Ophthalmic and Neurological Disorders in Patients with Giant Inactive Pituitary Adenomas Depending on the Nature of Tumor Growth

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ABSTRACT
68 patients with gigantic inactive adenomas of the pituitary gland were examined (from them men - 43, women -25). Middle age: men amounted to 37,12 years, women - 38, 15 years ago, the illness of the disease ranged from 2 months to 25 years.
Most often among patients met an endo-supraseller growth of the tumor -28 (41.1%). observations. The most pronounced violations of the visual fields in the form of amaurosis and the bitemporal hemianopsy was observed in patients with endo-supraselligar growth - amaurosis (10.7%), bitemporal hemianopsy (89.3%), as well as with a total growth option - amaurosis (23%), bitemporal hemianopsy (79.9%). The most pronounced neurological disorders in the form of hypotalamic-stem disturbances (pyramid symptoms, a decrease in reflexes and muscle tone diffuse) were observed in patients with a total growth option, with retrosellary growth and during germination in the brain.
KEYWORDS: giant, inactive, pituitary adenomas

ABSTRACT

NAG (inactive pituitary adenomas) are benign pituitary tumors arising from adenohypophysial cells, which accounts for one third of all pituitary adenomas. . Clinically manifested NAG usually, although not always, are macroadenomas, and patients often show symptoms associated with mass effects, such as headache, visual disturbances and/or cranial nerve dysfunction [1,2]. These tumors may also come to the doctor's attention as a random finding when MRI is performed for unrelated signs and symptoms [3] or, less often, as a result of hormonal deficiency of the anterior pituitary lobe or hyperprolactinemia due to compression of the pituitary pedicle [4]. Recommendations on the management of random NAGS have recently been published [5]. NAG can also manifest as sinonasal or nasopharyngeal tumors without contact with the Turkish saddle. In such cases, they should be differentiated from other types of tumors found in this area, such as primary or metastatic neuroendocrine tumors or olfactory neuroblastomas.

Visual signs and symptoms are a frequent manifestation of pituitary adenoma due to compression or ischemia of the optic nerves and the intersection of the optic nerves. Although bitemporal hemianopia is a classic manifestation of visual field deficiency, these tumors can cause additional visual disturbances. After endoscopic endonasal pituitary surgery, most patients have an improvement in visual symptoms. Preoperative factors, including the thickness of the retinal nerve fiber layer, severity of preoperative deficiency, duration of visual symptoms, tumor size, degree of resection, and patient's age, serve as possible predictors of postoperative visual outcomes [6].

A recent NAG guideline states that in asymptomatic, hormonally inactive tumors, the standard of treatment is a "wait-and-scan" strategy. In case of (impending) visual impairment, surgical treatment is performed by an experienced pituitary surgeon. If the surgical resection was incomplete or if the tumors recur, interdisciplinary methods of treatment should be considered (for example, repeated surgery, radiation therapy, observation). [7].

The aim of the study was to study ophthalmic and neurological disorders in patients with giant inactive pituitary adenomas.

Material and methods of research. We examined 68 patients with giant inactive pituitary adenomas (43 of them were men, 25 were women). The average age: men was 37.12 years, women - 38, 15 years, the duration of the disease ranged from 2 months to 25 years.

In our study, we relied on the classification of Kurokawa Y., (1998), who considers tumors larger than 30 mm and 40 mm to be giant, respectively.

In total, 60 TAG (transnasaladenomectomy of the pituitary gland) was performed in three Centers in Tashkent (PhD Akbutaev A.M., prof. Makhkamov K.I., rof. By Michael Powell from the UK) . Repeated operations on the pituitary gland were performed in 5 patients (7.3%), 5 (7.4%) patients received radiation therapy and 1 – chemotherapy (1.5%).

MATERIALS AND METHODS

General clinical (study of endocrine, neurological statuses), 2) instrumental (perimetry for all colors, fundus, visual acuity, 3) ECG, CT/MRI of the Turkish saddle and adrenal glands,

4)Ultrasound of internal and genital organs, etc.), 5) hormonal blood tests (STG, IGF-1, LH, FSH, PRL, TSH, ACTH, prolactin, testosterone, estradiol, progesterone, cortisol (RIA-blood serum studies were conducted on counters "Gamma-12" and "Strantg 300"). In addition, the postoperative material was subjected to histological diagnostics at the RSNPMC E MZRUz named after Academician E.H. Turakulov (histology cabinet).

The obtained data were processed using computer programs Microsoft Excel and STATISTICA_6. The arithmetic mean (M), the standard deviation of the arithmetic mean or the error of the arithmetic mean of all n repetitions (m) were calculated.The reliability of the differences in the level between the groups was assessed by the value of the confidence interval and the Student's criterion (p). The differences were considered statistically significant at $p<0.05$.

