METFORMIN TREATMENT OF HYPOTHALAMIC OBESITY – THE LESSON OF TWO CASES

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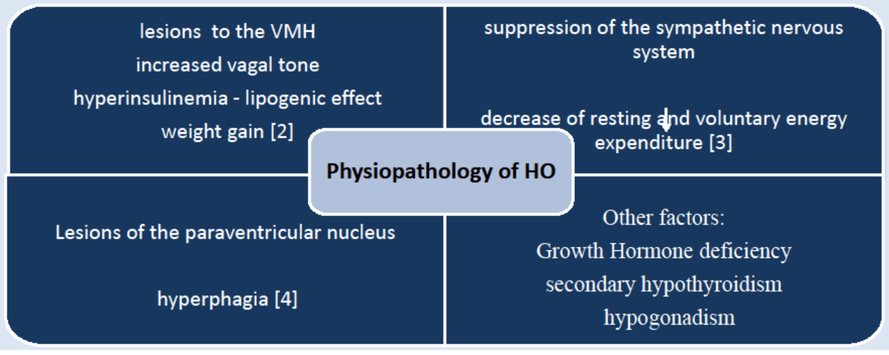
INTRODUCTION

- Hypothalamic obesity (HO) - a syndrome of intractable weight gain as a result of hypothalamic lesions [1]
- Causes: craniopharyngioma (more than 50 % of the cases), other posterior fossa tumors, infiltrative diseases of the hypothalamus, head trauma or pseudotumor cerebri [1,2]
- Treatment: lifestyle interventions, pharmacotherapy (sympathomimetic drugs and drugs that counteract the increased vagal tone) and surgery
- Metformin - antidiabetic drug also used in nondiabetic obese patients as it has been demonstrated that it promotes weight loss. Metformin alone has not been tested in patients with HO
- We present two cases of HO (an adult and a pediatric patient) in which successful weight loss was obtained following treatment with Metformin



CASE PRESENTATION 1

- 44 year old female patient admitted for:
  - severe headache
  - visual acuity loss in both eyes
  - secondary amenorrhea
  - polyuria, polydipsia
- Cranial CT scan -> craniopharyngioma
- October 2006 – transcranial surgery; November 2009 – second surgery (tumor recurrence)
- Following surgeries: - severe HO (she gained 45 kg)
  - panhypopituitarism treated with 5 mg Prednison/day, 100 µg Euthyrox/day, Climara 1 patch/week, Duphaston 10 mg/day, 10 days/month
  - diabetes insipidus treated with Minirin MELT 120 µg 2x1/day

	Weight (kg)	BMI (kg/m²)	Insuline (µU/ml)	HOMA-IR
October 2006 Preoperative	**105**	**34,3**		
October 2007 1 year postoperative	**114**	**37,3**		
December 2007	**119**	**38,8**		
January 2009	**120**	**39,2**		
November 2009 – reintervention for tumor recurrence				
January 2010	**117**	**38,2**	**40,4**	**9,87**
➔ Sibutramine 10 mg/day is initiated				
June 2010	**136**	**44,4**	**22,7**	**4,76**
➔ Sibutramine is replaced with Orlistat 3 x 120 mg/day				
June 2011	**150**	**49,01**	**34,2**	**7,17**
➔ Orlistat is replaced with Metformin 2 x 850 mg/day				
October 2011	**137**	**44,7**	**69,5**	**13,21**
➔ Metformin dose is increased at 2 x 1000 mg/day				
November 2011	**135**	**44,1**	**30,7**	**6,59**
October 2012	**126**	**41,1**	**32,2**	**5,56**
October 2013	**116**	**37,9**	**24,5**	**4,96**

