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Eye signs in craniopharyngioma

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Although craniopharyngiomas comprise only 3 per cent of all intracranial tumours (Walsh and Hoyt, 1969), they represent 13 per cent of intracranial neoplasms in childhood (Frazier, 1936; Ingraham and Scott, 1946) and 30 per cent of all new growths in the hypophyseal area (Love and Marshall, 1950). Since ocular signs are frequently the presenting feature of these tumours, many of the patients being first seen at an eye clinic, their recognition by the ophthalmologist is clearly of great importance. Certainly early diagnosis is desirable, since modern advances in treatment have resulted in better prospects for successful eradication of the growth, if its detection is timely and its location favourable.

At the Institute of Neurological Sciences (INS), Glasgow, approximately three new cases are discovered each year, and in this communication we report the results of a 20-year study.

Material and methods

Altogether 45 patients, 22 men and 23 women (mean age 25 years), suffering from craniopharyngioma and treated at the INS during the past 20 years, were the subjects of this retrospective study. One of us (RJSS) had examined most of the patients throughout the 20 years and was responsible for the ophthalmological examinations, comprising visual acuity, ocular movements, pupil reactions, ophthalmoscopy, and visual field testing using the Bjerrum screen.

Results

Fig. 1 shows that the patients were divided equally into male and female categories ranging from 2 to 61 years. They can be placed in three groups of approximately the same numbers, children of 13 years and under, young adults of 14 to 29 years, and older adults of 30 years and over. While more than half presented in the first two decades of life, and more than two-thirds before the age of 30, many were above that age before symptoms were manifest.

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In Fig. 2, the main presenting clinical features are shown. Headache was a prominent symptom in all the age groups at the time of hospitalization, varying in duration from 2 days to 23 years, and was particularly prevalent in children. The high incidence of loss of visual acuity, visual field defects, and optic atrophy or papilloedema is shown and the importance of these signs is emphasized as 22

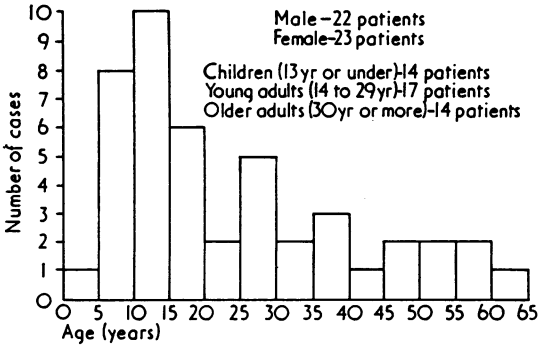

FIG. 1 *Age and sex distribution in 45 cases of craniopharyngioma*

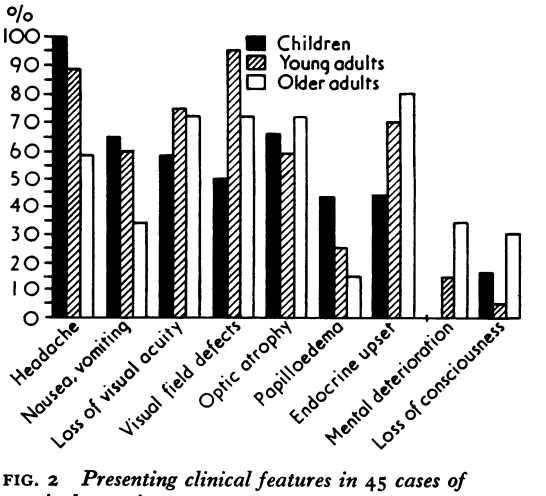

FIG. 2 *Presenting clinical features in 45 cases of craniopharyngioma*

(49 per cent) of the patients in this series had been examined at an eye clinic before being seen by the neurosurgeon.

VISUAL ACUITY

In 27 cases (60 per cent) visual acuity was reduced to 6/12 or less in one eye or both. Although diminished vision was noted less frequently in the children in this series than in either of the adult groups (50 per cent of children, 64 per cent of adults), the difference is not statistically significant. In two children and three adults visual acuity was not recorded because of the patient's age or level of consciousness.

