Changes of Visual Functions in Patients With Pituitary Adenoma

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***Key Words**: pituitary adenoma; visual functions; Farnsworth-Munsell 100 hue test.*

***Summary.** Background and Objective. The aim of this study was to evaluate associations between visual functions (visual acuity, perimetry, optic nerve disc condition, and color contrast sensitivity) and pituitary adenoma (PA) diameter.*

Material and Methods. In the study, 20 patients with PA, which was confirmed by computed tomography or magnetic resonance imaging scans, were examined. The patients were divided into 2 groups: those with a PA diameter of ⩽1 cm (14 eyes) and with a PA diameter of >1 cm (26 eyes). The control group comprised 40 healthy age- and gender-matched persons (80 eyes). The diameter of PA, visual acuity, and perimetry were analyzed; the F-M 100 hue test for color discrimination was used in patients with PA.

Results. Visual acuity was better in the control group as compared with both groups of patients (1.0 vs. 0.90 [SD, 0.50] and 0.64 [SD, 0.21]; P=0.01; respectively). The results of the Farnsworth-Munsell 100 hue test were also better in the control group compared with the patients with PA of ⩽1 cm and >1 cm (error score of 80.1 [SD, 53.0] vs. 131.8 [SD, 30.6] and 244.68 [SD, 51. 6], respectively; P=0.011). There was a very strong positive correlation between the error score of the F-M 100 hue test and PA diameter (r=0.905), but the correlation between the error score and visual acuity (r=–0.32), perimetry (r=0.21), and eye fundus changes (r=0.36) and PA diameter was weak.

Conclusions. Our results showed that PA can cause the impairments of visual acuity, perimetry, and color contrast sensitivity. The computerized F-M 100 hue test can be one of the methods for an early diagnosis of chiasm damage in patients with PA.

Introduction

The pituitary gland is a small endocrine gland, weighing about 0.5 g. It is slightly larger in the brain of women than men. Pituitary adenoma (PA) is the most common pathological process occurring in the sella turcica. PAs account for 12%–15% of all brain tumors (1). Ezzat et al. (2) reported the estimated prevalence of pituitary adenomas to be 14.4% and 22.5% in pooled autopsy and radiological series, respectively. Davis et al. (3) reported that pituitary adenomas occurred with a prevalence rate of 190–280 cases per 1 000 000. It is a benign tumor originating in adenohypophysial cells of the anterior lobe of the pituitary gland (4). The classification of PAs is based on the secretion of hormones. It can be a secreting (functional) or a non-secreting (nonfunctioning) pituitary adenoma. According to the size, adenomas are classified into microadenomas (⩽10 mm) and macroadenomas (>10 mm) (5). Women have a 2-fold increased risk of developing PA in comparison with men (4). Most commonly, PA is a nonmalignant tumor; however, it tends to renew/recur itself (6). Usually this tumor is soft and has no capsule, which could isolate it from the surrounding mass of microglia. That is the reason why it can grow and infiltrate the surrounding structures. Adenomas may cause symptoms in 2 ways: 1) due to tumor-related hypersecretion or hyposecretion of hormones. In this case, the tumor causes compression to a normally functioning hypophysis; or 2) due to compression of PA to the surrounding structures (5).

PA can often cause injury to the optic chiasm. Hypophysis is in the sella turcica, 8–13 mm lower than the optic chiasm. Therefore, when it increases, it can easily compress the optic nerve fibers in the chiasm. Microadenomas can have a negligible effect on the visual system or on the function of other glands, whereas macroadenomas can cause visual function impairment (7–9). Visual function impairment depends on the diameter of PA and its contact with optic pathways. If PA is small, it cannot reach the optic chiasm, and visual function impairment may not be observed (10). When PA compresses the frontal part of the optic nerve, impairments in visual field, visual acuity, and color contrast sensitivity are possible. Visual impairments can also be triggered by a microadenoma when it grows directly to the optic pathways and causes swelling of the pituitary gland (5).

