Analysis of the recovery of third nerve function after direct surgical intervention for posterior communicating aneurysms

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Jefferson (1947) reported 55 cases of isolated third nerve palsy caused by intracranial aneurysm; 23 were treated by carotid ligation and, on reviewing all survivors, he found that:

"Although considerable recovery takes place in time, the nerve in my experience almost never regains function so completely that there is perfect mobility of the globus oculi in all directions and with parallel visual axes."

Others have reported improvement after carotid ligation. Hamilton and Falconer (1959) found that all third nerve palsies improved with surgery, although they state that slight persisting weakness of the extraocular muscles was not assessed. Cantu (1969) graded the amount of third nerve recovery after carotid ligation. Grades I and II were regarded as satisfactory while III and IV were unsatisfactory. Grade I included those with slight pupillary abnormality or a restriction of less than 30 per cent. in the functional amplitude of any muscle; Grade II could include diplopia in upward gaze, intermittent horizontal diplopia, ptosis of small degree, or minor examples of aberrant regeneration (such as the pseudo-Graefe sign). He stated:

"Recovery of third nerve function was dramatically better in patients undergoing carotid ligation (nine satisfactory, five unsatisfactory) compared to non-surgical management (one satisfactory, five unsatisfactory)."

Raja (1972) used the same grading system on 42 patients with an aneurysm-induced third nerve palsy. He found that carotid ligation within 14 days of the onset of the palsy gave a better chance of recovery than ligation performed after 14 days.

Botterell, Lloyd, and Hoffman (1962) suggested that full recovery from a complete third nerve paresis occurred if direct surgical attack on the aneurysm was undertaken within 10 days of the onset of the paresis. Two of their patients, who had incomplete palsies pre-operatively, recovered fully after the paresis had been present for more than 10 days. However, Paterson (1968), in 28 cases also treated by direct surgical attack, found that:

"... although recovery from the third nerve palsy was complete from a subjective point of view, on testing ocular movements, all patients had some slight impairment of upward gaze in the originally affected eye."

The statistical significance of all these figures is doubtful. With Fisher's test (1934), none of them reaches the 5 per cent. probability level.

The present paper reports the results of a detailed orthoptic analysis of 26 cases of third nerve paresis associated with a posterior communicating aneurysm. The neurosurgical aspects of this series have been published elsewhere.

Material

This paper includes only cases of an oculomotor paresis due to an aneurysm of the internal carotid artery arising at or near to the junction of the posterior communicating artery, and treated surgically by a direct intracranial approach.

100 patients had such a procedure in the series reported by Soni (1974) of 175 posterior communicating aneurysms.* 38 patients were noted to have a preoperative third nerve paresis. Of these, eleven died within a few weeks of operation, five died of unrelated causes, two were living abroad, and one was untraced. The remaining nineteen were all seen by an orthoptist (V.A.S.).

In 62 patients there were no signs of a third nerve paresis preoperatively, although nine were noted to have a third nerve paresis for the first time immediately after operation. One died within a few days of the operation and one 4 years later. The remaining seven are reported although Cases 1 and 6 were seen by only one member of us (S.R.S.) and did not have a full orthoptic examination.

Cases 6 and 7 have been classified as cases of postoperative paresis in spite of having abnormal pupils before operation:

Case 6

Noted on admission to have a "minor inequality of the pupils which could well have been within normal limits". Postoperatively, there was a complete left third nerve palsy, gross right homonymous hemianopia, and a right hemiparesis.

Case 7

Admitted 12 days before operation after a subarachnoid haemorrhage. 6 days preoperatively she developed a left hemiparesis and left homonymous hemianopia as well as a dilated right pupil, but there was no ptosis. At operation, the aneurysm was found to be adherent to the third nerve. Postoperatively there was definite right ptosis and diplopia.

Method of assessment

The patient was asked about ocular symptoms; if diplopia occurred, its type was recorded, and the following were noted:

- (1) Visual acuity for distance and near, with and without glasses.
- (2) Cover test with head erect and also with any compensatory head posture.
- (3) Pupil size when viewing distance and near, direct and consensory responses.
- (4) Near-point rule was used to assess uniocular accommodation and binocular convergence.
- (5) Ocular movements were observed with special reference to any abnormality. A Hess chart was plotted which was later graded by the orthoptist and ophthalmologist (independently) into normal, slight, or severe defects. Ptosis was measured and the lids were observed on depression and elevation of the globe, with special reference to abnormal movements. All patients were examined for the pseudo-Graefe phenomenon.

