Treatment of hypothalamic obesity with GLP-1 agonists and extreme diet in a patient with hypothalamic infiltration

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Introduction

Hypothalamic damage can lead to intractable weight gain known as Hypothalamic Obesity (HO) (1). The pathogenesis of HO includes e. g. increased parasympathetic tone causing increase in insulin resulting in lipogeneses in the liver and adipose tissue (2).

HO has been resistant to all kinds of intervention but long acting incretin glucagon-like receptor (GLP-1R) agonist, has been used (3) and can bind to receptors in the hypothalamus (HT) increasing satiety and also reduce stomach emptying (4).

Methods

The HT injury was graded by the of Pascual et al (5) and Puget et al (7) **Figure I.**

The hypothalamic volume was estimated by Gabery et al (6) (**Figure II).**

Case presentation

A young woman presented with headache and vision loss but with normal weight (75 kg). She was operated by the zygomatiotemporal rout on the suspicion of a craniopharyngioma. After operation her weight doubled due to hypothalamic damage (**Fig III**).

- The microscopic examination revealed inflammatory cells of mainly neutrophilic type and T-lymphocytes.
- Immuno-histochemistry identified scattered CD3+ and CD45RO+ T lymphocytes.
- No malignant transformation was recorded.
- Cerebrospinal fluid cytology showed no malignant cells, but only plasma cells, granulocytes and a few lymphocytes.
- Further tests excluded lymphoma, germinoma or sarcoidosis.

The operation reduced the inflammation infiltration and 4 months postoperatively she was started on 30 mg and it was further reduced by tapering the dose during a 5 years follow up **(Fig III)**.
The hypothalamic volume was estimated to 63 mm^3 (right side) and 22 mm^3 (left side), resulting in a total hypothalamic volume of 85 mm^3. In comparison, a normal HT volume is 850 mm^3.

Twice the patient's weight was reduced dramatically by a very strict caloric diet (Xtravaganza 500 kcal/day) but as soon as ordinary diet was introduced, her weight increased dramatically **(Fig III)**. She was treated with (GLP-1R) agonists and metformin for her DM type II and with supplementation of her pituitary insufficiencies.

Figure III

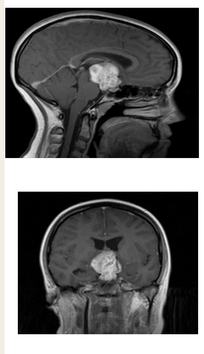


Fig 1. Preoperative MRI July-08, a contrast enhancing lesion (37 x 34 x 42 mm) in midline with suprasellar extension compressing the optic chiasm and displacing the MB and 3rd ventricle, which are unidentified, MB angle (MBA) was obtuse, and HT grade 2 (Puget).

