

# The Frequency and Neuroimaging Characteristics of Macro- and Giant Pituitary Adenomas

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## Abstract

Data from 3 medical centers of Tashkent city, in which 156 patients (76 men and 80 women) with pituitary macroadenomas (PMA) and giant pituitary adenomas (GPA) were treated during 3 years (between 2015 and 2017), were retrospectively analyzed. The results of the study showed that the different variants of PMA/GPA suprasellar growth might serve as a neuroimaging marker of tumor aggressiveness, namely, supra-infra-latesellar and supra-infra-tellular growth observed in 68 (43.5%) patients, as well as invasive tumor growth in 108 (69.2%) patients. Transsphenoidal removal is a relatively safe and effective method, even in PMA and GPA with suprasellar extensions, in most of the cases. (*International Journal of Biomedicine*. 2019;9(1):72-74.)

**Key Words:** giant pituitary adenomas • pituitary macroadenomas • magnetic resonance imaging • transsphenoidal hypophysectomy

## Abbreviations

**GPA**, giant pituitary adenomas; **NFPA**, non-functioning pituitary adenoma; **PA**, pituitary adenomas; **PMA**, pituitary macroadenomas; **PG**, the pituitary gland; **SIR**, Standardized Incidence Rates; **TSHS**, transsphenoidal hypophysectomy.

## Introduction

Pituitary adenomas constitute 10%–15% of intracranial tumors, and occur in 17%–25% of the population.<sup>(1)</sup> Most pituitary adenomas are benign, but approximately one third of them are invasive, encroaching upon the bones, dura, and/or other adjacent structures.<sup>(2,3)</sup> Functioning PMA and GPA have large growth volumes and endocrinological abnormalities. Pituitary adenomas are classified as “giant” when their diameter exceeds 4 cm.<sup>(4)</sup> GPA has the potential for widespread, multi-directional extension. These tumors are very difficult to treat and can behave aggressively.<sup>(5,6)</sup>

According to M. Gruppeta and J. Vassallo,<sup>(7)</sup> the prevalence for macroadenomas was 40–67/100 000 people and the SIR was 1–90/100 000/year. Giant pituitary adenomas (>40 mm) constituted 4–8% of the whole cohort of PAs and the SIR was 0–18/100 000/year. In 2004, WHO<sup>(4)</sup> classified pituitary adenomas into typical adenomas, atypical adenomas, or carcinomas.

Various classifications have been proposed but there is no evident terminology to describe large pituitary tumors.<sup>(8)</sup> JC Zakir et al. showed that parasellar invasion prevails as a strong predictive factor for tumor recurrence.<sup>(9)</sup> Severe suprasellar extension should be considered as invasion parameter and could impact prognosis.

An original study comparing the clinical spectrum of giant prolactinomas with ordinary macroprolactinomas was performed by Espinosa and colleagues.<sup>(10)</sup>

Despite the histological benign nature, the management

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of PMA and GPA is very difficult.<sup>(6,7,11-17)</sup> Transsphenoidal surgery is recognized as the optimum technique for the management of pituitary adenomas, as it helps preserve normal pituitary function and allows recovery of visual function.<sup>(6,18,19)</sup> As a consequence, the transsphenoidal approach is the first choice in the surgical treatment of MPA or GPA with suprasellar extensions.<sup>(6,20-22)</sup>

The purpose of this study was to determine the frequency and neuroimaging characteristics of macro- and giant pituitary adenomas according to seeking medical care.

## Materials and Methods

We retrospectively analyzed data from 3 medical centers of Tashkent city (RSSPMC of Endocrinology, the Republican Research Center of Neurosurgery, and the Republican Scientific Center for Emergency Medical Aid), in which 156 patients (76 men [mean age of 37.1 years] and 80 women [mean age of 38.2 years]) with PMA and GPA were treated during 3 years (between 2015 and 2017). The duration of the disease ranged from 2 months to 25 years. As the surgical management, TSHS was performed in 137 (87.8%) cases (surgeons: R.B. Fayzullaev, MD, PhD; Akbutaev MD; Prof. K. I. Makhkamov, MD, PhD; Prof. Michael Powell, MD, PhD) with repeated operations in 8 (5.1%) cases. Six (3.8%) patients received radiotherapy and 1 - chemotherapy.

Methods of investigation included: 1) general clinical examination, assessment of endocrine/neurological status; 2) instrumental methods of examination (visual field perimetry, colour vision, fundus oculi, visual acuity, ECG, CT/MRI of sella turcica and adrenal glands, ultrasound of reproductive organs); 3) determination of blood hormones (GH, IGF-1, LH, FSH, PRL, TTG, ACTH, testosterone, estradiol, prolactin, progesterone, cortisol) in RIA using "Gamma-12" and "Strantg 300," and 4) histological examination of postoperative specimens.