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The long-lasting compression of the chiasm induces primary optic nerve atrophy, which directly impairs the visual function. Functionally active PAs usually appear with specific clinical symptoms because of hormone hypersecretion. Functionally active PAs cause less damage to the visual function than the nonfunctioning gland, because functioning PAs become symptomatic due to hormone secretion. Nonfunctioning PAs can grow slowly, compress the optic chiasm, which is directly above the pituitary gland, and cause progressive visual loss (11). Among patients with intracranial tumors, the PA prevalence is high, and diagnosing the tumor, an overall visual system examination is required.

The aim of this study was to evaluate associations between visual functions (visual acuity, perimetry, optic nerve disc condition, and color contrast sensitivity) and PA diameter.

Material and Methods

A total of 20 patients diagnosed with PA (40 eyes, study group) and 40 healthy patients (80 eyes, control group) were enrolled into the study. PA was confirmed by computed tomography (CT) or magnetic resonance imaging (MRI) scans. The patients in the study group were divided into 2 groups according to the PA diameter: patients with the PA diameter of 1 cm and less (14 eyes) and patients with the PA diameter of more than 1 cm (26 eyes).

The inclusion criteria were as follows: 1) PA identified and confirmed by CT/MRI; 2) good patient's general condition; 3) patient's consent to take part in the study.

The exclusion criteria were as follows: 1) infectious eye diseases (history of keratitis, acute or chronic uveitis), glaucoma, optic nerve diseases, degeneration or dystrophy of the central part of the retina, high-degree refraction defects, lens opacities because of obscurity or poor photography quality of eye fundus; 2) systemic disease (diabetes, malignant diseases, systemic connective tissue disease, chronic infectious diseases, tissue or organ transplant surgery; 3) brain tumors of other localization; and 4) patient's refusal to participate in the study.

In this study, visual acuity as well as the transparency of the cornea and lens and the fundus were investigated in patients. Biomicroscopy was performed in order to assess the corneal and lenticular transparency. Noncorrected and best-corrected visual acuity (measured in decimals from 0.1 to 1.0) was evaluated using Landolt's rings (C optotypes) by Snellen test types at a 5-m distance from the chart.

The lenses were evaluated by biomicroscopy. The lenses were examined using a slit lamp, positioning the illumination source at a 45-degree angle and the light beam split to a 2-mm width.

To reach the best-corrected visual acuity, refraction was performed during each examination. The intraocular pressure was measured in order to exclude the patients with glaucoma. Moreover, the pupils of the subjects were dilated with 1% tropicamide. After dilation of the pupils, funduscopy was performed with an ophthalmoscope of the direct monocular type and the slit-lamp using a double aspheric lens of +78 diopters.

The Farnsworth-Munsell 100 hue test (F-M 100 hue test), which is a computer test of color sensitivity, was applied to all the patients (Fig. 1). The test was carried out under artificial daylight illumination; care was taken to use the same instructions during all the testing sessions.

The F-M 100 hue test required the arrangement of color samples by tone. The majority of samples were of the same brightness and intensity in color. Four boxes containing 85 plastic color samples were provided. Two color samples in each box were repeated and used as supportive colors, while other color samples were arranged so that a consistent transition of tones between the two supportive colors were achieved. The color samples were in such a manner as to cover the entire range of tones. The samples differed in tone, but their colors were approximately of the same brightness and intensity. Two minutes were given for each box series, though the speed of accomplishment of the test was not highly accentuated. A sequence number was assigned to each color sample. The result was evaluated by the total number of differences between the number of the color sample chosen by a subject and the number of the color sample actually belonging to the position. The degree of color distinction was assessed. The sensitivity of colors might be very high (when the number of mistakes is up to 20), normal (up to 100), or impaired (more than 100).

Stimuli were generated and presented on a color monitor for calibration. The chromaticity of the monitor phosphors was calibrated using a spectrometer (VIS-LIGA of STEAG microParts GmbH). The computerized test was compared with the original test using a Bland and Altman plot (12).

