Sponastrime dysplasia: presentation in infancy

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EDITOR—The case of a white female with sponastrime dysplasia is presented.

Case report

The patient is the first and only child of healthy, non-consanguineous parents. During routine ultrasound scanning, the fetus was noted to have extremely short limbs and a tentative diagnosis of achrondroplasia was made. The pregnancy was otherwise uncomplicated. The baby was delivered at 40 weeks' gestation by emergency caesarian section because of breech presentation. Birth weight was 2460 g and length 44 cm (both below the 3rd centile). During infancy and early childhood, her height remained well below the 0.4th centile.

Examination showed a small baby with midface hypoplasia and a small, slightly upturned nose. With increasing age, the prominent forehead, saddle shaped nose, and midface hypoplasia became more obvious. There was rhizomelic and mesomelic shortening of her upper and lower limbs (fig 1). She was noted to have short, broad hands and feet with deep palmar creases, short toes, and dimples in the elbows and knees. In addition, she had marked generalised joint laxity except at the elbows where extension was limited. A skeletal survey at 5 months was not diagnostic, but achondroplasia was excluded.

Chromosomal analysis was normal (46,XX).

At 4 months of age, she was noted to have an eczematous skin rash, and there followed several hospital admissions for recurrent chest infections; investigations showed hypogammaglobulinaemia. Both the skin rash and the hypogammaglobulinaemia gradually normalised, effectively excluding a diagnosis of a short limbed dwarfism syndrome in association with immunodeficiency.

Despite a dysplastic (but not dislocated) left hip, crawling and walking were not delayed; however at 2 years of age she developed a waddling gait, and at 2 years 5 months a dislocated left hip was diagnosed. At 3 years, an open varus reduction and derotation osteotomy was performed. She made good recovery from her operation, and at 4 years 3 months the internal fixator was removed.

Developmental milestones were reached at appropriate ages, and mental development was normal.

RADIOGRAPHIC FINDINGS

The radiographic findings are illustrated in figs 2-7.

Spine (figs 2 and 3)

These *x* rays show the typical changes in the shape of the vertebral bodies as described by Langer *et al* in 1996 and again in 1997[2 3]: platyspondyly improving with the patient's age; a distinct junction (apparent in early/mid-childhood) between the anterior and posterior parts of the vertebral bodies (this is as a result of the anterior portions having convex end plates compared to the straight end plates of the posterior portions); a central anterior beaking of the vertebral bodies; and increasing concavity of the posterior surfaces of the vertebral bodies (posterior scalloping).There is a progressive kyphoscoliosis and mild osteopenia. Additionally, there is loss of the normal increase in interpedicular distance from L1 to L5 which can be appreciated in the radiograph taken at birth (fig 2A).

Long bones (figs 4-7)

Characteristic changes in the proximal femora consist of a pronounced bony projection of the lesser trochanter, short femoral necks, and loss of the normal metaphyseal flare. These give a "spanner-like" appearance to the proximal

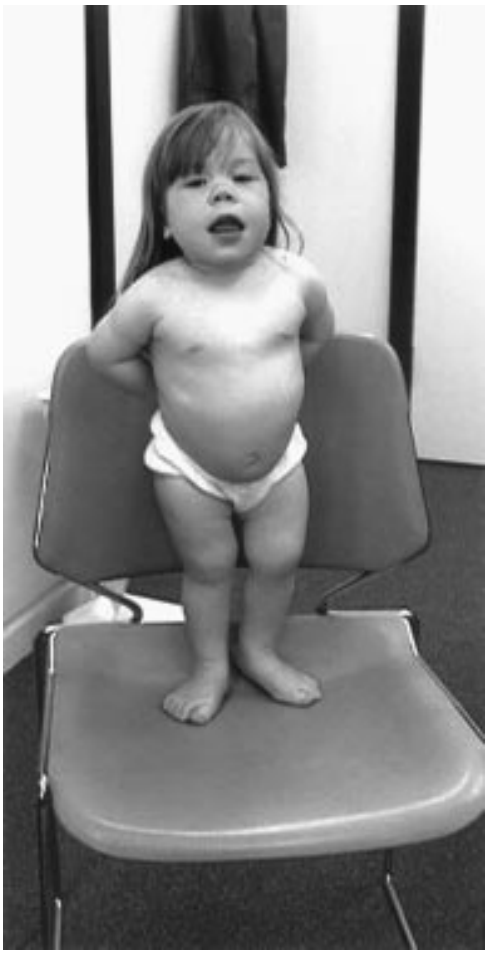

Figure 1 Clinical photograph of patient aged 4 years 8 months. Note the significant (rhizomelic) shortening, prominent forehead, and depressed nasal bridge.