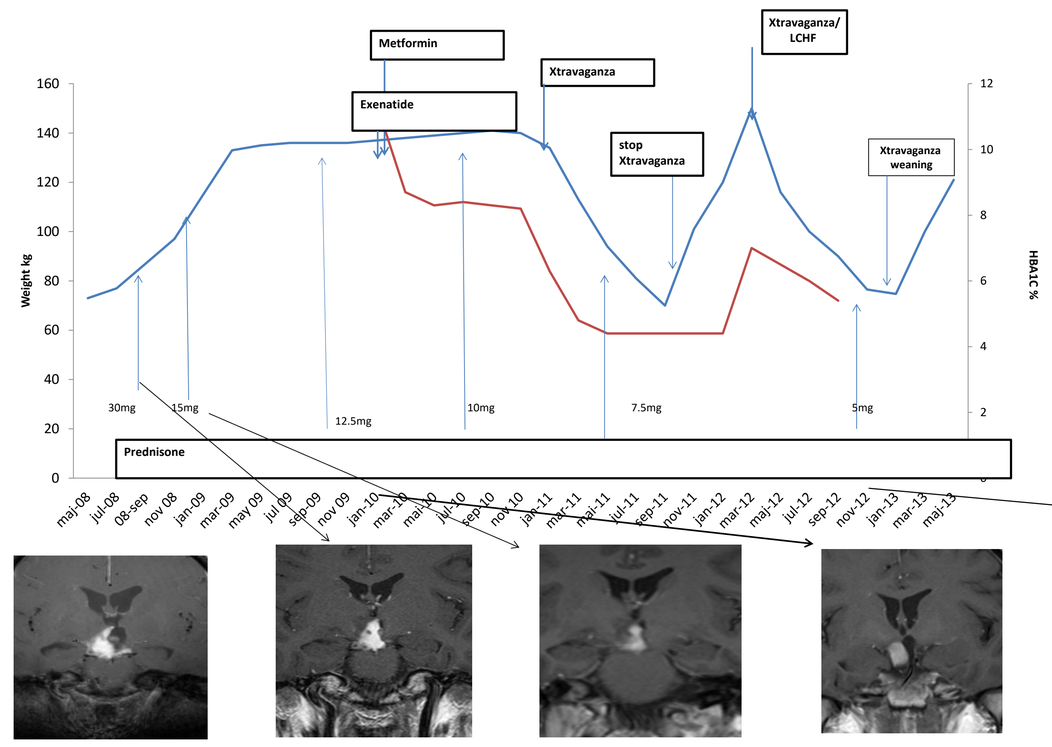


Fig 2. Postoperative MRI (2 days after op) 16x14x21 mm .**MBA obtuse**

Fig 3. Start on Prednisone Nov--08 . MBA was > 90 with Grade 1-2 (Puget).

Fig 4. One month on Prednisone(12 x 11 x 16 mm). Obtuse MBA

Fig 5. Reduction in constrast enhancing lesion. (12 x 10 x 14 mm) Jan-10

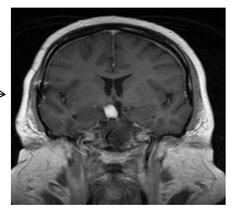


Fig 6. Nov-12 Unchanged lesion

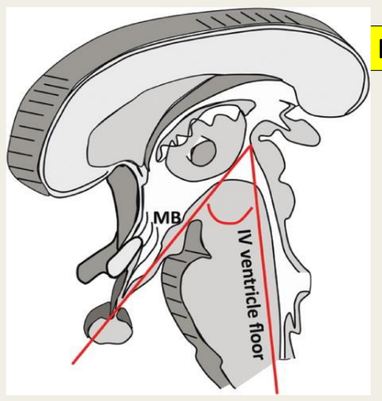
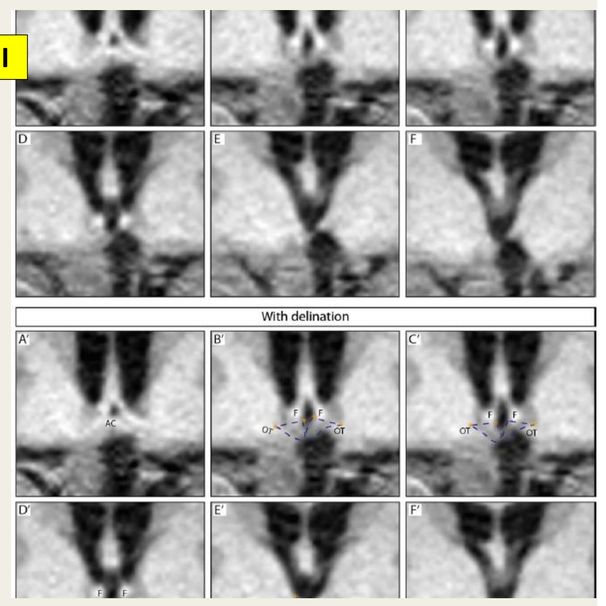
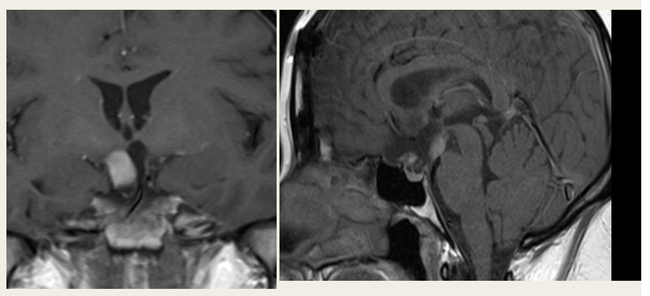


Figure I

The MBA, displayed by the MBs on mid-sagital MRI, was defined as the angle formed by the intersection of a plane tangential to the base of one of the MBs with the plane tangential to the floor of the fourth ventricle (**Figure I, and Figure I)**

Figure II





In October 2013 an MRI showed an anterior part of the HT with some fluid but posterior HT seemed now unaffected. The size of the inflammation was 11x15x10 mm, and MBA was about 90 °.

Conclusion

This case report illustrates the attenuation of hypothalamic inflammation with prednisone.
It shows also that extreme diet is successful in reducing weight, in combination with a GLP-1R agonist in HO.
The relative contribution of the GLP-1R analog was possibly minor.
Further, it shows brutally how difficult it is to maintain a weight reduction after such a rapid and extreme diet introduction, which causes a further downregulation of basal metabolic rate.

References

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