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SPONDYLOEPIPHYSEAL DYSPLASIA, TARDA
NATURAL HISTORY

INTRODUCTION:

The following summary of the medical expectations in Spondyloepiphyseal Dysplasia, Tarda (SEDT) is neither exhaustive nor cited. It is based upon the available literature as well as personal experience in the Midwest Regional Bone Dysplasia Clinics (MRBDC). It is meant to provide a guideline for the kinds of problems that may arise in individuals with this disorder, and particularly to help clinicians caring for a person recently diagnosed. For specific questions or more detailed discussions, feel free to contact MRBDC at the University of Wisconsin – Madison [phone – 608 262 6228; fax – 608 263 3496; email – modaff@waisman.wisc.edu].

SEDT is rare, thought to affect about 1 in 150,000 individuals. It is an X-linked, recessive disorder. This means that only males are typically affected and are born to unaffected carrier females There will be no male to male transmission of either the disorder or the poorly functional gene that causes it, and, therefore no affected sons will be born to affected fathers. See under Genetics and Molecular Biology, below.

Unlike many bone dysplasias, SEDT is always delayed in presentation. Most often features are not recognized until around 6 to 8 years of age. Sometimes diagnosis is even delayed beyond these ages. Most often slowing growth brings an affected boy to attention. Significant joint symptoms may arise soon thereafter.

Radiologic changes in the spine are unequivocal in those who are affected, with a classic 'humped up' appearance of the vertebral bodies on lateral spine films. Epiphyseal abnormalities are considerable more subtle.

What are not concerns include the following. Life expectancy is normal. Intellectual function is normal. SEDT causes no internal anomalies of any organs. Only bony complications arise in those affected.

MEDICAL ISSUES TO BE ANTICIPATED

PROBLEM: **GROWTH**
EXPECTATIONS: Growth in infancy and childhood is normal. Beginning at around 6 or 8 years of age slowing of growth arises. In addition, it is at this time that body disproportion becomes evident. The disproportionate effect on the spine results in individuals having shortened trunks. In addition, there is usually sternal protrusion, a short neck and relatively long arms and legs. Reported adult height in affected males range from 4'1" to 5'8". Typically, ultimate adult stature is in the range of 4'9" to 5'3".
MONITORING: There are no growth charts available. Plotting linear growth on regular growth standards may provide some guide to whether growth velocity is being maintained.
INTERVENTION: There is no known specific treatment. Although there have been no trials in SEDT, growth hormone etc. is <u>not</u> likely to be effective since this disorder is secondary to intrinsic abnormality of bone growth. Limb lengthening is not appropriate, since this will result in even greater body disproportion.

PROBLEM: **JOINTS**
EXPECTATIONS: Hip pain is often the first joint symptom. In general, pain doesn't arise until late childhood or adolescence (and sometimes even later). The pain is secondary to premature degenerative arthritic changes. Such changes can affect other large joints, too, but usually disproportionately involve the weight bearing joints. Smalls joints tend to be spared.
MONITORING: Periodic clinical history regarding severity of pain and functional difficulties should be sought. Radiologic assessment can be reserved for those with symptoms.
INTERVENTION: Limitations of repetitive weight bearing activities (prohibition of long distance running, backpacking etc.) and other activities that result in repetitive stress on the hips, such as rope jumping, trampoline use etc., can slow degenerative arthritic change. Low impact or no impact aerobic activities should be encouraged. Collision sports and other activities that result in a high risk for joint injury should be proscribed since such trauma can further predispose to degenerative arthritic changes. Maintaining appropriate weight will also minimize impact on weight bearing joints. Glucosamine may be of some benefit in delaying onset of or decreasing severity of osteoarthritis, but this remains controversial. Pain management is the same as in idiopathic osteoarthritis. Use of a motorized scooter for long distance mobility is warranted whenever osteoarthritic problems become severe - sometimes as early as adolescence. Many will have total hip replacement, often in the 30s or 40s.

PROBLEM: **THORACOLUMBAR SPINE PAIN**
EXPECTATIONS: Back pain is frequent. It is not evident whether this is or is not secondary to arthritic changes.
MONITORING: Clinical monitoring.
INTERVENTION: Conservative management (nonsteroidal anti-inflamatories, physical therapy etc.) is appropriate.

PROBLEM: **SCOLIOSIS**
EXPECTATIONS: Adolescent onset of scoliosis is common although no population-based estimates of frequency seem to be available.
MONITORING: Clinical monitoring, probably yearly, beginning in mid-childhood and continuing until full completion of growth is appropriate.
INTERVENTION: Rarely is the scoliosis severe. Occasional individuals require bracing. Virtually never will spinal surgery be needed.

PROBLEM: **CERVICAL SPINE**
EXPECTATIONS: Odontoid hypoplasia and cervical spine instability are present uncommonly.
MONITORING: Flexion, neutral and extension lateral cervical spine radiographs should be obtained at the time of initial diagnosis. If normal, no additional assessment is needed. If instability is identified, consider further assessment using multi-position magnetic resonance imaging of the cervical spine.
INTERVENTION: Even with normal radiographs, nonetheless probably avoidance of exceedingly high risk physical activities such as football, rugby, trampoline etc. is prudent. If instability is found, then more serious activity limitations, in an effort to avoid marked head or neck trauma, are necessary. Only very rarely is surgical fusion needed to stabilize the cervical spine.

PROBLEM: **ADAPTIVE**
EXPECTATIONS: In general short stature is not so severe that major environmental adaptations are needed.
MONITORING: -
INTERVENTION: -

GENETICS AND MOLECULAR BIOLOGY

As noted above, SEDT is an X-linked genetic disorder. It seems to be a true recessive so that carrier females usually show no clinical manifestations of the process. Only males will have the features and potential medical problems outlined. Carrier females will have a 50% chance that each of their sons will be affected. Affected males have no chance that any of their children will be affected, but will have risk of passing the poorly functional gene on to daughters who, in turn, may then have affected sons.

Most, or perhaps all, X-linked SEDT arises from mutations in a gene called *SEDLIN*. When diagnosis is uncertain, *SEDLIN* testing can be completed.

Even in the same family, the identical mutation can cause quite considerable variably expressed features.