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The frequency of various giant pituitary adenomas on retrospective data

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Background

The adenoma of pituitary glands, recently called neuroendocrine pituitary tumors along with neuroendocrine tumors (Pitnets) from other organs,[1] are common neoplasms that are formulated from 10% to 20% of intracranial tumors.[2]

Classification of endocrine tumors of the World Health Organization 2017.[3] has been utilized, which determines the adenoma of the pituitary gland in accordance with their profile of hormones pituitary and transcription factors.[3,4]

A significant proportion of the pituitary adenoma (from 22% to 54% in different series) will manifest themselves with signs and symptoms of the mass effect, and not excessive secretion of hormones, and is defined as clinically non-functional pituitary adenoma (NFPA).[5-7]

Among the large number of existing classifications of hypertension, there are no classifications that reflect the total tumor sizes, the path of its distribution, the nature of growth, hormonal activity, which represents certain difficulties for the formation of a detailed clinical diagnosis, surgical treatment tactics and correction of hormonal disorders.[8,9] It is widely discussed, despite the effectiveness proven in a number of work, the feasibility of the use of radiation treatment at gigantic ag in connection with a large number of complications.[10,11]

Magnetic resonance imaging (MRI) is a diagnostic method that is one of the most modern, safe (without radioactivity or radiations) and a qualitative method for the diagnosis of various organs and systems of the human body.[12]

As it is a known fact, that MRI is a method that allows to investigate the structure of the pituitary gland (front and rear lobes, the intermediate share is also differentiated), to identify and evaluate the size and prevalence of the volumetric formations of the pituitary gland (adenoma, cysts, craniopharygioma, etc.), determine the presence of hemorrhages and their prescription, Assess the effectiveness of conservative and surgical treatment of pituitary diseases.

It allows you to reveal a tumor, as well as estimate its position in the Turkish saddle and relationship with the surrounding structures of the brain, primarily by chiasm and visual nerves.

According to Chohan MO, et al.[13] in 2016, a new bulk threshold of 20 cm (3) was proposed as the most accurate for MRI tomography of giant pituitary adenomas.

According to Zakir JC, et al.,[14] although some hypophized adenomes can have aggressive behavior, the overwhelming majority of benign. There are still disputes about predicting factors regarding the biological behavior of these specific tumors. Present study estimates the potential invasion and proliferation markers compared with the current classification structures and epidemiological parameters. The study included 50 patients who were operated for the tumor, more than 30 mm in size, with an average postoperative observation of 15.2±4.8 years. The pituitary magnetic resonance was used to assess the resumption of growth, invasion and stretching to adjacent tissue. Three fabric biomarkers were analyzed: P53, KI-67 and C-ERBB2. Ki-67 ($p = 0.23$) and C-ERBB2 ($P = 0.71$) did not have a significant attitude to the status of the development of the tumor. P53 ($p = 0.003$), parasellar invasion ($p = 0.03$), and classification, grade 2b ($p = 0.01$) were associated with the worst outcome of the disease.

All of the above served as the reason for the present study.

The present study aims – to perform a comparative description of neuroendocrine disorders in patients with giant pituitary adenomas.

Material and methods

We studied data from 3 Centers in Tashkent (RSSPMC Endocrinology of PHM named by akad. Yo.Kh. Turakulov, Scientific Center for Neurosurgery and Scientific Center for Emergency Medical Aid of the Ministry of Health of the Republic of Uzbekistan), according to which 68 patients with giant pituitary adenomas of various etiologies were hospitalized for 3 years (period 2015-2017). (of which men - 43, women -25). Average age: for men amounted to 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), which considers tumors to be more than 30 mm and 40 mm in size, respectively, as gigantic.

A total of 60 TAGs (transnasal pituitary adenomectomy) were performed in three Centers in Tashkent (MD Phayzullaev R.B., PhD. Akbutaev A.M., Prof. K. Makhkamov, Prof. Michael Powell from the UK). Repeated operations on the pituitary gland were performed in 5 patients (7.3%). Radiation therapy was received by 5 (7.4%) patients and 1 chemotherapy (1.5%).

Research methods included: 1) general clinical (examination of endocrine, neurological status), 2) instrumental (perimetry for all colors, fundus, visual acuity, 3) ECG, CT / MRI of the Turkish saddle and adrenal glands, 4) internal ultrasound and genital organs, etc.), 5) hormonal blood tests (STH, IGF-1, LH, FSH, PRL, TSH, ACTH, prolactin, testosterone, estradiol, progesterone, cortisol (RIA studies of blood serum were performed on Gamma counters -12 "and" Strantg 300"). In addition, the postoperative material was subjected to histological diagnosis in RSSPMC E MHRUz named after academician Y. Turakulov (histology office).

Statistical calculations were performed in the Microsoft Windows software environment using the Microsoft Excel-2007 and Statistica version 6.0, 2003 software packages. The data obtained are reflected in the dissertation in the form M ± m, where M is the average value of the variational series, m is the standard error of the average value. The significance of differences between independent samples was determined by the Mann-Whitney and Student methods.

Results and discussion

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

Table 1 Distribution of patients by gender and age

Age , years	The number of men	The number of women
13 -15 years	-	-
16 – 29	11	9
30-44	14	7
45-59	13	7
60-74	5	2
75 and more	-	-
Total : n = 68	43	25

Table 2 shows the distribution of patients according to the nature of the formation of the sellar region and the type of treatment received.

