

# Hyperproduction Hydrogenic of STH Patology Generation of Clinical - paraclinical Disorders

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*Pituitary adenomas are benign tumors ; they arise from epithelial pituitary cells and they represent 10-15% of intracranial tumors. They can be found at 3% up to 20% of the population, on autopsy series. Cephalalgia is a precocious symptom which keeps going over the disease. The aspect as a whole of the person who suffers from this disease in the phase of established malady is characteristic: a very flat-shaped body, massive and stubby thus justifying the comparison with a pachyderm. Hands and legs are disproportionately bigger, like paddles, facies is disharmonic, facial features become coarse, with oblate forehead and massive prominent pregnant mandible. The joints disproportionately bigger, have limited, painful movement. The patient also presents visceral hypertrophy with numerous dysfunctions from various apparatus and systems.*

**Keywords:** pituitary adenoma, STH hyposecretion, dysmorphism, acromegaly, visceromegaly

Pituitary adenomas are benign tumors from the epithelial pituitary cells and they represent 10-15% of intracranial tumors. They can be found at 3% up to 20% of the population, on autopsy series [1,2]. These tumors can be hormonally active; they clinically manifest by acromegaly (excessive secretion of growth hormone), Cushing syndrome (ACTH and secondary of cortisol excess), amenorrhea-galactorrhea syndrome (prolactin excess) or it can be hormonally inactive (dysfunctional clinical tumors) [3,4]. Furthermore, pituitary adenomas can grow to sizes which can determine compression effects over the neighbouring structures, defending the pituitary insufficiency, vision disorders and, rarely, intracranial hypertension. From the historical point of view pituitary tumors are mostly benign. The adenoma secreted by PRL or prolactin is the most frequent type of secretive pituitary tumor (about 39%), followed by GH secretive adenomas and ACTH secretive tumors. Non-functional tumors represent only 10 % of pituitary adenomas whereas TSH secreting tumors, gonadotrophins or alpha subunits are rare [5]. Regarding the age of apparition, the pituitary hypersomatotropism determines two distinctive clinical forms: gigantism, when it appears in childhood and acromegaly when it appears after the bones overgrowth. Acromegaly has a gradual slow progressive evolution [6-8]. Cephalalgia is a precocious symptom which maintains over the disease. The aspect as a whole of the person who suffers from this disease in the phase of established malady is characteristic: a very flat-shaped body, stubby and massive thus justifying the comparison with a pachyderm. Hands and legs are disproportionately bigger, like paddles, the facies is disharmonic, facial features become coarse with oblate forehead, massive prominent pregnant mandible. Although the muscular system is well developed, muscular force is diminished. The joints disproportionately bigger, have limited, painful movement. The patient also presents visceral hypertrophy with numerous dysfunctions from the various systems [12].

## Experimental part

This study was performed at Craiova Emergency County Hospital, having a retrospective component (after

observation files) and a perspective one (by direct supervision), over a 6 years period [9]. Within the study there were included 80 patients with pituitary adenomas- 27 prolactinomas, 19 GH secreting adenomas and 34 non-secreting tumors.

The patients were investigated by determining the STH, taking usual blood analyses and also evaluating the breathing function and making a cardiovascular, neurological, ophthalmological, psychological evaluation and CT or RMN examination of the GH secreting pituitary tumor. For the 19 patients diagnosed with acromegaly, GH dosing was performed, resulting in values higher than the upper limit (ie above 5ng / mL in men or over 10ng / mL in women).

Although the high diagnostic accuracy of IGF1 (greater than baseline GH) is known, we did not have this possibility in our study. There are cases of normal and elevated IGF1 acromegaly in the literature. This imposes the introduction of this criterion as a method routine in studying acromegaly

After some authors with experience in the management of patients with acromegaly, diagnosis can only be missed if only criteria based on GH values are used. For diagnosis and monitoring of acromegals, GH should be used along with the serum titer of IGF1 [10].

In acromegaly patients, GH media was 20.96ng / mL, with a minimum of 6.8ng / mL and a maximum of 72.7ng / mL

It is described in literature the inconsistency between GH (sometimes small) values and clinical appearance.

