

# The Frequency of Macro and Giant Pituitary Adenomas of the Chiasm-Sellar Area on the Base of Retrospective Analysis

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### The purpose of the study

To study the frequency and clinical and hormonal characteristics of patients with giant formations of the chiasm-sellar region (CSR) according to a retrospective analysis.

## ABSTRACT

### Relevance

The treatment of giant pituitary adenomas (PA) is not only the lot of neurosurgeons, but also other specialists, first of all, endocrinologists, because arising (or aggravating) after surgery or radiation therapy in almost all patients with hypopituitarism (and often panhypopituitarism) requires substitution (sometimes lifelong) or corrective hormonal therapy (Ugryumov VM 1963, Starkova NT 1983, Vaks VV 1999, Greenman Y et al 1996). Nevertheless, there is currently no algorithm correction of hormonal disorders in patients with PA in the early and late postoperative period, meanwhile, it is the latter largely determine their quality of life. The causes of the continued growth of the tumor and its determining factors, as well as the tactics of surgical or conservative treatment in these cases, have not been clarified. Among the large number of existing classifications of PA, there are no classifications that fully reflect the size of the tumor, the ways of its spread, the nature of growth, hormonal activity, which presents certain difficulties for the development of a detailed clinical diagnosis, tactics of surgical treatment and correction of hormonal disorders. There is widespread discussion, despite the effectiveness proved in a number of papers, the feasibility of applying radiation treatment for giant PA due to a large number of complications (Sheline GE, 1979; Tsang RW et al., 1996; Sasaki R. et al., 2000), at present, the results of surgery of giant pituitary adenomas cannot be considered satisfactory, and the postoperative treatment tactics are far from perfect. Considerable postoperative lethality, a high level of disabled people dictates the need for further targeted study of this problem, aimed at improving the results of treatment [1-3]. All the above determines the relevance of this research topic. All the above was the reason for conducting this research.

## Material and methods of research

For the period from 2015 to 2017 years we performed a retrospective analysis of data from three Centers in Tashkent, namely the RSRSPC of Endocrinology of the Ministry of Public Health of the Republic of Uzbekistan, the Republican Scientific Center for Neurosurgery and the Republican Scientific Center for Emergency Medical Care. A total of 121 adult patients with macro-

and giant pituitary adenomas were analyzed. Of them - men - 59 (48.9%), women - 62 (51.1%). Middle age: men were 37.12 years old, women - 38, 15 years old. Disease duration ranged from 2 months to 25 years. All patients were divided into 2 groups: group 1 - patients with pituitary macroadenomas - 53 (43.8%) cases and group 2 - patients with giant pituitary adenomas - 68 cases (56.1%). The research methods included:

- a) general clinical (complaints, anamnesis, filling in the subject patient questionnaire, research of endocrine, neurological statuses, anthropometry - height, weight, FROM, OB, BMI).
- b) instrumental (perimetry for all colors, fundus, visual acuity, ECG, densitometry, CT/MRI (computed tomography / magnetic resonance imaging) of the Turkish saddle and adrenal glands, etc.).
- c) hormonal blood tests (STG, IFR-1, LH, FSH, prolactin, TSH, ACTH, free testosterone, estradiol, cortisol, free thyroxin).
- d) biochemical blood tests (LDL, HDL, cholesterol, triglycerides, calcium, chlorides, sodium, etc.). Based on the completed studies, the following results were obtained.

The obtained data were processed using computer programs Microsoft Excel and STATISTICA\_6. The significance of quantitative differences (n>12) was determined by the Wilcoxon method for unrelated ranges, to determine the reliability of small samples (n<0.05. The mean values (M), standard deviations of the mean (m) were calculated.<12), the non-parametric randomization criterion for the Fisher components for independent samples was used. Differences between groups were considered statistically significant at P [4-9]. The significance of differences in the level between groups was assessed by the magnitude of the confidence interval and student's criterion (p). Differences were considered statistically significant at p<0.05.