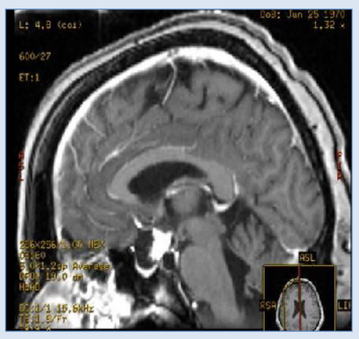


Fig. 1 Cranial MRI before the second surgery

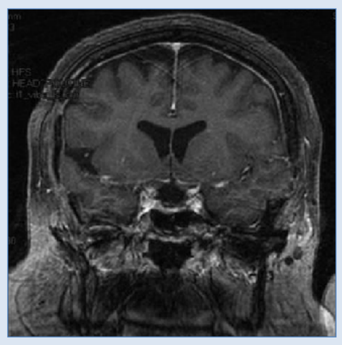


Fig. 2 Postoperative cranial MRI

CASE PRESENTATION 2

- 6,4 year old female patient admitted for:
  - chronic headache
  - decreased growth
- Cerebral MRI: suprasellar tumor -> transcranial surgery
- Histopathologic diagnosis - mixed germ cell tumor (grade 3 immature teratoma and germinoma -> chemotherapy and radiotherapy
- Following surgery:
  - panhypopituitarism treated with 2,5 mg Prednison/day, 75 µg L-Thyroxine/day
  - diabetes insipidus treated with Minirin MELT 60 µg 2x1/day
  - severe hypothalamic obesity (she gained 32 kg in 2.5 years)
  - dyslipidemia
  - steatohepatitis

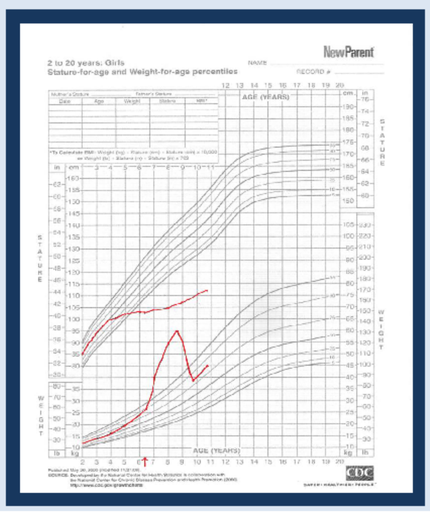
Before treatment with Metformin
Weight: 60 kg HOMA-IR: 7,61 ALT: 102 U/L
BMI: 50 kg/m2 Chol: 286 mg/dl AST: 168 U/L
TG: 460 mg/dl

After 2 months of treatment
Weight: 55 kg (-5 kg) HOMA-IR: 4,98 ALT: 54 U/L
BMI : 48 kg/m2 Chol: 220 mg/dl AST: 72 U/L
TG: 390 mg/dl

After 6 months of treatment
Weight: 42 kg (-18 kg) HOMA-IR: 4,69 ALT: 23 U/L
BMI: 36 kg/m2 Chol: 188 mg/dl AST: 41 U/L
TG: 220 mg/dl

After 1 year of treatment
Weight: 39 kg (-21 kg) HOMA-IR: 3,26 ALT: normal
BMI: 33.4 kg/m2 Chol: 208 mg/dl AST: normal
TG: 184 mg/dl

After 2 years of treatment
Weight: 45 kg (+ 6kg) HOMA-IR: 4,13 ALT: normal
BMI: 35.8 kg/m2 Chol: 216 mg/dl AST: normal
TG: 263 mg/dl



← **Fig. 3 The second patient's growth chart. (Red arrow –suprasellar tumor diagnosis)**

DISCUSSION AND CONCLUSIONS

- Hypothalamic obesity is a severe, debilitating disease that affects a large proportion of the patients with hypothalamic lesions, leading to multiple complications and an impaired quality of life.
- Both our patients developed hypothalamic obesity following surgery for craniopharyngioma and teratoma respectively. They experienced rapid weight gain which was resistant to lifestyle interventions and Sibutramine or Orlistat therapy.
- Metformin proved to be safe, well tolerated and effective in promoting weight loss in our two patients.
- Hamilton et al, 2011 observed a decrease in weight gain and BMI in children with HO due to intracranial damage, after 6 month of treatment with Metformin and Diazoxide [5].
- Larger, long-term and placebo-controlled studies are required in order to confirm the efficiency of Metformin alone in patients with hypothalamic obesity.

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