Coll. Antropol. **26** (2002) 2: 601–608
UDC 617.731:616.43-008.6
Original scientific paper

Chiasma Syndrome in Acromegalic Patients – Correlation of Neuroradiologic and Neuroophthalmologic Findings

Ž. Gnjidić[1], R. Iveković[2], Z. Rumboldt[3], M. Malenica[1], B. Vizner[4] and M. Berković[4]

[1] Department of Neurosurgery, University Hospital »Sestre milosrdnice«, Zagreb, Croatia
[2] Department of Ophthalmology, University Hospital »Sestre milosrdnice«, Zagreb, Croatia
[3] Department of Radiology, University Hospital »Sestre milosrdnice«, Zagreb, Croatia
[4] Department of Internal Medicine, University Hospital »Sestre milosrdnice«, Zagreb, Croatia

A B S T R A C T

The study evaluated neuroophthalmologic and computerized tomography (CT) findings in 100 patients with somatotrophic adenoma and clinical picture of acromegaly, who underwent transsphenoidal adenomectomy. Prior to the surgery, visual field was normal in 77 patients. The diameter of adenoma in these patients ranged from 8 to 30 mm on CT, and the average value was 13.5 mm. Various kinds of visual field disturbances were present in 23 patients. The diameter of their adenomas ranged between 18 to 35 mm, with the average of 24.7 mm. Compared to visual field defects, CT findings of suprasellar adenoma extension were better correlated with chiasma syndrome ($p < 0.001$). All patients with suprasellar mass greater than 10 mm had chiasma syndrome. Degenerative adenoma changes (hemorrhagic necrosis), which precipitate abrupt increase in size of the tumor, were more frequently seen in patients with chiasma syndrome. The incidence of chiasma syndrome directly correlates with the degree of suprasellar extension of the tumor.

Introduction

The most common clinical manifestations of mass lesions in sellar region are hypopituitarism and neuroophthalmological disorders. Sellar tumors often cause vision disturbances by compression of the optic nerves or chiasma, or ophthalmoplegia, due to displacement of III, IV, or VI cranial nerves within the cavernous sinus.

Received for publication October 5, 2002

Chiasma syndrome is characterized by vision deterioration, and visual field defects. It occurs only in large adenomas with suprasellar extension, which compress the optic chiasma and the optic nerves. Visual acuity disturbances usually do not correlate with visual field defects, except in the most advanced cases, which were not focus of this research.

Visual field defects or oculomotor nerve paresis usually occur late in the course of the disease, and are sometimes referred to as 'slowly progressing compressive optic neuropathies'[1,2]. Many patients, due to gradual and slow development of visual field defects, either seek medical help at a more advanced stage, or not at all. If the symptoms occur suddenly, pituitary adenoma apoplexy should be considered[3,4].

Although CT has greatly helped in detection and follow-up of pituitary tumors, visual field testing is still part of the standard algorithm for such patients, especially during pregnancy and at evaluating conservative therapy.

Out of series of over 1,000 patients with different sellar mass lesions, operated by transsphenoidal approach, we selected 100 patients with somatotrophic adenoma and clinical picture of acromegaly for this study[5]. The aim of the study is analysis of correlation between morphologic changes demonstrated by CT and visual field defects.

Patients and Methods

The study includes 100 patients with a clinical picture of acromegaly in which a somatotrophic adenoma was histologically verified. There were 46 males and 54 females aged 19 to 65, with the average age of 40.1 years.

All of the patients underwent thorough diagnostic workup prior to the operation according to same clinical, radiological, endocrinological, and neuroophthalmological criteria, and were operated by the same neurosurgical method. The postoperative testing was done 3 months after the surgical procedure. The decrease in growth hormone (GH) concentration under 5 ng/ml in the test of 6-hour basal secretion, so called 'normalization' was achieved in 90% of patients. Before and after the surgical procedure all of the pa-