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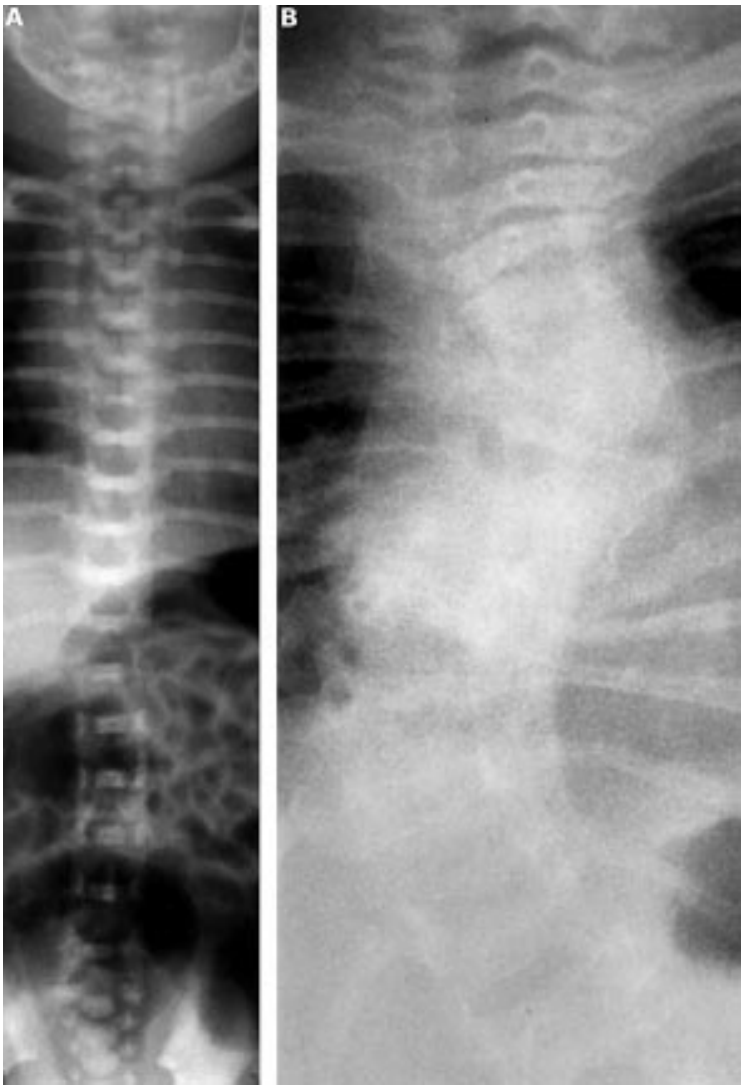

Figure 2 (A) AP spine at birth, showing platyspondyly and loss of the normal increase in interpedicular distance from L1 to L5. There is no significant curvature of the spine. (B) AP spine at 4 years 8 months. A kyphoscoliosis has developed. Note the relative increase in height of the vertebral bodies (improved platyspondyly) and the mild osteopenia.

