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## Changes in visual abnormalities after endonasal endoscopic surgery for giant pituitary adenoma with extension to the ventricular system

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**Purpose:** To assess the features of visual impairments in patients with giant pituitary adenoma (GPA) with extension to the ventricular system showing different directions of tumor growth and chiasm positions to improve the early diagnosis of the chiasmal syndrome.

**Material and Methods:** We retrospectively examined medical records of 41 patients with GPA showing extension to the ventricular system who were treated at the Endonasal Neurosurgery Department, the Romodanov Neurosurgery Institute between 2016 and 2021. Patients were divided into three groups based on the direction of tumor extension and chiasm position: group 1, antesellar extension and/or postfixed chiasm (14 patients); group 2, suprasellar extension and/or normal chiasm (12 patients); group 3, retrosellar extension and/or prefixed chiasm (15 patients). Patients underwent clinical neurological, otoneurological and eye examination.

**Results:** Of the 41 patients, 38 (92.7%) had reduced visual acuity and/or or visual field defects. In the current study, 53.7% of patients had nonfunctional GPA, which makes diagnosis in the early stages (when the tumor is small) challenging. Bitemporal hemianopsia and severe chiasmal syndrome were prevalent among patients with normal or postfixed chiasm, and 14% of eyes were blind among these patients. Moderate chiasmal syndrome was prevalent, 1.2% of eyes were blind and 7.3% of patients had no visual deficiency among patients with prefixed chiasm. In addition, homonymous hemianopsia was found in 7 patients (17.5%) with prefixed chiasm, and was caused by the effect on the posterior chiasm and visual pathways. Mean visual acuity and visual field mean defect (MD) values were statistically significantly better in patients with post-fixed or normal chiasm.

**Conclusion:** Visual field defects atypical for tumors of the chiasmal and sellar region may emerge depending on the topographic relationship between the chiasm and the GPA.

### Keywords:

Giant pituitary adenoma, extension to the ventricular system, position of the chiasm, compressive optic neuropathy, homonymous hemianopsia, endoscopic transnasal surgery

### Introduction

Pituitary adenomas (PAs) are the most common primary benign intracranial tumors of the chiasmal and sellar region (CSR); they comprise approximately 12–15% of all intracranial tumors [1, 2, 3].

The clinical picture depends on tumor size and type, rate and direction of tumor growth as well as whether or not the tumor is secreting one or more of a variety of hormones. Various approaches to the classification have been put forward to take into account these features.

The Yasargil classification of 1996 [4] reflects PA growth directions in details, with extrasellar extensions of the pituitary mass classified as follows: IIIa suprasellar suprachiasmatic (extension of the PA beyond the diaphragma sellae, causing optic nerve/chiasm complex (ONCC) compression); IIIb suprasellar retrosellar (upward and behind); IIIc parasellar-cavernous (lateral extension

into the cavernous sinus (CS)); and IIId paninvasive (extends in all directions). The Knosp classification is an MRI tool used to define CS invasion in the 2017 World Health Organization classification [5].

PAs are classified as either macroadenomas ( $\geq 10$  mm) (or microadenomas ( $< 10$  mm)). Giant PAs are tumors 40 mm or greater in maximal diameters, although there is no consensus for the criteria, and they account for 5-27% of all adenomas in surgical series [6-10]. Due to their size, management of these tumors is a surgical challenge when they cannot be excised radically [11, 12].

Histologically, PAs are classified according their activity into somatotroph, lactotroph, corticotroph, gonadotroph, plurihormonal and hormonally inactive

pituitary adenomas [13]. The detection of the presence of hormonal activity enables early disease diagnosis [14, 15, 16].

The topographic relationship between the chiasm and sella turcica is important for emergence of visual impairment in tumors of the CSR, and depends on the length of the intracranial portion of the optic nerve. Chiasmatal compression by a tumor of the CSR results in visual impairments in the form of the chiasmatal syndrome, which is characterized by reduced visual acuity, temporal hemianopsia, and descending optic atrophy. The normal chiasm overlies the diaphragm sellae and the pituitary gland, the prefixed chiasm overlies the tuberculum, and the postfixed chiasm overlies the dorsum (Fig. 1). When the chiasm is prefixed, the optic nerves are short, the chiasm sits forward over the sella, and the optic tracts are short. When the chiasm is postfixed, the optic nerves are long, the chiasm sits posteriorly over the sella, and the optic tracts are short. The chiasm is in the normal position in approximately 70-80% of cases, prefixed in 9-15% of cases, and postfixed in 11-15% of cases [17, 18, 19].

Giant PAs (GPAs) with extension to the ventricular system are located close to critical vascular and nervous structures like the internal carotid artery, anterior carotid arteries and their branches, cavernous sinuses, optic nerves, chiasm, and the pituitary gland with its blood vessels. These tumors have a special clinical course due to their extension to the ventricular system, which results in abnormal cerebrospinal fluid (CSF) dynamics and symptoms of increased intracranial pressure [11, 12, 20, 21].

Given the size and extension to the ventricular system of GPAs, their radical resection is associated with a high risk of damage to surrounding structures, which may result in visual impairments, hormonal insufficiency and other abnormalities [3, 10, 22, 23, 24, 25].

The transition from microsurgery to endoscopic transsphenoidal pituitary neurosurgery made it possible to perform endoscopic transnasal excision of a GPA with total resection of a large mass and minimal surgical

invasion, thus reducing complications common in classical transcranial surgery for GPA. The annual number of endoscopic transnasal surgeries for CSR tumors increases year by year. The main advantages of endoscopic transsphenoidal surgery include the wide panoramic view offering better visualization of critical structures with the subsequent potential for reduced complications. Thus, the surgeon has the opportunity to increase the percentage of resection and use a smaller surgical window with a favorable cosmetic outcome [25, 26].

Despite recent advances in neuroimaging techniques, the use of modern microsurgical endoscopic instruments and the potential for safe radical tumor resection, the mortality in surgery for GPA is still high.

Chiasmatal compression by a GPA results in visual impairments which are characteristic for macroadenomas, emerge at the "ophthalmic stage" of PA development and are the most prominent in the clinical picture.

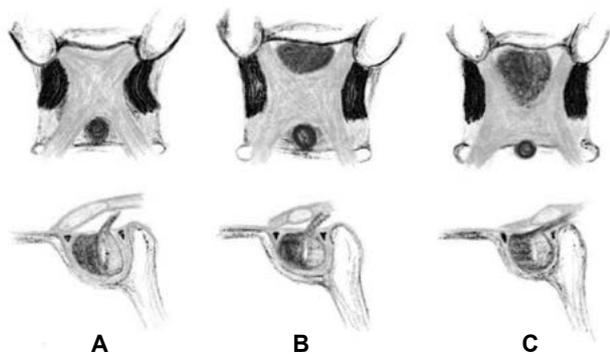
**The purpose** of the study was to assess the features of visual impairments in patients with GPAs with extension to the ventricular system showing different directions of tumor growth and chiasm positions to improve the early diagnosis of the chiasmatal syndrome.

#### Material and Methods

We retrospectively examined medical records of 41 patients (82 eyes; age, 19 to 78 years; mean age, 53.2±11.5 years; 17 (41.5%) women and 24 (58.5%) men) with GPA showing extension to the ventricular system who were treated at the Endonasal Neurosurgery Department, the Romodanov Neurosurgery Institute between 2016 and 2021. Surgeries were performed with the aim of achieving tumor resection, and most tumors were excised radically. Gross-total or subtotal resection was achieved in 30 patients (73.2%), partial resection in 5 patients (12.2%), and biopsy in 6 patients (14.6%). All surgeries were performed through the endoscopic endonasal approach. Inclusion criteria were a tumor size (in any direction) ≥ 40 mm as assessed by magnetic resonance imaging (MRI); the endoscopic endonasal approach; tumor extension to the third ventricle and/or frontal horns of the lateral ventricles; and histologically verified pituitary adenoma.

Patients underwent clinical neurological, otoneurological and eye examination. Neuroimaging procedures (native and contrast-enhanced brain MRI and computed tomography (CT)) were performed to assess tumor size, location and associations with surrounding vascular and neural structures. A 1.5-T MRI system (Intera 1.5T/I system, Philips Medical Systems, Best, the Netherlands) was utilized. The MRI of brain and pituitary gland were obtained using T1-weighted image (WI) and T2WI. The eye examination included visual acuity assessment, biomicroscopy, kinetic and static perimetry, and direct and indirect ophthalmoscopy, and was performed on day 1-2 after admission and day 5-7 after surgery (the early postoperative period).

Best-corrected visual acuity was classified as normal (1.0), mild impairment (0.7-0.9), moderate impairment



**Fig. 1.** Anatomical positions of the optic chiasm (top images: superior views; bottom images: sagittal views): prefixed chiasm (A), normal chiasm (B), and postfixed chiasm (C).

(0.4-0.6), severe impairment (0.1-0.3), very severe impairment (< 0.1) and blindness (zero). Static automated perimetry was performed with the Centerfield 2 Perimeter (Oculus, Wetzlar, Germany) using the neurological 30-2 threshold test program and Neuro screening program. The mean defect (MD) was used to assess visual loss severity. Visual field loss severity was classified as mild visual field loss (Grade 1; MD, -2 dB to -4 dB), moderate visual field loss (Grade 2; MD, -4 dB to -12 dB), severe visual field loss (Grade 3; MD, -12 dB to -20 dB), and very severe visual field loss (Grade 4; MD, worse than -20 dB).

The severity of chiasmal syndrome was assessed taking into consideration bilateral visual acuity and visual field defect as assessed by MD with a proprietary methodology being developed: mild chiasmal syndrome (bilateral visual acuity, 1.0 or better; MD, -4 dB or better); moderate chiasmal syndrome (bilateral visual acuity, 0.1 or better; MD, -4 to -12 dB); and severe chiasmal syndrome (bilateral visual acuity, worse than 0.1 in at least one eye; MD, worse than -12 dB in at least one eye).

Patients were divided into three groups based on the direction of tumor extension and chiasm position: group 1, antesellar extension and/or postfixed chiasm (14 patients, 34.1%, 28 eyes); group 2, suprasellar extension and/or normal chiasm (12 patients, 29.3%, 24 eyes); group 3, retrosellar extension and/or prefixed chiasm (15 patients, 36.6%, 30 eyes).

The study involved human subjects, adhered to the tenets of the Declaration of Helsinki, and was approved by the Ethics Committee of the Romodanov Neurosurgery Institute (Committee Meeting Minutes of 13.12.2019). Informed consent was obtained from all patients. This study was not conducted on animals. The data were input into an Excel spreadsheet. Statistical analyses were conducted using Statistica 6.0 (StatSoft, Tulsa, OK, USA) software. Results are presented as the mean and standard deviation ( $M \pm SD$ ). Student's unpaired t test was used to determine differences between independent groups. The level of significance  $p \leq 0.05$  was assumed. Pearson's  $\chi^2$  and Fisher's exact tests were used to detect any variation from the expected distribution of data.

## Results

Of the 41 study patients, 38 (92.7%) had and 3 (7.3%) had no visual impairment (reduced visual acuity and/or visual field defects). The duration of visual impairment symptoms ranged from 4 months to 7 years; typically, a gradual reduction in visual acuity was seen. There were 25 (61%) hormonally inactive PAs, 6 (14.6%) corticotroph PAs, 4 (9.8%) somatotroph PAs, 5 (12.2%) lactotroph PAs, and 1 (2.4%) thyrotroph PA.

Table 1 shows mean preoperative and postoperative visual acuity and MD values. There was a significant difference ( $p < 0.05$ ) in visual acuity and MD of patients in groups 1 and 2 versus patients in group 3.

Preoperatively, of the 28 eyes (14 patients) in group 1, 2 (7.1%) had a VA of 1.0; 6 (21.5%), a VA of 0.7-0.9; 5 (17.9%), a VA of 0.4-0.6; 6 (21.4%), a VA of 0.1-0.3; 2

(7.1%), a VA <0.1, and 7 (25%) were blind. Visual field defects were observed in 28 (100%) eyes: 8 (28.6%) had temporal hemianopsia with a central scotoma, 8 (28.6%) had absolute or relative temporal hemianopsia only, 6 (21.4%) had a residual nasal visual field, and 1 (3.6%) had a central scotoma with temporal visual field loss. In addition, visual field was not measurable in 5 eyes (17.8%) of this group. Of the 14 patients, 1 (7.1%) exhibited mild chiasmal syndrome, 4 (28.6%), moderate chiasmal syndrome, and 9 (64.3%), severe chiasmal syndrome. Bilateral primary descending optic atrophy (OA) was observed in 13 patients (92.9%, 26 eyes). Total OA was found in 7 eyes, and partial OA, in 21 eyes.

Preoperatively, of the 24 eyes (12 patients) in group 2, 4 eyes (16.7%) had a VA of 1.0; 2 (8.3%), a VA of 0.7-0.9; 2 (8.3%), a VA of 0.4-0.6; 8 (33.4%), a VA of 0.1-0.3; 3 (12.5%), a VA <0.1, and 5 (20.8%) were blind. Visual field defects were observed in 22 eyes (91.7%): 8 (33.3%) had temporal hemianopsia with a central scotoma, 6 (25.1%) had absolute or relative temporal hemianopsia only, 3 (12.5%) had a residual nasal visual field and 2 (8.3%) had a central scotoma with temporal visual field loss. In addition, visual field was not measurable in 3 eyes (12.5%) of this group. Of the 12 patients in group 2, 5 (41.6%) exhibited moderate chiasmal syndrome, 7 (58.4%), severe chiasmal syndrome and no patient exhibited mild chiasmal syndrome. Primary descending OA was observed in 12 patients (100%): bilateral OA was found in 9 eyes (75%), and unilateral OA, in 3 eyes (25%). Total OA was found in 4 eyes, and partial OA, in 20 eyes.

Reduced visual acuity and/or visual field defects were found in 12 patients (24 eyes) and not found in 3 patients (6 eyes) in group 3. Of the 30 eyes (15 patients) in group 3, 15 (50%) had a VA of 1.0; 3 (10%), a VA of 0.7-0.9; 5 (16.7%), a VA of 0.4-0.6; 5 (16.7%), a VA of 0.1-0.3; 1 (3.3%), a VA <0.1, and 1 eye (3.3%) was blind. In group 3, visual field defects were observed in 24 eyes (80%): 14 (46.7%) had homonymous hemianopsia only, 5 (16.7%) had temporal hemianopsia with a central scotoma, 3 (10%) had temporal hemianopsia only and 1 (3.3%) had a residual nasal visual field. In addition, visual field was not measurable in 1 eye (3.3%) in this group. Of the 15 patients in group 3, 1 (6.7%) exhibited mild chiasmal syndrome; 7 (46.7%), moderate chiasmal syndrome, and 4 (26.6%), severe chiasmal syndrome. Primary descending OA was observed in 10 patients (66.7%): 9 patients (60%) had bilateral OA, and 1 patient (6.7%), unilateral OA. OA was partial in all these 10 patients (19 eyes). Papilledema was found in 1 patient (3.3%; 2 eyes).

Symptoms of increased intracranial pressure (headache) were observed in the presence of the PA expanding the sella in 29 patients (70.7%). Significant parasellar extension caused trigeminal branch compression manifested by trigeminal neuralgia or hyperesthesia in the region of innervation of V1 and V2 in 3 patients (7.3%). CSF flow abnormalities in the form of hydrocephalus were seen in 23 patients (56.1%). Of these, 7 patients were diagnosed with

**Table 1.** Preoperative and postoperative visual acuity and visual field mean defect (MD) in patients with giant pituitary adenoma showing invasion of the ventricular system

No.	Group of patients (n, number of eyes)	Visual acuity (M±SD)		MD (M±SD) dB	
		Preoperative	Postoperative	Preoperative	Postoperative
1	Group 1, n = 28	0.4±0.06	0.5±0.08	11.58±0.84	9.67±0.87
2	Group 2, n = 24	0.35±0.07	0.36±0.07	16.33±0.97	13.52±0.71
3	Group 3, n = 30	0.7±0.07	0.75±0.07	5.44±0.46	4.76±0.38
	P <sub>1</sub>	p=0.32		p=0.12	
	P <sub>2</sub>	p=0.91		p=0.02	
	P <sub>3</sub>	p=0.62		p=0.26	
	P <sub>1-2 preoperative</sub>	p=0.59		p=0.00	
	P <sub>1-2 postoperative</sub>	p=0.19		p=0.00	
	P <sub>1-3 preoperative</sub>	p=0.00		p=0.00	
	P <sub>1-3 postoperative</sub>	p=0.02		p=0.00	
	P <sub>2-3 preoperative</sub>	p=0.00		p=0.00	
	P <sub>2-3 postoperative</sub>	p=0.00		p=0.00	