### The Results of the Study and their Discussion

Table 1 shows the distribution of patients by sex and age. Distribution of patients according to the topographic-anatomical classification of the side of growth of the pituitary adenoma by Kadashev B.A. (2007) showed that pituitary adenomas with a total growth variant were most often observed - 27 cases (22.4%), infra-suprastossellar growth - 28 cases (23%), infra-suprasellar

growth - 28 cases (23%) . It was these cases that differed more vivid clinical symptoms, due to the direction of tumor growth. Table 2 shows the distribution of patients according to the nature of the formation of the sellar region. From Table 2 NFPA was the most frequent - 72 cases out of 121 (56%). At the same time, 51 patients (98%) out of 53 in group 1 underwent surgical treatment - transnasal pituitary adenectomy (TAG). 55 patients (80%) of 68 in group 2 were subjected to surgical treatment - transnasal adenectomy of the pituitary gland. A total of 106 TAGs were performed in both groups. Repeated operations on the pituitary gland were performed in 8 patients (7%) of both groups. Radiation therapy was received by 6 (5%) patients and 1 by chemotherapy. It was found that panhypopituitarism was the most common in group 2 patients - in 32 of 68 patients (44.4%), postoperative panhypopituitarism occurred in 59 of 68 patients (55.5%), while in group 1 panhypopituitarism did not be observed. Bitemporal hemianopsia was also observed with a greater frequency in patients of group 2-41 cases out of 68 (61.1%). In addition, secondary amenorrhea was also more frequent in patients of group 2-27 cl (33.3%). Such disorders as secondary osteopenia, delayed physical and sexual development were identified only in group 2 patients. Thus, the most pronounced neuroendocrine and ophthalmologic disorders occurred in patients of group 2.

**Table 1:** The distribution of patients by sex and age.

Age, years	Men, n		Women, n	
	1 <sup>st</sup> group	2 <sup>nd</sup> group	1 <sup>st</sup> group	2 <sup>nd</sup> group
13 -15	-	-	1	-
16 - 29	5	11	9	9
30-44	5	14	12	7
45-59	5	13	12	7
60-74	2	4	3	2
75 and >	-	-	-	-
Total: n = 121	17	42	37	25

**Table 2:** The distribution of patients according to the nature of the formation of the sellar region.

The diagnosis	The patient's number		TAG, et all		Radiotherapy	
	1 gr	2 gr	1 gr	2 gr	1 gr	2 gr
Nonfunctional pituitary adenomas (NFPA)	31	41*****!!!	29	37 ((((((	1 (	2
Craniopharyngioma	3	6**{!!	3	3	-	-
Somato tropinoma	10	10**	8	7	-	-
Prolactinoma	10	7!***	10	5	-	-
Hemangioblastoma	-	1	-	1*(	-	2
Astrocytoma	-	1*	-	1+CT	-	1+ChT
meningioma	-	1	-	1	-	-

**Note:** TAG - Trans nasal adenectomy of the pituitary gland, - relapse growth! - stromal hemorrhage, (- repeat RT operation - number of patients who received radiation therapy, chemotherapy, CT - combination therapy.

The most pronounced disorders of the neurological status - endocrine encephalopathy, hallucinations (1 case), inadequate condition (1 cases), amaurosis (9 cases), ischemic stroke (2 cases), pathological reflexes, impaired muscle tone - decreased - were observed in patients 2 during the germination of a tumor in the brain, the groups are the anterior, middle, or posterior cranial fossa, with the growth of the tumor in the ventricles of the brain and both cavernous sinus [5-10]. The most pronounced violations of the visual fields in the form of bitemporal hemianopsia were observed in patients of both groups with endo-suprasellar growth - 18 cases (14.8%), with a total growth variant - 36 cl (30%), with endo-supra-infrasellar growth - 28 sl (23%) and supra-infra-laterosellar

growth - 28 cases (23%). Complications such as hemorrhage into the tumor in 6 out of 58 (10%), tumor recurrence in 14 out of 58 (24%) were found only in 2 grams of patients. Tables 3,4 give the average basal plasma hormone levels by group. As can be seen from Tables 3,4, the most significant decrease in the mean values of basal levels of plasma tropic hormones - GH, LH, FSH, ACTH - was recorded in patients of group 2. In addition, these patients also significantly reduced levels of cortisol, while in patients of group 1 plasma cortisol was on average within the normal range [11-15]. Thus, the most pronounced neuroendocrine complications were found in patients with giant pituitary adenomas.

