Why are Males with Compressive Optic Neuropathy Predisposed to Developing Cranial Nerve Palsy and Binocular Vision Problems?

Inez Eveline Elderman, DipOrth[1]
Meri Vukicevic, PhD[2]

[1]Department of Ophthalmology & Neuroscience, Royal Melbourne Hospital, Melbourne, Australia
[2]Department of Clinical Vision Sciences, La Trobe University, Melbourne, Australia

ABSTRACT

Background: The aim of this study was to investigate the prevalence and characteristics of diplopia and cranial nerve palsies in a group of consecutive patients presenting with suspected compressive optic neuropathy.

Methods: Fifty patients aged 17 to 93 years diagnosed with a brain tumour and possible compressive optic neuropathy were referred to an outpatient orthoptic clinic. The orthoptic investigation included an ocular motility assessment to determine the characteristics of the problems reported. All patients presented with a diagnosed brain tumour and possible compressive optic neuropathy.

Results: Thirteen patients (26%) presented with complaints of diplopia pre-operatively and a cranial nerve palsy was found in 8 of these patients (61.5%) and all were male. This result was statistically significant ($\chi^2 = <0.001$).

Conclusion: The prevalence of cranial nerve palsy found in this cohort of participants was consistent with some of the literature. Interestingly only males with compressive optic neuropathy were affected with cranial nerve palsy. It was not possible, however, to identify a causal factor in this study.

Key words: compressive optic neuropathy; cranial nerve palsy, diplopia.

INTRODUCTION

Compressive optic neuropathies resulting from tumours cause progressive vision loss. Pituitary adenomas cause the most commonly occurring compressive optic neuropathies and account for 6 to 12 % of all intracranial tumours[1,2]. Tumours are usually grouped by size, with a micro-adenoma being less than 10 millimetres (usually arising within the pituitary fossa) and macro-adenomas being larger than 10 millimetres (which grow within the sella and spread from below, superiorly resulting in optic pathway and optic chiasm compression). Classification of the tumour can also be based upon the mass effect of the pituitary secretary function, although one tumour can secrete more than one hormone[3].

Pituitary apoplexy is also associated with pituitary adenomas and is present in 2 to 22% of patients. Males may be more susceptible to the condition[4-7]. The diagnosis is often dependent upon the exact definition of apoplexy used and this varies between researchers. Apoplexy can be diagnosed when only haemorrhage is present in the pituitary gland and this may lead to a higher incidence of the condition. Presenting symptoms of apoplexy usually include severe headache, nausea, vomiting, altered consciousness, ocular paresis and visual field loss caused by haemorrhage or ischaemic infarction of the pituitary tumour[8, 9].

Cranial nerve (CN) palsy present as a result of pituitary tumour has been well documented[8,10-13]. There also seems to be a correlation between paralysis of the cranial nerves, pituitary apoplexy, aneurisms, pituitary adenomas and meningiomas[10,14,15]. Aneurisms can cause CN damage by the sudden dilation of the aneurism and intra-neural haemorrhage and research suggests that women over the age of 50 years are more affected by intra cavernous aneurisms[16]. Meningiomas are more common in women than in men and may cause compressive optic neuropathy and CN palsies[13]. The other mechanism that can cause CN damage occurs when the adenoma grows laterally out of the sella and into the cavernous sinus. This causes compression of the cranial nerves resulting in paralysis[10,15,17]. CN palsy occurs in 10% of patients with pituitary adenoma and CN III is reported as most often affected, followed by CN VI and CN IV respectively[18] although differing rates of CN involvement have been reported. A large retrospective study of 508 patients by Kim[11] found that 2.4% of patients had CN dysfunction and retrospective investigation revealed

Correspondence: **Meri Vukicevic**
Department of Clinical Vision Sciences, La Trobe University, VIC 3086, Australia
Email: m.vukicevic@latrobe.edu.au

that all had apoplexy, with a higher incidence of CN palsy in males. In a much smaller retrospective study investigating 40 patients with pituitary apoplexy, Lubina[9] reported an incidence of 40% of patients with CN palsy. Another large retrospective case series by Elkington[17] found that only 5% of patients had CN palsy and of 98 patients with symptoms of diplopia[14] of these 14% presented with paresis. The researcher suggested that the reason for diplopia symptoms in the remaining patients without paresis can be attributed the phenomenon of "hemifield slide" resulting from a bi-temporal visual field defect where there is difficulty in accurately registering the image in the intact hemifield. The consensus among all researchers, however, is that CN III is the most commonly affected nerve. It also appears that decompression of the tumour reduces the CN palsy and improves ocular motility[5,11].

The aim of this prospective study was to investigate the prevalence and characteristics of diplopia and CN palsy in consecutive patients presenting with a brain tumour and with a possible compressive optic neuropathy.

METHODS

This study comprised of 50 consecutive patients diagnosed with a brain tumour and a possible compressive optic neuropathy who were referred by a neurosurgeon to an outpatient orthoptic clinic for investigation of their ocular status within one month prior to neurosurgery. All procedures used in the study were approved by the hospital human research and ethics committee and all participants provided written consent for testing procedures. In addition, patient anonymity was preserved at all times.

A comprehensive ocular history was taken for each participant, including the reason for referral to the orthoptic clinic. Complaints of diplopia were documented and thorough investigation of visual acuity and ocular motility was conducted pre- and post-operatively. The ocular motility examination included a cover test at near and distance and prism cover test in 9 positions of gaze. Where participants complained of diplopia, careful assessment was conducted to differentiate diplopia resulting from paralytic or non paralytic strabismus and also between binocular and monocular diplopia. Where there was evidence of a manifest strabismus or decompensating phoria with corresponding diplopia, this was classified as binocular diplopia. Monocular diplopia, which occurred when viewing with only one eye and was due to pathology of the cornea or lens, was also documented.

If a participant was found to have an ocular motility disorder, a complete diagnosis was made, based upon the orthoptic investigation. To ensure that the researcher was blind to any potential cause of CN palsy, the participant's neurology results were examined after the initial diagnosis. This included results of MRI or CT scans, radiology reports operation reports and correspondence letters which enabled determination of evidence of lateral extension of the optic neuropathy which may have caused compression of CN III, IV or VI in the cavernous sinus. Any evidence of aneurism, apoplexy, haemorrhages or signs of previous brain surgery were also documented. Retrospective analysis of patients' neurological records was also conducted to confirm which participants had true compressive optic neuropathy.

RESULTS

The age range of the participants in this study was 17 to 93 years with a mean age of 53 years (SD=16.2). There was a slightly higher ratio of males (58%) compared with females (42%). All participants underwent surgery to remove the tumour and trans-sphenoidal resection was performed on 48 participants (96%). The remaining 2 participants underwent craniotomy. Evidence of previous brain surgery was found in 12 participants (24%). However, this was investigated retrospectively and was based upon investigation of the participant's clinical file; it is therefore possible that some participants with previous surgery were missed in this analysis. Signs and symptoms of apoplexy or haemorrhage were found in 10 participants (20%) and were based on the participant's clinical file for documented apoplexy. This finding may have also been skewed due to the method of investigation of this particular variable.

The most commonly occurring pathology was macro adenoma, found in 68% of participants and the retrospective analysis of the patient files indicated that 35 participants (70%) had compression of the optic pathway. An overview of tumour types and confirmed visual pathway compression is show in Table 1.

The best corrected visual acuity of each participant was measured pre- and post-operatively and was found to range between 6/4 and 6/60 at both testing times with an average acuity of between 6/6 and 6/7.5. Seventy six percent of participants had visual acuity better than 6/6 in the right eye prior to surgery and post surgery 88% were found to have visual acuity better than 6/6. For the left eye, 72% had acuity better than 6/6 with 84% of participants with acuity

Table 1. Tumour type and confirmed compression

Tumour Type	Frequency (%)	Confirmed Compression (%)
Macro adenoma	34 (68%)	29 (58%)
Micro adenoma	5 (10%)	0 (0%)
Cyst	8 (16%)	4 (8%)
Craniophayngioma	1 (2%)	1 (2%)
Meningioma	2 (4%)	1 (2%)
Total	50 (100%)	35 (70%)

better than 6/6 post operatively. The improvement in visual acuity was found to be statistically significant for both eyes after removing the tumour (Right eye: Z=-3.39, P<0.05; Left eye: Z=-2.09, p<0.05).

