Clinical Features Associated With Lesions Other Than Pituitary Adenoma in Patients With an Optic Chiasmal Syndrome

LUIS J. MEJICO, MD, NEIL R. MILLER, MD, AND LI MING DONG, PHD

• PURPOSE: **Pituitary adenomas are the most common cause of an optic chiasmal syndrome, and treatment of these lesions is considerably different from the treatment of most of the other lesions in this region. Although the diagnosis of a pituitary adenoma is usually inferred from the results of neuroimaging, lesions other than pituitary adenomas can have an appearance that suggests an adenoma. The objective of our study was to determine whether there are clinical findings that suggest a lesion producing a chiasmal syndrome is something other than a pituitary adenoma.**

• DESIGN: **Retrospective, case-controlled, analysis of medical record data.**

• METHODS: **The records of the Neuro-Ophthalmology Unit of the Wilmer Eye Institute were searched for patients with a chiasmal syndrome who had been evaluated before treatment and for whom pathologic or laboratory confirmation of the etiology was available. Presenting clinical features of these patients were recorded, and analyses with both a single variable and multiple variables were performed to determine whether there were any features that could identify with a high degree of probability the etiology of the lesion producing the syndrome.**

• RESULTS: **The search revealed 149 patients who met the inclusion criteria, including 90 patients with pituitary adenomas and 59 patients with other lesions. Variables that were highly suggestive of an etiology other than pituitary adenoma included symptomatic visual loss, younger age, unilateral optic disk pallor, a relative afferent pupillary defect, and an absolute or a complete visual field defect or one was greater inferiorly than superiorly.**

• CONCLUSION: **Although no single clinical feature can be used to determine the specific nature of a lesion that produces an optic chiasmal syndrome, certain features are highly suggestive of an etiology other than pituitary adenoma. When these features are present, the likelihood that a suprasellar lesion is a pituitary adenoma is much lower, regardless of the appearance on neuroimaging. (Am J Ophthalmol 2004;137:908–913. © 2004 by Elsevier Inc. All rights reserved.)**

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From the Neuro-Ophthalmology Unit (L.J.M., N.R.M.) and Clinical Trials and Biometry Unit (L.M.D.), Wilmer Eye Institute, Johns Hopkins Hospital, Baltimore, Maryland.

Inquiries to: Luis J. Mejico, MD, Department of Neurology, 90 Presidential Plaza, Syracuse, NY 13202; fax: (315) 464-7328; e-mail: mejicol@upstate.edu

THE OPTIC CHIASM MAY BE DAMAGED BY A VARIETY of lesions, both intrinsic and extrinsic. In most cases, some form of bitemporal field defect may be associated with unilateral or bilateral reduction in visual acuity and color vision from damage to one or both optic nerves. If only one optic nerve is affected or there is a significant asymmetric bilateral optic neuropathy, a relative afferent pupillary defect (RAPD) will be present.

Once the diagnosis of a chiasmal syndrome is made, the challenge is to determine what type of lesion is responsible and the optimal treatment for the lesion. This usually requires neuroimaging; however, in some settings, neuroimaging results may be misleading. The following is an illustrative case report.

A 26-year-old man complained of new-onset fatigue, sexual dysfunction, cold intolerance, weight gain, decreased facial hair growth, constipation, headaches, and bilateral blurred vision of 6-months duration. Workup revealed multiple endocrine abnormalities suggestive of panhypopituitarism, as well as a slightly elevated serum prolactin level. A magnetic resonance image (MRI) was obtained (Figure 1), a diagnosis of pituitary adenoma was made, and the patient was scheduled for transsphenoidal removal of the lesion. The patient was referred for neuroophthalmology consultation prior to surgery.

