Gonadal function of female patients with Noonan syndrome

Sophie Moniez 1, Yline Capri 2, Catherine Pienkowski 1, Benoit Lepage 3, Safouane Hamdi 4, Audrey Cartault 1, Isabelle Oliver 1, Béatrice Jouret 1, Gwenaëlle Dienne 1, Jean-Pierre Salles 1,5, Hélène Cave 2, Alain Verloes 2, Mathé Tauber 1,5, Armelle Yart 6, Thomas Edouard 1,5

1 Endocrine, Bone Diseases, and Genetics Unit, Children’s Hospital, Toulouse University Hospital, Toulouse, France; 2 Departments of Genetics, Robert-Debré University Hospital, APHP, Paris, France; 3 Department of Epidemiology, Toulouse University Hospital, Toulouse, France; 4 Laboratory of Biochemistry and Hormonology, Toulouse University Hospital, Toulouse, France; 5 INSERM UMR 1043, Centre of Pathophysiology of Toulouse Purpan (CPTP), University of Toulouse Paul Sabatier, Toulouse, France; 6 INSERM UMR 1048, Institute of Cardiovascular and Metabolic Diseases (I2MC), University of Toulouse Paul Sabatier, Toulouse, France

Context: Abnormalities in the hypothalamo-pituitary-gonadal axis have long been reported in Noonan syndrome (NS) but few data are available in particular in female patients.

Objective: The aim of this study was to evaluate the gonadal function of NS females from childhood to adulthood.

Design: We performed a retrospective chart review in female patients with a genetically confirmed diagnosis of NS.

Patients and Methods: Two patient groups were identified. The ‘paediatric group’ (n = 19) consisted of NS girls/adolescents with available clinical (including Tanner stages and age of first menstruations) and/or hormonal data (including gonadotropins, inhibin B, and anti-Müllerian hormone [AMH]) who were followed at the Children’s Hospital, Toulouse, France, between 2008 and 2018. The ‘adult group’ (n = 99) consisted of women who were referred for molecular testing to the Department of Genetics of Robert-Debré Hospital, Paris, France.

Results:

In the ‘paediatric group’, 12 (63.2%) children had entered puberty and the age at pubertal onset and at menarche were 12.0 and 14.7 years respectively, corresponding to a delay of 1.15 to 2 years compared with the general healthy population. The patterns of secretion as well as the values of serum AMH and inhibin B were normal in NS girls and adolescents, suggesting a normal ovarian function.

In the ‘adult group’, the mean age of first menstruations available in 30 women was 14.7 years (range: 9.6 – 19.0 years). Sixty-one women (61.6%) had 1 to 4 children and none of the 99 women reported involuntary childlessness nor treatment for infertility.

Conclusions:

NS females display normal albeit delayed onset at puberty and a normal ovarian function.