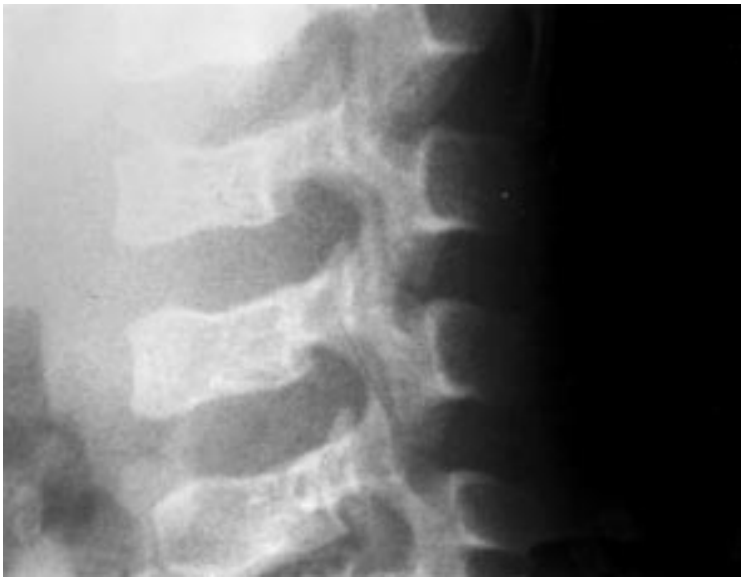

Figure 3 Lateral spine at 2 years 6 months. The platyspondyly is less marked than in infancy. There is a distinct junction between the anterior and posterior portions of the vertebral bodies and posterior scalloping.

femora (fig 4A), which becomes less marked with time (fig 4B). There was progressive development of coxa vara deformity, which although complicated by dislocation on the left, could be appreciated bilaterally.

Vertical metaphyseal striations are best seen around the knee and in the distal radius. These striations developed with age, and were not demonstrable radiologically until 4 years 8 months (figs 5 and 6).

There is retardation of bone age (fig 5) when compared to the standards of Greulich and Pyle (2 years 6 months at a chronological age of 4 years 8 months, SD 11.65 months). A pseudoepiphysis of the first metacarpal is seen, a finding which has also been seen in several other patients.[3 4] All epiphyses are small for age and slightly irregular.

Other features include a predominantly rhizomelic shortening of the limbs and flaring of the distal humeral metaphyses, giving them a rather bulbous appearance which becomes more pronounced with time. In addition, there is a curious appearance of the proximal humeral diaphyses (fig 7), consisting of a linear radiolucency affecting the medial cortex and running obliquely. Beneath this, there is cortical thickening (buttressing) and mild angulation of the humeral shaft. This appearance, reminiscent of focal fibrocartilagenous dysplasia, was bilaterally symmetrical.

Discussion

Sponastrime dysplasia is a rare but distinct entity which can be categorised as a spondyloepimetaphyseal dysplasia. The acronym was derived by Fanconi *et al*[6] from the *spo*ndylar and *na*sal alterations which occur in addition to the *stri*ations of the *me*taphyses. It has been documented in several sets of sibs,[2 3 5 6] but in the 13 cases reported to date (including ours) the parents have been non-consanguineous. It would appear that sponastrime dysplasia is inherited as an autosomal recessive disorder although germline mosaicism is a possibility.

Other than ours, 12 cases of true sponastrime dysplasia have been reported,[2–6] of which only one, described by Langer *et al*,[2] was an infant. Comparing the findings of Langer *et al*[2] to those in our patient, there would appear to be specific findings which may allow the diagnosis of sponastrime dysplasia to be made at birth and in infancy. Clinically these are non-specific and include midfacial hypoplasia, a saddle shaped nose, short limbs, and short stature. Radiological features, however, are more specific; the proximal femora have a characteristic radiological "spanner-like" appearance with a bony projection of the lesser trochanter, short curved femoral necks, and loss of the normal metaphyseal flare. This appearance of the proximal femora becomes less apparent with age. In the spine there is a significant platyspondyly with loss of the normal progressive widening of the interpedicular distances from L1 to L5. While present in all eight of the previous cases in which the result of spinal radiography was available, this is the first time that the gradual reduction in interpedicular distance has been