VISUAL FIELDS

The results of visual field examinations are especially informative in this disease. As a presenting feature field loss was detected in 50 per cent of the children, 94 per cent of the young adults, and 71 per cent of those over 30 years of age. Bitemporal hemianopia was present in 12 patients (27 per cent) on first admission. In two of these the fields altered during the course of the illness, becoming homonymous in one case. In addition, a further six patients developed bitemporal hemianopia at a later stage of their illness. Prechiasmal field defects were apparent as presenting signs in nine patients (20 per cent); five had temporal field loss in one eye and central scotomatous loss in the second eye, two showed central or paracentral scotomata in one eye and no defect in the other, and two presented with false homonymous hemianopia. Honomyous hemianopia was the presenting feature in five patients (11 per cent), the optic tracts being involved in three of these and the other two being of the false type attributable to lateral displacement of one optic nerve and involvement of crossing fibres at the anterior chiasmal border. Altogether 11 of our patients (24 per cent) demonstrated a homonymous hemianopia at some stage of their illness, this appearing as a late sign in five (11 per cent). Evidence of tract involvement was present in two (5 per cent) of these. Pleomorphism, that is a distinct change from one type of field defect to another, was found in 10 cases (22 per cent). These changes are exemplified by a 14-year-old boy who survived for $3\frac{1}{2}$ years during which he exhibited bilateral paracentral scotomata, bilateral centro-caecal scotomata, bitemporal hemianopic paracentral scotomata, homonymous hemianopic sector defects, and a unilateral sector defect with general depression in the fellow eye.

Of the remaining patients in this series, full fields were demonstrated initially in nine (20 per cent), while another five (11 per cent) had generally depressed fields. Finally, in five cases (11 per cent) perimetry was impossible.

PAPILLOEDEMA AND OPTIC ATROPHY

A total of 18 (40 per cent) patients were shown to have raised intracranial pressure during their first admission to hospital. Of these, 12 had papilloedema (six children and six adults), and the remaining six had atrophic optic discs, most showing the appearance of primary optic atrophy. Altogether 27 (60 per cent) of our 45 cases had optic atrophy when first hospitalized, and in each age group optic atrophy was commoner than disc swelling, although the children had a higher incidence of papilloedema than the adults.

MISCELLANEOUS OCULAR SIGNS

Strabismus was demonstrable in seven patients (15 per cent), two adults and five children. One of the adults exhibited a transient sixth nerve paresis due to raised intracranial pressure, the other a concomitant convergent squint dating from childhood (see Case 8). All five children had concomitant squints, three convergent and two divergent. In each there was a marked loss of visual acuity in the squinting eye due to pressure by the tumour (see Cases 32 and 42). It is of interest that two of the children had been subjected to squint surgery before presenting at the INS.

An awareness of diplopia, in the absence of squint or palsy, due to defective binocular vision was noted by one adult who had a complete bitemporal hemianopia (Case 39).

Finally, nystagmus of a rotatory type, was seen in one patient, an 8-year-old child with a blind convergent eye and bilateral optic atrophy in whom the intracranial pressure was normal.

ENDOCRINE DISTURBANCES

Table I shows the varied manifestations of pituitary and hypothalamic dysfunction common in all age groups, affecting 29 (64 per cent) of the patients. However, endocrine imbalance was more frequently manifest in the older age groups, being discovered in 70 per cent of young adults and 79 per cent of those over 30 years of age, compared with 43 per cent of the children.

MENTAL SYMPTOMS

Of the older adults five (36 per cent) had a history of loss of memory, depression, retardation, and periods of disorientation or of marked personality change. In two patients an organic dementia had been diagnosed.

Table I *Features of pituitary or hypothalamic dysfunction in 45 cases of craniopharyngioma*

Symptoms	*Children*	*Adults*		*Total*	
		Young	*Older*	*No.*	*Per cent*
Thirst and polyuria nocturia incontinence	4	1	7	12	27
Increase in weight, obesity	3	3	4	10	22
loss of weight	1		1	2	4
Small stature	3	6		9	20
Hypogonadism amenorrhoea sterility loss of libido sparseness of body hair shaving less frequently		9	7	16	36
Skin pallor myxoedematous appearance		1	6	7	16
Somnolence periods of unconsciousness	3	3	5	11	24

RADIOLOGY

Table II shows that routine skull *x* rays in the children revealed abnormalities in all of them and suprasellar calcification in all but one (93 per cent). In contrast, only 76 per cent of the young adults and 50 per cent of the older adults demonstrated abnormal plain *x* rays of the skull, with suprasellar calcification showing in 32 per cent of all adults.

Discussion

Craniopharyngioma is a benign tumour, entirely of ectodermal origin, arising from squamous cell rests derived from the primitive buccal epithelium (Rathke's pouch). These cell rests occur mainly on the infundibulum between the undersurface of the brain and the upper surface of the pituitary (Erdheim, 1904; Carmichael, 1931; Susman, 1932), and it is from these sites that the great majority of craniopharyngiomas develop. The tumour may be wholly suprasellar or partly intrasellar, growing by epithelial proliferation and resulting in masses of avascular solid tissue in which calcification may occur, as well as cysts filled with cellular debris and cholesterol crystals (Matson, 1969). Indeed, about 90 per cent contain cysts, some of which reach very large proportions (Jennett, 1970). Very variable in size and extent, the tumours produce many different symptoms and signs depending on direction of growth, and degree of compression or distortion of the optic pathways, pituitary, hypothalamus, or third ventricle (Figs 3 and 4). Further-

Table II *X ray changes in 45 patients with craniopharyngioma*

Changes found	*Children*	*Adults*		*Total*	
		Young	*Older*	*No.*	*Per cent*
Plain *x* ray of skull					
normal		4	6	10	22
abnormal	14	13	7	34	76
Widening of sutures	5	1		6	13
Digital impressions on vault	2			2	4
Enlarged pituitary fossa	6	8	1	15	33
Erosion of dorsum sellae	8	5	7	20	44
Suprasellar calcification	13	7	3	23	51
Intrasellar calcification	3	2	1	6	13
Skull *x* ray not available			1	1	2

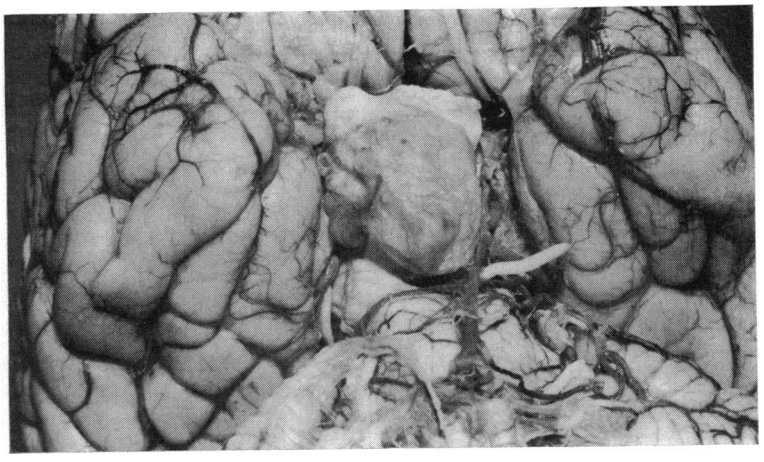

FIG. 3 *A 24-year-old woman (Case 45) who had a craniopharyngioma partially removed 9 months before her death. Hypothalamic structures are obscured by cystic craniopharyngioma which has compressed optic chiasma and displaced it anteriorly*

more, fluctuations in the patient's clinical state are characteristic of craniopharyngiomas, and are said to occur both in solid tumours (perhaps due to local oedema) and in the cystic variety (from intermittent emptying of the cyst into the ventricles; Russell and Pennybacker, 1961). In addition, although the tumour is benign, its growth may at times show the characteristics of an invasive neoplasm (Grover and Rorke, 1968).