On examination, the patient's Snellen visual acuity was 20/40 in the right eye (OD) and 20/20 in the left eye (OS). He correctly identified 4.5 of 10 Hardy-Rand-Rittler (HRR) pseudoisochromatic color plates OD and eight of 10 OS. Both pupils reacted briskly to light, and there was

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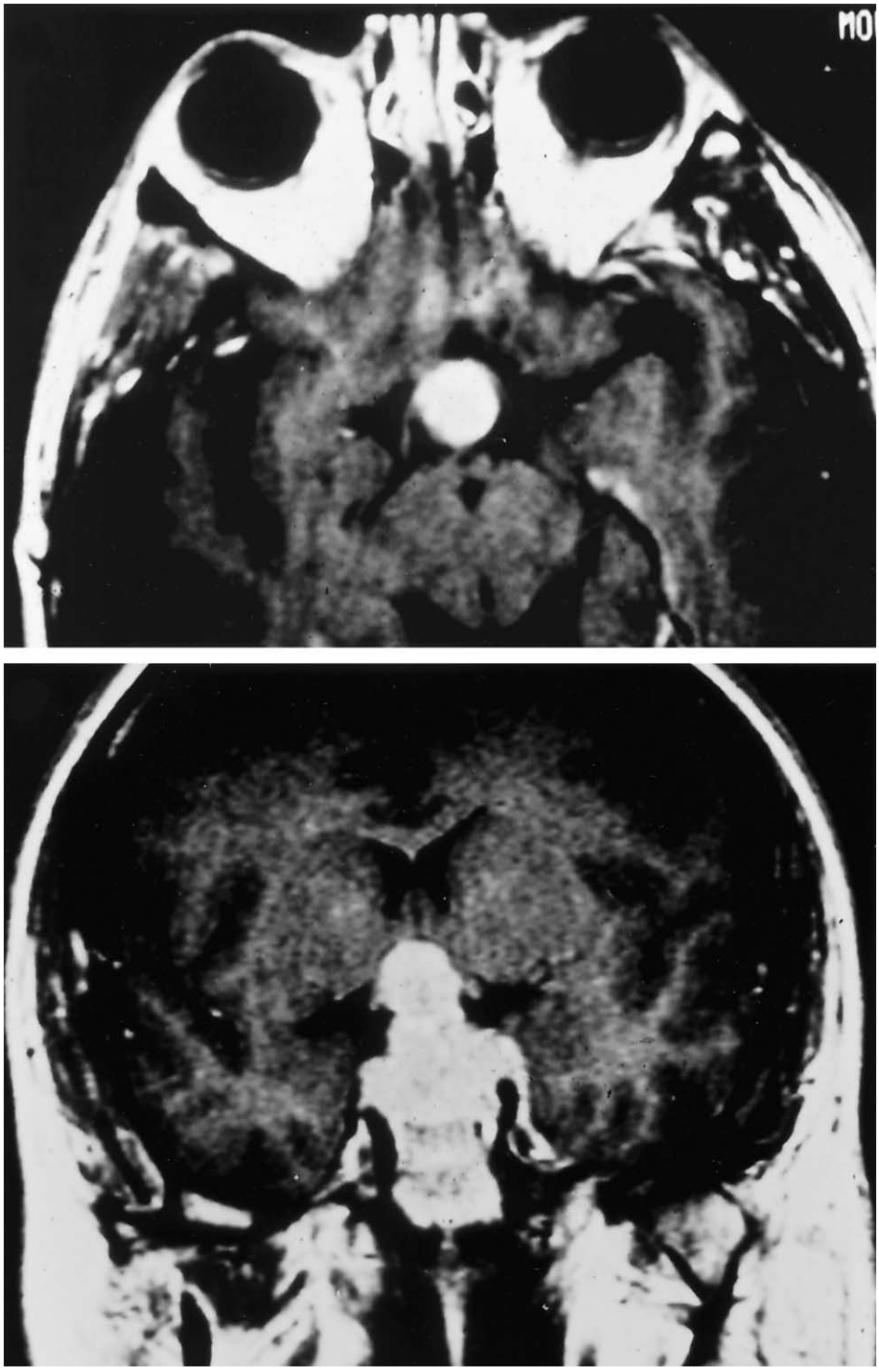

FIGURE 1. Gadolinium-enhanced T1-weighted axial and coronal magnetic resonance images show generalized enhancement of a large mass involving the sellar and suprasellar regions.

no RAPD. His ocular motility and slit-lamp examinations revealed no abnormalities. Dilated funduscopic examination revealed normal optic disks, vessels, maculae, and peripheral retinas in both eyes. Results of kinetic and static perimetry (Figure 2) revealed a bitemporal inferior incomplete relative hemianopia, suggesting a lesion affecting the superior decussating fibers of the body of the optic chiasm. This, in turn, suggested that the lesion was likely superior to the chiasm, rather than inferior to it, as would be expected with a pituitary adenoma.

