Carvajal syndrome - rare entity of cardiocutaneous syndrome in a child from the Mediterranean part of Croatia - report on a new mutation of a desmoplakin gene

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Introduction: Within the arrhythmogenic right ventricular cardiomyopathy (ARVCM) there are two entity forms referred to as the Naxos syndrome and the Carvajal syndrome. If ARVCM also has a palmoplantar keratoderma with distinctive hair features (wooly hair) it is described as the Naxos syndrome, but if cardiomyopathy is spread on both ventricles with even more severe changes on the left ventricle, the entity is referred to as the Carvajal syndrome.

Objective: To describe a child with a biventricular dilated cardiomyopathy with a dominantly left sided cardiomyopathy with palmoplantar hyperkeratosis and wooly hair, and to present a molecular-genetic analysis of a gene which codes desmoplakin; one known database mutation as a non sense mutation was found: c.3791G>T, p.Glu1265X on exon 23 and one variant not yet presented in the database (http://www.arvcdatabase.info): variant p.Asp297His, c.889G>C on exon 7.

Case study: A 4.5 years old boy from the Croatian Mediterranean basin was hospitalized for clinical symptoms of global biventricular cardiac insufficiency (hepatomegalia, positive venal pulse, pulmonary edema), with extreme cardiomegalia and high pro-BNP values. He had palmoplantar hyperkeratosis and peculiar hair (wooly hair), and echocardiography revealed biventricular dilatation with severe LV hypocontractility. After a short-term stabilization using conventional therapy (diuretics, ACE inhibitors, digitalis), he became dependent on inotropic support. He was candidate for heart transplant, but died before available donor. Child’s mother also has dilated cardiomyopathy which extends on both ventricles with decreased contractility (EF 35%). Due to arrhythmogenic episodes which commenced when she was 40, an ICD was implanted in the mother. A molecular-genetic analysis was performed for the child. We also presented a pathologic anatomical finding with special emphasis on presenting the histological analysis of right and left ventricle.

Conclusion: We present a patient with a triad of symptoms (biventricular cardiomyopathy, palmoplantar hyperkeratosis, wooly hair) making the Carvajal syndrome which is a rare entity form of the Naxos syndrome, i.e. arrhythmogenic cardiomyopathy of the right ventricle. Detailed molecular-genetic analysis has confirmed a new mutation for desmoplakin synthesis on exon 23 and a peculiar pathohistological finding on right and left ventricle.