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PROGRESSIVE PSEUDORHEUMATOID SPONDYLOEPIPHYSEAL DYSPLASIA
NATURAL HISTORY

INTRODUCTION:

Known by a variety of names (Juvenile Progressive Pseudorheumatoid Dysplasia, Progressive Pseudorheumatoid Dysplasia, etc.), this is a rare disorder, thought to affect around 1 in 200,000 individuals. Its consequences are progressive and can be quite severe. Affected individuals are normal at birth, with age of onset ranging from around 2 years to 12 years of age, and an average of about 4 years. It is diagnosed on the basis of clinical and radiologic characteristics. As its name implies, often early signs and symptoms suggest the presence of rheumatoid arthritis. However, the usual laboratory evaluations for that entity are uniformly normal. Radiographs should allow unequivocal diagnosis, but when uncertainty remains, then molecular genetic testing could be pursued.

MEDICAL ISSUES TO BE ANTICIPATED

PROBLEM: **LIFE EXPECTANCY**
EXPECTATIONS: Despite its progressive character and severe consequences in adulthood, there is no evidence that individuals with this disorder have any decreased life expectancy. Furthermore, there are no extraskeletal abnormalities or complications.
MONITORING: -
INTERVENTION: Affected individuals and their families should be reassured regarding these issues.

PROBLEM: **LARGE JOINTS**
EXPECTATIONS: Individuals experience non-inflammatory, progressive limitation of movement secondary to bony swelling. Most often the first affected joints are the hips (and sometimes the hands). Early stance and gait anomalies are often the first recognized issues – waddling gait and a ‘Z-stance’ secondary to hip and knee contractures and a compensatory hyperlordosis of the lower spine. All large joints eventually are affected. Hips are most often most severely involved. Knees and elbows seem to be particularly severely affected as well. All affected joints display progressively limited movement. The ultimate consequences of joint movement limitation are disabling without intervention. Joint failure can be anticipated in young adulthood.

MONITORING: Periodic clinical assessment of joint movement, levels of pain and activities of daily living.
INTERVENTION: Physical therapy for range of motion therapy for superimposed soft tissue contractures, and, particularly, aquatic therapy, seem to provide some benefit. Mobility aids (e.g. cane, walker, motorized scooter etc.) become essential. Ultimately, joint replacement will be needed to allow better mobility and reduce severity of pain. Generally hip replacement is usually first and should be carried out whenever pain and limited movement become disabling. Often knee replacement surgery will be needed, too. Vocational counseling needs to take into account chronic limitations of mobility.

PROBLEM: **SMALL JOINTS**
EXPECTATIONS: Although hand abnormalities appear early, small joint involvement seems to be less disabling than effects on large joints. There is prominent swelling of the interphalangeal joints, but often with only little pain. However, this may cause fine motor functional difficulties because of stiffness.
MONITORING: Periodic clinical assessment of joint movement, levels of pain, fine motor function and ability to carry out routine activities. This should include monitoring by an occupational therapist in the school setting to insure that educational issues do not arise secondary to fine motor dysfunction.
INTERVENTION: In school age children, modification of assignments, early keyboarding, etc. may be needed. At any age, adaptive devices and equipment may be required to allow adequate fine motor function. These features, too, need to be considered in vocational counseling.

PROBLEM: **SPINE**
EXPECTATIONS: Platyspondyly (decreased vertical dimension of the vertebral bodies) is diagnostically important but is of no relevance otherwise. Scoliosis is common but usually mild and only rarely will require bracing or surgery. Often there is very marked limitation of neck movement secondary to vertebral fusions.
MONITORING: Yearly assessment for scoliosis until maturity. No effective treatment for limitation of neck mobility seems to exist.
INTERVENTION: Bracing or surgery as required, using usual criteria.

PROBLEM: **PAIN**
EXPECTATIONS: Pain is a major issue throughout the lives of affected individuals. Often hip pain is the most severe but is relieved by hip replacement surgery. Pain is non-inflammatory, similar to but evidently more severe than that resulting from osteoarthritis.
MONITORING: Inquiry regarding pain and pain management should be made with every medical contact.
INTERVENTION: Pain Clinic referral is usually appropriate and needed. All modalities of pain management should be considered.

PROBLEM: **MUSCLE WEAKNESS**
EXPECTATIONS: Generalized muscle weakness has been frequently reported. It is not clear whether this is a primary, intrinsic consequence of this disorder or if it arises mostly from disuse. Nor is it clear whether this is always but variably present or that it only is present in some affected individuals. Some individuals have muscle atrophy on examination.
MONITORING: Muscle strength screening should be part of periodic health assessments.
INTERVENTION: Efforts to limit disuse atrophy and weakness should be pursued through physical therapy, development of an adapted exercise program etc.

PROBLEM: **CLUBFOOT**
EXPECTATIONS: This has been occasionally reported in children subsequently diagnosed with Progressive Pseudorheumatoid Spondyloepiphyseal Dysplasia. It does not appear to be different from idiopathic clubfoot.
MONITORING: -
INTERVENTION: Usual orthopedic interventions are appropriate.

GENETICS AND MOLECULAR BIOLOGY

Progressive Pseudorheumatoid Spondyloepiphyseal Dysplasia is an autosomal recessive, single gene process. This means that parents who have had one affected child have a 25% risk than any next child will be similarly affected. In contrast, an affected individual will have only about a 1/900 chance that they might have an affected child (secondary to the unusual chance that their partner is a carrier of the same poorly functional gene).

Progressive Pseudorheumatoid Spondyloepiphyseal Dysplasia appears always to be secondary to loss of function mutations in a gene called *WISP3*. Molecular testing of *WISP3* is available in circumstances where diagnosis is otherwise uncertain.