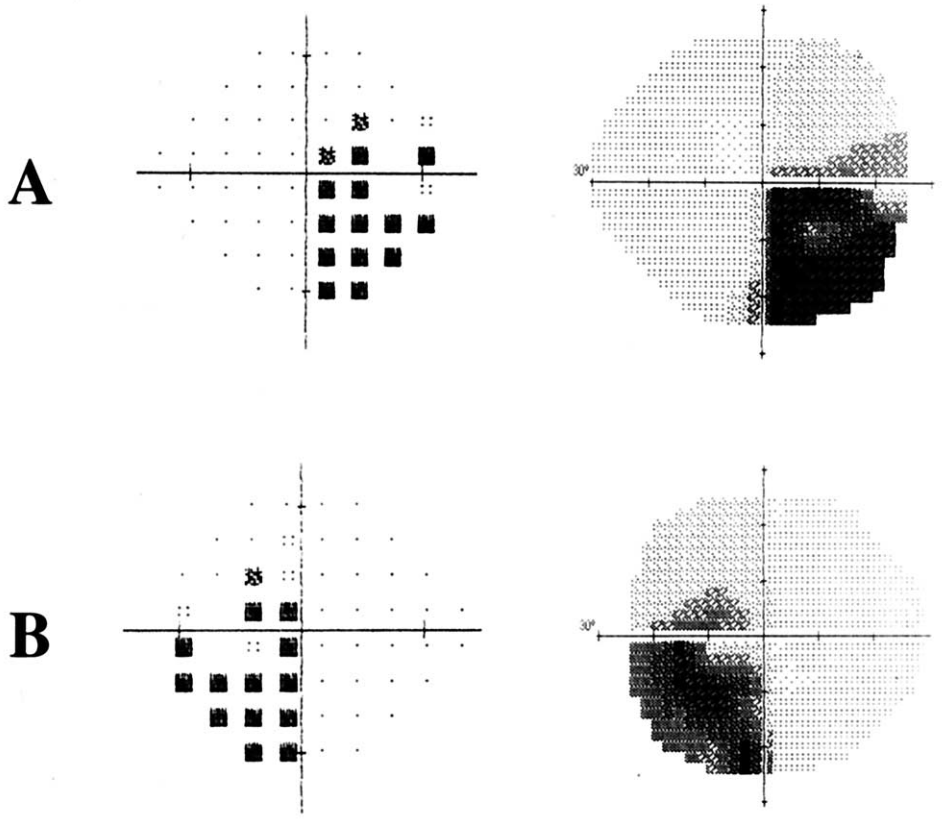

FIGURE 2. Findings from automated perimetry (Humphrey 24–2 threshold program; Zeiss Humphrey Systems, Dublin, California) of the right (A) and left (B) eye show a bitemporal inferior quadrantanopia on gray scale (right) and pattern deviation (left).

Based on the results of the neuroophthalmologic examination, we indicated to the neurosurgeon that it was unlikely the lesion was a pituitary adenoma, and he decided to perform a craniotomy rather than transsphenoidal surgery. At surgery, the lesion proved to be a germinoma, and the patient subsequently was treated with radiation therapy.