## Dosing technique - methods for dosing the straight (hormone of growth)

hGH (somatotropin) is essential in the growth process, and in adults it plays an important role in metabolic activities. It is synthesized in the acidophilic cells of the anterior pituitary and its secretion from the intracellular storage granules is regulated by hormone-releasing hormone (GHRH) hormones and SRAT (somatotropin release-inhibiting factor); their synthesis depends on neurotransmitters, such as serotonin, dopamine, norepinephrine, and growth hormone releasing peptides.

It is also secreted in response to effort, stress, deep sleep, hypoglycemia, glucagon, insulin, thyroid hormones,

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estrogen, testosterone and vasopressin. Plasma exists in several monomeric and oligomeric isoforms (*big GH* and *big big GH*). Circulating GH-binding protein, which is similar to the extracellular domain of the tissue receptor of hGH5.

hGH stimulates the production of RNA, protease synthesis, mobilizes fatty acids from deposits and has transient insulin antagonist effects; elevated prolonged levels may induce alteration of glucose tolerance [5].

The secretion of hGH is pulsatile, but in adults plasma concentrations are stable, hGH oscillations are attenuated by GHBP. The plasma half-life is 20 min [5].

If the pituitary secretion of hGH is deficient or excessive in different stages of growth, it will determine the occurrence of nanism and gigantism. An excess of adult growth hormone will generate acromegaly.

The test is useful for confirming hypo- or hyperpituitarism, so that appropriate therapy can be initiated as soon as possible.

Determination of the hormone can be performed under both basal and post stimulation conditions (exercise, arginine, glucagon or insulin) or suppression (after 100 g of glucose).

Absence of response or inadequate response to stimulation tests is associated with hypopituitarism.

In case of gigantism or acromegaly, there is a lack of suppression or incomplete suppression after glucose administration. Furthermore, patients with acromegaly may have paradoxical increases in hGH in the suppression test1.

Patient training - junction (fasting) and after at least 30 minutes of rest, to determine the basal concentration3;

Harvested specimen - venous blood 3

Vacuum container without anticoagulant, with / without separator gel.

Processing required after harvest - separate the serum by centrifugation; work the serum immediately; if this is not possible, the serum freezes;

Sample volume - minimum 0.5 mL ser.

Method - immunoenzymatic with chemiluminescent detection .

Reference values - are age and sex dependent (tabel 1)

**Table1**  
REFERENCE VALUES OF hGH

Age and sex	Reference values (ng / mL)
Adults • Women <60 years	<10
• Women >60 ani	1-14
• Men <60 ani	<5
• men >60 ani	0.4-10
Newborns	15-40
children	<20
After stimulation	>5 (growth compared to basal level)
	>10 (maximum response to basal level)
After suppression	<2

Conversion factor: ng / mL =  $\mu$ g / L.

Detection limit - 0.01ng / mL

Limits and interferences

A single determination of hGH has a limited value due to marked fluctuations in serum concentration. Stimulation or suppression tests provide much more information.

Elevated levels can be met postprandial, after physical activity, deep sleep, stress, anxiety, sex hormone deficiency, especially androgens, hypo-, hyperthyroidism, adrenal hyperfunction, increased levels of free fatty acids; low levels can occur in hunger, cachexia, protein deficiency, metabolic imbalance diabetes.

## Results and discussions

Recent studies mention a 1/1 women/men proportion for the GH secreting adenomas, but in this study we registered 11 women and 8 men with GH secreting adenomas (fig. 1).

Regarding distribution on age groups specific studies showed that the occurrence of investigated pathology is more frequent for the age group of 40 - 60 years. In our study we found 4 cases (5%) with ages between 40 -49 years, 7 cases (8.75%) with ages between 50 - 59 years, and only 3 cases (3.75%) with ages between 30 -39 years, no patient below 30 years and the rest of 5 cases with ages over 60 years (fig. 2).

As for the 19 patients diagnosed with acromegaly there has been performed GH dosing and as a result there were higher values than the upper limit (over 5ng/mL for men or over 10ng/mL for women). At the acromegalic patients The GH average was 20.96ng/mL, with a minimum of 6.8ng/mL and a maximum of 72.7ng/mL.

