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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-operatory 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-operatory 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-operatory 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

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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 somatotropinoma 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
Conjugated bilirubin	0.22	0-0.5	mg/dl
Total bilirubin	0.5	0.2-1.2	mg/dl
Ionic serum calcium	4.1	3.9-4.9	mg/dl
Total serum calcium	9.5	8.4-10.2	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 phosphor – 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
P1NP	**99.34**	**14.28-58.92**	**ng/ml**
Parathormone (PTH)	30.07	15-65	pg/ml

D. Adrenal axes

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

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

Parameter	December 2020	March 2021	July 2021	
IGF1 (ng/ml)	**400.2**	**435.4**	**340.3**	
T Trans-sphenoidal hypophystectomy				
Parameter	August 2021	October 2021	Units	Normal ranges
IGF1 (ng/ml)	176.1	186.5	ng/ml	46-238

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

GH (ng/ml)	December 2020	March 2021	July 2021	Neurosurgery	August 2021	Units
Value 1	1.81	1.63	1.72		0.862	ng/ml
value 2	1.08	1.51	3.01		0.381	ng/ml
Value 3	2.18	2.04	1.23		0.237	ng/ml
Value 4	1.37	0.695	1.21		0.985	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 p 53 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).

TABLE 3. *Central DXA on post-menopausal acromegalic woman (BMD = bone mineral density; TBS = trabecular bone score)*

DXA regions	BMD (g/cm^2)	T-score (SD)	Z-score (SD)
lumbar 1-4	1.048	-1	-0.1
femoral neck	1.09	0.4	1.4
total hip	1.233	1.8	2.5

Follow-up

Post-operatory success of acromegaly neurosurgery requires (anyway) a subsequent long term follow-up of the patient.

DISCUSSION

Three aspects worth to be mentioned in relationship with this case. First is the early detection of the disease at the moment when clinical examination was not suggestive for acromegaly. Thus early intervention was feasible. The remission of GH excess after neurosurgery depends on tumor size and practical experience of the neurosurgeon/center (5,6). The easy access to cerebral and pituitary imaging techniques like computed tomography or magnetic resonance imaging allows premature revealing of a somatotropinoma nowadays (7,8).The patient we introduced had an association of other benign endocrine tumor at the level of uterus, stomach, *etc*. These tumors may be incidental or due to GH/IGF1 excess or they share a common genetic backup with the pituitary adenoma as seen in multiple endocrine neoplasia type 1 etc. (9,10). Also, The lady had a high level of bone resorption marker CrossLaps in addition to increased serum bone formation marker P1NP and a mild deficiency of vitamin D which was replaced with daily 1000 UI/ day. Acromegaly may cause a higher fracture risk especially at vertebral level; false positive normal DXA results due to arthrosis might be found (11,12,13). Acromegalic subjects may display a lower TBS (as seen here) due to GH/IGF1 – related bone quality impairment; bone turnover markers as well as bone quality are expected to improve once the GH/IGF-1 levels are controlled (14,15,16).

CONCLUSIONS

Awareness of health practitioners of different specialties including family physicians is essential for an early diagnostic of a GH secreting tumor before the traditional phenotype is registered. Early management means a major risk reduction of associated co-morbidities.

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