Acromegaly without acral anomalies

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Abstract

Early recognition of a pituitary secretor tumor offers a better prognostic; thus acromegaly might be recognized before the actual clinical picture of acromegaly is detectable. This is a 59-year old, non-smoking female admitted for: post-operative evaluation of acromegaly. The clinical evaluation is non-specific. One year prior she was diagnosed with acromegaly based on cerebral imaging assessment due to intermittent headache. She was treated with cabergoline a few months before neurosurgery was done; post-operative panel showed complete remission of acromegaly. Prompt detection of the disease allowed the early intervention with a very good outcome. The remission of GH excess after neurosurgery depends on tumor size and practical experience of the surgeon. The longer time of high growth hormone levels exposure the higher is the risk of cardio-metabolic and oncologic complications.

Keywords: acromegaly, pituitary tumor, acral, IGF1, GH

INTRODUCTION

Early recognition of a pituitary secretor tumor offers a better prognostic; thus acromegaly might be recognized before the actual clinical picture of acromegaly is detectable (1,2). The longer time of high growth hormone levels exposure the higher is the risk of cardio-metabolic and oncologic complications (3,4).

We aim to introduce a female case with early diagnostic of acromegaly and prompt case management.

CASE PRESENTATION

Admission

This is a 59-year old, non-smoking female admitted for: post-operative evaluation of acromegaly. The family medical history is irrelevant. The clinical evaluation is non-specific.

Medical history

She was diagnosed with acromegaly one year prior and initially she was treated with dopamine agonist cabergoline up to 3 mg/week for eleven months, then trans-sphenoidal hypophysectomy was done. The nuclear magnetic resonance examination at diagnostic showed a pituitary adenoma of 12/8/6 millimeter. Her medical history also includes: total hysterectomy for uterine fibroma 7 year prior, surgery for a nasopharyngeal cyst a few weeks before the diagnostic of acromegaly and a recent endoscopic removal of gastric polyp. The acromegaly was detected starting from a
cerebral and pituitary magnetic resonance imaging which was performed for non-specific headache.

**ASSESSMENTS**

The biochemistry panel shows hypercholesterolemia (Table 1).

**TABLE 1.** Biochemistry panel of 59-year old female known with acromegaly; evaluation after somatotropina was removed

| Parameter                  | Value   | Normal ranges | Units |
|----------------------------|---------|---------------|-------|
| Uric acid                  | 4       | 2.6-6         | mg/dl |
| ALT (Aspartate aminotransferase) | 16.7   | 0-31          | U/l   |
| AST (Alanine transaminase)  | 16.6    | 0-32          | U/l   |
| Total bilirubin            | 0.22    | 0-0.5         | mg/dl |
| Total cholesterol          | 245     | 0-200         | mg/dl |
| Serum phosphorus           | 4.4     | 2.3-4.7       | mg/dl |
| Fasting glycaemia          | 83.1    | 70-105        | mg/dl |
| HDL-cholesterol            | 79.3    | 40-60         | mg/dl |
| LDL-cholesterol            | 151.8   | 60-160        | mg/dl |
| Potassium                  | 5       | 3.5-5.1       | mmol/l|
| Magnesium                  | 2.1     | 1.6-2.55      | mg/dl |
| Sodium                     | 145     | 136-145       | mmol/l|
| Total proteins             | 7.3     | 6.4-8.3       | g/dl  |
| Triglycerides              | 111     | 0-149         | mg/dl |
| Urea                       | 25.2    | 15-50         | mg/dl |
| Creatinine                 | 0.72    | 0.5-1.2       | mg/dl |

The endocrine and calcium metabolism assays pointed out remission of acromegaly, a mild vitamin D deficiency (Table 2). The patient started menopause at the age of 43 without hormone replacement therapy. She was treated with cabergoline before surgery for a few months.

**TABLE 2 (A+B+C+D+E+F+G).** Endocrine and phosphorus – calcium metabolic on acromegalic patient 6 weeks after pituitary neurosurgery for a growth hormone producing tumor

### A. Thyroid panel

| Parameter                        | Value   | Normal ranges | Units |
|----------------------------------|---------|---------------|-------|
| TSH (Thyroid Stimulating Hormone) | 0.5     | 0.5-4.5       | µUI/ml|
| FT4 (Free levothyroxine)         | 11.44   | 9-19          | pmol/l|
| ATPO (Anti-thyreoperoxidase antibodies) | 0.33   | 0-5.61        | UI/ml |
| Calcitonin                       | 1.74    | 5.17-9.82     | pg/ml |