Note: P<sub>1</sub>, comparing postoperative and preoperative values for group 1; P<sub>2</sub>, comparing postoperative and preoperative values for group 2; P<sub>3</sub>, comparing postoperative and preoperative values for group 3; P<sub>1-2 preoperative</sub>, comparing preoperative values between groups 1 and 2; P<sub>1-2 postoperative</sub>, comparing postoperative values between groups 1 and 2; P<sub>1-3 preoperative</sub>, comparing preoperative values between groups 1 and 3; P<sub>1-3 postoperative</sub>, comparing postoperative values between groups 1 and 3; P<sub>2-3 preoperative</sub>, comparing preoperative values between groups 2 and 3; P<sub>2-3 postoperative</sub>, comparing postoperative values between groups 2 and 3; p, significance of difference between characteristics

the Hakim-Adams triad of gait disturbances, cognitive impairment, and urinary incontinence. There was MRI evidence of the extension of PA to the third ventricle only in 28 patients (68.3%), frontal horns of the lateral ventricles only in 28 patients (68.3%), and both these areas in 4 patients (9.8%). An abnormal CSF flow was due to the unilateral or bilateral occlusion of the foramen of Monro (asymmetric and symmetric hydrocephalus, respectively).

Surgical treatment for pituitary adenoma resulted in improvement in both visual acuity and visual fields, but the difference was not significant.

After treatment, the VA improved from  $0.4 \pm 0.06$  to  $0.5 \pm 0.08$  ( $p = 0.32$ ) in group 1, from  $0.35 \pm 0.07$  to  $0.36 \pm 0.07$  ( $p = 0.91$ ) in group 2, and from  $0.7 \pm 0.07$  to  $0.75 \pm 0.07$  ( $p = 0.62$ ) in group 3. In addition, the MD improved from  $11.58 \pm 0.84$  dB to  $9.67 \pm 0.87$  dB ( $p = 0.12$ ) in group 1, from  $15.33 \pm 0.97$  dB to  $13.52 \pm 0.71$  dB ( $p = 0.02$ ) in group 2, and from  $5.44 \pm 0.46$  dB to  $4.76 \pm 0.38$  dB ( $p = 0.26$ ) in group 3.

### Discussion

To the best of our knowledge, the current study is the first to analyze in detail the ophthalmological outcome of endoscopic endonasal surgery for GPA with extension to the ventricular system in a rather large sample of patients. Particularly, previously, the largest sample of patients treated with endoscopic endonasal approach for GPA with

extension to the ventricular system was that reported by Jamaluddin and colleagues (2021) [27] ( $n = 8$ ), but they did not analyze the ophthalmological outcome. In the current study, we examined the features of visual impairments in patients with GPA with extension to the ventricular system and showing various anatomical positions of the optic chiasm.

Diagnosis of nonfunctional PA at an early stage, when the tumor size is small is challenging. In the current study, 53.7% of patients had nonfunctional PA, which is consistent with the findings of Gnanalingham and colleagues (2005) [28]. Although bitemporal heteronymous hemianopsia is believed to be the classical visual field defect of disorders that involve the optic chiasm, the defect emergence depends on the topographic relationship between the chiasm and the tumor. Bitemporal hemianopsia was prevalent among patients with normal or postfixed chiasm (17 patients; 41.5%), whereas homonymous hemianopsia was found in 7 patients (17.5%) with prefixed chiasm. Homonymous hemianopsia is not a typical visual field defect in skull-base tumors and is caused by the effect of the tumor on the posterior chiasm and visual pathways. There have been scarce reports on the development of homonymous hemianopsia in tumors of the CSR [23, 29].

Moderate chiasmatal syndrome was prevalent, 1.2% of eyes were blind and 7.3% of patients had no visual

deficiency among patients with prefixed chiasm. In addition, mean visual acuity and MD in these patients were statistically significantly better than in patients with post-fixed or normal chiasm, and severe chiasmal syndrome was prevalent and 14% of eyes were blind among the latter patients. This indicates that the compressive effect of the tumor on the chiasm was less substantial in patients with prefixed chiasm than in those with post-fixed or normal chiasm, due to the GPA extending to the visual pathways.

Surgical treatment resulted in an improvement in visual acuity and visual field defects in the three groups, but the difference was not statistically significant. Mean visual acuity and MD were statistically significantly better in patients with post-fixed or normal chiasm.

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#### **Disclosures**

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**Ethics Statement:** This study included human participants, was approved by the local bioethics committee and adhered to the tenets of the Declaration of Helsinki. Appropriate informed consent was obtained from all patients. This study did not include animal experiments.

**Disclaimer:** The opinions presented in this article are those of the authors and do not necessarily represent those of their institutions.

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**Abbreviations:** CSR, chiasmal and sellar region; CT, computed tomography; MD, mean defect; MRI, magnetic resonance imaging; OA, optic atrophy; PA, pituitary adenoma.