SYNDROMES

Spondyloepiphyseal dysplasia

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Summary Spondyloepiphyseal dysplasia (SED) includes a group of conditions affecting the vertebrae and epiphyses following a mutation in a collagen gene. These disorders are broadly categorised in to congenita and tarda subtypes. This article briefly reviews these two subtypes and summarises the latest evidence in the literature regarding their genetics, diagnosis and treatment.

Introduction

Spondyloepiphyseal dysplasia (SED) is the name given to a group of disorders that cause deformation of vertebrae and abnormal growth at epiphyseal centres of peripheral bones. Severity and extent of symptoms vary widely and a range of radiographic features is seen. However, invariably spinal changes are seen as platyspondyly and the appearance of ossification centres, which are hypoplastic and irregular, is delayed. The main clinical outcomes are short stature (with a disproportionately short-trunk), chest malformations and early onset joint degeneration. The genetic abnormalities underlying SED are heterogeneous.

SED is split into two main categories, SED congenita and SED tarda. Other rare forms of SED with slightly different radiological and clinical features are reported. The two main forms are described below.

Spondyloepiphyseal dysplasia congenita (SEDC)

Epidemiology and genetics

SEDC is transmitted with an autosomal dominant inheritance pattern. SEDC has consistently been shown to correlate with defects in the gene COL2A1 on the long arm of chromosome 12, whose product is needed to form normal type II collagen. Type II collagen is found in cartilage, vitreous humour and the nucleus pulposus. Mutations of COL2A1 associated with SEDC have been found at multiple sites. The prevalence is approximately 3.4 per million population.5
Clinical presentation
The severity of symptoms and range of radiological changes are variable. SEDC presents at birth (antenatal testing is possible) with short stature and/or other clinical and radiological features. There is often exaggerated lumbar lordosis with associated hip flexion contractures and the abdomen protrudes. The neck is short and there may be pectus carinatum as well as a barrel-shaped chest. Other associated features include a flat face, cleft palate and talipes equinovarus deformity.

As development continues abnormal gait may become obvious due to coxa vara. Delayed ossification of capital femoral epiphyses can cause deformation and predispose to precocious OA. Thoracic scoliosis or kyphosis can develop in adolescence and may be rigid and severe. Atlantoaxial instability (and consequent spinal cord compression) is also common due to hypoplasia of the odontoid (or Os odontoideum) and can cause myelopathy, or occasionally sudden death.

Associated ocular involvement, in the form of myopia, retinal detachment or cataracts, is common.

SEDC has been divided into severe and mild variants. Severe disease causes very short stature, grossly affected hips, severe coxa vara and increased risk of myelopathy. Mild disease results in height just under the 3rd percentile and mild coxa vara. Both variants can be diagnosed at birth but cannot be differentiated until 3–4 years of age.

Radiological features
Radiological features of SEDC

Chest
- Broad thorax
- Abnormal ribs

Spine
Children
- Delayed ossification centers
- Varying degrees of platyspondyly (Fig. 1)
- Posterior wedging of vertebral bodies
- Odontoid hypoplasia

Adults
- Intervertebral disc spaces decrease
- Anteroposterior diameter of the vertebral bodies decreases
- Lordosis
- Progressive kyphoscoliosis
- The thoracolumbar junction shows the most marked abnormalities

Hips
- Coxa vara is almost always present (Fig. 2)
- Femoral head flattened and irregular (Fig. 2)
- Distal femur flattened and irregular (Fig. 3)

Knees
- Genu valgum (Fig. 3)

Treatment

- Non-surgical
  - Includes input from ophthalmology and neurology and pulmonary function monitoring.
Surgical (to relieve symptoms and improve function)

- Spinal column
  - Treatment of scoliosis may start with bracing but some will need a spinal fusion. In young patients aged 3–10 years a distraction rod inserted with no spinal fusion can limit the condition until fusion is undertaken at spinal maturity. Often lumbar lordosis is improved upon surgical correction of hip flexion deformity.
  - For atlanto-axial instability or for patients with myelopathy, atlanto-axial fusion may help symptoms. Fusion to the occiput may be needed if the posterior ring of the atlas is too small.
  - In some cases of coxa vara, a valgus or valgus-extension transtrochanteric osteotomy may help.
  - Varus supracondylar femoral osteotomy or a proximal tibial and fibular osteotomy can be useful if patients have symptomatic genu valgum.

The risk of any operation is increased due to atlano-axial instability, decreased pulmonary function resulting from an abnormal thorax and rigid spine deformities.

Spondyloepiphysial dysplasia tarda (SEDT)

The term SEDT was first used in 1957 by Maroteaux et al. to describe a condition that showed X-linked inheritance and presented with features characteristic of SED but of milder severity and later onset. Other case reports have diagnosed patients who have mild SED-type changes as having SEDT, and have described autosomal dominant and autosomal recessive inheritance. SEDT therefore is used in the literature to label different genetic diseases. Here, SEDT (X-linked) is discussed.

Epidemiology and genetics

The prevalence of SEDT has been estimated as 1.7/million in Britain. Only males are affected (X-linked). The gene responsible for SEDT is SEDL (sedlin), and has been mapped to the short arm of the X chromosome (Xp22). The molecular basis for SEDT is unknown as the sedlin region produces a protein involved in intracellular transport rather than any connective tissue or cytoskeletal protein. Therefore, it is proposed that the mutated gene product is associated with the process of organising or regulating skeletal development resulting in abnormal endochondral bone formation.

Clinical presentation

Bannerman criteria for diagnosis of SEDT

- X-linked recessive inheritance
- Short stature first evident between 5 and 14 years of age
- Shortness due to impaired growth of spine
- Radiologically characteristic flattening of vertebrae with central humping
- Dysplastic changes of femoral heads and neck
- Minor changes in other bones

Appearance is often normal at birth, so the clinical presentation is of short stature that typically becomes obvious around the time of puberty, when the trunk seems to stop growing. Back pain is usually the first complaint and can be followed by decreased spinal mobility. Hip pain, scoliosis and barrel-shaped chest may develop. Premature osteoarthritis of large joints, in particular of the hip, follows. Some patients suffer from scoliosis and/or kyphosis.

Radiological features

Radiological features of SEDT

Chest
- Increased thoracic anteroposterior and transverse diameters

Shoulders
- Epiphyseal involvement (symmetrical) (Fig. 3)

Pelvis
- Narrowing of the bony pelvis

Spine (mainly in lower thoracic and lumbar region)
Children (changes are progressive)

Irregular generalised platyspondyly
No ossification at the upper and lower anterior margins of the vertebral bodies
"Humping" of the vertebrae (characteristic feature of SEDT): mounds of bone in the posterior and central parts of superior and inferior vertebral end-plates

Adults
Disc degeneration with narrowing of intervertebral spaces (height loss in adult life)

Hips
Deep acetabulae
Short femoral necks
Abnormal femoral heads which lead to mild but early degenerative changes

Knees
The distal femurs flattened
Epiphyseal involvement (Symmetrical)

Treatment

- Surgical
  - Scoliosis should be managed as for adolescents with idiopathic scoliosis. If bracing is not successful posterior fusion may be needed.
  - Precocious osteoarthritis of the major weight bearing joints, especially the hips, is the main complication of SEDT, and if relief is not provided by valgus or valgus-extension intertrochanteric osteotomy, patients will often need arthroplasty.

References

11. Wynne-Davies R, Gormley J. The prevalence of skeletal dysplasias. An estimate of their minimum frequency and the

Figure 3 Epiphyseal involvement in distal femora with flattening of the condyles and genu valgum as seen in SED. Left lateral, Right anteroposterior view.