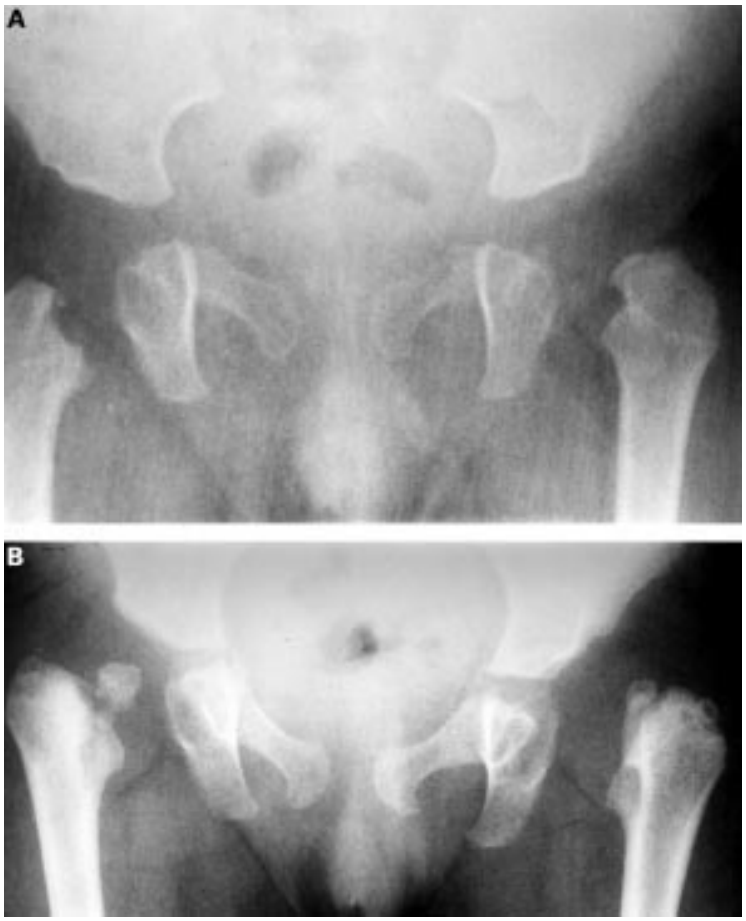

Figure 4 (A) The hips at 13 months. (B) The hips at 3 years 1 month. The spanner-like appearance of the proximal femur seen in the infant period (and early childhood) will become less obvious with age. The left hip is subluxed. The patient subsequently developed bilateral coxa vara.

confirmed in the neonate and infant. As in other reported cases,[4–6] patients may develop a scoliosis, which, as in our patient, may be significant.

Lachman *et al*[5] obtained biopsies from the iliac crests of two patients with sponastrime dysplasia. Light and electron microscopic examination findings suggested a specific morphological appearance for sponastrime dysplasia. Unfortunately, despite open surgery, a histological sample was not obtained in our patient to confirm this appearance.

Short stature is a universal finding. The severity of short stature seen in our patient (fig 1) was made worse by the development of a progressive (and significant) kyphoscoliosis (fig 2B).

Our patient developed bilateral coxa vara deformity, which has been documented in two other patients.[3] There have been two published cases of patients who both developed thoracolumbar scoliosis warranting surgery[5]; our patient has also developed a significant scoliosis.

Including our patient, mild osteopenia has been described in all eight of the patients in whom this information is available.

This is the first case of sponastrime dysplasia in which transient hypogammaglobulinaemia has been reported.

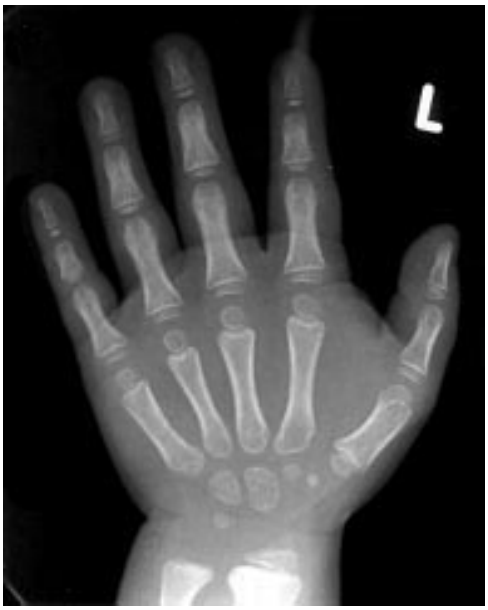

Figure 5 Left wrist and hand at 4 years 8 months. Bone age is delayed (2 years 6 months according to the standards of Greulich and Pyle). The first metacarpal has a pseudoepiphysis. Note the metaphyseal striations of the distal radius.

In our patient, there was a predominantly rhizomelic limb shortening and prominence of the distal humeral metaphyses which had a rather bulbous appearance. These changes have not previously been described in sponastrime dysplasia.

