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Congenital heart defect in patient with Noonan Syndrome and RIT1 mutation.

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Background: Noonan syndrome (NS) is a genetically heterogeneous, autosomal dominant disorder due to mutations in genes, the majority coding proteins with an established role in the RAS/MAPK signalling pathway. *RIT1* mutations have recently been identified as a new cause of NS. The aim of the study is to evaluate the prevalence and anatomic types of congenital heart defect (CHD) in NS patients heterozygous for mutations in this gene.
Methods. From January 2015 to January 2016, 9 patients with NS-causing *RIT1* mutations have been diagnosed. All patients had 2D-color Doppler echocardiographic and ECG evaluation. CHD was diagnosed in all of them.
Results. Pulmonary valve stenosis (PVS) was the most recurrent defect accounting for six cases. Hypertrophic cardiomyopathy (HCM) and atrial septal defect ostium secundum type were observed in four and three cases, respectively, while partial atrioventricular canal defect (pAVCD) and ventricular septal defect (VSD) was documented in one individual each. All patient with PVS had also supravalvular pulmonary stenosis and dysplastic pulmonary valve. HCM was associated with PVS and muscular VSD in one patient, with PVS in an additional one. One patient with HCM with biventricular obstruction had cardiac transplantation at the second year of age. Lymphatic anomalies were present in 3 patients, including recurrent chylothorax in two cases, lymphedema of lower limbs in one.
Conclusions. 1) the prevalence of CHD in patients with *RIT1* mutations is relatively high and needs further studies to be underlined; 2) a great variety of anatomic abnormalities in CHD is detected ranging from the classic PVS and HCM to the uncommon pAVCD; 3) HCM can be severe; 4) complications due to lymphatic anomalies should be taken into account in these patients especially at the postoperative stage due to higher risk of chylothorax.