Arthrogryposis

Causes, Consequences and Clinical Course in Amyoplasia and Distal Arthrogryposis

Background. Arthrogryposis Multiplex Congenita, AMC, is a heterogeneous condition defined as multiple congenital joint contractures in two or more body areas. The pathogenesis is impaired fetal movements. Amyoplasia, the most frequent form, is a sporadically occurring condition with hypoplastic muscles and joint contractures. Distal arthrogryposis (DA) syndromes are often hereditary, and joint involvement is predominantly in hands and feet. Arhrogryposis with CNS involvement includes chromosomal and other syndromes.

Aims. The purpose of this study was to investigate patients with arthrogryposis, to classify the different occurring forms, and to investigate causes, muscle and joint involvement, motor function, treatment and outcome.

Methods. Patients were identified via pediatric rehabilitation centers. Family and case history including perinatal findings were recorded. Physical investigation included joint range of motion, muscle strength and motor function. In patients with DA molecular genetic and, in selected cases, muscle morphologic investigations were carried out.

Results. 131 patients with arthrogryposis were investigated. The most frequent diagnoses were amyoplasia and DA. In amyoplasia, community ambulators had the best muscle strength, household ambulators had severe contractures in legs but good muscle strength in arms, and non-ambulators had the most severe contractures and muscle weakness. Muscle strength was found to be more important than joint range of motion for motor function.

In DA, muscle weakness was present in 44% of investigated patients. Mutations in sarcomeric muscle protein genes were found in seven families with autosomal dominant and in one child with sporadic DA. In one family with a mutation in *TNNI2* there were mild myopathic findings, in one family with mutation in *TPM2* no obvious myopathy, and in patients from three families with *MYH3* mutations mild myopathic findings. Clinical findings were found to be highly variable between families and also within families with DA.

Conclusions. Different forms of arthrogryposis were identified. In amyoplasia, attention should be directed at development of muscle strength with early stimulation of active movements. Immobilisation should be minimized. DA syndromes are clinically and genetically heterogeneous conditions. Fetal myopathy due to sarcomeric protein dysfunction can cause DA. An early multidisciplinary team evaluation for specific diagnosis and planning of treatment is recommended.

Key words. Arthrogryposis, amyoplasia, distal arthrogryposis, muscle involvement, motor function, contractures, muscle morphology, sarcomeric protein dysfunction.

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I. **Kroksmark AK, Kimber E, Jerre R, Beckung E, Tulinius M**
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Distal arthrogryposis: Clinical and genetic findings
Manuscript

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