Results

Table I (overleaf) lists the patients in order of duration of third nerve paresis before operation. It is apparent that there was no complete recovery if signs had been present for

* One additional patient traced after original series prepared

Table I Findings in 26 cases

Case no.	Sex	Age (yrs)	Eye	Duration of 3rd nerve paresis (days)	Interval between first symptoms and operation (days)	No. of subarachnoid haemorrhages	Duration of follow-up (yrs)	Full recovery	Time elapsed before recovery (mths)	Hess chart defect
1	M	32	L	—	28	1	2	+	6	—
2	M	34	R	—	4	1	5	+	21	No
3	F	40	R	—	6	1	6	+	1	No
4	M	44	L	—	10	2	4	+	6	No
5	M	32	L	—	42	2	3	+	< 36	No
6	F	56	L	—	20	1	12	—	—	?
7	F	47	R	—	12	1	4	+	4	No
8	F	57	R	1½	31	1	4	+	26+	No
9	F	33	R	3	11	2	12	+	< 60	No
10	M	43	R	4	8	1	3	+	4	No
11	F	37	L	5	10	—	3	—	—	+
12	F	54	L	5	18	1	14	—	—	++
13	M	44	L	7	14	—	13	—	—	Too ill
14	F	47	R	8	8	—	2	—	—	++
15	F	53	R	9	30	3	5	+	12	No
16	F	39	L	10	11	—	6	—	—	++
17	F	30	R	10	21	—	18	—	—	++
18	F	25	R	11	14	—	1½	—	—	+
19	M	41	R	12	19	1	13	—	—	++
20	F	58	R	20	20	1	10	—	—	++
21	F	66	R	21	23	—	2½	—	—	++
22	F	63	L	21	30	1	9	—	—	++
23	M	51	R	30	60	—	8	—	—	++
24	F	54	L	43	43	1	4	—	—	++
25	F	61	L	60	270	—	3	—	—	++
26	F	59	L	90	90	2	13	—	—	++

more than 9 days. Postoperative onset of third nerve paresis was associated with complete recovery in six of the seven cases.

Full recovery occurred in four patients out of eight in whom a third nerve paresis had been present for less than 10 days before craniotomy. Of the other four, two developed signs of aberrant regeneration, and two were followed for less than 3 years.

Case 11

Presented 10 days before surgery with severe headache above the left eye which radiated to the back of the neck. 5 days before surgery, she was unable to open her left eye. At operation, the third nerve was noted to be grossly swollen and discoloured. 3 years later, she has a minimal deficit on the Hess screen, and weakness on depression; the left pupil is larger than the right but there is no ptosis.

Case 12

2½ weeks before surgery severe pain developed in the ophthalmic division of the fifth cranial nerve. 5 days preoperatively she developed a partial third nerve paresis which became complete 4 days later. The same day she became comatose and direct surgical exploration revealed the aneurysm. She has a sluggish left pupil 14 years later; there is no ptosis but the left eye adducts on attempted elevation.

