FIVE-YEAR RESPONSE TO GROWTH HORMONE IN CHILDREN WITH NOONAN SYNDROME AND GROWTH HORMONE DEFICIENCY: OUR EXPERIENCE AND REVIEW OF THE LITERATURE

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OBJECTIVES

Noonan syndrome (NS) is an autosomal dominant disorder characterized by specific features including short stature, distinctive facial dysmorphic features, congenital heart defects, hypertrophic cardiomyopathy, skeletal anomalies and webbing of the neck. Molecular screening has shown that the majority of individuals with NS have a mutation in the PTPN11 gene. Noonan syndrome children may show an impaired growth hormone (GH)/insulin-like growth factor axis. Moreover, recombinant human GH (rhGH) has been shown to improve growth rate in patients with NS, although data are still limited. We assessed growth response following GH therapy in GH-deficient NS patients (NSGHD) and compared it with idiopathic GH deficient (IGHD) sex and age-matched patients. We also evaluated the safety of rhGH therapy in NS patients with GHD.

METHODS

We enrolled 5 (2 M and 3 F) GH-deficient NS patients (NSGHD, mean age 8.5 years) and in 5 (2 M and 3 F) idiopathic GH deficient (IGHD, mean age 8.6 years) patients and followed them for the first five years of GH therapy (0.25 mg/Kg/week). We also evaluated the safety of rhGH therapy in NS patients with GHD.

RESULTS

At the beginning of GH treatment, height and growth rate were statistically lower in NSGHD children than in IGHD ones. During the first three years of rhGH therapy, NSGHD patients showed a slight improvement in height (from -2.71 SDS to -2.44 SDS) and growth rate (from -2.42 SDS to -0.23 SDS), although the values were always significantly lower than in IGHD children. After five years of rhGH treatment, height gain was higher in IGHD children (mean 28.3 cm) than in NSGHD patients (mean 23.6 cm). During the first five years of rhGH therapy, regular cardiological and haematological check-ups were performed, leading to the conclusion that rhGH therapy was safe.

CONCLUSIONS

Pre-pubertal NS children with GHD slightly increased their height and growth rate during the first years of GH therapy, although the response to rhGH treatment was significantly lower than in IGHD children. Furthermore, the therapy appeared to be safe since no severe adverse effects were reported, at least during the first five years. However, a close follow-up of these patients is mandatory, especially to monitor cardiac function.