A new locus for brachydactyly type A2 maps to chromosome 20p

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Introduction:
Brachydactyly, or shortening of the digits, is due to the anomalous development of the phalanges or metacarpals. As an isolated feature, the different types of brachydactyly have been classified on an anatomical and genetic basis into five groups, A-E, including three subgroups (A1-A3) by Julia Bell [1951].

Bell’s classification of brachydactyly:

Brachydactyly A2, an autosomal dominant hand malformation, is characterized by short and laterally deviated second and fifth fingers. Also, the first and second toes can be affected in a similar way. The other fingers and toes are for the most part of normal form (see exemplary cases).

Recently, heterozygous missense mutations in the gene coding for bone morphogenetic protein receptor 1b (BMPR1B) were shown to cause brachydactyly A2 in some families by acting in a dominant negative manner (Lehmann et al, PNAS, 2003)1.

Besides our recent report, families with brachydactyly type A2 have been published only a few times in the literature. In 1919 Mohr and Wriedt2 first described this form of brachydactyly in a large Norwegian family. In this pedigree, a possible homozygote affected child as a result of a consanguineous marriage of two affected parents with an isolated brachydactyly, was mentioned to have a very severe skeletal phenotype.

Another description of a large Brazilian family of German origin with very severe skeletal phenotype. Parents with an isolated brachydactyly, was mentioned to have a child as a result of a consanguineous marriage of two affected parents with an isolated brachydactyly, was mentioned to have a very severe skeletal phenotype.

Another description of a large Brazilian family of German origin with 117 family members affected by isolated brachydactyly A2 was published by Freire-Maia et al, 19803. In addition, his clinical report indicated a higher fertility in affected women than in unaffected individuals.

We had the chance to perform a linkage study in 26 family members of this Brazilian pedigree presenting with brachydactyly type A2 (see pedigree).