TABLE 1
ADENOMA DIAMETERS (MM) MEASURED ON CT, GROUPED ACCORDING TO THE DEGREE OF SUPRA- AND PARASELLAR EXTENSION

Degree of extension	N	Min.	Max.	X	SD
No suprasellar extension	61	8	24	12.3	3.826
No parasellar extension	57	8	28	13.68	5.359
Suprasellar extension up to 5 mm	18	10	30	18.7	5.727
Parasellar extension up to 5 mm	30	8	30	18.87	5.987
Suprasellar extension 6 to 10 mm	8	18	30	22.9	5.055
Parasellar extension 6 to 10 mm	9	10	30	16.44	8.278
Suprasellar extension over 10 mm	13	20	35	25.85	3.997
Parasellar extension over 10 mm	4	20	35	27.75	6.344

tients had ophthalmologic evaluation: visual acuity, slit-lamp and fundus examinations as well as Goldmann perimetry. Examinations were performed before and after surgery and were classified as either normal or abnormal. If visual field examinations were abnormal they were divided in three categories: bitemporal hemianopsia, hemianopsia (left- or right-sided) or amaurosis. If there was a clinical suspicion of cranial nerve III, IV, or VI lesion, or a parasellar extension of the tumor on CT with signs of cavernous sinus infiltration, an examination of diplopia by Hess-Lancaster method was done[6–10]. In specific cases visual evoked potentials were done as well.

CT was done with 2 mm collimation in coronal plane, from the base of the anterior clinoids to the dorsum sellae. All patients were intravenously given 60 ml of urotrophic iodinated contrast (380 mg/ml) prior to the examination. Following the scan, images were also reconstructed in the sagittal plane[11–14]. Since pituitary adenomas are often of irregular shape, we used the largest dimension as the measure of diameter in all patients. Suprasellar extension was measured from the line connecting the anterior and posterior clinoids to the superiormost point of the adenoma. Tumor extension beyond the line connecting the anterior and posterior clinoids was considered evidence of lateral parasellar spread.

Results

The diameters of the suprasellar and lateral parasellar tumor extension as measured on CT are shown in Table 1.

The average values of the adenoma diameters in the group of patients with normal visual field and patients with defects in the visual field showed statistically significant ($p<0.001$) difference (Table 2).

A normal visual field was found in 77 patients (Table 3). The adenoma diameter in these patients as measured on CT was from 8 to 30 mm, with the average value of 13.48 mm, with a SD of 4.84. Various kinds of visual field defects were present in 23 patients. The diameter of their adenomas as measured on CT was from 8 to 35 mm, with the average 24.65, with a SD of 4.40.

The preoperative and postoperative visual field examinations are presented in Tables 4 and 5. In 82 patients the visual field findings remained unchanged. In 16 cases there was improvement following surgery, and in two there was deterioration. In 11 patients with bitemporal hemianopsia the visual field normalized in one eye, while remaining on the other side. In one patient with amaurosis on the right and hemianopsia on the left, visual field showed improvement on the left, while amaurosis remained on the right.

TABLE 2
INCIDENCE OF CHIASMA SYNDROME AT DIFFERENT STAGES OF SUPRASELLAR TUMOR EXTENSION VISUALIZED ON CT

Degree of suprasellar expansion	Normal visual field N=77	Chiasma syndrome N = 23
Intrasellar adenoma (N = 61)	60 (98.3%)	1 (1.7%)
Extension over 5 mm (N = 18)	16 (88.9%)	2 (11.1%)
Extension 6 to 10 mm (N = 8)	1 (12.5%)	7 (87.5%)
Extension over 10 mm (N = 13)	0 (0%)	13 (100%)

$^2 = 79.47$, df = 3, $p < 0.001$

TABLE 3
VISUAL FIELD PRIOR AND AFTER SURGERY

Visual field findings	Prior to the operation	After the operation
Normal visual field on both sides	77	86
Bitemporal hemianopsia	18	3
Right normal, left hemianopsia	1	6
Left normal, right hemianopsia	1	2
Right hemianopsia, left amaurosis	2	2
Left hemianopsia, right amaurosis	1	0
Right amaurosis, left normal	0	1
Total	100	100

TABLE 4
CHANGES IN THE VISUAL FIELD AFTER THE OPERATION

Visual field findings	Number of patients
Unchanged	82
Postoperative improvement	16
Postoperative deterioration	2
Total	100

Only one patient had paresis of the right oculomotor nerve, as confirmed by the double vision test by Hess-Lancester, prior to surgery. Postoperatively, the paresis has partly regressed. One patient had a transitory paresis of the right oculomotor nerve in the first three postoperative days. In the remaining 98 patients there were no postoperative cranial nerve defects.