Diplopia	Adduction on attempted elevation	Pseudo- Graefe phenomenon	Defective elevation	Defective depression	Ptosis	Pupil dilation	Visual acuity		Synoptophore readings	
							R	L	Fixing right	Fixing left
No	—	—	—	—	—	—	Not done		Not done	
No	—	—	—	—	—	—	6/6	6/5	+3 R/L ¹	
No	—	—	—	—	—	—	6/5	6/6	+4 ⊕	
No	—	—	—	—	—	—	6/6	6/6	0	0
No	—	—	±	—	—	—	6/6	6/6	+2 ⊕	
No	+	—	+	+	—	—	Not done		Not done	
No	—	—	—	—	—	—	6/9	6/9	+2°	+1°
No	—	—	—	—	—	—	6/9	6/9	+2 ⊕	
No	—	—	—	—	—	—	6/9	6/9	0	
No	—	—	—	—	—	—	6/5	6/4	+3 ⊕	
+	—	—	—	+	—	+	6/4	6/18	0 R/L ¹	+2 R/L ¹
++	+	—	—	—	—	+	6/5	6/5	-2 R/L ⁷	-2 R/L ¹⁹
See text	—	—	+	+	—	—	6/9	6/18	Hirschberg +15	
+	—	—	+	+	+	+	6/6	6/6	+4 R/L ⁷	+4 L/R ²
No	—	—	Both	—	—	—	6/5	6/5	+1 ⊕	
+	+	+	+	+	+	+	6/6	6/12	-7 ⊕	-5 L/R ³
+	+	—	+	+	+	++	6/7.5	6/5	+4 ⊕	+4 ⊕
+	—	—	—	+	—	—	6/6	6/6	+2 ⊕	+2 ⊕
+	+	+	+	+	—	+	6/5	6/5	+2 L/R ¹	+2 ⊕
+	+	—	+	—	—	+++	6/36	6/24	at 15° down	L/R ⁴
++	—	—	+	+	+	++	6/12	6/6	+8 L/R ³⁸	+8 L/R ¹³
++	+	—	+	+	—	+	6/9	oc.	-10 L/R ²	-5 L/R ¹²
+	+	—	+	+	—	++	6/18+	6/5	+10 L/R ⁹	+6 L/R ⁵
++	+	+	+	+	+	+	6/6	6/18	-17 R/L ⁶	-10 R/L ⁸
+	—	—	+	+	+	+	?	?	-5 ⊕	-8 ⊕
+	+	—	+	+	+	+	6/5	6/5	+10 R/L ²⁸	

Case 13

There was pain in the left side of face and eye for 2 weeks, and a drooping lid 1 week before surgery. Angiography showed bilateral posterior communicating aneurysms. The left aneurysm was clipped directly although there was considerable bleeding. Postoperatively, he had a left hemiparesis and dysarthria. 13 years later, he was confined to a wheelchair and could not co-operate for a Hess screen test. The left pupil was sluggish, there was defective elevation and depression, and on attempted depression of the eye, it became adducted.

Case 14

There was a history of headaches for 2 years which were especially severe for 1 month before surgery. 8 days preoperatively, she had diplopia, ptosis, a dilated pupil, and impaired movements of the right globe. 6 months after operation she showed only slight ptosis, a slightly enlarged pupil, and absent elevation. 2 years postoperatively, these minimal signs are still present, together with diplopia on looking up.

The remaining eleven cases (*i.e.* those with third nerve signs of 10 days' duration or more) are summarized in Table I.

The time taken for full recovery of third nerve function varied from 1 month to at least 2 years.

In sixteen cases with residual evidence of a third nerve paresis, follow-up varied from 15 months to 18 years. Signs of aberrant regeneration were found in eleven cases (6, 12, 13, 16, 17, 19, 20, 22–24, 26). In ten cases, the eye was noted to become adducted on attempted elevation, and in one case to become adducted on attempted depression (Case 13).

In only three cases (16, 19, 24) did the classical pseudo-Graefe sign appear (*i.e.* elevation of the upper lid on downward gaze.) However, in four other cases (17, 21, 24, 25), the lid movements were abnormal in that the upper lid failed to descend, on downward gaze.

Pupillary abnormalities noted in thirteen cases (11, 12, 14, 16, 17, 19–26) mainly comprised an increase in pupil size and sluggish reactions. No case of an atypical Argyll Robertson pupil was found.

Discussion

The striking result is that full recovery of third nerve function occurred, but only in those cases in which it had been present for less than 10 days before craniotomy. Recovery did not appear to be related to the preoperative severity of the paresis (although insufficient detail is given in the case notes for a reliable analysis).

Comparing the eight patients who had third nerve symptoms for less than 10 days, of whom four recovered completely, with eleven patients who had third nerve symptoms for more than 9 days, of whom none recovered completely, this is likely to occur by chance in less than 5 per cent. (*i.e.* statistically “probably significant”) see Table IIA. If the pareses developing postoperatively are included, there is a significant difference at the 1 per cent. level (Table IIB). This is also true if Case 7 (with 6 days’ pupillary involvement) is included as one of preoperative paresis (Table IIC).