Clinical cases such as the one presented here suggest that it would be useful to know from the clinical picture as much as possible about the nature of the lesion causing a chiasmal syndrome. The information can then be used, along with the results of neuroimaging, to guide both the nature and speed of the subsequent assessment as well as the appropriate management of the lesion. Furthermore, in view of the unique anatomic configuration of the optic chiasm and its relationship to the surrounding structures, we wondered if it was possible to determine with a high degree of probability the nature of a lesion producing a chiasmal syndrome based on specific features of the clinical examination. We therefore conducted a study to determine the value of various clinical features at time of presentation, including the pattern of visual field loss, in differentiating among the many etiologies of the chiasmal syndrome.

DESIGN

RETROSPECTIVE, CASE-CONTROLLED, ANALYSIS OF MEDICAL record data.

METHODS

THE RECORDS OF THE NEURO-OPHTHALMOLOGY UNIT from the Wilmer Eye Institute at the Johns Hopkins Hospital between July 1975 and July 1999 were searched for patients coded as having an optic chiasmal syndrome, defined as the presence of a binocular, relative or absolute temporal visual field defect with or without decreased visual acuity, color vision, or both, or a unilateral optic neuropathy associated with a superior temporal defect in the contralateral eye. Patients who had been evaluated preoperatively in the unit and whose etiology subsequently was confirmed by pathologic or laboratory testing were identified, and the following data were collected for each patient: age at diagnosis; sex; duration and nature of visual symptoms such as blurred vision, double vision, and difficulties with side vision; best-corrected or pinhole

visual acuity; color vision using HRR plates; pupillary function; appearance of the optic disks; and visual field defect. Visual field characteristics were also analyzed in detail. The techniques employed to plot visual fields included tangent screen examination, kinetic perimetry using a Goldmann perimeter, and static perimetry using a Humphrey automated perimeter. Some patients underwent visual field testing with more than one technique. The density of the field defect, either relative or absolute, was noted in cases in which more than one isopter were used with kinetic techniques. Field defects were classified as complete or incomplete based on the extent of the defect. For example, a hemianopic field defect that covered 75% of the affected hemifield was considered incomplete. The side (that is, right, left, bilateral, etc.) and type of field defect (that is, hemianopia, quadrantanopia, scotoma, etc.) were documented. Finally, the location of the field defect (that is, superior, inferior, or equal superior and inferior) was noted.

Logistic regression was performed to examine the influence of each individual factor on odds ratio in favor of diagnosis other than pituitary adenoma. Stepwise procedure was performed among all the above-mentioned variables except on some features of visual field defects because of sparse categories within each of these variables. A χ^2 P value of $\leq .1$ was used as a criterion for a factor to enter or stay in the model in the stepwise procedure. For visual acuity in the analysis, Snellen notation was converted to logMAR by taking log10 of the inverse of Snellen notation. Notations such as counting fingers, hand motion, and no light perception were assigned a logMAR of 2.3, 2.6, and 2.9, respectively, to avoid treating them as missing data. A P value less than .05 was considered statistically significant.

RESULTS

THE RECORDS SEARCH IDENTIFIED 149 PATIENTS WHO MET the inclusion criteria. These patients had the following lesions: pituitary adenoma (90 patients), meningioma (16 patients), craniopharyngioma (15 patients), traumatic injury (eight patients), glioma (seven patients), aneurysm (four patients), germinoma (two patients), metastatic tumor (three patients), and other (one patient each with sarcoidosis, Rathke cleft cyst, dermoid cyst, and sphenoid sinus mucocele). The age of the subjects ranged from 11 to 86 years, with a mean of 48 years. Women accounted for 43% of the study population. Race information was available for 141 subjects. Among them, 18% were black, 79% were white, and 3% were coded as "other."

When examining the effect of each individual factor regardless of other factors with logistic regression, we found that patients were more likely to have a lesion other than pituitary adenoma if they had one of the following clinical features: visual symptoms consistent with an optic neuropathy or optic chiasmal process such as blurred vision or difficulties with side vision, unilateral optic disk pallor, an RAPD, an absolute or a complete visual field defect, or a field defect that was greater inferiorly than superiorly (Table 1). For example, subjects without pituitary adenoma were 3.8 times more likely to have visual symptoms compared with those with pituitary adenoma. Worse visual acuity and color vision were also found to be associated with an etiology other than pituitary adenoma. There was a trend toward older age in the pituitary adenoma group: the odds of not having pituitary adenoma for a subject was 0.84 of that of a subject who was 10 years younger (data not shown); however, the effect of age was not statistically significant ($P = .07$).