In the group of 77 patients with normal visual field, signs of old hemorrhage or cystic changes were intraoperatively found in only 2 (2.6%) cases. Out of 23 patients with visual field defects, 18 (78.2%) had macroscopic signs of hemorrhagic adenoma necrosis. The correlation between the frequency of chiasma syndrome occurrence and suprasellar tumor extension is shown in Table 2. In patients with suprasellar tumor extension under 5 mm, in almost 90% of the cases visual fields were normal. On the other hand, almost 90% of the patients with suprasellar tumor spread of 6 to 10 mm had abnormal visual fields.

Discussion

Clinical manifestations of the compressive spatial lesions of pituitary adenoma, such as various kinds of hypopituitarism, diabetes insipidus, overproduc-

TABLE 5
COMPARISON OF THE CHANGES IN THE VISUAL FIELD ON ONE OR BOTH SIDES BEFORE AND AFTER SURGERY

	Prior to the operation	After the operation
Normal visual field	77	86
Visual field defects on both sides	21	5
Visual field defects on one side	2	9

$^2 = 14.80$, df = 2, $p < 0.0001$

tion of pituitary hormones, chiasma syndrome and the cavernous sinus syndrome are indicative of a pathological process in sellar and perisellar region. However, they frequently appear as late signs of large adenomas[15].

The frequency of the visual field defects of 23% in the presented series is much greater than in other reported studies, and indicates higher incidence of adenomas with suprasellar extensions or a late presentation in our patients[16–18]. In some other nonselective pituitary adenoma series the incidence of late presentation was even more frequent. For instance Kalousek in the group of 60 patients with pituitary adenomas finds 4 (6%) patients with clinical signs of oculomotor nerve paresis, and 31 (51%) patients with signs of chiasma syndrome[12]. However, from his work it is not clear how many of the studied patients were with nonfunctional adenomas and how many with somatotrophic and other functional adenomas. It is well known that patients with nonfunctional adenomas most commonly present with very large adenomas, which exhibit significant mass effect, including chiasma syndrome and the cavernous sinus syndrome. If we analyze the reports from ophthalmologic institutions, the frequency of the neuroophthalmologic defects is even greater[19,20].

According to the CT results, it is evident that in this series macroadenomas were predominant. Suprasellar extensions of the adenoma were noticed in 39 and parasellar in 43 cases. Much smaller number of patients had ophthalmologic abnormalities (23% had visual field defects and only 1% signs of oculomotor nerve compression).

By comparing the adenoma diameter, as measured on CT in patients with and without visual field defects, a statistically significant difference was proven ($p < 0.001$), indicating a correlation between the adenoma diameter and the visual field defects. Suprasellar expansion of macroadenoma in our series was graded in several levels as opposed to the majority of other series where tumors are classified only into macro and microadenoma. Our classification thus allows us to be more precise in grading the degree of suprasellar expansion. All of the patients with the suprasellar extension over 10 mm had chiasma syndrome (Table 4). These results correlate well with the results by Huang et al[21]. Ikeda et al had a similar study employing magnetic resonance imaging (MRI), and obtained almost identical results[22]. Therefore, surgical therapy is arguably the best choice for adenoma measuring 10 mm or more, in order to avoid chiasma lesion.

After the extirpation of the adenoma and chiasma decompression a marked improvement of the visual field occurred (Tables 3–5). In some this effect was very impressive, and the patients were noticing improvements only a few hours following the surgery. In majority the improvement of visual function was more gradual, and sometimes it was developing over a number of weeks following the surgical procedure.