The appearance of the proximal humeri was reminiscent of focal fibrocartilaginous dysplasia, a known cause of tibia vara. On plain film it appears as a tongue-like cortical defect. It affects the medial cortex and leads to varus deformity centred at the lesion. On MRI, there is no associated soft tissue mass.[13] Although it has previously been reported in the upper limb,[14] to our knowledge it has never been seen bilaterally. Histologically, there is abnormal growth and remodelling of fibrocartilaginous tissue at the growth plate interface between the tendon and its bony attachment.[15 16] Comparing this with the histological findings of Lachman *et al*[4] in sponastrime dysplasia, we wonder if a similar (abnormal) process is occurring in the two conditions. Interestingly, neither the humeral shaft changes nor the metaphyseal striations around the wrist and knees were radiologically obvious at birth or in infancy, but became apparent in mid-childhood (4 years 8 months). The natural history of focal fibrocartilaginous dysplasia is that of spontaneous resolution[17]; as we have neither histology nor radiographs beyond 4 years 8 months in our patient, we feel that radiographic follow up may be useful.

Fig 8 shows the patient's metacarpophalangeal pattern profile (MCPP) performed at 4 years 8 months according to the method of Garn *et al*.[18] All 19 bones had negative Z values, confirming shortening. Z scores ranged from −1.2 (distal phalanx 3) to −3.6 (metacarpal 3). The normal Z score range for the metacarpals is +2 to −2. All metacarpals in this patient had a value of less than −2, again confirming

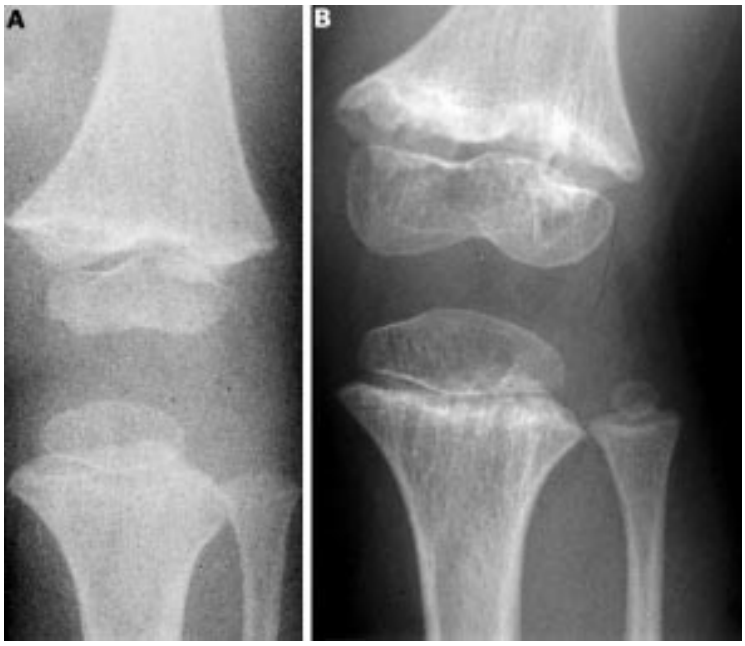

Figure 6 Left knee at (A) 2 years 6 months and (B) 4 years 8 months. Metaphyseal striations around the knee become more obvious with age.

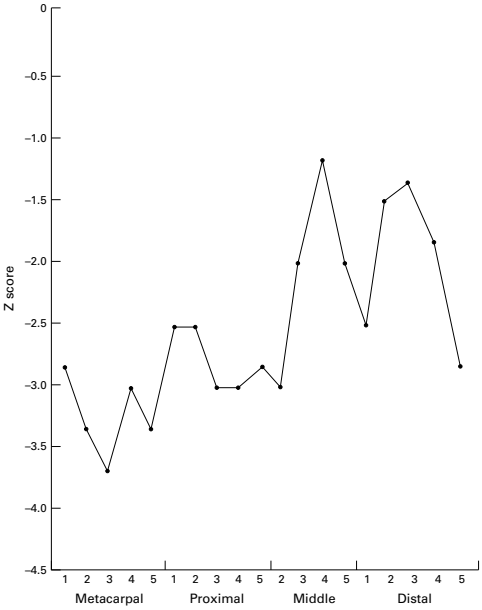

Figure 8 Metacarpophalangeal pattern profile (4 years 8 months). An up and down pattern variation (especially of the phalanges) and brachymetacarpy are illustrated.