TABLE 1. Influential Clinical Factors on Odds Ratio of Not Having a Pituitary Adenoma: Logistic Regression With Single Independent Variables

Variable	Point Estimate (Odds Ratio)	95% Wald Confidence Limits	*P* Value
Disc			
Normal OU vs other	0.250	0.107–0.584	.004
Pallor OU vs other	0.355	0.139–0.906	—
Visual symptom			
Presence vs absence	3.836	1.470–10.007	.004
RAPD			
OD vs no	2.899	1.167–7.194	.05
OS vs no	1.835	0.839–4.016	—
Visual acuity			
OD (logMar)	2.197	1.216–3.968	.005
OS (logMar)	2.181	1.216–3.912	.005
Color vision			
OD	0.962	0.883–1.047	.36
OS	0.871	0.794–0.956	.003
Extension			
Complete vs incomplete	5.780	1.972–16.949	.0005
Density			
Absolute vs relative	4.292	1.088–16.949	.03
Location			
Superior vs inferior	0.237	0.071–0.784	.02
Equal vs inferior	0.516	0.153–1.742	—

OD = right eye; OS = left eye; OU = both eyes; RAPD = relative afferent papillary defect.

We also conducted logistic regression with multiple independent variables using stepwise analysis to select influential variables. The effect of the selected variables on the odds ratio in favor of a diagnosis other than pituitary adenoma in the presence of other variables are displayed in Table 2. Patients who had a combination of the following features were unlikely to have a pituitary adenoma: younger age, unilateral optic disk pallor, an absolute or a complete visual field defect, or a field defect that was greater inferiorly than superiorly (Table 2). Among these

TABLE 2. Influential Clinical Factors on Odds Ratio of Not Having a Pituitary Adenoma: Logistic Regression With Mulitple Variables*

Variable	Point Estimate (Odds Ratio)	95% Wald Confidence Limits	P Value
Age (yr)	0.971	0.949–0.993	.01
Disc			
Normal OU vs other	0.309	0.114–0.839	.02
Atrophy OU vs other	0.238	0.077–0.740	—
Extension			
Complete vs incomplete	6.250	1.709–22.727	.005
Location			
Superior vs inferior	0.188	0.052–0.688	.04
Equal vs inferior	0.235	0.059–0.943	—
Visual acuity			
OD	1.802	0.898–3.648	.10
OS	1.873	1.007–3.483	.05

OD = right eye; OS = left eye; OU = both eyes.
*Selected with the help of stepwise procedure.

factors, the extension and location of the visual field defect had the greatest prognostic effect. The odds in favor of a lesion other than pituitary adenoma for subjects with complete visual field defect was 6.25 times that of subjects with incomplete visual field defect, and the odds for subjects with an inferior field defect was 5.32 (1/0.188 from Table 2) times that of subjects with superior field defect. Interestingly, the effect of age became significant ($P = .01$) after adjusting for other factors; however, visual symptoms such as blurred vision, double vision or difficulties with side vision, a color vision deficit, presence of an RAPD, and density of the field defect dropped out from the model with multiple independent influential variables, suggesting that their prognostic effects were likely to be represented by other factors in the model. In addition, the effect of each selected variable in the analysis with multiple variables (Table 2) was similar to its effect in the analysis with single variables (Table 1), suggesting that the effects of age, disk appearance, and the extent and location of the field defect were important regardless of the effect of other factors.