Should we separate bilateral from the unilateral visual field defects it is possible to notice the decrease of bilateral visual field lesions and a significant increase of normalized vision bilaterally, as well as an increase of unilateral visual field defects. This observed difference is highly statistically significant ($p < 0.0001$) (Table 5), and implicates a positive effect of transsphenoidal surgery in treatment of chiasma syndrome caused by pituitary adenoma, as Visot have previously concluded[23].

Visual field defects were postoperatively present in 14 patients. In 12 the defects remained as irreversible lesions, and two patients, who preoperatively had normal visual field findings, developed a slight suppression of the left temporal vi-

sual field (Table 4). Both patients postoperatively demonstrated »empty sella«, which may be explained by herniation of the chiasma into the operatively created space and stretching over the dorsum sellae[24]. Adams reported similar findings, however, he proposed operative vascular damage as a possible explanation[17]. The incidence of this complication is unfortunately not small (2%), but the same incidence was reported in other large series as well[25].

In 16 patients, following the extirpation of the adenoma and chiasma decompression, an either partial or total improvement of the visual field occurred, and in the remaining 82 patients the visual field was not changed. Our data confirm findings of a previous study, which demonstrated low reliability of visual field defects as a sign of a successful surgery[26]. In 16 patients in whom an improvement of the visual field occurred, there could have been an intrasellar residue, which would not affect the clinical development of acromegaly, while the effect of the chiasma decompression and the improvement of the visual field were achieved.

A recurring somatotrophic adenoma would have to surpass the preoperative dimensions and also to have suprasellar extension, to eventually result in worsening of perimetry, indicating the presence of a mass lesion in the region. At the same time all other diagnostic indicators would undoubtely indicate acromegaly.

In adenomas of patients with normal visual field there were signs of hemorrhage or cystic changes in only 2.6% of the cases, while these changes were common in the group of patients with narrowed visual field (78.2%). These degenerative changes of the tumors, caused by ischemia or hemorrhage, frequently occur without symptoms. However, sometimes they have a very dramatic course, with acute development of the chiasma syndrome, cavernous sinus syndrome, and meningeal syndrome, possibly with fatal consequences[27]. This clinical entity, known as pituitary adenoma apoplexy, occurred in four patients in our series. Intraoperatively there were signs of hemorrhage and necrosis of a part of the adenoma. Similar findings are reported in other studies as well[28–30].

Despite the fact that according to the CT findings, 43% of patients had adenomas showing signs of parasellar expansion, only one patient had oculomotor nerve paresis, while other cranial nerves of the cavernous sinus were not affected. The incidence of this occurrence is much smaller than in other series[31]. On CT scans, as well as intraoperatively, in this patient a large invasive adenoma was found infiltrating cavernous sinus and expanding almost to the semilunar ganglion. Two months after the transsphenoidal surgical procedure, which created decompression, a partial improvement of the nerve function occurred. Three months later a transcranial resection of the residue was done, followed by irradiation, but further recovery was not achieved.

One patient, also with parasellar propagation of the tumor, following the surgery had a transitory III nerve paresis which spontaneously regressed on the fourth postoperative day. During the attempts of most radical removal of the part of the tumor infiltrating right cavernous sinus in this patient, strong venous bleeding occurred. The paresis is most probably a consequence of the nerve compression by the implanted muscle tissue, and surrounding hematoma.

Out of 39 patients with CT signs of suprasellar adenoma extension, 23 had visual field defects, while out of 43 patients with CT signs of the parasellar extension, only one had cavernous sinus syndrome. This may be due to fibrous trabecules and cavernous sinus septa, which decrease the direct pressure of the

adenoma onto the nerves situated in its lateral wall. Interposition of the carotid artery between the adenoma and the cavernous sinus nerves, may compensate for the direct pressure of the adenoma on the nerves.

The evaluation of neuroophthalmologic and neuroradiologic findings in 100 patients with somatotrophic adenoma and clinical picture of acromegaly operated on by transsphenoidal microsurgical selective adenomectomy, brought us to following conclusions:

Chiasma syndrome is correlated to the degree of suprasellar adenoma spread. All patients with suprasellar extension over 10 mm had visual field defects, irreversible in some cases, despite satisfactory surgical decompression. Therefore, all patients with pituitary adenoma showing suprasellar spread should undergo neuroophthalmological examination.

