Growth hormone hypersecretion in children with NF1 and optic pathway gliomas

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Optic pathways glioma (OPG), the most frequent tumor in children with Neurofibromatosis type 1 (NF1), is a optic nerve low-grade glioma, that may involve hypothalamus and post-chiasmal regions.

Central precocious puberty (CPP) is a known endocrinopathy associated with OPG in NF1, while growth hormone excess (GHE) has rarely been reported.

Aims of the study

1. to verify the presence of GH excess and/or CPP in patients with NF1
2. to find a possible correlation of GH hypersecretion and the MRI patterns of OPG.

Methods

We selected all patients with NF1 and OPG followed in our hospital between 2008 and 2014.

⇨ **All of them** underwent auxological evaluation.

⇨ **Children with clinical signs of gigantism** (height >2 SD and/or growth velocity >2 SD) were submitted to biochemical study, including IGF-I, IGFBP-3, FT4, TSH, PRL, OGTT for glucose, insulin and GH levels, and bone age.

⇨ **Children with clinical signs of CPP** underwent GnRH test for LH and FSH, testosterone/estradiol evaluation, bone age and pelvic ultrasound in girls.

⇨ **MRI patterns of gliomas** were reassessed by the same neuroradiologist.

Results

⇨ **Sixty one** patients with NF1 and OPG (35 boys, age 2.1-17.9 years) were included in the study.

⇨ In all patients except one (patient 3) **OPG** had been previously diagnosed. Patient 3 underwent MRI because of increased HV. He had no other neurological or detectable ophthalmological signs.

⇨ Seven out of 61 (11.5%) presented clinical signs of **gigantism**. In all of them GHE was confirmed by IGF-I and IGFBP-3 levels >2 SD. Lack of GH levels suppression after OGTT was demonstrated in 4 cases (Tab. 1).

⇨ **CPP** had been diagnosed in patient 2 six months before the inclusion in this study. Complete biochemical and clinical control of puberty with LH-RH analogue treatment had been reached at the time of GH secretion study. In other 3 children isolated CPP was demonstrated.

⇨ MRI in all children with gigantism showed **extension of OPG** at least to chiasmal region.

Cases	Sex	Age (ys)	Height (SD)	Tanner	HV(cm/ys)	HV (SD)	Bone Age	OGTT GH nadir (ng/ml)	IGF-I (ng/ml)	IGF-I range (ng/ml)	IGF-I percentile	IGFBP-3 (µg/ml)	IGFBP-3 range (µg/ml)	IGFBP-3 percentile	MRI
1	F	3.6	2.53	I	20.0	10.2	6.1	1.8	457	29-212	>97th	5.9	0.9-4.3	>97th	ON-OC-R
2	M	5.1	2.1	II	10.9	4.3	8	1.46	565	35-264	>97th	6.2	1.1-5.2	>97th	ON-OC
3	M	4.9	3.1	I	10.0	3.1	5.0	3.53	390	35-264	>97th	4.8	1-4.7	>97th	ON-OC
4	M	4.1	2.1	I	12.0	5.2	4.6	0.52	477	34-258	>97th	6.3	1-4.7	>97th	ON-OC
5	M	5.5	1.2	I	11.0	4.0	6.0	0.22	433	35-264	>97th	4.8	1.1-5.2	95th-97th	ON-OC
6	M	3.1	2.2	I	12.0	3.1	2.8	0.39	446	41-323	>97th	5.2	0.9-4.3	>97th	ON-OC
7	M	5.5	2.9	I	9.3	2.9	7.0	3.9	415	50-412	>97th	NA	NA	NA	ON-OC

Tab. 1 – Clinical and biochemical data, and tumor localization of NF1 patients with GHE.
HV: height velocity; ON: optic nerves; OC: optic chiasm; R: retrochiasmatic pathways.

Our study shows that GHE in children with NF1 and OPG is not so rare as previously reported and seems more frequent than CPP.

There is an evident correlation between extension of glioma and presence of GH hypersecretion.

In NF1 children, gigantism should be considered as a possible sign of OPG and as an indication to perform brain MRI. On the other hand, children with NF1 and OPG involving chiasm or post-chiasmal regions should be evaluated considering the risk of GHE.

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