LONG-TERM REMISSION (CURE?) OF ACROMEGALY AFTER DISCONTINUATION OF SOMATOSTATIN ANALOGS

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INTRODUCTION. The prevalence of acromegaly is estimated to range from 38 to 80 cases per million, and the annual incidence of new patients is 3 to 4 cases per million, with a higher prevalence in Europe. Growth hormone (GH) and insulin-like growth factor 1 (IGF-1) act both independently and dependently to induce hypersomatropism. In a metaanalysis of 4464 patients treated with a somatostatin analog (SSA), average GH control rates and IGF-1 normalization rates were 58% and 59%, respectively (1). Usually, the disease relapses biochemically within few months after treatment withdrawal. We describe 2 rare cases with apparent cure of the disease after treatment with somatostatin analogs.

CASE 1
A 50 years woman came with typical acromegalic features, headache and carpal tunnel syndrome.

Acromegaly confirmed by:
- GH in oral glucose tolerance test (OGTT): 4.9 ng/ml;
- IGF-1 for age and sex = 3.8 x upper limit of normal (931 ng/ml, N < 244);
- She had normal visual field examination and no other hormonal dysfunction.
- Pituitary MRI showed a sellar mass of 14/13/15 mm.

Treatment 1: transsphenoidal pituitary surgery.

2 months after surgery: GH nadir in OGTT was elevated (8.3 ng/ml), with an IGF-1 of 2.6 x ULN (651.5 ng/ml).
- Pituitary MRI: sellar mass of 9/8/12 mm.

Treatment 2: Octreotide LAR 30 mg/28 days for 3 years, achieving control after association with cabergoline 2 mg/wk: random GH 0.85 ng/ml, with normal IGF-1 (212.4 ng/ml, N < 244).
- Pituitary MRI: minimum tumor shrinkage (11/8/7 mm).

After treatment withdrawal: At 6 months and 2 evaluations after medication withdrawal, the patient has no aggravations of acromegalic signs.
- Normal GH nadir in OGTT: 0.51 – 0.94 ng/ml.
- Slightly elevated IGF-1 (1.2 x ULN).
- Pituitary MRI: stable 11/8/7 mm pituitary nodule.

CASE 2
A 53 years old obese female patient came for acral enlargement, acromegalic features and paroxysmal hypertension (up to 220/160 mmHg).

Acromegaly confirmed by:
- GH in OGTT: 6.6 ng/ml;
- IGF-1 for age and sex = 2.9 x ULN (1130 ng/ml, N < 380);
- She had left ventricular hypertrophy on ecocardiography. No visual field impairment; no pituitary insufficiency.
- Pituitary MRI: sellar mass of 18/16/19 mm.

Treatment 1: transsphenoidal pituitary surgery.

2 months after surgery: GH nadir in OGTT was mildly elevated (1.2 ng/ml), with IGF-1 of 1.36 x ULN (326 ng/ml, N < 238);
- Pituitary MRI: sellar mass of 11.3/7/13.5 mm.

Treatment 2: Octreotide LAR 20 mg/28 zile for 3 years, during which the clinical features improved and she achieved disease control: normal GH nadir in OGTT 0.33 ng/ml, with normal IGF-1 (192 ng/ml N < 229);
- Pituitary CT: significant tumor shrinkage (sellar mass of 4/6 mm).

After treatment withdrawal: At 1.5 yrs and 3 yrs evaluations after SSA withdrawal, she has stable obesity (BMI 34.5 kg/m²) and improved clinical features.
- Normal GH nadir in OGTT (0.7 – 0.3 ng/ml);
- Slightly elevated IGF-1 (1.1 x ULN);
- Pituitary CT: stable 4/6 mm pituitary nodule.

Treatment 3: she received Cabergoline 1 mg/wk for 5 months, which did not improve the IGF-1 level (1.2 x ULN).

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<th>Case 1</th>
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DISCUSSION
A substantial number of patients (48.0–72.4%) have persistent acromegaly despite treatment with surgery, medical therapy, and/or radiotherapy and ~2–8% of patients who achieve remission with surgery experience disease recurrence within 5 years (2).

There are potential areas of improvement in the monitoring of patients with acromegaly, such as integrating other clinical and molecular biomarkers to complement GH/IGF-1 in assessing treatment response, such as sKlotho (3), Ki-67 levels, positive AIP mutation, large tumor size, or sparse granular pattern (4, 5).

Cure after SSA has rarely been reported. It is possible that the apparent cure described in our patients is a long-term remission of the disease, and they should be followed-up.

CONCLUSION
With an improved array of therapeutic options available, it is possible to provide long-term disease control to a majority of patients with acromegaly. However, it has rarely been reported cure of acromegaly after somatostatin analogs. If this apparent cure is a long-term persistent suppression of GH secretion as a result of SSA therapy or a true cure of the disease, only long-term follow-up will tell.

References: