Humphrey visual field analysis, visual field defects, and ophthalmic findings in patients with macro pituitary adenoma

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ABSTRACT

Objectives: To evaluate the Humphrey visual field parameters in patients with pituitary adenoma and classify the visual field defects in this patient group.

Methods: Forty primary pituitary adenoma patients underwent neuro-ophthalmological examination and Humphrey Perimetry 30-2 visual field test at Baskent University, Departments of Ophthalmology, and Neurosurgery, between 2003 and 2005. Global indices, mean±SD and pattern standard deviation (PSD) of pituitary adenoma patients (group 1) were taken as the test parameters and compared with age- and sex- matched controls (group 2).

Results: There were no significant differences between groups 1 and 2 with respect to mean age or gender distribution ($p>0.05$). The MD and PSD results of group 1 according to the age groups and gender were not statistically significant ($p>0.05$). The MD and PSD results of subjects in group 2 were within normal limits, and no special visual field defects were observed. When compared with healthy controls, the MD and PSD values of patients with hypophyseal adenomas were statistically significantly ($p<0.05$). In group 1, the mean adenoma size was 13.34 mm and no statistically significant correlation was found between the adenoma size and either the MD or PSD values ($p>0.05$). Sixteen (40%) patients had visual field defects, the specific complete bitemporal hemianopsia was found in 5 (12.5%) patients. Only in 3 patients (7.5%) the primary diagnosis was made by ophthalmologic examination.

Conclusion: Although ophthalmologists rarely have a role in the primary diagnosis of hypophyseal adenoma, routine ophthalmologic examination is still important. To detect early visual field abnormalities, automated perimetry should be performed as a part of routine examination in patients with suspected hypophyseal adenomas.

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Hypophyseal adenomas account for approximately 12% of clinically symptomatic intracranial tumors.[1] These neoplasms are benign but can cause visual loss or visual field defects by compressing the optic chiasm or the optic nerve.[2,3] Thirty percent to 96% of patients with a hypophyseal tumor experience a slow progression of visual symptoms.[4] Hypophyseal adenoma can be diagnosed early with modern imaging techniques such as high-resolution computed tomography and magnetic resonance imaging. These tumors can also be identified at an early stage because they produce neuroendocrine symptoms before visual loss and other problems occur. In patients in whom a hypophyseal adenoma is hormonally inactive, it is more common to identify visual symptoms, such as visual field defects, at the time of diagnosis.[5] Assessment of the visual field is particularly important in the diagnosis and monitoring of chiasmal lesions. Visual field defects can be diagnosed by manual perimetry or automated static perimetry. In this study, we used a Humphrey perimeter (Zeiss Humphrey Systems, CA, USA) to examine patients with a primary hypophyseal adenoma, and we compared the results with those in healthy controls. We also classified the types of visual field defects that were detected in the patients with an adenoma.

Methods. The study consisted of 40 patients with a primary pituitary adenoma (group 1) and 35 age-matched and gender-matched healthy controls (group 2). All group 1 patients were diagnosed and monitored by staffs of Baskent University, Faculty of Medicine, Departments of Neurosurgery, and Neuro-Ophthalmology between 2003 and 2005. The controls were recruited from our outpatient clinic. The study was conducted in accordance with the ethical guidelines set forth in the 1975 Declaration of Helsinki. Local ethics Committee and Institutional Review Board Approval were obtained [KA06/187]. The medical record of each of the 40 patients was reviewed, and presenting complaints were recorded. The diagnosis of hypophyseal adenoma was confirmed by the results of magnetic resonance imaging, and lesion size was determined by measuring the diameter of the lesion on images in the coronal plane.

Each patient and control underwent the same ophthalmologic and visual field examinations. The ophthalmologic examination included an assessment of best-corrected visual acuity (BCVA) and a slit-lamp evaluation of the anterior and posterior segments. Color vision was evaluated by showing pseudoisochromatic test (Ishihara) cards, and pupillary function was also assessed by swinging flash light test. Any individual whose BCVA result was lower than 20/30 because of a cataract or a retinal condition was excluded from the study. Patients who have macro pituitary adenoma were included in the study. Visual field analysis was performed with automated perimetry (the Humphrey Perimetry 30-2 program), and all tests were performed by the same experienced technician. Each subject underwent 2 tests on the same day, and the results from the second test were recorded for statistical analysis. If the perimetry test results were unreliable (for example if an extreme difference between the 2 tests results, a high fixation loss, or a high rate of false-positive or false-negative results [up to 20%] was noted) that individual was excluded from the study.

Results for the global indices, mean deviation (MD), and the pattern standard deviation (PSD) in groups 1 and 2 were compared. The Mann-Whitney U test and the Kruskal-Wallis tests were used to compare MD and PSD scores after the subjects had been separated by age group. Kendall's tau rank correlation was used to assess for relationships between tumor size and MD and between tumor size and PSD and to analyze the relationship between the tumor size, visual acuity level, and degree of color vision.

Results. The patients with hypophyseal adenoma (group 1) consisted of 17 women (42.5%) and 23 men (57.5%); mean age, 50.13 ± 14.4 years (range, 14-77 years). The controls (group 2) consisted of 19 women (54.3%) and 16 men (45.7%); mean age, 45.3 ± 11.5 years (range, 23-65 years). Two (5%) of the 40 patients in group 1 were <30 years, 3 (7.5%) were between 31 and 40 years of age, 14 (35%) were between 41 and 50 years, 15 (37.5%) were between 51 and 60 years, and 6 (15%) were >60 years. There were no significant differences between group 1 and 2 with respect to mean age or gender distribution (p>0.05 for all).

Table 1 lists the presenting complaints of the patients in group 1. Ten patients (25%) (age range: 21-50, mean age: 41.7 ± 10) presented with neuroendocrinological complaints.

The mean MD and PSD results for the right and left eyes of the subjects in group 1 and 2 are shown in **Table 2**. When group 1 and 2 were compared in terms of MD, the difference was statistically significant; the mean MD value of group 1 was significantly lower than that of group 2 (p<0.05). The difference between group 1 and 2 in terms of PSD value were statistically significant as well; the mean PSD value of group 1 was higher than that of group 2 (p<0.05).

In group 1, the mean adenoma size was 13.34 mm (**Figure 1a**). Statistical analysis revealed no significant correlation between tumor size and MD or PSD values. For tumor size and MD, Kendall's tau correlation was -0.387 for left eyes and -0.304 right eyes. For tumor size and PSD, Kendall's tau correlation was 0.430 for left eyes and 0.393 right eyes; p>0.05 for both. There was also no correlation between tumor size and visual acuity level or color-perception degree. Kendall's tau correlation of visual acuity was -0.459 for right eyes and -0.049 left eyes. For tumor size and color perception, Kendall's tau correlation was 0.032 for right eyes and -0.006 left eyes, p>0.05 for both. In group 1, visual field analysis revealed unilateral non-specific temporal depression in 5 patients (12.5% of total) and bilateral non-specific temporal depression in 3 patients (7.5%). Complete bitemporal hemianopsia was detected in 5 patients (12.5%) (**Figure 1b**). One patient (2.5%) exhibited incomplete superior temporal quadranopsia bilaterally, and 2 (5%) exhibited complete quadranopsia bilaterally (**Figures 2a and 2b**). The visual field defects observed in that group are summarized in **Table 3**.

In only 3 the tumor was initially diagnosed by ophthalmologic examination. Those 3 patients were then referred for a neurosurgical consult. Of those 40 patients, 4 (10%) demonstrated mild optic disk pallor bilaterally at the initial investigation, 2 (5%) showed signs of third cranial nerve palsy, 3 (7.5%) exhibited a mild-to-moderate color-vision defect, and none had an afferent pupillary defect.

Discussion. Hypophyseal adenomas are the third most common primary intracranial neoplasms in people ≥60 years of age. These lesions are the most common cause of chiasmal dysfunction in adults,[4] and they most often produce symptoms in patients in their fifth and sixth decades.[6] However, the incidence of hypophyseal adenoma in patients aged ≥60 years has decreased because of earlier diagnosis.[7] In our study, the mean age of the patients with pituitary adenoma was 50.13 ± 14.4

Table 1 - Presenting complaints in patients with hypophyseal adenoma.

Presenting complaint (n=40)	n	(%)
Reduced vision	4	(10)
Reduced visual field	6	(15)
Headache	12	(30)
Amenorrhea, galactorrhea, impotence	10	(25)
Diplopia, ptosis	2	(5)
None	6	(15)

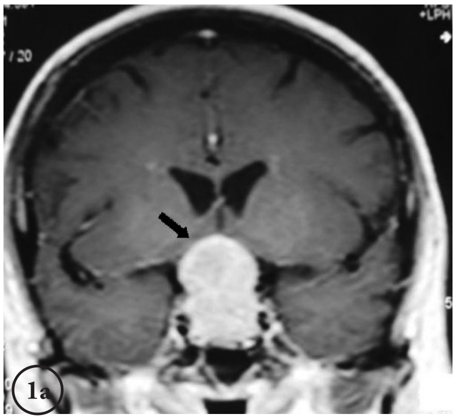
Table 3 - Visual field defects in patients with hypophyseal adenoma.