One of the striking features in this series was the variation, observed with progression of the disease, in visual acuity and more significantly in visual field loss. More information can thus be gleaned from repeated field testing than from any single measurement. Bitemporal hemianopia was present at the time of diagnosis in only 27 per cent of our patients, an appreciably smaller proportion than one would expect in pituitary adenoma (Lyle and Clover, 1961; Smith, 1964; Wilson and Falconer, 1968). Moreover, during the course of the illness, the bitemporal picture altered in two patients, becoming homonymous in one—a development rarely encountered in pituitary adenoma in which a bitemporal hemianopia if present tends to be persistent. In addition the bitemporal loss in pituitary tumour, whether a hemicentral scotomatous defect or a classical bitemporal hemianopia, tends to progress in an orderly fashion particularly in midline inferior lesions (Wilson and Falconer, 1968). A further six (13 per cent) of our patients developed bitemporal field loss at a later stage of their illness, and in three the hemianopia was inferiorly quadrantic, a finding unusual in pituitary adenoma. It should be noted that bitemporal hemianopia can be seen similarly as a late development in suprasellar meningioma, but is never expected in aneurysm before rupture. Full fields were found initially in nine (20 per cent) of the patients in this study, and this may be regarded as a high incidence compared with pituitary adenomas or suprasellar meningiomas. Indeed, suprachiasmal craniopharyngiomas can extend upwards away from the visual pathways. The prechiasmal field defects which were apparent as presenting signs in nine (20 per cent) of this

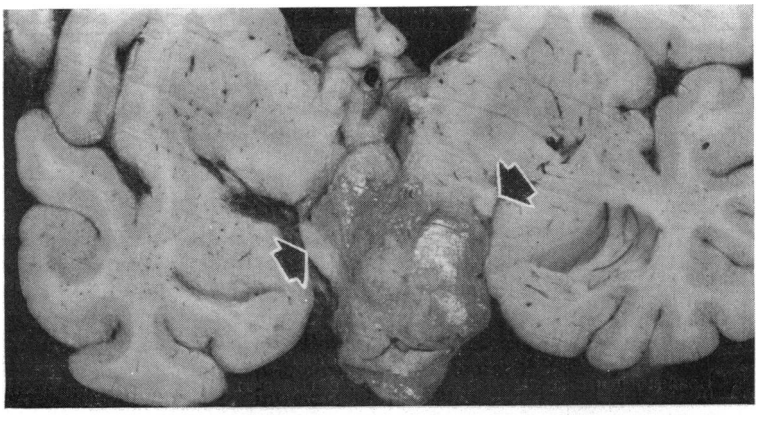

FIG. 4 *Coronal section (Case 45) showing tumour extending upwards into third ventricle. Optic tracts are arrowed. At time of diagnosis of tumour patient's visual fields were full, but 3 months before death she had left-sided homonymous hemianopia*

series, are of a type frequently encountered in pituitary adenomas extending anteriorly between the optic nerves. Homonymous hemianopia is relatively common in craniopharyngioma (Beckmann and Kubie, 1929), and was a presenting feature in five (11 per cent) in this study, the optic tracts being involved in three patients. Tract homonymous hemianopia is an infrequent presenting field defect in pituitary adenoma but, when it does so, once again the defect persists. As we have seen, pleomorphism, a distinct change from one type of field defect to another, was detected in ten (22 per cent) of our patients. This is a characteristic feature of craniopharyngioma and could be related to intermittent emptying of cyst fluid into the ventricular system (Isayama, 1970).

In children, two main presenting syndromes are found (Russell and Pennybacker, 1961). First, there are those who have mainly symptoms and signs of raised intracranial pressure, resulting from obstruction of the third ventricle by the tumour. Secondly, there are those who present with visual failure from compression of the visual pathways. In a few children endocrine and growth abnormalities dominate the clinical picture, and in this series one child presented as a pituitary dwarf. On the other hand, adults with craniopharyngioma most frequently present with visual failure and optic atrophy.

It should be remembered that, in those patients who have raised intracranial pressure, optic atrophy may be found rather than papilloedema. As pointed out by Huber (1961), an atrophic disc is as a rule incapable of developing the typical signs of choking, and in these cases it is impossible to say whether the atrophy is primary from optic nerve pressure, or postpapilloedematous, or both (Smith, 1964).

Strabismus is not uncommonly found in craniopharyngioma patients. There are three groups.