RESULTS AND DISCUSSION

Table 1 shows the distribution of patients by gender and age.

Table 3 .
Distribution of patients by gender and age

Age ,years	**Numberofmen**	**Numberofwomen**
13 years-15 years	-	-
16 – 29	11	9
30-44	14	7
45-59	13	7
60-74	5	2
75 andolder	-	-
Total: n = 68	43	25

The next stage of our research was to study the nature of tumor growth, since the manifest of clinical symptoms depends on it. Table 2 shows the distribution of patients according to the nature of the formation of the cellular region and the type of treatment received.

As can be seen from Table 2, hemorrhage in the pituitary stroma occurred in 6 (8.9%) cases and of them prevailed in patients with NAG – 3 cases (4.4%). Recurrence of tumor growth after TAG occurred in 15 patients out of 67 (22.4%), while most often with NAG – 6 cases out of 15 (40%).

Table 2.
Distribution of patients by type of treatment received.

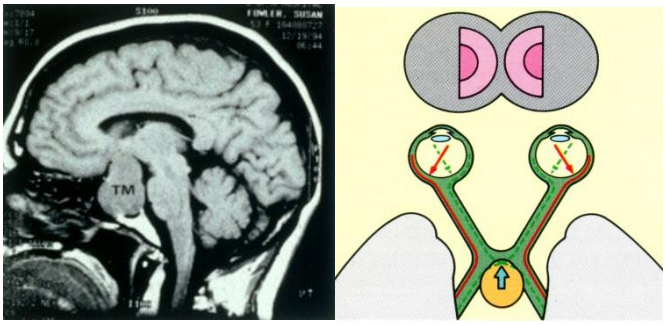
Diagnosisofthedisease	**Number patients**	**TPA**	**NoP**
IPA	42******!	37((((	2

Note: IPA – inactive pituitary adenoma, TPA – transnasal pituitary adenomectomy, *- relapse of growth, ! – hemorrhage in the stroma, (- repeated surgery, LT - the number of patients who received radiation therapy, CT - chemotherapy , CT – combination therapy

Figure 1 shows an MRI and a diagram of disorders in endosuprasellar tumor growth.

Fig. 1, a, b. Pituitary macroadenoma. Endo-suprasellar growth: bitemporal hemianopia

a) **b)**



Patients of this group are characterized by chiasmal syndrome, i.e. visual field loss: bitemporal hemianopia, initial left- (or right)third-party homonymous hemianopia, complete left- (or right)third-party homonymous hemianopsia, scotomas, etc.

Among our patients, this growth variant was observed in 28 cases (41.1%).

Figure 2 shows an MRI and a diagram of disorders in endo-laterosellar tumor growth.

For patients of this group, the most characteristic are a decrease in visual acuity in one eye, unilateral headaches, damage to the oculomotor nerves - III, IV, V, VI PMN

It should be emphasized that usually most of the acidophilic cells producing STH and prolactin are located in the posterolateral part of the adenohypophysis. Some acidophilic cells produce both STH and prolactin. These are mammo-somatotrophic cells.

Taking this into account, the earliest loss of STH should be expected among patients with endo-laterosellar growth of pituitary tumor. We observed 9 cases (13.2%).

Fig. 2, a, b. Pituitary macroadenoma. Endo-laterosellar growth: decreased visual acuity in one eye, unilateral headaches, lesion of III, IV, V, VI PMN

