TYPEFACE:
TIMES NEW ROMAN
TYPE SIZE: 12

NOONAN AND MULTIPLE LENTIGINES SYNDROMES: 23 YEAR EXPERIENCE IN ONE CENTRE

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During my 23 years in Ottawa, I have seen 50 individuals with a diagnosis of Noonan syndrome, 24 females and 26 males, from neonates to 70 years of age, and 2 with multiple lentigines syndrome. Most are Caucasian, however 4 are of African descent, one is Asian, one Native Canadian and 2 are of mixed ancestry. Many have been followed for a decade or more. Eleven were seen before mutation testing was available and carry a clinical diagnosis and three families have chosen not to have testing. One result is pending. In the cohort of 37 where full molecular testing has been completed, 21 (58%) have a mutation in *PTPN11*, 2 (5%) in *SOS1*, one (3%) in *RAF1* and one (3%) in *BRAF*. The remaining 12 (33%) have convincing features and no identifiable mutation. Where molecular status is known, all mutations are de novo except one. Mean parental age was 32.5 (maternal) and 34.5 (paternal) years.

Birth weight exceeded the normal range for gestational age in 64%, with polyhydramnios (21%), increased nuchal skin laxity (30%), cystic hygroma (9%), hydrops (3 babies) and neonatal lymphedema (3) reported. In infancy, gastro-esophageal reflux occurred in 26% and failure to thrive in 59%. Short height in a quarter of individuals is less than 3%. Absolute macrocephaly is found in 9% while relative macrocephaly is considerably more common. Typical facial appearance is found in 88%.

Seventy percent have normal intelligence although specific learning disability is found in a quarter and one in four has needed individual educational programming. Nonetheless, all adults have completed high school, 83% attended college and all are employed. Anxiety is reported by 6% and ADHD noted in 41%. While no-one has hydrocephalus, 6 (20%) have ventriculomegaly and one has a Chiari malformation. Hypotonia is/was present in a majority.

Pulmonary valve stenosis (52%), hypertrophic cardiomyopathy (22%) and atrial septal defect (22%) are the most frequent cardiac structural defects, with arrhythmia reported in more than one might expect (14%). Cryptorchidism was found in 62% of male neonates. Other genitourinary anomalies are found in 22%. Pubertal delay is not a feature of this cohort. Half the group has easy bruising with coagulopathy recognized in 5. Ptosis (24%), myopia (34%), and hypermetropia (19%) are the commonest eye findings. Five individuals have hearing loss, 2 of whom require aids.