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First Evidence of Maternally Inherited Mosaicism in TGFBR1 in Loeys Dietz Syndrome. Literature Review of TGBR1&2 Mosaicism.

Baban A.(1), Magliozzi M.(2), Adorisio R.(1), Secinaro A.(3), Dietz H.(4), Vricella L.(4), Drago F.(1), Novelli A.(2), Amodeo A.(5)
1Pediatric Cardiology and Cardiac Arrhythmia/Syncope Unit, Department of Pediatric Cardiology and Cardiac Surgery, Bambino Gesù Children's Hospital and Research Institute, Rome, Italy.
2Laboratory of Medical Genetics, Bambino Gesù Children's Hospital and Research Institute, Rome, Italy.
3Department of Imaging, Bambino Gesù Children's Hospital and Research Institute, IRCCS, Rome, Italy.
4Howard Hughes Medical Institute and Institute of Genetic Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA; Division of Pediatric Cardiology, Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA; Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA.
5 Mechanical Assistance Device Unit, Department of Pediatric Cardiology, Bambino Gesù Children's Hospital and Research Institute, Rome, Italy.

The index patient is the only male child of Caucasian non-consanguineous parents, both having normal echocardiographic findings at baseline visit. The mother was operated for recurrent hemorrhage originating from the right buccal artery. She also recently presented with diminished right visual acuity for spontaneous vitreous detachment. On physical examination, the mother disclosed no signs of cranio-facial abnormalities.
Aortic dilatation of the proband was confirmed after birth and follow-up was instituted and carried out at another institution, where the diagnosis of oculo-cutaneous albinism was also made. PE disclosed macrosomia and bifid uvula. The suspicion of the coexistence of two distinct genetic defects was raised: oculo-cutaneous albinism and Loeys Dietz Syndrome (LDS). NGS approach identified a previously repoted, heterozygous, missense mutation c.1460G>A (p.Arg487Gln) of TGFBR1 (data confirmed by Sanger). Parents was tested for segregation study which identified a maternally inherited mutation in mosaicism. Specifically, the rate of mosaicism was 18% in peripheral blood cells and buccal cell swab DNA and around 10% in DNA extracted from the hair root cells. The child was operated for aortic root replacement that was complicated by severe haemorhage and complete AV block that needed pacemaker positioning. He was discharged and is doing well at 5 months follow up.
Maternal head to pelvis MRI showed vascular asymmetry at head and neck regions mainly prevalent right vertebral and left carotid arteries without significant signs of arterial tortuosity. The volume rendering reconstruction of the gadolinium enhanced MR angiography showed mild tortuosity at the arch and mild ectatic proximal abdominal aorta and peculiarly the left ventricle vertical long axis cine image in diastolic phase revealed multiple myocardial clefts at the inferior basal segment and anomalous distribution of mitral papillary muscle without signs of regurgitation. The aorta showed a uniform dilatation of the abdominal aorta. Peculiarly the left ventricle showed myocardial inferobasal cleft.
Literature review of mosaicism in TGFBR1 and TGFBR2 mutations are included.
This is the first report of somatic mosaicism of a TGFBR1 mutation of a mother of a child with classic LDS.