Neonatal haematological complication in Noonan syndrome: future concerns about growth hormone therapy

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P1 category - Syndromes : mechanisms and management

INTRODUCTION

Noonan syndrome (NS) is an autosomal-dominant inherited condition defined clinically by a short stature, specific phenotype, congenital heart disease, bleeding and hematologic abnormalities (particularly leukaemia).

There is a genetic heterogeneity, with all mutations involved in the RAS/mitogen-activated protein (MAP) kinase pathway and with PTPN11 gene mutations counting for almost 50% of patients.

METHODS

We report a case of a newborn girl with antenatal diagnosis of NS who developed, shortly after birth a juvenile myelomonocytic leukemia (JMML)-like picture.

During the intrauterine life, the foetus developed a bilateral pleural effusion.
An amniocentesis was performed and the diagnosis of NS (p.G503R c.1507G>C **mutation** in exon 13 of the **PTPN11 gene**) was made.

The baby was born at 30 weeks of gestation, with 1370 g and 38,5 cm.

RESULTS

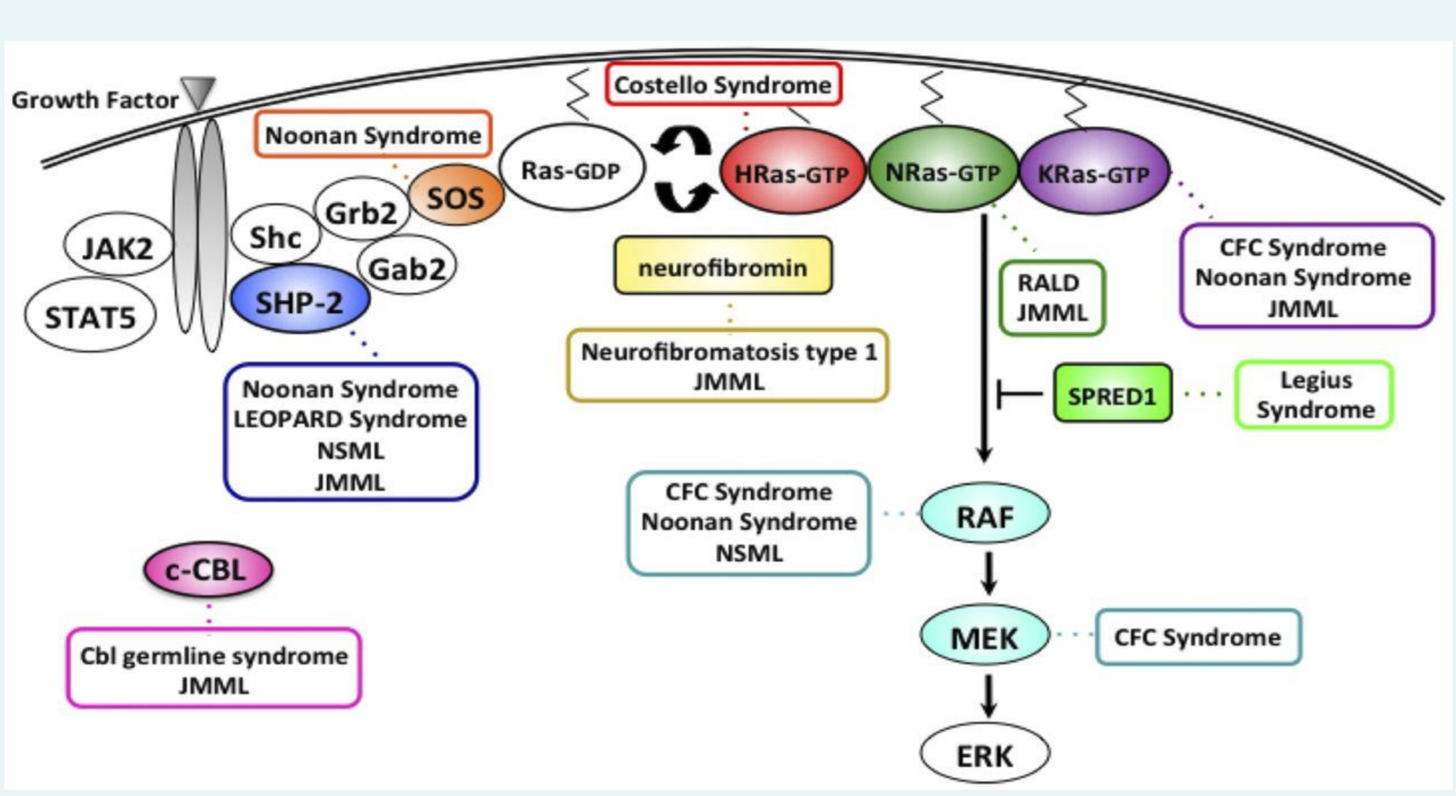
1) The **retrospective diagnosis** of NS was made in the mother and maternal grandmother.

2) At the **age of 10 days**, the peripheral blood profile (**leukocytosis - 45.000/mm3** and **thrombocytopenia - 70.000/mm3**) and the bone marrow smear morphology (**myelodysplasia**) fulfilled the international criteria for JMML.

   - The clonality of this myeloproliferation was negative and a spontaneous regression was noted.

   - A regular follow-up was started with the child registered in a European long-term follow-up concerning the risk of malignancy in NS.

3) At the age of 1 year 9 months, the toddler is well-appearing, with characteristic facial appearance and **short stature** (height is 69,5 cm, on -1 DS on Noonan growth chart).



CONCLUSIONS

Neonatal NS diagnosis provided important clues for early multidisciplinary approach.

A myeloproliferative disorder, even with spontaneous resolution, in a child with NS and PTPN11 germline mutation deserves a very close clinical follow-up.

Growth hormone therapy to promote growth should be considered in relation to the genotype, the stature gain and the potentially amplified malignancy risk.

References

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