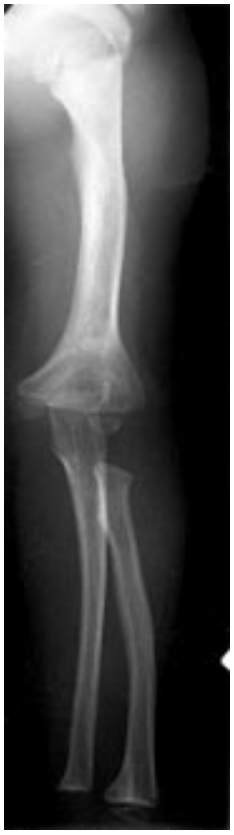

Figure 7 Left upper limb at 4 years 8 months. There is rhizomelic shortening. The humeral metaphyses are bulbous and there is a linear radiolucency of the medial cortex of the proximal humeral diaphysis running obliquely with cortical thickening (buttressing) below this. This appearance became apparent in mid-childhood.

brachymetacarpy as a feature of sponastrime dysplasia. Fig 8 illustrates an up and down variation in the hand pattern, particularly affecting the phalanges. In our patient, this is not as pronounced as in the cases of Cooper *et al*[4] and Fanconi *et al*.[6] The MCPP obtained by Camera *et al*[7] shows a much flatter pattern, further supporting the likelihood of a different condition in their patient. The pattern variability index (OZ) in this patient, based on the method described by Garn *et al*,[19] was calculated to be 0.51. A score greater than 0.7 is said to indicate hand dysmorphogenesis; Cooper *et al*[4] calculated a value of 0.73 for their patient. Their patient was 6 years 7 months old and ours 4 years 8 months; age is therefore an unlikely explanation for the differences and MCPP analyses are required in more patients with sponastrime dysplasia, in order to evaluate its use in aiding the diagnosis.

Intelligence in patients with true sponastrime dysplasia is normal. Several patients reported as cases of sponastrime dysplasia[7–9] are likely to be cases of spondyloepimetaphyseal dysplasia (SEMD) with large joint dislocations (first characterised by Hall *et al*[10]). The two sisters described by Camera *et al*[11] and the patient described by Verloes *et al*[12] do not seem to have either sponastrime dysplasia or SEMD with large joint dislocations. Table 1 summarises and compares the findings in these conditions.

As previously reported,[2 3] the metaphyseal striations are not a prominent feature in the early stages, and in our patient were not radiologically apparent until the child was almost 5

Table 1 Differential diagnosis of sponastrime dysplasia

Feature	*Sponastrime*	*SEMD with large joint dislocations*[10]	*Camera et al*[11]	*Verloes et al*[12]
Intelligence	Normal	Normal	Severe retardation	Severe retardation
Short stature	+	+	+	+
Midface hypoplasia	+	+	+	+
Saddle nose	+	+	+	+
Rocker bottom feet	−	−	−	+
Joint laxity	+	++	?	+
Hypotonia	+	+	+	+++
Large joint dislocations	−	++	−	−
Osteopenia	+	−	+	+++
Microcephaly	−	−	+	+
Wormian bones	−	−	−	+
Striated metaphyses*	+/++	+	+	−
Irregular metaphyseal margins*	+	−	−	−
Epiphyseal involvement	+	++	+	−/+
Delayed bone age	+	+	+	+
Scoliosis	+/+++	+	−	+
Characterisic age related vertebral changes*	++	−	−	−
Lumbar lordosis	+	+	+	−
Reduction in interpedicular distances from L1 to L5	+	+	−	−
Gracile metacarpals	−	+	?	−
Brachymetacarpy	+	−	?	+
Pseudoepiphyses of metacarpals	+	−	−	+
Long slender phalanges	−	+	?	−
MCPP	Up - down variation	?	?	Relatively flat

*Major radiological diagnostic features of sponastrime dysplasia.
+ mild; ++ moderate; +++ severe; − absent; ? not mentioned in paper.

years of age, so sponastrime dysplasia was not considered as a possible diagnosis; indeed this patient has previously been presented by Slaney *et al*[1] as a new syndrome of spondyloepimetaphyseal dysplasia, eczema, and hypogammaglobulinaemia. We therefore tend to agree with Langer *et al*[2 3] who feel that less emphasis should be placed on these striations and more on the findings in the spine. They suggest that the condition be called "spondylometaphyseal dysplasia with midface hypoplasia and depressed nasal bridge". However, because of the mild epiphyseal abnormalities, and because it is now present in textbooks and databases as sponastrime dysplasia, we feel that "spondyloepimetaphyseal dysplasia (SEMD), sponastrime type" is a more appropriate term.

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