P309

GLP-1 Receptor Agonist in a Patient with Craniopharyngioma-Related Obesity.

M.C. Antoniou[a], P.Diaz-Escagedo[a], T. Bouthors[a], E. Elowe-Gruau[a], S. Stoppa-Vaucher[a], M. Messerer[b], M. Hauschild[a]

[a] Pediatric Endocrinology and Diabetology Unit, Service of Pediatrics. Centre Hospitalier Universitaire Vaudois (CHUV), University of Lausanne, Switzerland
[b] Department of Clinical Neurosciences, Neurosurgery Service and Gamma Knife Center. Centre Hospitalier Universitaire Vaudois (CHUV), University of Lausanne, Switzerland.

Background and Objective

Craniopharyngioma is a histologically benign tumor with aggressive clinical presentation, whose management constitutes a big challenge. Hypothalamic syndrome with consecutive obesity occurs in up to 35% of patients at diagnosis, but dramatically increases after treatment [1,2]. Glucagon-like peptide 1 (GLP-1) receptor agonists have been successfully used in adults with hypothalamic obesity, showing a BMI decrease and metabolic profile improvement [3]. Data on GLP-1 receptor agonist treatment for children and adolescents is limited.
Herein, we present a clinical case of a male adolescent treated with GLP-1 receptor agonist for hypothalamic obesity, secondary to craniopharyngioma.

Case Presentation

A 15.8 year-old male presented for evaluation of delayed puberty and progressive growth failure.

Family history:
- Oldest of 4 children born to a Swiss non-consanguineous couple. Uneventful family history.

Personal medical history:
- Born full term, eutrophic, after an uneventful pregnancy.
- Clift-lip operation during the 1st year of life.
- Developmental milestones normally achieved.

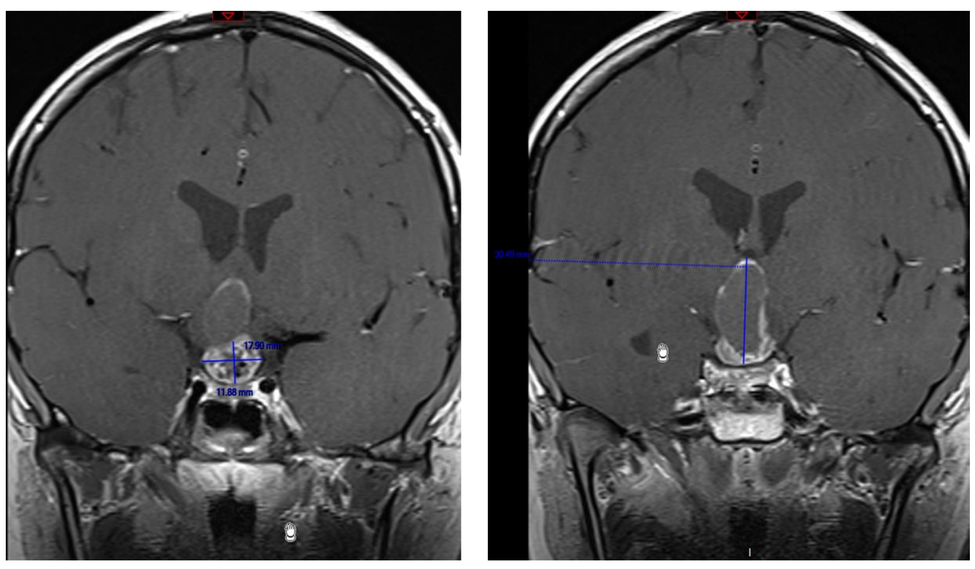
Clinical examination at 15.8 years:
- Height-SDS: -2.59; BMI-SDS: +0.82. No dysmorphic signs. Normal olfaction.
- Tanner: A1PP3G2, Testicular volume: 4ml bilaterally
- Bilateral gynecomastia.
- Normal neurological and ophthalmologic examination.

Laboratory and radiologic evaluation

		Patient	Reference value
Testosterone	*nmol/l*	0.6	0.1-17.6
Prolactin	*µg/l*	5	<20
TSH	*mU/l*	0.927	0.5 - 4.5
freeT4	*pmol/l*	17	9 - 25
IGF-1	*µg/l*	213	212 - 1043
IGFBP3	*mg/l*	5.49	3.2 - 10.4
ACTH	*pg/ml*	10	10 - 70
Cortisol	*nmol/l*	451	170 - 630
AMH	*pmol/l*	1286	5-800
Inhibin-B	*pg/ml*	137	60-300

LHRH stimulation test

	LH	FSH
	mU/l	*mU/l*
0'	0.5	3
15'	3.8	4.6
30'	6.4	6.4
60'	7.0	8.8
90'	6.2	9.6
120'	6.5	10.6



MRI 15.8 y: Supra-sellar tumor with cystic and solid component, extending to the hypothalamus and compressing the optic chiasma. Presence of intratumoral calcifications.