**Table 3:** The average value of plasma hormones in patients of group 1 (n = 53).

Hormones	The average level	P	Control	The norm
LH	1,58±0,4	<0,05	12,3±2,1	8,7 ME/L (6,0-12,0)
FSH	2,5±0,3	< 0,05	8,2±0,3	6,1 ME/L (1,0-8,0)
PRL	27,3±0,6	<0,05	5,3±0,5	5,7 ng/ml
Free testosterone	48,5±3,5	>0,05	44,3±9,3	8.69-54.69 ng/ml
ACTH	413, 6±7,4	>0,05	564,1±23,1	До 50 ng/ml
IF-1	0,77±0,01	<0,05	3,1±0,4	134-836 ng/ml
STH	122,6±10,1	>0,05	112,9±13,6	2-5 ng/ml
Free thyroxine	443,3±22,8	>0,05	673,9±24,6	60-160nmol/l
Cortisol	1,58±0,4	<0,05	12,3±2,1	норма утро 260-720 nmol/l

Note. P - significance of differences compared with the control group.

**Table 4:** The average value of plasma hormones in patients of group 2 (n=68).

Hormones	The average level	P	Control	The norm
LH	1, 53±0,03	<0,05	12,3±2,1	8,7 ME/L (6,0-12,0)
FSH	3,9±0,4	<0,05	8,2±0,3	6,1 ME/L (1,0-8,0)
PRL	17,18±0,7	<0,05	5,3±0,5	5,7 ng/ml
Free testosterone	30,7±7,9	>0,5	44,3±9,3	8.69-54.69 ng/ml
ACTH	45,3 ±12,3	<0,05	564,1±23,1	До 50 ng/ml
IF-1	0,08 ±0,01	<0,05	3,1±0,4	134 - 836 ng/ml
STH	102, 6±16,3	>0,5	112,9±13,6	2-5 ng/ml
Free thyroxine	180,2±22,1	< 0,5	673,9±24,6	60-160 nmol/l
Cortisol				норма утро 260-720 nmol/l

## Conclusions

- In total, over the period 2012-2017, 68 patients with giant pituitary adenomas were treated in three Centers in Tashkent city, among which inactive pituitary adenoma was the most common - 41 cl (60%), less often - somatotropinoma - 10 cl (15%), prolactinoma - 7 cl (10%), craniopharyngioma - 6 cl (9%).
- The most pronounced neuroendocrine and ophthalmologic disorders occurred in patients of group 2 with giant pituitary adenomas.
- Neuroendocrine (GHD, panhypopituitarism, hypopituitarism, infertility, secondary amenorrhea), ophthalmological (GD, amaurosis, etc.) and stem disorders (pyramidal symptoms,

reduced reflexes and muscle tone diffusely) were observed in patients with a total growth variant in giant hyphenopaque patients with giant adrenal genes, reduced reflexes and muscle tone diffusely) were observed in patients with a total growth variant in giant hybrids, reflexes and muscle tone diffusely).

d) In patients with giant pituitary adenomas, a decrease in the level of GH, FSH, LH, ACTH (55%), that is, panhypopituitarism on the background of cerebral and stem symptoms, is primarily noted.

e) Neurovisualization marker of tumor aggressiveness can be different variants of its total growth, namely: supra-infra-laterosellar growth, supra-infrasellar growth observed in 56 patients (46.2%) of both groups.

Clinic-hormonal description of patients with giant pituitary adenomas". In this scientific article, the authors discussed the results of studies of 121 patients with various volume formations of the sellar area, of which 59 men (48.9%) and 62 women (51.1%) women [16-21]. Depending on the size of the pituitary adenoma, detected on CT/MRI, the patients were divided into two groups: group 1 patients - macroadenomas (from 20 to 30mm) - 53 (43.8%), and group 2 patients - giant (more 30mm) - 68 (56.1%). Pituitary adenomas with a total growth pattern were most often observed - 27 cases (22.4%), infra-suprastoserellar growth - 28 cases (23%), infra-suprasellar - 28 cases (23%), It was these cases that differed brighter clinical symptoms due to the direction of tumor growth. NFPA was the most common - 72 cases out of 121 (56%). At the same time, 51 patients (98%) out of 53 in group 1 underwent surgical treatment - transnasal pituitary adenectomy (TAG). 55 patients (80%) of 68 in group 2 were subjected to surgical treatment - transnasal adenectomy of the pituitary gland. A total of 106 TAGs were performed in both groups. Repeated operations on the pituitary gland were performed in 8 patients (7%) of both groups. Radiation therapy was received by 6 (5%) patients and 1 by chemotherapy. It was found that the most pronounced neuroendocrine complications were found in patients with giant pituitary adenomas.

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