As can be seen from table 2, the most common patients with NFPA were 42 patients out of 68 (61.7%), somatotropinomas were observed in second place in frequency - 10 cases (14.7%), and prolactinoma in third place - 7 cases (10.4%), in 4th place - craniopharyngioma - 6 cases (8.9%). Hemangioblastoma, astrocytoma of the optic nerve, and meningioma in 1 case (1.5%) were least common. It should be noted that hemorrhage in the pituitary stroma was observed in 6 (8.9%) cases and of these 3 cases (4.4%) prevailed in patients with NFPA. Relapse of tumor growth after TAG was found in 15 patients out of 67 (22.4%), while most often in cases of NFPA - 6 cases out of 15 (40%). Table 3 presents the frequency of various neuroendocrine disorders in the examined patients.

Table 2 The distribution of patients according to the nature of the formation of the cellar region and the type of treatment received

Diagnosis of Disease	The number of patients	TPA	RT
NFPA	42******!!!	37 (((((	2
Craniopharyngioma	6**(!!	3	-
Somatotropinoma	10**	7	-
Prolactinoma	7!***	5	-
Hemangioblastoma	1	1*(	2
Astrocytoma	1*	1+KT	1+XT
Meningioma	1	1	-

Note: NFPA, non-functional pituitary adenoma; TPA, transnasal pituitary adenomectomy;* - growth recurrence,! - hemorrhage in the stroma, (- reoperation, RT, the number of patients who received radiation therapy; CT, combination therapy

It was found that panhypopituitarism was most common in 32 of 68 patients (47.0%), postoperative panhypopituitarism was found in 59 of 68 patients (86.7%). Bitemporal hemianopsia was also observed with greater frequency in 41 cases out of 68 (60.2%). In addition, secondary amenorrhea in 27 cases (33.3%). Thus, there was a polymorphism of symptoms.

The most pronounced violations of the neurological status - endocrine encephalopathy, hallucinations (1 case), inadequate condition (1 case), amaurosis (9 cases), ischemic stroke (2 cases), pathological reflexes, impaired muscle tone - decrease - were observed in 5 patients with the germination of a tumor in the brain — the anterior, middle or posterior cranial fossa, with the growth of the tumor in the ventricles of the brain and both cavernous sinuses.

The most pronounced visual field disturbances in the form of bitemporal hemianopsia were observed in patients with endo-suprasellar growth - 28 cases (41.2%), with the total growth variant - 26 cases (38.2%). Table 3 gives the average basal plasma hormone levels.

Table 3 The average value of plasma hormones in patients of group 2 (n = 68)

Hormones	Mean value	P	Control	Norm
LH	1, 53 ±0,03	<0,05	12,3±2,1	8,7 ME/L (6,0-12,0)
FSH	0,94 ±0,04	<0,05	8,2±0,3	6,1 ME/L (1,0-8,0)
Prolactin	17,18 ±0,7	<0,05	5,3±0,5	5,7 ng/ml
ACTH	30,7 ±7,9	>0,5	44,3±9,3	До 50 pg/ml
IGF-1	45,3 ±12,3	<0,05	564,1±23,1	134 – 836 ng/ml in adults
STH	0,08 ±0,01	<0,05	3,1±0,4	2-5 ng/ml
Free T4	102, 6 ±16,3	>0,5	112,9±13,6	60-160 nmol/l
Cortisol	180,2 ±22,1	< 0,5	673,9±24,6	260-720 nmol/l
Free T	1, 53 ±0,03	<0,05	12,3±2,1	8.69-54.69 ng/ml

Note: P - significance of differences compared with the control group, IGF-1, insulin-like growth factor 1; Free T, free testosterone; Free T4, free thyroxine

The most significant decrease in the average values of basal levels of plasma tropic hormones - STH, LH, FSH, ACTH - was recorded in patients with panhypopituitarism - 32 cases (p <.0.01).

In addition, it was precisely in patients that cortisol levels were also significantly reduced, while in other patients, plasma cortisol was on average within normal limits.

Comparative characteristics of patients showed that in patients with giant pituitary adenomas pronounced neuroendocrine, neurological and ophthalmic disorders were noted. So, neuroendocrine (GHD, panhypopituitarism, hypopituitarism, infertility, secondary amenorrhea), ophthalmic (Bitemporal hemianopsia, amaurosis, etc.) were characteristic of total tumor growth and suprasellar growth. Diencephalic stem disorders (pyramidal symptoms, decreased reflexes

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and muscle tone diffusely) were observed in patients with total growth option, with retrocellular growth and with germination in the brain. In patients with giant pituitary adenomas, there is primarily a decrease in the levels 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 pituitary tropic hormones.

Conclusions

Our results showed that in all patients with giant pituitary adenomas, one or another degree of severity of neuroendocrine disorders is observed, worsening as the pituitary tumor grows. The nature of the disorders has a number of specific (Bitemporal hemianopsia, scotomas, hypopituitarism, damage to the cranial nerves) and nonspecific symptoms (pyramidal symptoms, diffuse decrease in muscle tone, reflexes) depending on the side of growth, tumor size.

The most pronounced neuroendocrine, neurological and ophthalmic disorders were observed in patients with a total growth option.

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None.

Conflicts of interest

All authors declare that there is no conflicts of interest.

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