Visual field defect	n	(%)
Bilateral incomplete superior temporal quadranopsia	1	(2.5)
Bilateral complete quadranopsia	2	(5)
Complete bitemporal hemianopsia	5	(12.5)
Temporal depression (unilateral or bilateral)	5/3	(12.5/7.5)

Table 2 - Mean deviation and pattern standard deviation in the right and left eyes of patients with hypophyseal adenoma and in controls.

Patient classification	Mean deviation (dB)		Pattern standard deviation (dB)	
	Right eye	Left eye	Right eye	Left eye
Patients with a hypophyseal adenoma (group 1)	-5.15 (SD ± 5.38)	-4.28 (SD ± 4.45)	4.55 (SD ± 4.26)	4.10 (SD ± 3.52)
Healthy controls (group 2)	-1.73 (SD ± 1.51)	-1.74 (SD ± 1.65)	1.50 (SD ± 0.70)	1.46 (SD ± 0.59)

SD - standard deviation



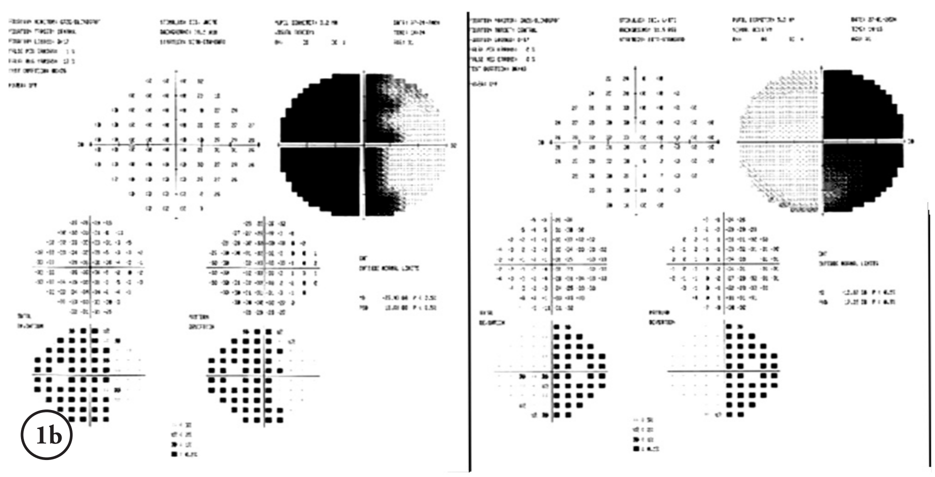


Figure 1 - **a)** T1-weighted magnetic resonance imaging shows a pituitary tumor (12 x 12 mm) in a 33-year-old woman. Note that the tumor compresses the optic chiasm superiorly and posteriorly and invades the cavernous sinus in the right border **b)** Humphrey visual field testing reveals bitemporal hemianopsia.

years. Although 15% of the patients had no complaints and the diagnosis of their tumor was incidental, 25% of the 40 patients had an endocrinologic complaint such as amenorrhea, galactorrhea, or impotence. We suggest that this high percentage of endocrinologic complaints resulted in an earlier diagnosis of pituitary adenoma. Ophthalmologic findings of hypophyseal adenomas are unilateral or bilateral reduction in visual acuity, visual field defects, paralytic strabismus, loss of color vision, and optic disc pallor. In our study, most commonly observed symptoms were reduced vision (4 [10%]), visual field defects (6 [15%]), and diplopia-ptosis (2 [5%]) of the patients. While defective color vision was detected in 3 patients (7.5%), optic disk pallor was observed in 10% of the patients studied.

The visual field abnormalities encountered in patients with hypophyseal adenomas include unilateral and bilateral superotemporal defects, bilateral hemianopsia, bitemporal hemianopic scotomas, anterior crossing scotoma, monocular scotomas, and temporal depression.[8] Even in patients with a visual acuity of 20/20, the initial symptom of a pituitary adenoma may be a defect in the visual field. The crossing inferonasal nerve fibers are the earliest to be affected by adenomas that grow upward, which causes superotemporal visual field defects. However, as that type of tumor enlarges, all crossing fibers are exposed to pressure, and the classic presentation of bitemporal hemianopsia develops. In patients with a chiasmal lesion, the reduction in vision occurs vertically. Although chiasmal lesions usually cause bilateral visual field defects, monotemporal defects may also be seen.[9] Two previous studies reported visual field defects in 86% and 70% of patients with hypophyseal adenoma,[2,10] but another study found that only 9% of

