PW4-8

Cardiac anomalies in Noonan sydrome: experience in 64 patients

Banaudi E., Riggi C., Baldassarre G., Ferrero G.B. *, Silengo M.*, Agnoletti G.*
Department of Cardiology and Genetics, Paediatric Hospital Regina Margherita, Turin, Italy*

Introduction: Noonan Syndrome (NS) is a variagate autosomal dominant disorder, related to mutations in the genes of RAS/MAPK pathway. NS is frequently associated with short stature, facial dysmorphism, congenital heart defects (CHD) (70-80% of cases), impaired blood clotting, lymphatic dysplasia, learning problems. Common CHD are pulmonary valve stenosis (PVS), hypertrophyc cardiomyopathy (HCM) and septal defects.
Patients and methods: We describe cardiac involvement and genotype in a cohort of 64 patients born from 1986 to 2010, who had a clinical diagnosis of NS in our centre.
Results: We evaluated 64 patients with clinical diagnosis of NS; in 46 the genotype is known. Fifty-five patients (86%) have cardiac anomalies, in 41 of these the molecular diagnosis was made as shown in the table. Fifteen (27%) patients needed surgical or interventional treatment, which was successful in 14 (93%). We also identified a subgroup of 17 (31%) patients in whom NS was suggested by the presence of minor cardiac anomalies.

Genotype	N (%)	CHD (n,%)	PVS (n)	HCM (n)	Septal defects (n)	Other (n)
PTPN11	32 (50)	28 (44)	22	5	6	1
SOS1	8 (12,5)	6 (9)	5	0	1	0
KRAS	0	0	0	0	0	0
RAF1	3 (4,7)	3 (4,7)	1	2	0	0
BRAF	1 (1,5)	1 (1,5)	0	0	1	0
SHOC2	2 (3,1)	2 (3)	1	1	0	1
Unknown/under investigation	18 (28)	15 (25)	8	2	1	1
Sum	64 (100)	55 (86)	37	10	7	2

Conclusion. In our series the presence of CHD in NS is higher than that previously reported and is frequently associated with PTPN11 genotype. Unlike what is generally thought we observed that cardiac surgery or interventional treatment are highly effective. One third of this population has insignificant cardiac involvement, which however lead to the genetic diagnosis.