a) **b)**

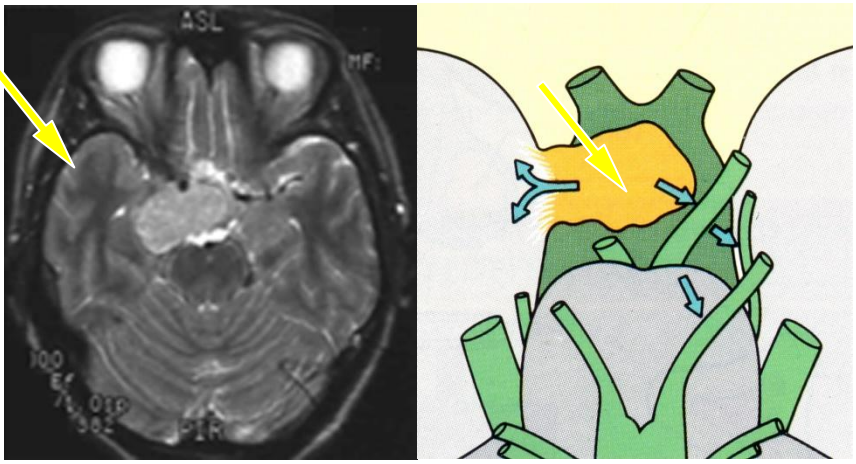
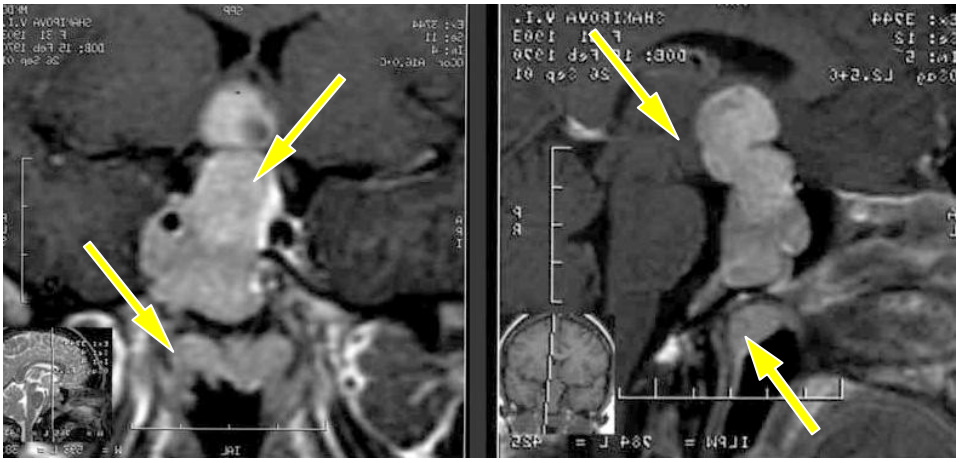


Figure 3 shows an MRI and a diagram of disorders with total tumor growth.

Fig. 3 a,b. Pituitary macroadenoma. Endo-supra-infra-retro-ante-laterosellar growth

a) **b)**



For patients of this group, the direction of tumor growth is characterized by all of the above violations, as well as pyramidal symptoms due to damage to the motor pathway. We had 26 cases (38.2%).

Figure 4 shows an MRI and a diagram of disorders in endo-antesellar tumor growth.

For patients of this group, the direction of tumor growth is characterized by disorders caused by growth into a lattice maze, orbit. We observed 3 cases (4.4%).

Fig. 4, a, b. Pituitary macroadenoma. Endo-antesellar growth: into a lattice maze, into an orbit

a) **b)**

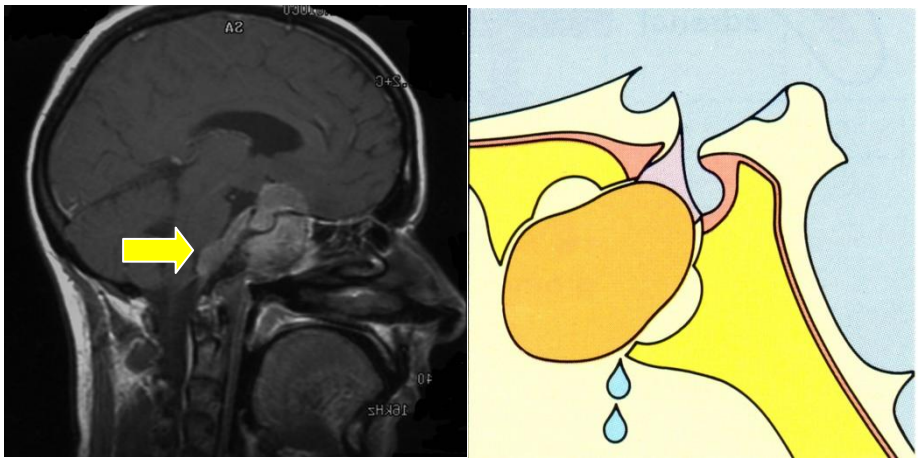
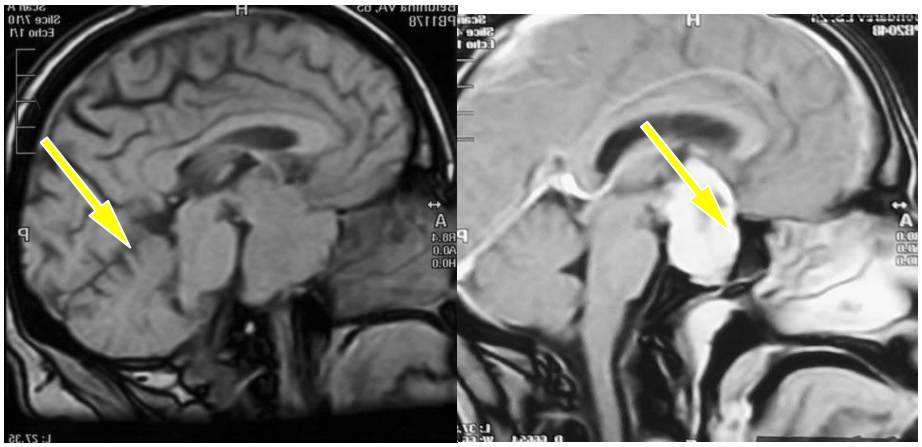


Figure 5 shows an MRI and a diagram of disorders in endo-infrasellar tumor growth.

