INTRODUCTION

A few patients with Noonan Syndrome (NS) have been reported to harbour pathogenic variants in LZTR1 gene. RAS/MAPK pathway regulation by LZTR1-mediated ubiquitination provides an explanation for the role of LZTR1 in human disease. Pathogenic variants in this gene could hence lead to NS phenotype. Four patients with mutations in this gene due to a different genetic transmission pattern and compatible NS phenotype are herein characterized.

PATIENTS

CONCLUSIONS

Albeit functional studies are still required to confirm causality of each mutation in LZTR1 leading to NS, this gene ought to be incorporated into RASopathy genetic panels. Whole exome sequencing may add the opportunity to re-analyze the study in patients with no molecular confirmation as new genes related to the clinical diagnosis are discovered. Patients with pathogenic mutations in LZTR1 seem to exhibit characteristic NS facial features but variable expression in heart, stature and neurodevelopment, where dominant inheritance may associate a milder phenotype.