Although some patients began their treatment due to vision disturbances, which were very exactly determinated and lead to the final diagnosis, neuroophthalmological diagnostic methods have no significant role in the long term follow up of acromegalic patients. Therefore, biochemical indicators have the leading role (basal values of GH, IGF-I, TRH test), followed by neuroradiological methods (CT and MRI).

In all 100 patients CT revealed the adenoma, its size, structure, associated bony changes, and extrasellar tumor expansion. We emphasize that in many communities CT is still a more accessible method, but MR due to numerous preferences in 'imaging' of the sellar region has the absolute advantage[32–35]. Today, MR is the neuroimaging study of choice for evaluation of the sellar region, however CT represents a valuable alternative.

Transsphenoidal surgical approach proved to be a reliable technique not only for intrasellar adenomas, but also for large tumors with extrasellar extension, accompanied by neuroophthalmologic disturbances. This approach is especially recommended as an emergency method in cases of pituitary apoplexy, which is frequently followed by sudden, often irreversible visual dysfunctions. This method, involving minimal surgical trauma, provides the possibility of urgent tumor reduction and decompression of different perisellar structures.

REFERENCES

1. KOVAČIĆ, M., T. GRAČNER, Coll. Antropol., 25 Suppl. (2001) 57. — 2. PERIĆ, S., B. CEROVSKI, P. PERIĆ, Coll. Antropol., 25 Suppl. (2001) 67. — 3. McFADZEAN, R., F. C. OPHTH, D. DOYLE, R. RAMPLING, E. TEASDALE, G. TEASDALE, Neurosurgery, 29 (1991) 669. — 4. MILLAZO, S., P. TOUSSAINT, F. PROUST, G. TOUZET, D. MALTHIEU, Eur J. Ophtalmol., 1 (1996) 69. — 5. GNJIDIĆ, Ž.: Evaluacija kliničkih, radioloških i laboratorijskih parametara kod akromegaličkih bolesnika operiranih transsfenoidalnim pristupom. Ph.D. Thesis. (School of Medicine, University of Zagreb, Zagreb, 1994). — 6. KOVAĆEVIĆ, S., B. CEROVSKI, Z. BUJGER, Z. PAŠTAR, J. PETROVIĆ, Coll. Antropol., 25 Suppl. (2001) 63. — 7. TRAUTMANN, J. C., E. R. LAWS, Am. J. Ophtalmol., 96 (1983) 200. — 8. RIVOAL, O., A. BREZIN, S. FELDMAN-BILLARD, J. P. LUITON, Ophtalmology, 107 (2000) 991. — 9. PARMAN, D. N., A. SOFAT, R. BOWMAN, J. R. BARTLETT, G. E. HOLDER, Br. J. Ophtalmol., 84 (2000) 1024. — 10. GROCHOWICKI, M., A. VIGHETTO, S. BERQUET, Y. KHALFALLAH, G. SASSOLAS, Br. J. Ophtalmol., 75 (1991) 219. — 11. DAVIS, P. C., J. C. HOFFMAN, G. T. TINDALL, I. F. BRAUN, Am. J. Neuroradiol., 6 (1985) 711. — 12. KALOUSEK, M., Rad. JAZU, 20 (1985) 109. — 13. MAROTTI M., M. LOVRENČIĆ, M. KALOUSEK, Liječ. Vjes., 10 (1984) 429. — 14. ELSTER, A. D., Radiology, 187 (1993) 1. — 15. FELDKAMP J., R. SANTEN, E. HARMS, A. AULICJ, U. MODDER, W. A. SCHERBAUM, Clin. Endocrinol., 51 (1999) 109. — 16. GRISOLI, F., T. LECLERQ, P. JAQUET, Surg. Neurol., 23 (1985) 513. — 17. ADAMS, C. B. T., Acta neurochirurgica (Wien), 94 (1988) 103. — 18. YAMADA, S., K. TAKADA, Y. OZAWA, T. SHIMIZU, S. SAWANO, Y. SHISHIBA, T. SANO, M. USUI, Endocrine Journal, 44 (1997) 395. — 19. LESTAK, J., J. VLADYKOVA, L. HOUSTAVA, Cesk. Oftalmol., 51 (1995) 165. — 20. FU, X., H.

