Long acting octreotide treatment in children with growth hormone excess and neurofibromatosis type 1-optic pathway tumors

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Introduction

Growth hormone (GH) excess in children with neurofibromatosis type 1 (NF-1) has been reported in some sporadic cases. Whether GH excess stimulates progressive optic pathway glioma (OPG) growth is of concern. The scheme treatment with octreotide long-acting release (LAR) has not been well characterized yet.

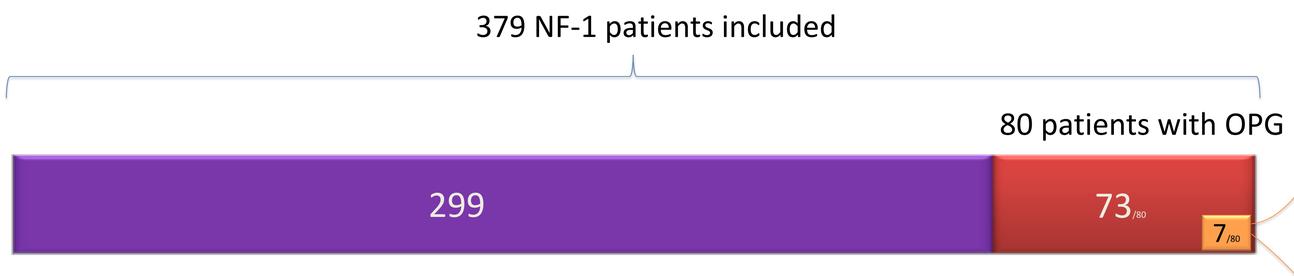
Objective

To describe the treatment regimen in children with NF-1/OPG and GH excess treated with octreotide-LAR

Population and methodology

Descriptive study including NF-1 patients with OPG and GHE who were followed in tertiary hospital in an interval between 2008 and 2018. The diagnosis of GH excess was established from acceleration of growth, high levels of insulin-like growth factor 1 (IGF-1 >1DS) and the absence of GH suppression during the glucose tolerance test (GH > 1 ng/dl)

Results



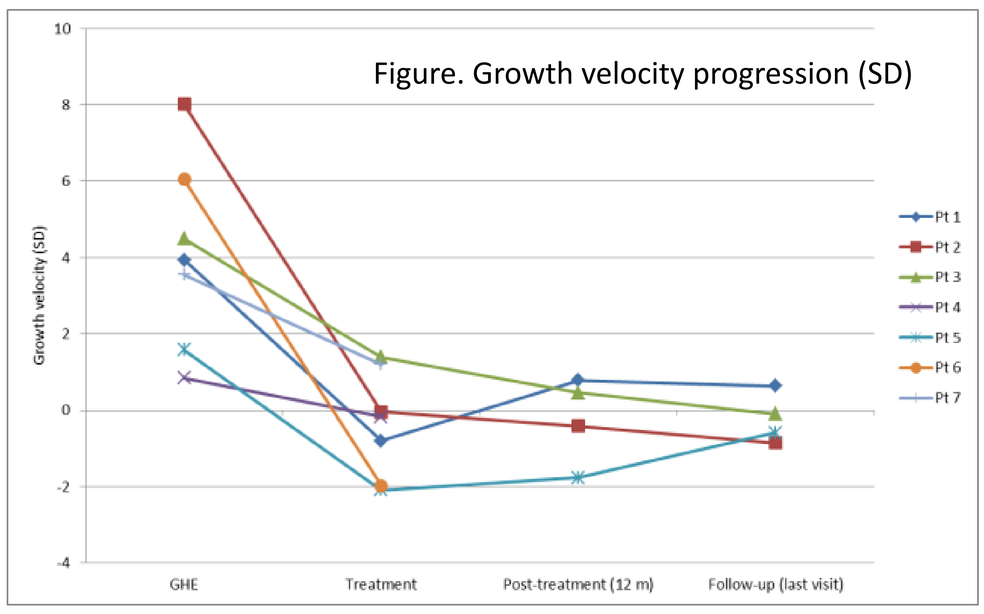
Seven patients were identified as having GH excess in the presence of NF-1 and optic pathway tumor.
All prepubertal (5 boys, 82%) and with a mean age (SD) of 4.4 ± 1.9 years.

Table. Description of patient demographics and octreotide treatment regimen

Patient	Sex	Age (years)	MPH* (SD)	Height (SD)	Growth velocity cm/year at GHE diagnosis (SD)	IGF-1** [range] (ng/mL)	Tumor progression	Octreotide treatment long-acting release (intramuscular)	Treatment duration (months)	IGF-1 normalization during treatment/ post-treatment
1	M	3,5	-0,38	1,80	12,6 (3.94)	289 [33-150]	Yes	10 mg/28 days	16.1	Yes/Yes
2	M	7,9	1,41	2,62	12 (8.02)	651 [60-300]	No	10 mg/28 days	14.8	Yes/Yes
3	M	4,0	-0.21	0,86	12,5 (4,49)	587 [60-300]	Yes	10 mg/28 days	41.4	Yes/Yes
4	M	4,2	0.16	1,91	8.1 (0.84)	454 [60-300]	Yes	10 mg/28 days 20mg/28 days	24,3	Yes/Yes
5	M	5,3	-0,54	0,45	8 (1.58)	535 [60-300]	Yes	10 mg/28 days	14.9	Yes/Yes
6	F	3,4	-0,94	-0,40	13.4 (6.04)	444 [33-150]	No	10 mg/28 days	19,6 ongoing	Yes/ -
7	F	2,3	0,57	1.55	14 (3.55 SD)	245 [40-115]	Yes	10 mg/28 days	10,1	Yes/Yes

* MPH: Midparental height **IGF-1 reference ranges varied in November 2016 (change of testing method)

- The first two patients were initially treated with short-acting octreotide (subcutaneous single-daily dose, 1.5 µg/kg/day). After confirming efficacy and good tolerability, the scheme was moved forward to intramuscular octreotide-LAR.
- One out of the 5 patients initially treated with octreotide-LAR (10 mg/28 d) needed to be increased the dosage to 20 mg/28 days to normalize IGF-1 levels.
- After 3 months, 6/7 patients showed a normalization of IGF-1 and growth velocity. Treatment could be withdrawn in 6 patients after 20.21 ± 4.82 months. They remained stable for 25.94 months (range 2-49 months).
- In 5/7 patients (71%) GH excess occurred simultaneously with the tumor progress
- Except for mild diarrhea, no other side effects were observed.



Conclusions

We should consider the risk of GH excess in patients with NF-1- OPG, and be concerned as a possible sign of glioma´s progression. Treatment with octreotide-LAR was effective and safe. After treatment the growth and the IGF-1 levels remained within normal ranges, confirming GH excess reversibility.