Clinical evolution after diagnosis

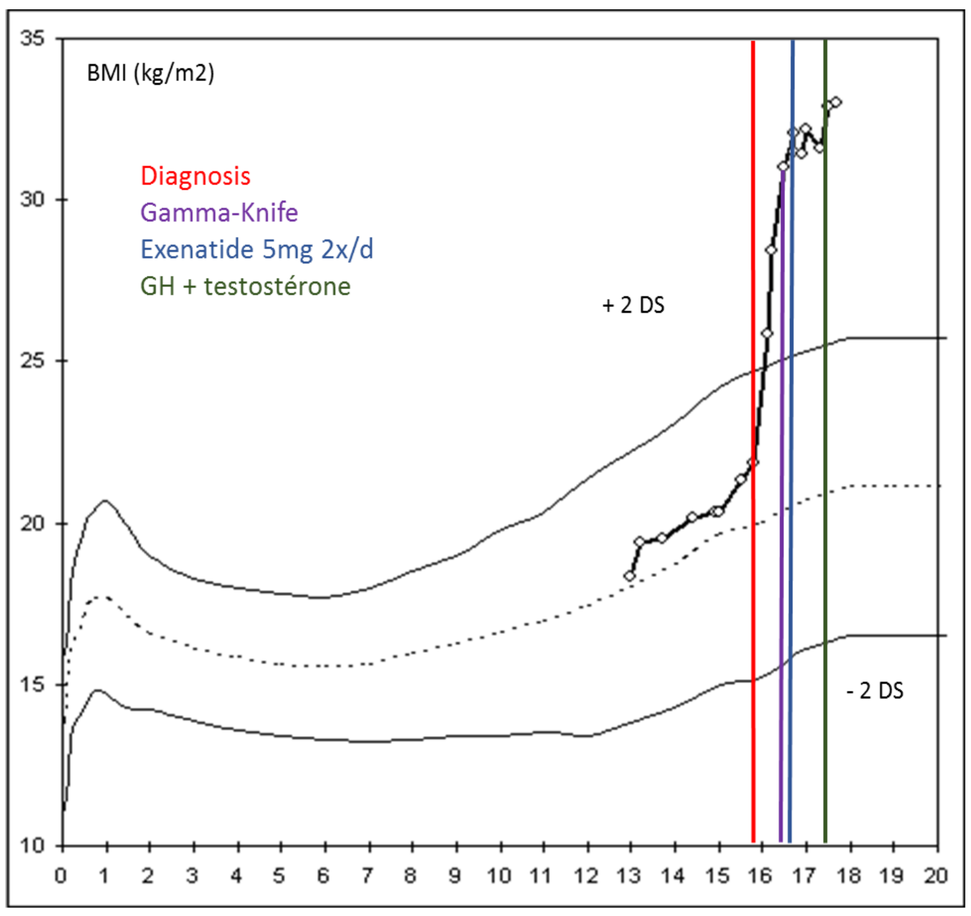
Tumor resection followed by:
- Persistant hemianopsia
- Panhypopituitarism, requiring L-thyroxin, vassopressin and hydrocortisone substitution
- Rapid onset of obesity, refractory to rigorous hygieno-dietetic measures

9 months post-operative: gamma knife radiotherapy
Latest brain MRI: residual mass of 4mm, empty sella turcica except for 1mm of anterior pituitary

11 months post-operative : introduction of Exenatide 5mcg, 2x/j→BMI stabilization
- Well tolerated
- No hypoglycemic events (flash glucose monitoring-FreestyleLibre®)
- Restoration of satiation and quality of life (QoL) improvement

17 months later: Testosterone and growth hormone substitution, further QoL improvement

BMI evolution chart



Discussion & conclusions

GLP-1 receptor agonist treatment appears to be promising in adolescents with hypothalamic obesity. Further studies with larger cohorts are required in order to evaluate longtime effectiveness on BMI and metabolic control.

References

1. Müller HL..Expert Rev Neurother. 2016 May;16(5):535-48. doi: 10.1586/14737175.2016.1166959.
2. Elowe-Gruau E, Beltrand J, Brauner R, Pinto G, Samara-Boustani D, Thalassinos C, Busiah K, Laborde K, Boddaert N, Zerah M, Alapetite C, Grill J, Touraine P, Sainte-Rose C, Polak M, Puget S. Childhood craniopharyngioma: hypothalamus-sparing surgery decreases the risk of obesity. J Clin Endocrinol Metab. 2013 Jun;98(6):2376-82
3. Bruno Geloneze et al, 2017. *Glucagon-Like Peptide-1 Receptor Agonists (GLP-1RAs) in the Brain-adipocyte axis.* Drugs 2017 77:493-503