WANG, Yen Ko Hsueh Pao, 12 (1996) 166. — 21. HUANG, W. C., L. S. LEE, Zhonghua YiXue Za Zhi (Taipei), 60 (1997) 245. — 22. IKEDA, H., T. YOSHIMOTO, Acta Neurol. Scand., 92 (1995) 157. — 23. VISOT, A., Presse Med., 30 (2001) 401. — 24. CZECH, T., S. WOLFSBERGER, A. REITNER, H. GORZER, Acta Neurochirurgica (Wien), 141 (1999) 45. — 25. ĆIRIĆ, I., A. RAGIN, C. BAUMGARTNER, D. PIERCE, Neurosurgery, 40 (1997) 225. — 26. MEHDORN, E., G. KOMMERELL, Klin. Mbl. Augenheilk., 180 (1982) 275. — 27. BILLS, D. C., F. B. MAYER, E. R. LAWS, D. H. DAVIS, M. J. EBERSOLD, B. W. SCHEITHOUER, D. M. ILSTRUP, C. F. ABBOUD, Neurosurgery, 33 (1993) 602. — 28. MULLER-JENSEN, A., D. LUDECKE, J. Neurol., 224 (1981) 267. — 29. GNJIDIĆ, Ž., L. NEGOVETIĆ, M. GNJIDIĆ, V. LUPRET, M. KALOUSEK, B. VIZNER, J. KORŠIĆ, (Monduzzi editore, Copenhagen, 1999.) — 30. FRAIOLI, B., V. ESPOSITO, L. PALMA, G. CANTORE, Neurosurgery, 27 (1990) 741. — 31. MILAZZO, S., P. TOUSSAINT, F. PROUST, G. TOUZET, D. MALTHIEU, Eur. J. Ophtalmol., 6 (1996) 69. — 32. NICHOLS, D. A., E. R. LAWS, O. W. HOUSTER, C. F. ABBOUD, Neurosurgery, 22 (1988) 380. — 33. MIKHAEL, M. A., I. A. CIRIC, J. Comput. Assist. Tomogr., 12 (1988) 441. — 34. KNOSP, E., E. STEINER, K. KITZ, C. MATULA, Neurosurgery, 33 (1993) 610. — 35. YOON, P. H., D. I. KIM, P. JEON, S. I. LEE, S. K. LEE, S. H. KIM, AJNR Am. J. Neuroradiol., 22 (2001) 1097.

Ž. Gnjidić

Department of Neurosurgery, University Hospital »Sestre milosrdnice«, Vinogradska 29, 10000 Zagreb, Croatia

HIASMA SINDROM U AKROMEGALIČNIH BOLESNIKA – KORELACIJA NEURORADIOLOŠKIH I NEUROOFTALMOLOŠKIH NALAZA

S A Ž E T A K

Cilj istraživanja je evaluacija neurooftalmoloških i nalaza kompjuterizirane tomografije (CT) u 100 bolesnika sa somatotrofnim adenomom i kliničkom slikom akromegalije koji su operirani metodom transsfenoidalne selektivne adenomektomije. Vidno polje je prije operacije bilo obostrano uredno u 77 bolesnika. Promjer adenoma u tih bolesnka kretao se od 8 do 30 mm na CT-u, a prosječna vrijednost iznosila je 13.5 mm. Različite oblike ispada vidnog polja imala su 23 bolesnika. Promjer njihovih adenoma kretao se od 18 do 35 mm, s prosjekom 24.7 mm. U usporedbi s poremećajima vidnog polja, nalazi supraselarne ekspanzije adenoma na CT-u su bolje korelirali s hijazma sindromom ($p < 0.001$). Svi bolesnici sa supraselarnim masama većim od 10 mm imali su hijazma sindrom. Degenerativne promjene adenoma, koje ubrzavaju povećanje promjera tumora su također bile važan predikativni faktor. Učestalost hijazma sindroma direktno korelira sa stupnjem supraselarne ekspanzije tumora.