Fig. 5, a, b. Pituitary macroadenoma. Endo-infrasellar growth: nasal breathing disorders, swallowing disorders

a) **b)**



Patients in this group of tumor growth directions are characterized by disorders of nasal breathing and swallowing (dysphagia). We observed 2 cases (2.9%).

Thus, endo-suprasellar tumor growth -28 (41.1%) was most common among our patients with giant inactive pituitary adenomas. observations. On the 2nd place there were variants with total growth – 26 cases (38.2%). On the 3rd place – with endo-laterosellar tumor growth – 9 observations (13.2%).. The least common were endo-antesellar (germination into the brain) and endo-infrasellar tumor growth – 3/2 cases, respectively, or (4,4%)./ (2,9%).

Table 3 shows a comparison of clinical symptoms depending on the nature of tumor growth.

Table 3.
Comparison of clinical symptoms depending on the nature of tumor growth (n=68) abs (%)

Violations	**Totaltumor growth N=26**	**Suprasellartumorgrowth N=28**	**Endo-laterosellartumorgrowth N=9**	**Endo-antesellartumorgrowth N=3**	**Endo-infrasellar tumor growth N=2**
Bitemporalhemianopia	20 (79,9%)	25 (89,3%)	-	-	-
Amaurosisisbilateral	6 (23%)	3 (10,7%)	-	-	-
Diencephalic - stemsymptoms	13 (50%)	-	9(100%)	5 (100%)	-
Neuroendocrinedisorders	26 (100%)	26 (92,8%)	-	1 (20%)	-
Brain - wideсимптомы	18 (69%)	-	-	5 (100%)	1 (50%)
Defeat of III, IV, V,VI pairs	15 (57,6%)	-	9(100%)	-	-
Symptoms of oral automatism, s-m Babinsky	12 (46,1%)	-	7 (77,8%)	5 (100%)	-

Note. CN – cranialnerves

As can be seen from Table 3, the most pronounced visual field disturbances in the form of amaurosis and bitemporal hemianopia were observed in patients with endo-suprasellar growth – amaurosis (10.7%), bitemporal hemianopia (89.3%), as well as in the total growth variant – amaurosis (23%), bitemporal hemianopia (79.9%). Comparative characteristics of patients showed that patients with giant pituitary adenomas had pronounced neuroendocrine, neurological and ophthalmological disorders. Thus, neuroendocrine (DHR, panhypopituitarism, hypopituitarism, infertility, secondary amenorrhea), ophthalmological (bitemporal hemianopsia, amaurosis, etc.) were characteristic of total tumor growth and suprasellar growth. Diencephalic-stem disorders (pyramidal symptoms, decreased reflexes and muscle tone diffusely) were observed in patients with a total growth variant, with retrosellar growth and with germination into the brain. In patients with giant pituitary adenomas, first of all, there is a decrease in the level of STH, FSH, LH, ACTH (47%), that is, panhypopituitarism against the background of cerebral and stem symptoms.

It should be emphasized that in general, patients had a decrease in the average values of tropic hormones of the pituitary gland.

The results we obtained showed that all patients with giant pituitary adenomas have neuroendocrine disorders of varying severity, worsening as the pituitary tumor grows. The nature of the disorders has a number of specific (HD, scotomas, hypopituitarism, cranial

nerve damage) and non-specific symptoms (pyramidal symptoms, diffuse decrease in muscle tone, reflexes) depending on the side of growth, the size of the tumor.

CONCLUSION

1) Endo-suprasellar tumor growth -28 (41.1%) was most common among our patients with giant inactive pituitary adenomas. observations.
2) The most pronounced visual field disturbances in the form of amaurosis and bitemporal hemianopia were observed in patients with endo-suprasellar growth – amaurosis (10.7%), bitemporal hemianopia (89.3%), as well as in the total growth variant – amaurosis (23%), bitemporal hemianopia (79.9%),
3) The most pronounced neurological disorders in the form of diencephalic-stem disorders (pyramidal symptoms, decreased reflexes and muscle tone diffusely) were observed in patients with a total growth variant, with retrosellar growth and with germination into the brain

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