1. Cases of concomitant squint, an esotropia or exotropia following marked loss of central vision in one or both eyes (Wybar, 1971).

Such a squint was present as an early feature in 30 per cent of the children in our study. The poor vision in the squinting eye may be dismissed as strabismic amblyopia, until it is realized that the visual acuity is deteriorating despite treatment. The presence of optic atrophy, or of a sluggish pupil, may be missed in a young child.

2. Cases of paralytic strabismus.

Its incidence in published groups of cases varies widely. Love and Marshall (1950) found third nerve palsy in 20 of 200 cases. Walsh and Hoyt (1969) mention third nerve paresis from direct pressure, and sixth nerve paresis from increased intracranial pressure. Hoff and Patterson (1972) found cranial nerve palsies in 25 per cent of children and 33 per cent of adults they reviewed. Wybar (1971) found two cases of third nerve palsy, and one of sixth nerve palsy, in 72 cases. Only one of our patients had an extraocular muscle palsy, a transient sixth nerve paresis, and it is very surprising that, in view of the massive size of the cystic tumour in many of our patients, there were not more cases of ophthalmoplegia.

3. Cases of so-called 'non-paretic diplopia', where the presence of a bitemporal hemianopia may so reduce the area of visual field overlap common to the two eyes that a disturbance of binocular vision results, there being episodes of diplopia in the absence of demonstrable ocular palsy or defect of ocular movement (Beckmann and Kubie, 1929; Lyle and Clover; 1961; Wybar, 1971).

The results of this series and others indicate that headache is a very common symptom in craniopharyngioma, particularly in children. Although usually frontal, it can sometimes be occipital or unilateral, and has no localizing value (Walsh and Hoyt, 1969). When present in the absence of raised intracranial pressure, it is presumably caused by stretching of the meninges or meningeal blood vessels (Matson, 1969).

It is well documented that mental deterioration may be the only evidence of craniopharyngioma in the older patient (Tiberin, Goldberg, and Schwartz, 1958; Walsh and Hoyt, 1969; Bartlett, 1971). Russell and Pennybacker (1961) give a full description of the mental symptoms shown by these patients, the earliest being a defect of recent memory, often fluctuating, and accompanied by episodes of somnolence and disorientation. More severely affected patients show, in addition, a generally progressive deterioration in intellect similar to the dementia seen in many types of degenerative brain disease. In this series mental symptoms appeared in five adults and in two instances organic dementia had been diagnosed.

The results of this study confirm that routine *x* ray of the skull is of diagnostic value in children suspected of having craniopharyngiomas; the great majority will show characteristic spotty calcification in the suprasellar area (93 per cent in this series). In adults, on the other hand, a normal *x* ray does not exclude craniopharyngioma (in our study 50 per cent of those over 30 years old were normal in this respect).

Case reports

CASE 8

A 20-year-old man, who was fit but slightly obese, attended the eye clinic because of gross deterioration of

vision for 4 years, the right eye being almost blind for 1 year. A childhood squint had become worse 5 years previously. He had had recent headaches. There was a right convergent squint, bilateral primary optic disc pallor, and a sluggish right pupil. Visual acuity in the left eye was 6/24 and there was a temporal hemianopia, while the visual acuity in the right eye was hand movements in the nasal half field only. There were no other neurological signs. *X*-ray studies revealed a huge cystic craniopharyngioma with a little suprasellar calcification, and craniotomy confirmed the presence of a massive cyst, its surface only 1 cm below the surface of the right frontal cortex, extending far back, and arising from the sella, having enlarged and destroyed the sella completely. No trace of the optic nerves was seen, and it appeared that they had been displaced laterally and incorporated in the cyst wall.

CASE 28

A 39-year-old housewife had had supraorbital headaches for 23 years, with occasional vomiting. Recently these symptoms had become worse. There had been amenorrhoea for 3 years, with marked weight gain and nocturnal frequency. She had a transient diplopia due to a short-lived right sixth nerve paresis, a low-grade bilateral papilloedema, and intermittent neck stiffness. Visual acuities were right 6/6 partly and left 6/12 partly; the visual fields were full. There was considerable difficulty in arriving at a correct diagnosis, and *x*-ray studies were inconclusive. It was felt that the most likely diagnosis was benign intracranial hypertension, and treatment with prednisolone produced an initial clinical response. However she had to be readmitted urgently a few months later with an exacerbation of raised intracranial pressure, and craniotomy revealed a craniopharyngioma encroaching on the third ventricle.