From the graphic below (fig.3) we can conclude that there is a direct correlation between the dimension of the tumor measured RMN and somatotrope secretion (the bigger diameter of the tumor is, the bigger is the quantity

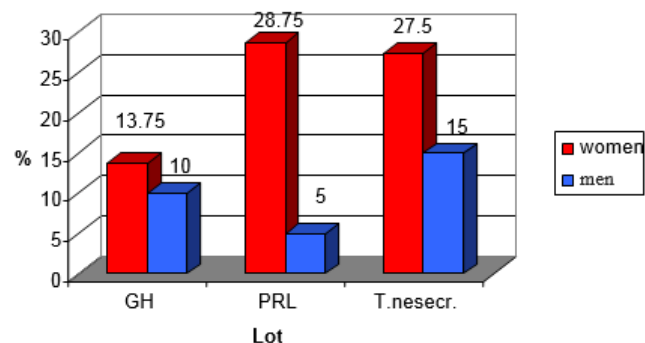


Fig 1. Gender and pathology distribution of subjects in the tumor group

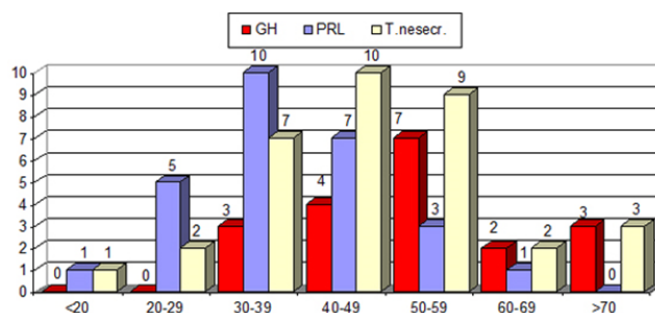


Fig.2. Distribution by age group of the tumor group

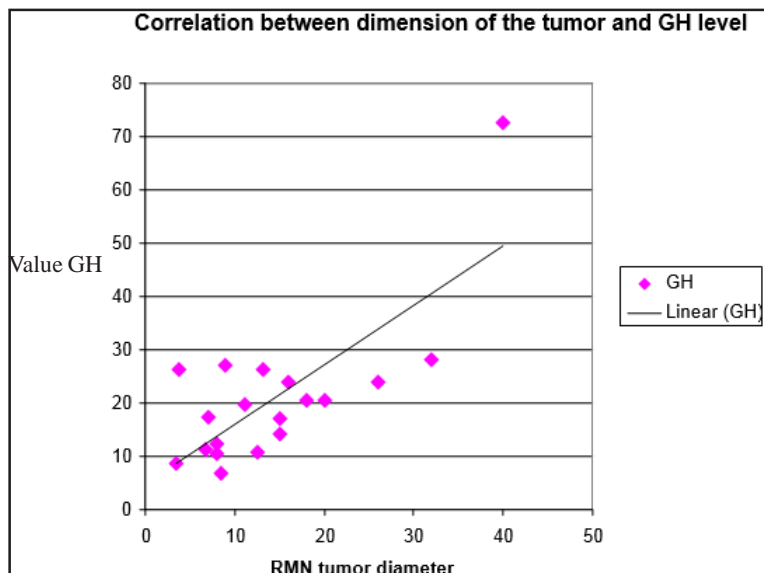


Fig.3. Correlation between hormonal secretion and tumoral volume

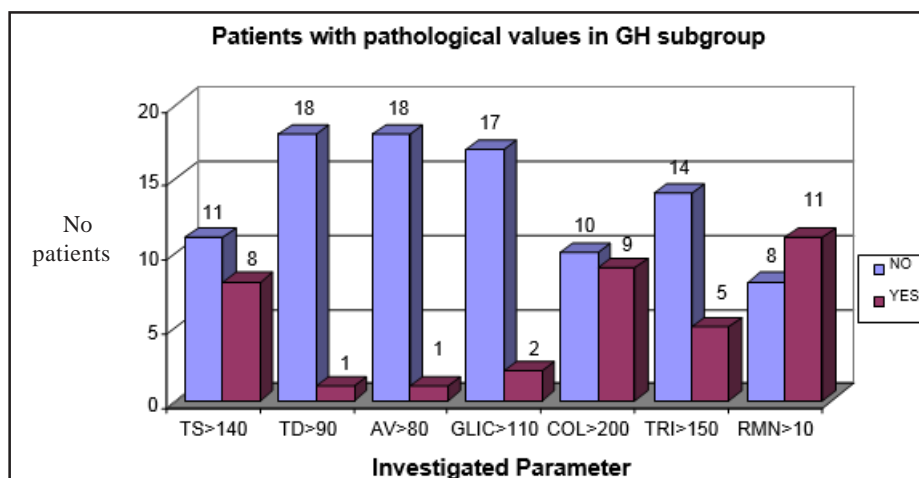


Fig. 4. Pathological values at acromegalic patients

of hormone), because the line of regression has a clear upward slope. This is underlined also statistically, the  $r$  correlation coefficient of Pearson having the value of 0.752, which overcomes the limit of significance of  $\pm 0.456$  of  $r$  for 19 subjects (17 freedom degrees). Within the acromegaly patients group we have obtained the following pathological values (fig.4) :

- Systolic HTA at 8 patients (57.9%) and diastolic HTA at 1 patient (5.3%);
- AV over 80 beats /min at 1 patient (5.3%);
- Glycemia over 110 mg/dL at 2 patients (10.5%), with diabetes mellitus type II confirmed at 1 patient;
- Hypercholesterolemia at 9 patients (47.4%);
- Hypertriglyceridemia (triglycerides over 150 mg) at 5 patients (26.3%);
- 11 patients (57.9%) had GH secretive macroadenoma GH and 8 patients (42.1%) had microadenoma (smaller than 10 mm diameter).

Regarding the patients from the present study, the percentage of those whose visual field was affected (8.75% representing 7 patients) is comparable to that whose patients didn't have any CV deficits-8 patients and visual acuity decrease was registered at 46.25% of the acromegalic patients [16].

From the 19 patients diagnosed with acromegaly, only 1 patient didn't have an EKG print, 4 patients (5%) had cardiomegaly with associative ischemic cardiopathy, 5 patients (6.25%) had ischemic cardiopathy symptoms but 9 patients (11.25%) had an EKG track of normal repose. [15] study there can be seen a three times growth of