Statistical analysis was performed using the computer program SPSS/W 13.0 (Statistical Package for the Social Sciences for Windows, Inc., Chicago, Illinois, USA). The data were expressed as absolute numbers (percentage) or means and standard deviation (SD). The Mann-Whitney *U* and Kruskal-Wallis tests were used for the comparison of 2 or 3 groups, respectively. The correlation between the diameter of PA and Farnsworth-Munsell 100 hue test, visual acuity, perimetry, and fundus changes was evaluated by using the Spearman's correlation coefficient. Differences were considered statistically significant if $P<0.05$.

Fig. 1. Farnsworth-Munsell 100 hue test

Results

Twenty patients (40 eyes) diagnosed with pituitary adenoma by CT/MRI were examined. There were 16 women (80%) and 4 men (20%). The mean age of the patients was 51 years (SD, 13.07). Of the 40 patients with a mean age of 50 years (SD, 10.3) in the control group (80 eyes), 30 were women (75%) and 10 were men (25%). The control and study groups were matched for age and gender.

In the control group, visual acuity was 1.0. Visual acuity was worse in the group of patients with PA of >1 cm as compared with the patients with PA of ⩽1 cm (0.64 [SD, 0.21] vs. 0.9 [SD, 0.50], $P<0.05$). A weak negative correlation was found between visual acuity and PA diameter ($r=-0.32$, $P<0.05$).

The results of the Farnsworth-Munsell 100 hue test were also better in the control group compared with the patients with PA of ⩽1 cm and >1 cm (error score of 80.1 [SD, 53.0] vs. 131.8 [SD, 30.6] and 244.68 [SD, 51.6], respectively; $P=0.011$) (Fig. 2). There was a very strong positive correlation between the error score of the F-M 100 hue test and the PA diameter ($r=0.905$, $P=0.008$).

Patients who were diagnosed with PA had visual field impairment. Visual field impairment was determined in 71% of the patients in the group with PAs of ⩽1 cm. Concentric visual field was found in 8 (57%) of eyes, 2 eyes (14%) had bitemporal hemianopsia, and 4 eyes (29%) had the intact visual field (Fig. 3). In the group with PAs of >1 cm, visual field impairment was determined in 86% of the patients; concentric constriction and bitemporal hemianopia was documented in 16 (63%) and 6 patients (23%), respectively. Visual acuity was intact in 4 patients (14%). Visual field impairment was more common in the patients with PA >1 cm, but the difference

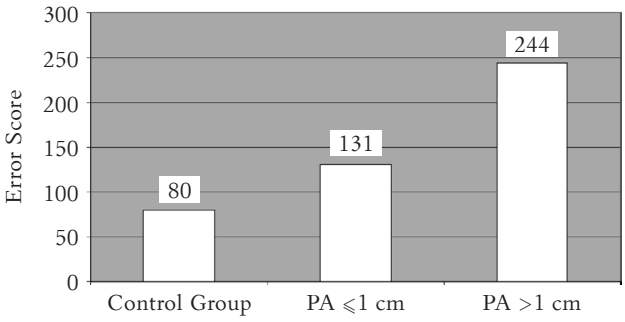

Fig. 2. Error scores of the Farnsworth-Munsell 100 hue test in 3 groups of the patients

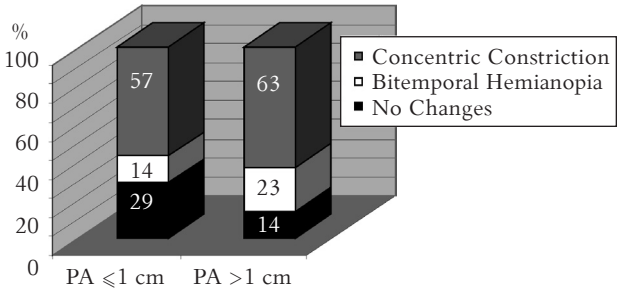

Fig. 3. Visual field impairments by pituitary adenoma diameter

was not significant. There was a weak positive correlation between visual field impairment and PA diameter (r=0.21, P<0.05).

The patients diagnosed with PA showed optic nerve disc changes in the fundus of the eye (Table). Optic nerve disc changes were significantly more common in the patients with PA than the healthy controls (20% vs. 50%, P=0.009), and there was a weak positive correlation between eye fundus changes and PA diameter (r=0.36, P<0.05).

Table. Optic nerve disc changes in patients with a pituitary adenoma (PA) diameter of ⩽1 cm and >1 cm

Change	Eyes, n (%)		*P* value
	PA ⩽1 cm	PA >1 cm	
Unchanged optic nerve disc	6 (15)	6 (15)	1.0
Optic nerve disc pallor	6 (15)	14 (35)	0.69
Optic nerve disc atrophy	2 (5)	6 (15)	0.26

Discussion

Visual functions in patients with PA were analyzed in this study. Our analysis revealed that PA can cause the impairments of visual acuity, perimetry, eye fundus, and color contrast sensitivity in patients with PA, and the computerized F-M 100 hue test can be one of the methods for an early diagnosis of chiasm damage in patients with PA.

Molecular genetic research has identified a number of genetic defects that might be involved in pituitary tumorigenesis. Few genes have been reported to be associated with inherited forms of pituitary tumors. Approximately 5% of all pituitary tumors arise in a familial setting (11). The etiology of pituitary adenomas has not been clearly understood until now. A relationship between adenomas and multivarious environmental factors, such as smoking, mobile phone use, etc., was studied. However, no scientifically confirmed environmental risk factors associated with the development of pituitary adenomas have been identified so far (13, 14).

PA affects people of all ages. It can occur at any age, but its prevalence increases with age (31). A study by Thomas et al. showed that the mean age of PA patients was 43 years (range, 16–69 years); the ratio of women to men was 1:2 (27). Other study by Elgamal et al. reported the mean patients' age of 42 years (range, 14–83) and a female-to-male ratio of 1.4:1 (16). In our study, the mean age of PA patients was slightly greater, i.e., 51 years (range, 25–70), and the ratio of women to men was 3.8:1.

The impairment of visual functions may be found in patients with PA. The present investigation showed that visual acuity impairment can be found even when the diameter of PA less than 1 cm (visual acuity, 0.9 [SD, 0.50]). The level of damage directly depended on the of diameter adenoma and the location of compression on optic pathways (15). Other researchers also determined visual acuity impairment in 54.8% of the patients (n=37) who were diagnosed with PA (16).

In literature, information about the impairment of color contrast sensitivity can only be found when visual acuity is altered, i.e. in advanced PA stages. Researchers have also determined a great impairment in color contrast sensitivity in patients diagnosed with PA (17). In Grochowski's opinion, the examination of contrast sensitivity is a susceptible method for the determination of visual pathway compression. However, it should not be used separately from other examination methods of the visual system (18). Gutowski et al. evaluated 11 patients who had tumors in the sella turcica and had no visual acuity and visual field impairment; however, color contrast sensitivity impairment was found (19).

Our study showed that the results of the F-M 100 hue test were better in the control group than in the groups with PA ⩽1 cm and >1 cm (80.1 [SD, 53.0] vs. 131.8 [SD, 30.6] and 244.7 [SD, 51.6], P=0.011; respectively). Dain et al. reported that the results of the F-M 100 hue test depended on the human race, but the difference was insignificant if the examination was performed in the same group of age and with the same pupil diameter. However, the mentioned authors noted that the difference was significant between Asians and brown-eyed Europeans (20). With reference to the study by Kinnear et al., the results of the F-M 100 hue test can vary depending on age. The authors reported the number of mistakes ranging from 43 to 364 (21). The researchers examined 10 patients (20 eyes) of the same age and ophthalmologically healthy patients similar to our group (50–59 years old); and the number of mistakes was 90, but in the group of 60–69-year-old persons, the number of mistakes increased to 120 (21). Based on the results of the F-M 100 hue test, Kessel et al. reported that the Danish healthy human population made 83 mistakes (SD, 79) (22). Our study of healthy human population showed very similar results, i.e., 80.1 (SD, 53).