In this study, fourteen participants (28%) complained of diplopia. Thirteen participants (26%) presented with complaints of diplopia at the first clinic visit and 1 participant complained of diplopia post-operatively as a result of a CNIII palsy with an onset after surgery. This participant was removed for the purposes of data analysis in this study.

CN palsy was found in 8 of the 50 participants (16%) and the most commonly occurring CN palsy involved CN III, followed by CN IV and CN VI respectively. Eight participants (61.5%) of the 13 who reported diplopia pre-operatively were also diagnosed with a CN palsy. Of the remaining 5 participants, 3 were diagnosed with a decompensating phoria and 1 with monocular diplopia as a result of cataract. The remaining participant, who did not present with CN palsy but with diplopia, had an unconfirmed diagnosis. He reported the diplopia to occur when he was feeling unwell or tired, but his clinical signs were complicated with the presence of cataract and bitemporal haemianopia. It is therefore possible that he could was suffering from either monocular diplopia, "hemifield slide" as described by Elkington[17] or decompensating phoria which could not be decompensated during the clinical visits.

Table 2 shows a summary of participants with complaints of diplopia. Of the participants with pre-operative CN palsy (n=9), all were male. The higher ratio of males was found to be statistically significant (χ^2 =<0.001).

Investigation of the clinical file revealed that an underlying cause of CN palsy could be found for 6 of the 8 participants (75%). Lateral extension of the tumour was found in 3 participants (37.5%) and 3 participants (37.5%) had evidence of apoplexy pre-operatively. Evidence of previous brain surgery was present in the remaining 2 participants (25%) and it is possible that residual scar tissue may have contributed to the CN palsy, however this could not be confirmed.

Thirty-five participants of the total group had compression on the optic pathways and 10 (28.57%) of these patients evidenced true compression with binocular vision problems. The evidence of compression was found on participants radiology reports. Within the group of participants with pre-operative CN palsy all had true compression and all were male.

The CN palsy was found to be reduced after decompression of the tumour in 2 participants (25%), stable in 3 (37.5%) and resolved in 3 participants (37.5%) within the first 1 to 3 months of presentation to the orthoptic clinic (Table 2).

Whilst apoplexy or evidence of haemorrhage within the pituitary gland was found in 10 of the 50 participants (20%), only 3 participants with binocular vision problems were found to have apoplexy (Table 2). There was no statistically significant difference in the rate of apoplexy present between participants with and without binocular vision problems (χ^2=0.40). Due to the extremely high proportion of males with CN palsy, the difference between males and females and presence of apoplexy for all participants in this study was also investigated but no statistically significant difference was found (χ^2 =0.58). There was one female patient who presented with complaints of diplopia, and

Table 2. Summary of participants with complaints of diplopia, investigated prospectively

ID	Age	Sex	Diplopia	CN palsy	Type of Compressive optic neuropathy	Reason for diplopia if no CN palsy present	Apoplexy	Status of CN palsy after surgery
IC	56	M	Binoc.	IV	Macro adenoma*	-	-	Reduced [(a)]
TK	17	M	Binoc.	III,IV & VI	Macro adenoma*	-	Yes	Resolved [(b)]
JL	70	M	Binoc.	VI	Macro adenoma*	-	-	Resolved
MM	41	M	Binoc.	III	Macro adenoma*	-	-	Stable[(c)]
OM	61	M	Binoc.	III	Macro adenoma*	-	-	Stable
RD	79	M	Binoc.	IV	Macro adenoma*	-	-	Stable
GS	69	M	Binoc.	III	Macro adenoma*	-	-	Reduced
WT	50	M	Binoc.	III	Macro adenoma*	-	Yes	Resolved
AT	42	M	Binoc.		Macro adenoma*	#	-	-
PR	44	F	Binoc.		Macro adenoma*	Decomp. phoria	-	-
MS	53	F	Binoc.		Meningioma	Decomp. phoria	-	-
PM	70	F	Binoc.		Macro adenoma*	Decomp. phoria	-	-
LP	66	M	Monoc		Micro adenoma	Cataract	-	-

