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Dilatation of aortic root, arachnodactyly, and arthrogryposis in a newborn as early manifestation of a Marfan syndrome with a new splice acceptor mutation

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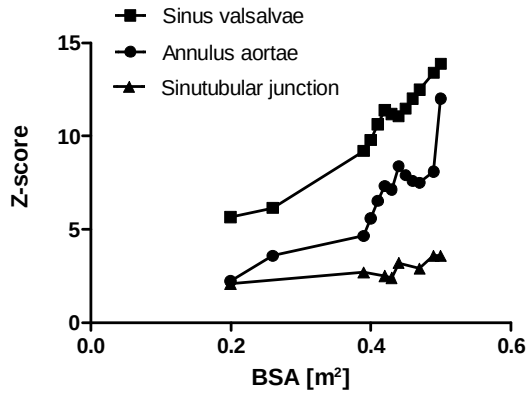
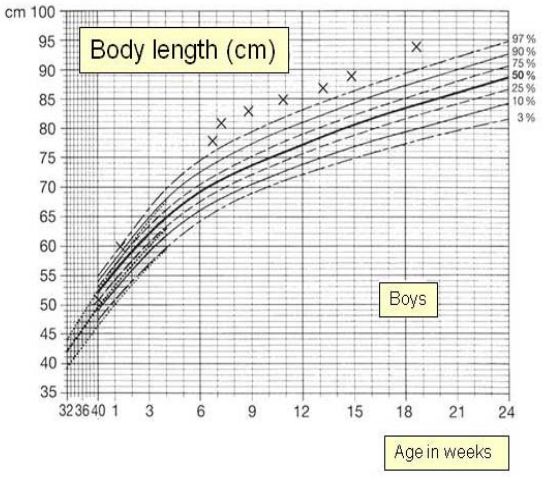
Introduction: Marfan syndrome is an autosomal dominant connective tissue disorder. The diagnosis relies on defined revised criteria (1, Ghent nosology, 2010) and is possible in over 95% due to detection of causative mutations in the fibrillin-1 gene. The revised criteria emphasize the cardiovascular manifestations and the ectopia lentis for diagnosis. The systemic manifestations are comprised in a new scoring system. However, the clinical phenotype is highly variable and the most severe forms get symptomatic in the neonatal period and early infancy. Therapy is medical and under certain conditions surgical. Prognosis depends on the progression of aortic root dilatation and consecutive aortic dissection or rupture.
Case: A term male newborn presented with a dilated aortic root (Z-score +5), arachnodactyly, joint contractures and facial progeria. In addition, a severe myopia (-17 dioptre) and a Morgagni hernia were detected. The score for systemic manifestation was nine. Molecular analysis showed a new heterozygous splice acceptor mutation in the fibrillin-1 gene (c.3965-1G>C). In the further course the patient developed a progressive dilatation of the aortic root in spite of medical therapy (ß-blocker and AT-1 antagonist), a severe thoracolumbar kyphosis and acceleration of the growth of his body length (see figures).





Discussion: The relevance of the mutation, the differential diagnosis in respect to connective tissue disorders considering the revised Ghent criteria, therapeutic interventions and the further course and prognosis are discussed.
Summary: Early diagnosis by detecting a causative mutation in the fibrillin-1 gene is important for exclusion of other diagnosis, optimal treatment and genetic counseling of the families.
[1] Loeys BL et al. (2010) The revised Ghent nosology for the Marfan syndrome. J Med Genet 47:476-85