The evaluation of visual field defects is very important in diagnosing PA, especially in primary stages of the development. Patients with PA have unique visual field defects – usually the visual field begins to constrict from the upper temporal sector (23). The prevalence of visual field defects in PA, with reference to various studies, varies from 37% to 96% (15, 24–26). Another very characteristic and unique symptom of PA is a constriction of the visual field from temporal sides to a complete bilateral temporal hemianopia. Thomas et al. reported that theoretically optic chiasm compression caused by PAs led to bitemporal defects. According to their results, bitemporal hemianopsia was the second most common presentation (27). Their study showed that visual field defects were determined in 94.6% of the patients. The unique visual field constricted from the temporal side for PA was determined in 69 of the 93 patients (74.2%). Bitemporal hemianopia was diagnosed in 19 patients (20.4%). In 24 patients (25.8%), 3 sectors of the visual field were lost. Nonspecific visual field defects for PA were determined in 19 patients (20.4%) (27). The results of our study are in line with the findings of these studies. Our study showed that in the group with a PA diameter of $\leqslant$1 cm, field defects were determined in 71% of patients. Of these patients, 57% had the concentric constricted vision field and 14% bitemporal hemianopia. In the group with a PA diameter of >1 cm, visual field defects were determined in 85% of patients. Of these patients, 63% had the concentric constricted field of vision and 23% bitemporal hemianopia. In the group with a PA diameter of >1 cm, visual field defects were twice as common in comparison with the group with a PA diameter of <1 cm. However, bitemporal hemianopia was more common in other scientific studies: the visual field was damaged in all the patients, and 50% of the patients were diagnosed with bitemporal hemianopia (28). Other nonspecific defects in the visual field were found in 55 eyes of 29 patients (44%), and 19 of them had bitemporal hemianopia (69%) (13). A study by Elegemal et al. also reported that 37 patients had visual field defects (65.5%) (16).

In a retrospective study by Kerrison et al., 62 patients with a mean age of 54 years (SD, 15 years; range, 22 to 83) were examined (33 men and 29 women). Visual field defects were analyzed before and after surgical treatment of pituitary adenoma and abnormal static threshold perimetry (29). The authors reported that the early fast phase (1 week after surgery) of improvement might lead to normalization of visual fields in some individuals. The early slow phase (1 month to 4 months) was the period of the most notable improvement. The late phase (6 months to 3 years) of mild improvement did not appear significant overall but may be marked in some individuals. Each of these phases might have one or more mechanisms underlying the observed improvement (29).

With reference to Monteiro et al., 30 patients (60 eyes) with pituitary adenoma were examined. All patients underwent neuro-ophthalmic examination and MRI before and after optic chiasm decompression. The study showed the tumor size to be the best predictive factor for visual loss, and the factors associated with visual recovery were the degree of optic atrophy, the severity of VF defect, and the tumor size. The authors reported that diagnosing pituitary adenomas before optic atrophy becomes severe might be related to a better prognosis in such patients (30).

The earliest defect of visual function is the impairment of color contrast sensitivity. The progressive impairment of color contrast sensitivity could warn about the development of the disease and progression; therefore, the examination of color contrast sensitivity is an informative and useful test to investigate visual functions.

Conclusions

Our results showed that PA can cause the impairments of visual acuity, perimetry, and color contrast sensitivity. Computerized F-M 100 hue test can be one of the methods for an early diagnosis of chiasm damage in patients with PA.

Statement of Conflict of Interest

The authors state no conflict of interest.

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