Familial non-syndromic thoracic aortic aneurysms and dissections – a life threatening disease.
Identification of novel genetic mutations of the ACTA2- and MYH11-gen in two families.

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Introduction: Aneurysms of the thoracic aorta (TAAD) occur sporadically in about 80% and familiar in about 20% of the cases. Non-syndromic familial thoracic aortic aneurysms and dissections (FTAAD) are characterized as TAAD in absence of clinical syndromes such as Marfan-, Loeys-Dietz- or vascular Ehlers-Danlos syndrome. FTAAD is a functionally heterogeneous disorder with autosomal dominant transmission. It is identified to date by mutations of TGFBR2 as well as of gens encoding structural proteins of the smooth muscle cells such as ACTA2 and MYH11. Mutations in the ACTA2 gen furthermore predispose to occlusive vascular disorders of the coronary and cerebral arteries as well as a bicuspid aortic valve and a PDA; extracardiac involvement may be present in the skin (livedo reticularis) and the eye (iris flocculi). Mutations of gen MYH11 are rare; in most patients a PDA is present.

Results: This report is on two families with an ACTA2- and a MYH11-mutation each, in which both a novel mutation has been identified. The ACTA2 family members are affected with PDA, dilation and aneurysm of the ascending and descending aorta including death because of dissection [missense mutation c.229A>T (p.Ile77Phe) in exon 3 of the ACTA2 gen]. The MYH11 family members suffered from valvular aortic stenosis and dilation and dissection of the thoracic aorta, associated with death [heterozygote mutation c.4975.5T>C within the intron 35 of the MHY11 gen].

Conclusions: FTAAD disease is a rare hereditary disorder with increasing clinical importance because of its potential lethal outcome. Patients with dilation/ dissection of the aorta should be thoroughly screened for involvement of the coronary and cerebral arteries, a PDA, or ocular and cutaneous signs; investigation of first degree family members is mandatory and a genetic counselling is obligatory.