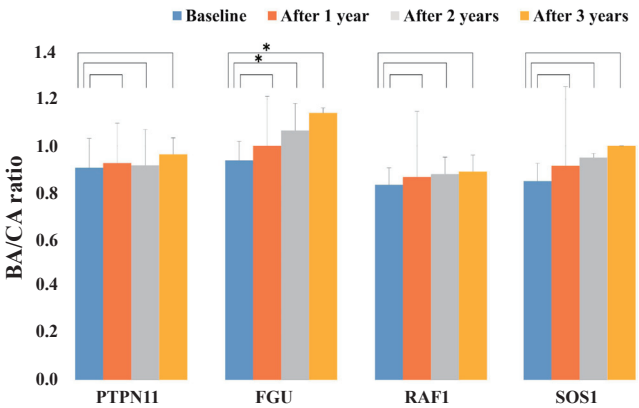
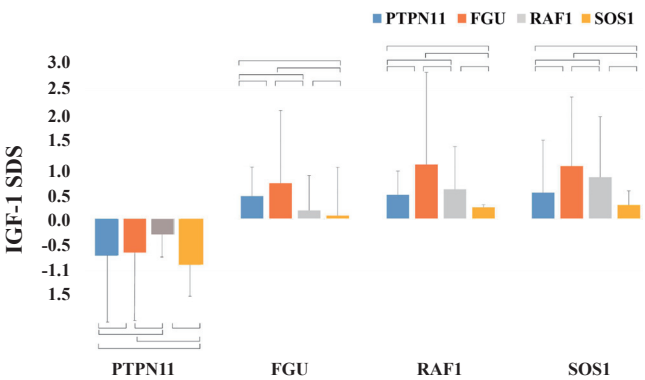
Supplementary Table 1. Evaluation of the endocrinological parameters of the 23 patients with prepubertal Noonan syndrome during GH treatment

Variable	Baseline	After 1 year	*P* value	After 2 years	*P* value	After 3 years	*P* value
CA (yr)	6.00 (2.00–10.00)	7.00 (2.08–11.17)	NA	8.42 (4.00–12.67)	NA	9.25 (5.00–13.17)	NA
BA (yr)	5.50 (1.50–9.83)	6.25 (2.42–11.42)	<0.0001	7.92 (3.17–14.67)	<0.0001	8.33 (4.25–18.25)	<0.0001
Height SDS	-2.30 (-6.79 to -0.49)	-2.11 (6.59–0.31)	<0.0001	-1.97 (-6.15–0.72)	<0.0001	-1.95 (-4.77–1.10)	0.001
GV (cm/yr)	5.52 (2.80–7.20)	8.90 (6.00–12.21)	<0.0001	8.18 (5.00–10.70)	<0.0001	7.80 (4.20–9.80)	<0.0001
IGF-1 SDS	-0.54 (-2.81–1.40)	0.51 (-1.81–2.82)	0.001	0.47 (-1.45–4.21)	0.001	0.73 (-1.06–3.80)	<0.0001
IGFBP-3 SDS	0.09 (-0.65–0.93)	0.35 (-0.40–1.03)	0.004	0.34 (-0.36–1.10)	0.032	0.31 (-0.41–0.91)	0.123
BA/CA ratio	0.90 (0.70–1.30)	0.92 (0.80–1.50)	0.014	0.93 (0.80–1.70)	0.007	0.98 (0.80–1.75)	0.026
BMI SDS	-0.88 (-2.42–1.48)	-0.53 (-3.10–1.51)	0.543	-0.79 (-2.82–1.64)	0.951	-0.83 (-2.16–1.56)	0.940

Values are presented as median (range).
Wilcoxon signed rank test was used to compare the response to GH therapy according to disease-causing genes.
BA, bone age; CA, chronological age; SDS, standard deviation score; IGF-1, insulin-like growth factor 1; SDS, standard deviation score; IGFBP-3, IGF binding protein 3; BMI, body mass index; NA, not available.



Supplementary Fig. 1. Sequential changes in bone age-to-chronological age (BA/CA) ratio during growth hormone (GH) treatment in patients with Noonan syndrome, including the *PTPN11,* FGU, *RAF1,* and *SOS1* groups. The Wilcoxon signed-rank test was used to compare responses to GH therapy according to disease-causing genes. The BA/CA ratio in the FGU group was significantly elevated after 3 years of GH therapy as compared with the other groups. **P*<0.05.



Supplementary Fig. 2. Comparison of changes in insulin-like growth factor 1 (IGF-1) standard deviation score (SDS) from before to during growth hormone (GH) treatment among patients with Noonan syndrome (NS) with different disease-causing genes. The Mann-Whitney *U* test was used to compare responses to GH therapy according to disease-causing genes. No statistical difference in improvement of IGF-1 SDS was found among the patients with NS in the *PTPN11,* FGU, *RAF1,* and *SOS1* groups.