



Richard M. Pauli, M.D., Ph.D.,
Midwest Regional Bone Dysplasia Clinics
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PSEUDOACHONDROPLASIA NATURAL HISTORY

INTRODUCTION:

The following summary of the medical expectations in Pseudoachondroplasia 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 children with this disorder, and particularly to help clinicians caring for a recently diagnosed child. 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].

Pseudoachondroplasia is unusual among the dwarfing bone dysplasias because diagnosis is often delayed. Indeed, both physical features and growth are normal in the first year or two of life, and radiological features are straightforwardly identified only after around one year of age. Therefore diagnosis in the absence of a positive family history is often delayed until 2 to 4 years of age, at which time slowing growth or waddling gait brings the affected child to medical attention.

MEDICAL ISSUES AND PARENTAL CONCERNS TO BE ANTICIPATED

PROBLEM: GROWTH

EXPECTATIONS: Initial growth in infancy is usually normal. Moderate to severe short stature is typical, with average adult height of about 120 cm (about 48 in). However, there is great variability, with adult heights ranging from about 90 cm (36 in) to 155 cm (61 in). Head growth is normal.

MONITORING: Rudimentary Pseudoachondroplasia-specific growth grids are available and should be used to monitor growth.

INTERVENTION: No known treatment. Growth hormone is not likely to be effective since this disorder is secondary to intrinsic abnormality of bone growth. Extended limb lengthening has been suggested but is controversial.

PROBLEM: DEVELOPMENT

EXPECTATIONS: Intelligence is normal. Variations in developmental patterns are to be expected because of short stature and joint instability.

MONITORING: Routine.

INTERVENTION: None.

PROBLEM: LEG POSITIONAL ABNORMALITIES

EXPECTATIONS: Beginning after orthograde weightbearing, nearly all develop some knee and leg position abnormality. By far the most common is varus deformity (bowleg) although some develop either bilateral knee valgus or a windsweep (valgus on one side and varus on the other). Progressive deformity, in conjunction with laxity and instability of the knees, results in activity associated pain.

MONITORING: Clinical monitoring for alignment, development of chronic knee pain, limitation of ambulation (usually secondary to pain).

INTERVENTION: Surgery should be delayed as long as possible since, if correction is done early, then repeated surgery is quite likely. Recurrence presumably arises because of persistent asymmetric growth at the growth plate. Often multilevel osteotomies are needed (i.e. correction at both the distal femoral and proximal tibial levels). Osteotomies require meticulous alignment and should be done by a pediatric orthopedist experienced in performing such surgery on individuals with pseudoachondroplasia.

PROBLEM: THORACOLUMBOSACRAL SPINE

EXPECTATIONS: There is high risk for kyphoscoliosis, usually beginning in late childhood or adolescence, eventually affecting at least 50% of individuals. Hyperlordosis of the lumbosacral region is common.

MONITORING: Clinical examination every 6 months. AP and lateral spine x-rays if any clinical indication of a kyphoscoliotic curve developing.

INTERVENTION: Kyphoscoliosis often will require bracing in childhood but only relatively infrequently will require surgical fusion. Hyperlordosis is far less of a concern, but if it results in low back symptoms, then an exercise program for strengthening of lower abdominal muscles and 'tucking under' may be helpful.

PROBLEM: CERVICAL SPINE

EXPECTATIONS: Although the risk may not be as great as in other forms of spondyloepiphyseal dysplasia, odontoid hypoplasia and/or cervical spine instability is present in a minority [perhaps about one in six]. Instability is more often seen in those with odontoid hypoplasia/os odontoidum. If present there is considerable risk for upper cervical cord compression [chronically or acutely].

MONITORING: Lateral cervical spine films [flexion, neutral and extension] should be obtained when the diagnosis of pseudoachondroplasia is first made; if abnormal or equivocal, repeat as part of complete assessment every 6 months. In those with possible neurologic abnormality, multiposition magnetic resonance imaging may help determine if surgical intervention is needed.

INTERVENTION: Treatment for severe, symptomatic instability is cervical fusion, which, however, is rarely needed.

PROBLEM: HIPS

EXPECTATIONS: Hip degeneration and premature osteoarthritis is nearly uniform and more than half will have total hip replacement, often in the 30s or 40s. Although requiring custom prostheses, such hip replacement can be successfully completed.

MONITORING: Radiologic assessment with symptoms.

INTERVENTION: Limitations of repetitive weight bearing activities and other activities that result in repetitive stress on the hips, such as rope jumping, trampoline use etc., can slow degenerative arthritic changes; Use of a motorized scooter for long distance mobility is warranted beginning at early school age.

PROBLEM: OTHER LARGE JOINT SYMPTOMS

EXPECTATIONS: Problems may include – ankle instability; shoulder subluxability; generalized morning stiffness.

MONITORING: Clinical monitoring.

INTERVENTION: AFOs may benefit if ankle instability is particularly severe. Morning stiffness may be relieved by use of an eggcrate mattress and morning baths or whirlpool.

PROBLEM: WRIST AND INTRINSIC HAND JOINT INSTABILITY

EXPECTATIONS: Profound hypermobility of the wrists and the intrinsic joints, along with marked brachydactyly, arise in childhood and may result in fatigue when doing fine motor functions such as writing, drawing etc.

MONITORING: Occupational therapy monitoring in school.

INTERVENTION: Initiation of early keyboarding and substitution of keyboarding for manual writing may be needed.

PROBLEM: ADAPTIVE

EXPECTATIONS: Considerable psychological and physical adaptive needs may arise later in childhood.

MONITORING: Assess for age appropriate needs.

INTERVENTION: School adaptations, stools, teacher involvement, Little People of America involvement.

GENETICS AND MOLECULAR BIOLOGY

Pseudoachondroplasia appears always to be caused by an autosomal dominant gene abnormality. This means that an adult with this disorder will have a 50% chance to pass this poorly functional gene on to each child. Not infrequently an individual with this disorder will be born to average statured parents. When this happens it usually is because of a new chance change (mutation) in

only the single egg or single sperm giving rise to the affected individual. However, instances of germinal mosaicism are not rare (and, in fact, before this phenomenon was recognized this led to the incorrect hypothesis that there was a recessive form of this disorder). Germinal mosaicism is sufficiently common that a risk of about 1-2% for recurrence after the birth of one affected child to parents of average stature is probably a reasonable estimate. If two parents of average stature already have more than one affected child, then recurrence risk is much greater and may approach 50%.

All individuals with pseudoachondroplasia have mutations in a gene which codes for Cartilage Oligomeric Matrix Protein (*COMP*). Other mutations at this same locus sometimes cause a clinically related but milder disorder called Multiple Epiphyseal Dysplasia.