DISCUSSION

THE RESULTS OF THIS STUDY DEMONSTRATE THAT CERtain clinical features are highly suggestive of an etiology other than pituitary adenoma in patients presenting with an optic chiasmal syndrome. The complex gross and microscopic anatomy of the optic chiasm and sella turcica area has attracted attention for hundreds of years, as has the nature and pathogenesis of the clinical findings produced by lesions in this region. One of the many anatomic features of the optic chiasm is that it tilts forward in an angle of about 15 to 45 degrees. In 80% of individuals, the chiasm is located directly above the pituitary gland (normal position), whereas in 15%, it is over the tuberculum sellae (prefixed), and in 5% it is located over the dorsum sellae (postfixed). A second anatomic feature of the optic chiasm relates to the pathways of its fibers. The ratio of crossed to uncrossed fibers within the chiasm is 53:47. Although uncrossed fibers, both dorsal and ventral, maintain their position at the lateral aspects of the chiasm and into the optic tracts, upper nasal quadrant fibers cross dorsally and posteriorly and lower nasal quadrant fibers cross more anteriorly.[1] Because of this unique anatomic configuration of the chiasm, lesions typically produce changes in visual sensory function, particularly visual field defects, that make the clinical diagnosis of chiasmal damage relatively straightforward. There remain many unanswered questions, however. For example, two of the issues raised by Traquair in 1917,[2] the exact mechanism by which chiasmal syndromes are produced and the relationship of visual field changes to the etiology of the lesion, remain largely unexplained.

Hughes[3] noted that if the chiasm is in a normal or a postfixed position, enlargement of the third ventricle will compress its posterosuperior aspect, causing bitemporal depression of the inferior fields; if the chiasm is prefixed, however, the ventricle will compress the posteroinferior aspect, causing bilateral central scotomas, nasal and arcuate defects, or even superior hemianopic defects. Based on nine cases, Adler and associates[4] concluded that bitemporal hemianopic scotomas were highly suggestive of craniopharyngioma and that a junctional scotoma suggested a pituitary adenoma. Hedges[5] proposed a way of explaining why the upper nasal field was preserved in advanced chiasmal syndromes. He placed a balloon in the sella turcica of monkeys, inflated it, and noted that as the balloon expanded into the suprasellar region and compressed the inferior aspect of the optic chiasm, the uncrossed upper fibers stretched and the lower ones relaxed. He likened this process to the effect on the skin of a flexed finger, in which the upper skin stretches and the under skin wrinkles and becomes less taut. Although Harrington criticized this study as being too simplistic,[5] no other mechanism has been proposed to date. In the largest report published of pituitary adenomas collected from 1935 to 1972, 42% of patients had visual complaints, and 70% had a chiasmal syndrome.[6] Among these, 94% had an incomplete visual field defect that was either equally severe superiorly and inferiorly or greater superiorly than inferiorly, whereas 1% were greater inferiorly. Optic disk pallor was observed in 34% of patients in this series, but there is no mention whether the pallor was unilateral or bilateral.

We are unaware of a previous study looking at the diagnostic value of various clinical features of the optic chiasmal syndrome in an attempt to identify the etiology of the condition and could find no reference to it in a

computerized search using MEDLINE. Even though pituitary adenomas tend to occur in young adults, we found that younger age predicted other lesions when combined with other specific features (Table 2). It is possible however, that presentation at younger age in other conditions, such as craniopharyngioma or trauma, could have influenced this finding. On the other hand, the robust effect of most other variables used in our study, in analyses with both single and multiple variables, suggests that their prognostic effects are independent of other factors. We did not include radiologic or endocrine data in this statistical model, nor did we compare these data with the clinical variables used, because the purpose of this study was to determine the value of various clinical ophthalmologic features at the time of presentation in differentiating among the many etiologies of the chiasmal syndrome. Indeed, our study indicates that some elements used in the routine clinical assessment of patients with chiasmal syndromes not only provide useful information with respect to baseline visual function and visual prognosis but also can be used to diagnose the etiology of the syndrome.

In conclusion, visual symptoms, younger age, unilateral optic disk pallor, an RAPD, an absolute or a complete visual field defect, a visual field defect that is greater inferiorly than superiorly, or a combination of these findings is highly suggestive of an etiology other than pituitary neoplasm. An awareness of the significance of these clinical findings may assist the clinician in the subsequent evaluation and management of a patient with an optic chiasmal syndrome.

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