Statistical analysis was performed using statistical software package SPSS version 20.0 (SPSS Inc, Chicago, IL). Categorical variables were analyzed using the Chi-square test. A probability value of  $P \leq 0.05$  was considered statistically significant.

## Results

Depending on the size of PA detected on CT/MRI, the patients were divided into two groups: Group 1 included 70/44.9% patients with PMA (from 20 mm to 30 mm in maximum diameter), Group 2 - 86/55.1% patients with GPA ( $\geq 40$  mm). Table 1 presents the distribution of patients by sex and age. In accordance with the topographic-anatomical classification by B. Kadashev,<sup>(23)</sup> endosellar adenomas were detected in 38/24.4% cases and endo-suprasellar in 5/3.2% cases, both of which were characterized by chiasmatic syndrome. Endo-supra-infra-ante-latero-retrosellar adenomas were detected in 48/30.7% cases, of which 3 were with extension into the anterior cranial fossa, 5 - into the ventricles, 1 - into the cavernous sinus, 2 - into both cavernous sinus and the middle cranial fossa. This group of adenomas contributed to the development of various neuro-endocrine disorders, as well as pyramidal symptoms due to affection of the motor path.

**Table 1.**

### The age-gender distribution of patients

Age, years	Number of men		Number of women	
	Group 1	Group 2	Group 1	Group 2
13	-	-	1	1
16-29	8	14	10	10
30-44	10	15	13	10
45-59	8	13	12	11
60-74	3	5	4	5
$\geq 75$	-	-	1	2
Total: n = 156	29	47	41	39

Infra-supra-laterosellar and infra-suprasellar adenomas were detected with the same frequency - 28/17.9% cases. These cases had more vivid clinical symptoms due to the direction of tumor growth. Disorders of nasal breathing and swallowing (dysphagia) were characteristic of patients with these adenomas.

The distribution of tumors in the sellar region is presented in Table 2. Thus, NFPA was the most frequent type (96/61.5%) ( $P < 0.05$ ), whereas somatotropinoma and prolactinoma numbered 23/14.7% and 20/12.8%, respectively. Itsenko-Cushing's disease was detected in two cases (1.3%).

**Table 2.**

### The distribution of patients according to the sellar region tumors and treatment

Nosology	Number of patients		TSHS		Radiation therapy	
	Group 1	Group 2	Group 1	Group 2	Group 1	Group 2
NFPA	43	53 (6*, 3^)	31	45 (5#)	1 (1#)	8
Craniopharyngioma	3	9 (2*, 2^, 1#)	3	6	-	1
Somatotropinoma	11	12 (2*)	8	10	-	2
Prolactinoma	12	8 (3*, 1^)	11	5	-	-
Hemangioblastoma	-	1	-	1 (1*, 1#)	-	2
Itsenko-Cushing's disease	2	-	1	-	-	-
Astrocytoma	-	1 (1*)	-	1 (1CT)	-	1 (1ChT)
Meningioma	-	1	-	1	-	-

\* - tumor regrowth, ^ - hemorrhage in stroma, # - reoperation, ChT - chemotherapy, CT - combination therapy, TSHS - transsphenoidal hypophysectomy.

According to MRI, necrosis of PG was diagnosed in one patient, hemorrhage in PG - in 6/3.8% cases. In 14 GPA patients, tumor growth continued after its removal. Malignant type of NFPA was detected in 2 patients.

Based on MRI of PG and X-ray classification by I.I. Dedov,<sup>(24)</sup> MPA with suprasellar growth were distributed as follows:

- Suprasellar growth within 10 mm above the pituitary fossa - 40 cases
- Suprasellar growth within 20 mm, with extension into the front pocket of the third ventricle (large PA) - 30 cases
- Suprasellar growth up to 30 mm, fills the anterior part of the third ventricle (very large PA) - 50 cases
- Suprasellar growth >30 mm (massive PA), rises above the level of the Monroe hole, or previous adenomas with asymmetrical lateral or multiple-sided growth (massive PA) - 36 cases

GPA showed invasive growth into surrounding anatomical structures in 69.2% of cases and pituitary apoplexy in 3.8% of cases, which was the main factor limiting the radical surgical capabilities and increasing the number of relapses.

**In conclusion**, the different variants of PMA/GPA suprasellar growth might serve as a neuroimaging marker of tumor aggressiveness, namely, supra-infra-latesellar and supra-infra-tellular growth observed in 68 (43.5%) patients, as well as invasive tumor growth in 108 (69.2%) patients. Transsphenoidal removal is a relatively safe and effective method, even in PMA and GPA with suprasellar extensions, in most of the cases.

## Competing Interests

The authors declare that they have no competing interests.

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