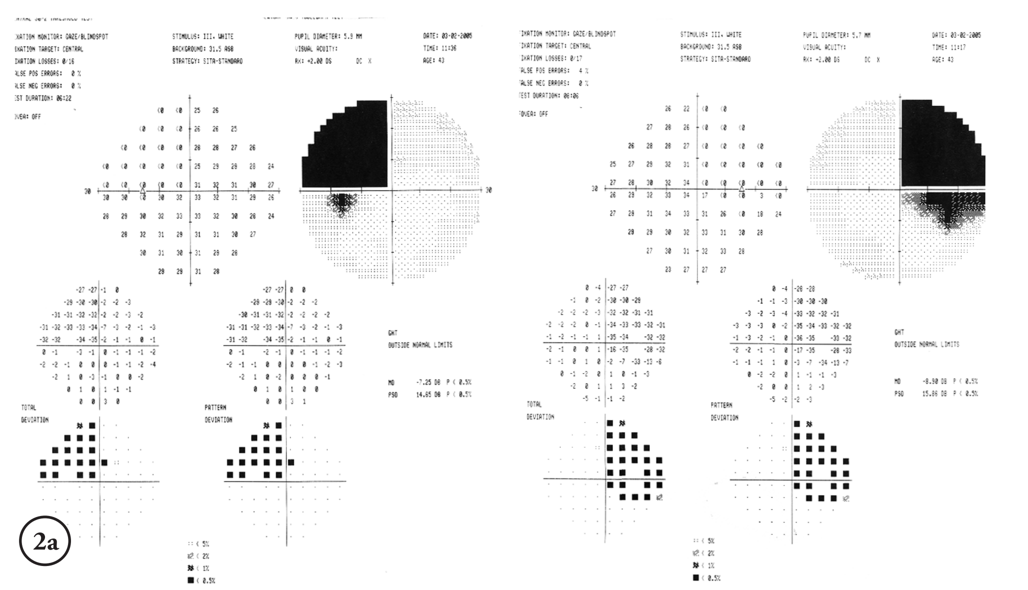


Figure 2 - **a**) A 43-year-old woman who presented with right-sided third cranial nerve palsy showed bilateral complete quadranopsia in Humphrey visual field test. **b**) Magnetic resonance imaging revealed a pituitary adenoma involving the sellar region.

such patients had an impaired field of vision.[1] In our study, visual field defects were found in 16 patients, although all those individuals had a corrected visual acuity that was better than 20/30. Only 8 patients (20%) had a specific visual field defect such as incomplete superior temporal quadranopsia, complete quadranopsia, or complete bitemporal hemianopsia. Unilateral non-specific temporal depression was detected in 5 (12.5%) patients, and bilateral non-specific temporal depression was identified in 3 patients (7.5%). We suggest that the advent of magnetic resonance imaging and the high diagnosis rate of hypophyseal adenoma by endocrinologists and gynecologists before neurosurgical referral decrease the incidence of patients' tumor-related ocular complications and visual field defects.

Different visual field examination methods can be used to diagnose and monitor patients with a hypophyseal adenoma and visual symptoms. In patients with a severe visual loss or in uncooperative patients, Goldmann kinetic perimetry may be performed.[11] However, state-of-the-art methods such as computerized visual field tests are simpler and more sensitive for optic nerve compression and chiasmal compression, especially in early stages of the disease.[11] In this study, all patients were examined with Humphrey visual field test, which is the dominant automated perimetry test, used in clinical practice. The superiority of automated perimetry was also reported by Fujimoto et al,[12] who examined ophthalmologically asymptomatic patients with hypophyseal adenoma in whom temporal hemianopsia was diagnosed with automated perimetry despite normal results with Goldmann kinetic perimetry.

One characteristic that renders automated perimetry more sensitive than Goldmann kinetic perimetry is its quantification. Among the parameters used in our study, the MD, and PSD values were significant determinants of the results of Humphrey perimetry. The MD is the mean value of the difference from the age-adjusted value at every test point, and PSD is the standard deviation of the difference between the threshold value and expected value at every test point. It is the measure of propagation of the difference of threshold value in different points of the visual field from other points.[13] In our study, the MD and PSD values were statistically significant between patients in groups 1 and 2, so we thought that these parameters can be used in diagnosis and in the follow-up of patients with hypophyseal adenoma.

In conclusion, in patients diagnosed with hypophyseal adenoma, neuro-ophthalmologic examination should be performed in addition to endocrine and radiological investigations. Although hypophyseal adenomas are usually diagnosed primarily by neurosurgeons, routine ophthalmologic examinations are still very important for the detection of visual loss and visual field defects and for the evaluation of disease progression. For detection of early visual field abnormalities, automated perimetry should be performed as a part of routine examination in patients with suspected hypophyseal adenoma or similar chiasmal dysfunction in addition to neuro-ophthalmic examination.

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