mortality from breathing causes. Functional breathing tests are abnormal not only at men but also at women. Total pulmonary capacity increases up to 81% at men and 56% at women, 36% present a narrowing of small pipes and 26% have their large bronchias narrowed. (155) Pipes' narrowing and apnea during sleeping, frequent at these patients, contributes to a high level of mortality at acromegalic patients [11,12] In this study, 18 patients out of 19, took the breathing functional exploration test. Patients were tested by using spirographic method, measuring the maximum exhaling volume per second (MEVS). After measuring the MEVS there resulted: 10 patients (52% of acromegalic people) didn't have a ventilation dysfunction of gentle obstructive type and 2 patients (11%) had a medium ventilation dysfunction [13] Depressive disorders and other kinds of disorders associated to acromegaly were: 10% of GH secretive pituitary tumor had a severe depression (closely related to present dysmorphism at these patients) 6.25% had an average depression, 5% a light depression and only 2.5% didn't present any symptoms of depression. The risk of depression at the acromegalic patients is higher than the risk of this psychiatric manifestation at other pituitary affections. Other symptoms noticed at acromegalic patients were : psycho-emotional lability, physical and psychical asthenia, loss of initiative, inhibition, *tendency of social isolation*, mnestic and prosex difficulties, insomnia/terrifying dreams, irritability, depressive ideation, panic attack, fatigue, anxiety, hallucinations [14].

## Conclusions

As for the frequency, adenoma secreted by GH represents the second type of pituitary adenoma after prolactinoma being characterized by clinical dysmorphism and multivisceral affection.

Within the studied group we had 11 women and 8 men with a frequent incidence of age group 40-60 years.

There was a direct correlation between the dimension of the tumor measured RMN and somatotrope secretion (the larger is the diameter of the tumor the bigger is the quantity of the hormone).

85% of the patients had systolic HTA, 1 patient (5.3%) had HTA diastolic, diabetes mellitus type 2 was found at 1 patient and dyslipidemia was presented at 9 patients.

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Manuscript received: 6.11.2018