### B. Gonadal axes

| Parameter                        | Value   | Normal ranges | Units |
|----------------------------------|---------|---------------|-------|
| FSH(follicle stimulating hormone)| 69.56   | 25.8-134.8    | mIU/ml|
| LH (Luteinizing hormone)         | 30      | 7.7-58.5      | mIU/ml|
| Estradiol                        | 5       | ≤5-138        | pg/ml |
| Prolactine                       | 0.77    | 4.79-23.3     | ng/ml |

### C. Calcium metabolism and bone turnover markers

| Parameter                              | Value   | Normal ranges | Units |
|----------------------------------------|---------|---------------|-------|
| 25-hydroxyvitamin D                    | 24.3    | 30-100        | ng/ml |
| CrossLaps                              | 0.82    | 0.162-0.436   | ng/ml |
| Osteocalcin                            | 40.5    | 11-43         | ng/ml |
| PINP                                   | 99.34   | 14.28-58.92   | ng/ml |
| Parathormone (PTH)                     | 30.07   | 15-65         | µg/ml |

### D. Adrenal axes

| Parameter                              | Value   | Normal ranges | Units |
|----------------------------------------|---------|---------------|-------|
| ACTH (Adenocorticotropic Hormone)      | 21.38   | 3-66          | µg/ml |
| Morning plasma cortisol                | 10.96   | 4.82-19.5     | µg/ml |

### E. IGF1 (Insulin-like Growth Factor) profile before and after neurosurgery

| Parameter                              | Value   | Normal ranges | Units |
|----------------------------------------|---------|---------------|-------|
| GH (ng/ml)                             | December 2020 | March 2021 | July 2021 |
| Value 1                                | 0.76    | 0.46-2.38     | ng/ml |
| Value 2                                | 1.08    | 0.862-1.67    | ng/ml |
| Value 3                                | 2.18    | 1.23-2.31     | ng/ml |
| Value 4                                | 1.37    | 0.985-1.21    | ng/ml |
| IGF1 (ng/ml)                           | August 2021 | October 2021 | Units |
| Value 1                                | 1.63    | 1.23-2.31     | ng/ml |
| Value 2                                | 1.50    | 1.23-2.31     | ng/ml |
| Value 3                                | 2.04    | 1.23-2.31     | ng/ml |
| Value 4                                | 0.695   | 1.23-2.31     | ng/ml |

### F. GH profile/24 hours (Growth Hormone) before and after neurosurgery

| Parameter                              | Value   | Normal ranges | Units |
|----------------------------------------|---------|---------------|-------|
| GH (ng/ml)                             | December 2020 | March 2021 | July 2021 |
| Value 1                                | 1.81    | 1.23-2.31     | ng/ml |
| Value 2                                | 1.08    | 1.23-2.31     | ng/ml |
| Value 3                                | 2.18    | 1.23-2.31     | ng/ml |
| Value 4                                | 1.37    | 1.23-2.31     | ng/ml |

### G. GH (growth hormone) in OGGT (oral glucose tolerance test) before and after neurosurgery

**December 2020**

| Time (minutes) | 0' | 30' | 60' | 90' | 120' |
|----------------|----|-----|-----|-----|------|
| GH (ng/ml)     | 1.39| 1.24| 1.09| 1.04| 1.14 |
| glucose (mg/dl)| 87 | 159 | 153 | NA  | 144  |

**March 2021**

| Time (minutes) | 0' | 30' | 60' | 90' | 120' |
|----------------|----|-----|-----|-----|------|
| GH (ng/ml)     | 1.63| 1.5 | 0.789| 0.695| 0.674|
| glucose (mg/dl)| 83 | 168 | 194 | NA  | 110  |

**July 2021**

| Time (minutes) | 0' | 30' | 60' | 90' | 120' |
|----------------|----|-----|-----|-----|------|
| GH (ng/ml)     | 1.21| 1.22| 0.953| 0.798| 0.823|
| glucose (mg/dl)| 76 | 148 | 125 | NA  | 76   |

July 2021: trans-sphenoidal hypophysectomy of the adenoma (immunohistochemistry report with positive GH, chromogranin A, and a Ki 67 proliferation marker of 3%, and p53 of less than 1%).

**August 2021**

| Time (minutes) | 0' | 30' | 60' | 90' | 120' |
|----------------|----|-----|-----|-----|------|
| GH (ng/ml)     | 0.985| 0.766| 0.119| 0.0779| 0.069|
| glucose (mg/dl)| 145.9| 178.7| 147.8| NA  | 58   |
Other investigations

Thyroid ultrasound showed a right thyroid lobe of 1.8 by 2 by 4.8 cm (centimeter), an isthmus of 0.4 cm, a left thyroid lobe of 1.8 by 1.7 by 4.5 cm, with inhomogeneous pattern, as well as a hypoechoic nodule at the level of right thyroid nodule of 0.6 by 0.5 by 0.6 cm. Central DXA (dual-energy X-ray absorptiometry) was within normal levels; TBS (trabecular bone score) was mildly reduced (Table 3).

