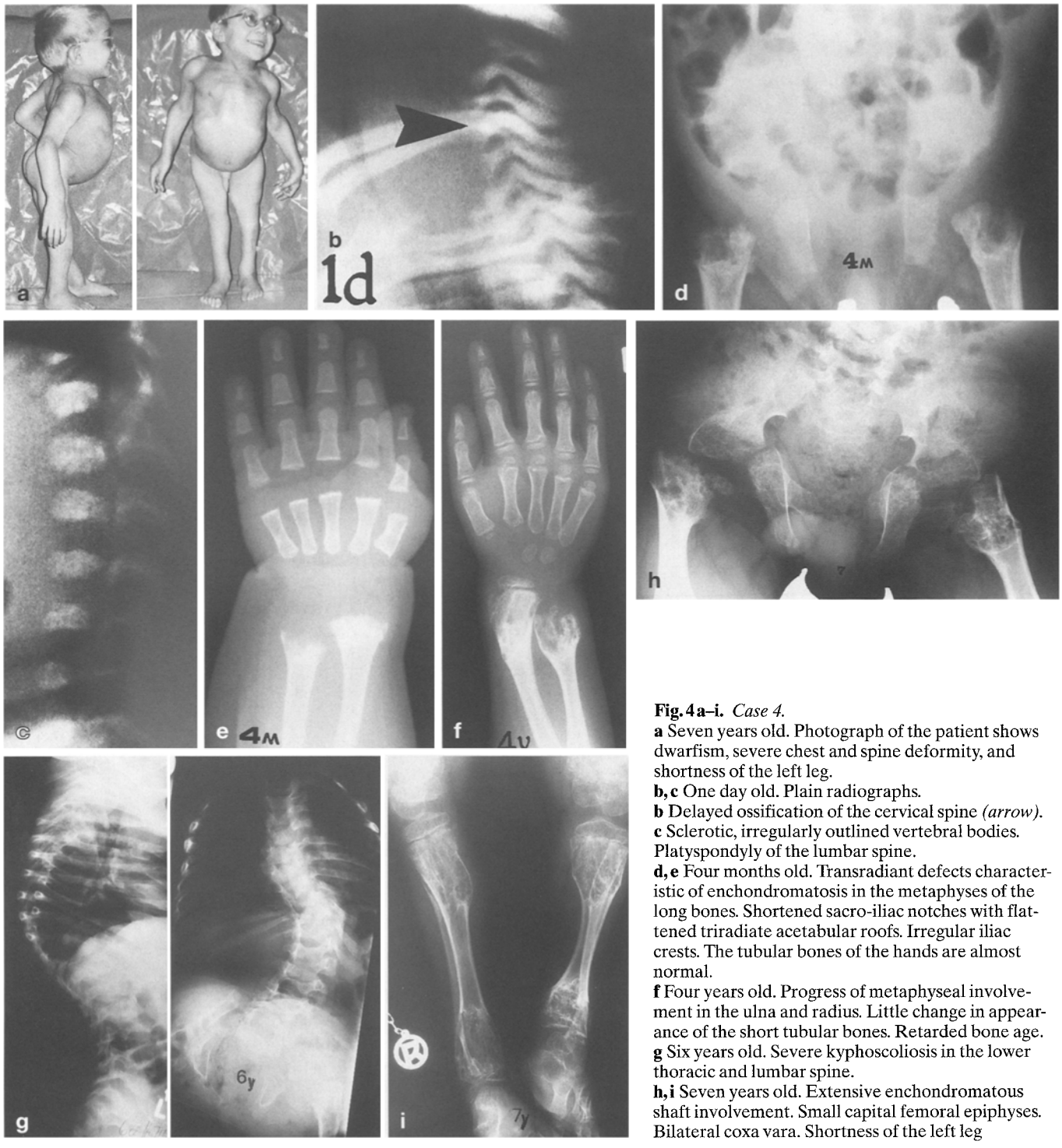

Fig. 4 a–i. *Case 4.*
a Seven years old. Photograph of the patient shows dwarfism, severe chest and spine deformity, and shortness of the left leg.
b, c One day old. Plain radiographs.
b Delayed ossification of the cervical spine *(arrow)*.
c Sclerotic, irregularly outlined vertebral bodies. Platyspondyly of the lumbar spine.
d, e Four months old. Transradiant defects characteristic of enchondromatosis in the metaphyses of the long bones. Shortened sacro-iliac notches with flattened triradiate acetabular roofs. Irregular iliac crests. The tubular bones of the hands are almost normal.
f Four years old. Progress of metaphyseal involvement in the ulna and radius. Little change in appearance of the short tubular bones. Retarded bone age.
g Six years old. Severe kyphoscoliosis in the lower thoracic and lumbar spine.
h, i Seven years old. Extensive enchondromatous shaft involvement. Small capital femoral epiphyses. Bilateral coxa vara. Shortness of the left leg

vertebral bodies. Long bone involvement varies and the changes in our case 4 were much more severe than in cases 1–3.

The classification of Kozlowski's case, reported as the micromelic type of spondylo-epimetaphyseal dysplasia [7], is uncertain, as is that of a Mauritian girl with enchondromatosis, dwarfism, limb asymmetry and deafness reported by Wallis et al. [8]. That patient's spine showed irregularity and flattening of the vertebral bodies but no malsegmentation or scoliosis.

We believe that dysspondyloenchondromatosis can be recognised, or may at least be suspected, at birth. A newborn with generalised enchondromatosis, delayed ossification of the cervical spine, lumbar platyspondyly and hypoplastic/dysplastic changes in the remaining vertebral bodies can be assumed to have dysspondyloenchondromatosis until proved otherwise. This diagnosis is supported further if asymmetry of the lower extremities is present and the small tubular bones are less affected than the long tubular bones. None of the patients

of Freisinger et al. [1] and none of the other cases previously reported had had a skeletal survey in the neonatal period, in contrast to the cases we describe.

We suggest that future examinations of patients with this condition should include tomograms, CT and MR of the spine, to evaluate precisely changes in the vertebral column and to exclude underlying spinal cord abnormalities.

All the cases reported hitherto were sporadic. They most probably represent new mutations or recessively inherited disorders.

The differential diagnosis of dysspondyloenchondromatosis includes other forms of enchondromatosis, metaphyseal dysplasias, spondylo-metaphyseal and spondylo-epimetaphyseal dysplasias. Other forms of enchondromatoses present a different pattern of enchondromatous changes. They are not generalised and are asymmetrical. The spine is not usually affected. Enchondromata and spine involvement are not present in metaphyseal dysplasias, and the latter rarely show such severe metaphyseal changes at birth. Spondylo-metaphyseal dysplasias are usually diagnosed later in life and do not show enchondromatous changes in the metaphyses. The spondylo-epimetaphyseal dysplasias may cause some confusion as they may present at birth and show metaphyseal and spine involvement. Limb asymmetry and malsegmentation of the spine might be a useful clue to diagnosis of dysspondyloenchondromatosis.

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