* Participants with evidence of compression on the pathways, investigated retrospectively. # Diplopia could be attributed to decompensating phoria, hemifield slide or cataract. (a) Reduced: the diplopic images are closer together and the angle of the strabismus was reduced compared with the first visit (b) Resolved: no diplopia, evidence of binocularity and no measured manifest strabismus (c) Stable: no change in diplopia or measured angle of strabismus compared with the first visit.

a meningioma was diagnosed when the researchers investigated the neurological reports retrospectively, but no evidence was found for a CN-palsy.

The relationship between previous brain surgery and binocular vision problems was examined as was the difference between previous brain surgery and CN palsy and no statistically significant relationships were found (Binocular vision: $\chi^2 = 0.27$; CN palsy: $\chi^2 = 0.43$).

DISCUSSION

Pituitary adenomas are reported as the most commonly occurring intracranial tumour[8,18] and the findings of this study are consistent with the literature. However, the prevalence of adenoma was significantly higher in this cohort of participants (78%) compared with the reported prevalence of between 6 and 12%. This finding may be skewed in this study as a large proportion of patients with compressive optic neuropathy are specifically referred to the orthoptic clinic.

The prevalence of CN palsy found in this cohort of participants was 16% and is similar to that reported by Elkington[17] and Ironside[2]. This differs significantly to the studies of Kim[11] and Lubina[9] who report a prevalence of 2.4% and 40% respectively. However, these researchers only included patients with evidence of apoplexy. A CN III palsy is described as the most commonly occurring palsy and the findings of this study are consistent with the literature.

The most interesting finding in this study was that only males with a compressive optic neuropathy were affected with CN palsy. It seems that males are more susceptible to developing apoplexy[4-7] and this may contribute to the development of a CN palsy. It was difficult to identify a causal relationship between CN palsy and apoplexy in this study, however as previously explained, the definition of apoplexy may differ and the presence of this condition was noted upon retrospective investigation of the participant's file notes and may have skewed the findings. Other possible causes for the higher presence of CN palsy in males such as the type of tumour, presence of apoplexy or haemorrhage or lateral extension of the tumour could not be identified as part of this study.

Almost a third of the participants in this study presented with diplopia of varying aetiology. This significant figure may be due to the fact that all participants were examined by an orthoptist, specifically trained in the detection and diagnosis of such ocular motility disorders. Diplopia was a presenting complaint to the orthoptic clinic and careful investigation of the aetiology of the diplopia was important to distinguish monocular from binocular and careful examination was also required to detect CN palsy. Whilst some binocular vision problems could be explained by decompensating phorias, most were as a result of CN palsy and it was found that the CN palsy was either reduced or completely resolved in a high proportion of participants after decompression of the tumour.

CONCLUSION

Whilst the researchers were not specifically investigating whether males or females were more likely to suffer with binocular vision problems, the finding of a higher prevalence of males with CN palsy cannot be answered here and is worthy of further research. A more thorough examination of the effects of the presence of apoplexy or the type and characteristics of the compressive optic neuropathy upon palsy is needed. However, this type of investigation was beyond the scope of the present study.

A significant proportion of patients with compressive optic neuropathy may present with diplopia or CN palsy. Often the symptom of diplopia is considered less important by neurosurgeons compared with the other symptoms experienced by the patients which, in the case of apoplexy, may be very severe. However, diplopia can be disconcerting for sufferers and patients require thorough investigation of the ocular motility problem when referred to an orthoptist and possible reassurance that, in the case of CN palsy, may resolve post trans-sphenoidal resection or craniotomy.

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