**REFERENCES**

1. Ganokroj P, Sunthomyothin S, Siwanuwan R, Chantra K, Buranasupkajorn P. Suwanwaliaikom S, Snabboon T. Clinical characteristics and treatment outcomes in acromegaly, a retrospective single-center case series from Thailand. *Pan Afr Med J*. 2021 Sep 10;10:40;31.

2. Albarel F, Elaraki F, Delemer B. Daily life, needs and expectations of patients with acromegaly in France: An on-line survey. *Ann Endocrinol (Paris)*. 2019 Apr; 80(2):110-116.

3. Zaroli-Hassan R, Conaglen HM, Conaglen JV, Elston MS. Symptoms and signs of acromegaly: an ongoing need to raise awareness among healthcare practitioners. *J Prim Health Care*. 2016 Jun;8(2):157-63.

4. Valea A, Ghervan C, Carsote M, Morar A, Iacob I, Tomesc F, Po DD, Georgescu C. Effects of combination therapy: somatostatin analogues and dopamine agonists on GH and IGF1 levels in acromegaly. *Clujul Medical*. 2015;88(3):310-313.

5. Dutta P, Hajela A, Pathak A, Bhansali A, Radotra BD, et al. Clinical profile and outcome of patients with acromegaly according to the 2014 consensus guidelines: Impact of a multi-disciplinary team. *Neurol India*. 2015 May-Jun;63(3):360-8.

6. Akoglu G, Melin A, Emre S, Ersoy R, Cakir B. Cutaneous findings in patients with acromegaly. *Acta Dermatovenerol Croat*. 2013;21(4):224-9.

7. Ribeiro-Oliveira A Jr, Barkan A. The changing face of acromegaly-advances in diagnosis and treatment. *Nat Rev Endocrinol*. 2012 Oct;8(10):605-11.

8. Borgen AE, Bugge ABD, Lund EL, Banner J. Undiagnosed acromegaly as an underlying cause of sudden death. *Forensic Sci Med Pathol*. 2021 Jun;17(2):322-326.

9. Cardinal T, Rutkowski MJ, Micko A, Shiroishi M, Jason Liu CS, Wrobel B, Carmichael J, Zada G. Impact of tumor characteristics and pre- and postoperative hormone levels on hormonal remission following endoscopic transsphenoidal surgery in patients with acromegaly. *Neurosurg Focus*. 2020 Jun;48(6):E10.

10. Ioachimescu AG. Acromegaly: achieving timely diagnosis and improving outcomes by personalized care. *Curr Opin Endocrinol Diabetes Obes*. 2021 Aug 1;28(4):419-426.

11. Carsote M, Ghemigian A, Valea A, Dumitrascu A. Acromegaly – related osteoporosis. *Romanian Journal of Clinical Research*. 2018;1(1):27-30.

12. Carrone F, Ariano S, Piccini S, Milani D, Mirani M, Balzarini L, Lania AG, Mazzolli G. Update on vertebral fractures in pituitary diseases: from research to clinical practice.
13. Cellini M, Biamonte E, Mazza M, Trenti N, Ragucci P, Milani D, Ferrante E, et al. Vertebral Fractures Associated with Spinal Sagittal Imbalance and Quality of Life in Acromegaly: A Radiographic Study with EOS 2D/3D Technology. Neuroendocrinology. 2021;111(8):775-785.

14. Godang K, Olarescu NC, Bollerslev J, Heck A. Treatment of acromegaly increases BMD but reduces trabecular bone score: a longitudinal study. *Eur J Endocrinol*. 2016 Aug;175(2):155-64.

15. Calatayud M, Pérez-Olivares Martín L, Librizzi MS, Lora Pablos D, González Méndez V, Aramendi Ramos M, Martínez Diaz-Guerra G, Hawkins F. Trabecular bone score and bone mineral density in patients with long-term controlled acromegaly. *Clin Endocrinol (Oxf)*. 2021 Jul;95(1):58-64.

16. Kužma M, Killinger Z, Jackuliak P, Vařuga P, Hans D, Binkley N, Payer J. Pathophysiology of growth hormone secretion disorders and their impact on bone microstructure as measured by trabecular bone score. *Physiol Res*. 2019 Nov 30;68(Suppl 2):S121-S129.