CASE 32

A 7-year-old boy presented with a 5 months' history of loss of visual acuity and headaches. At the age of 2 years he had developed a right convergent squint, which had been operated on when he was 4 years old. Subsequently he attended the eye clinic regularly. On admission he had a small residual right manifest convergence, the right eye was virtually blind with an amaurotic pupil, the left visual acuity was 6/9, and there was a complete left temporal hemianopia. The optic discs were pale with blurred edges. Skull *x* rays showed spotty suprasellar calcification. At operation a cystic craniopharyngioma was found compressing the right optic nerve and extending back under the chiasm.

CASE 39

A 35-year-old textile worker, a stout pale-faced placid woman who had never menstruated, complained of blurring of vision of 1 year's duration. She reported that objects doubled and letters ran into each other, but that on covering one eye the difficulty ceased. She consulted an optician who referred her to the eye clinic. Visual acuities were 6/18 in either eye, the optic discs were pale, and she had a complete bitemporal hemianopia. There was no sign of ocular palsy or of any defect of eye movement. The pupils reacted normally. Ventriculography revealed a smooth rounded filling defect in the anterior part of the third ventricle.

CASE 42

A 7-year-old boy was referred from a school eye clinic because of a left divergent squint of 6 months' duration. The visual acuity was 6/9 in the right eye and 6/24 in the left. There was no appreciable error of refraction, and the fundi were normal. There was a constant left manifest divergence of -15°, with eccentric fixation, and slight bilateral limitation of adduction. Occlusive therapy was started, but during the next few months he began to complain of frontal headaches and occasional vomiting, there was progressive visual loss, the left disc became paler, and the pupil less responsive to direct light. The visual fields were full except for a small paracentral scotoma just nasal to fixation in the left field. A skull *x* ray showed erosion of the dorsum sellae and floor of the pituitary fossa and starting of the sutures. Ventriculography revealed a suprasellar mass, and at operation a very large cystic craniopharyngioma was found.

Summary

A total of 45 patients with craniopharyngioma are reviewed, with particular reference to the presenting clinical features and neuro-ophthalmological findings. Of these 50 per cent had been referred in the first instance to an eye clinic. More than half the children presented with the clinical picture of raised intracranial pressure, although one-third of these had optic atrophy rather than papilloedema. One-third of the children had a history of concomitant strabismus, and only one patient had a paretic squint. The majority of the adults presented with visual failure and optic atrophy. Bitemporal hemianopia was fairly frequently found (27 per cent of our patients at the time of diagnosis) but was asymmetrical and unpredictable in its evolution. Homonymous hemianopia was relatively common, a presenting feature in 11 per cent of patients in this study. Full fields were found initially in nine patients (20 per cent), a high incidence compared with pituitary adenomas or suprasellar meningiomas. We consider pleomorphism, that is a distinct change from one type of field defect to another with progress of the disease, to be a characteristic feature of the tumour (as indeed are fluctuations in the clinical state and visual acuity); it was detected in 22 per cent of our patients. Endocrine disorders were common, especially in adults, and mental deterioration was a frequent presenting feature in patients over 30 years of age. Straight *x* rays of the skull are practically diagnostic of craniopharyngioma in children,

but in adults a normal *x* ray does not exclude the diagnosis.

We wish to thank our colleagues in ophthalmology and in neurosurgery whose patients we have been privileged to see. We are particularly indebted to Professor J. Hume Adams and Dr J. Williamson for their advice during the preparation of this paper. The photographs were supplied by Professor Adams, but the diagrams were prepared in the Department of Medical Illustration, Southern General Hospital. We also wish to thank Mrs M. E. Gowan, Head of the Orthoptic School, Glasgow, for her invaluable help. Miss Dorothy Brown provided impeccable secretarial support.

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