Botterell and others (1962) used the tenth day as a dividing line, and it is tempting to combine results. Botterell’s figures do not reach the 5 per cent. level (Table IID), but together with our figures, they easily reach the 1 per cent. level, whether one excludes or includes our postoperative third nerve palsies (Tables IIE, F).

Because the frequency of neurosurgical follow-up varied, it is difficult to state exactly when full recovery occurred. Thus Cases 9 and 15 were noted after 1 year to have definite evidence of a third nerve paresis, but after 5 years to be fully recovered. Case 8 was noted at 26 months still to have some ptosis, but at 55 months this patient was orthoptically normal and did not require the occlusion that she was still wearing.

Walsh (1957) gave a clinical evaluation of third nerve regeneration and, while noting one exceptional case, stressed that recovery of a third nerve paresis caused by an aneurysm was almost invariably associated with aberrant regeneration.

All our cases of aberrant regeneration have been followed for at least 3 years. Five other cases (11, 14, 18, 21, 25) are of particular interest in that they have been followed for less than this period. They still show signs of a third nerve paresis and may well develop aberrant regeneration later.

Cases 21 and 25 were last seen some 32 months after operation. They both had a severe defect on Hess testing and the lid failed to descend on downward gaze. Presumably these cases may develop, or are developing, aberrant regeneration. Cases 11 and 14 (already detailed) have been followed for 37 and 26 months respectively, but have been fairly static for the past 18 months. Case 18 has been followed for only 15 months; there has been progressive improvement and this patient appears to be heading for complete recovery.

It is generally accepted that third nerve regeneration does occur, and that misdirection of sprouting axons can occur. Consequently, after regeneration, as Walsh and King (1942)

Table II *Results related to duration of paresis before operation*

Duration of paresis (days)		9 or less	10 or more	Total	Statistical significance (Fisher's test)
A Preoperative only	Full recovery	4	—	4	5% > P > 1%
	Residual paresis	4	11	15	
	Total	8	11	19	
B All cases	Full recovery	10	—	10	P < 1%
	Residual paresis	5	11	16	
	Total	15	11	26	
C Excluding Cases 1-6	Full recovery	5	—	5	P < 1%
	Residual paresis	4	11	15	
	Total	9	11	20	
D Cases reported by Botterell and others (1962)	Full recovery	6	2	8	P > 5%
	Residual paresis	5	9	14	
	Total	11	11	22	
E Series A + D	Full recovery	10	2	12	P < 1%
	Residual paresis	9	20	29	
	Total	19	22	41	
F Series B + D	Full recovery	16	2	18	P < 1%
	Residual paresis	10	20	30	
	Total	26	22	48	

pointed out, any effort to move the eye will cause impulses to flow to all muscles innervated by the third nerve. It is not yet clear if this is simply misdirection of a fibre into the wrong sheath or a mass response through a glial scar. None the less, movements up or down are likely to counteract each other, while the medial rectus and levator palpebrae are free to move. Many authors have noted elevation of the lid on adduction, but it has not often been stressed that the eye may adduct on attempted elevation. It is mentioned by Duke-Elder and MacFaul (1972), who classified the signs of aberrant regeneration as follows:

- (1) Dyskinesia of the lid in horizontal gaze: elevation of the involved lid on adduction of the globe.
- (2) The pseudo-Graefe sign: retraction and elevation of the lid on downward gaze.
- (3) Limitation of upward and downward gaze with attempted retraction of the globe on vertical movement.
- (4) Adduction of the involved eye on attempted depression or elevation.
- (5) A pseudo-Argyll Robertson pupil, wherein the dilated pupil will not react to light but will contract on convergence and also on adduction in conjugate gaze.

(6) Uniocular vertical optokinetic response wherein the normal eye responds as usual but the involved eye shows suppressed vertical responses.

Our series suggests a rearrangement of this list in order of importance. Category 4 could thus be the most important sign of aberrant regeneration and is easily divided into two classes:

- (a) Adduction on attempted elevation (10 of 11 cases = 91 per cent.)
- (b) Adduction on attempted depression (only 1 case = 9 per cent.)

Next in importance is Category 2, the pseudo-Graefe sign, found in three cases (27 per cent.).

Category 3 is difficult to assess in terms of true aberrant regeneration. Limitation of gaze may be due solely to the paresis and hence retraction of the globe is essential. However, if lid elevation occurs, it may mask retraction of the globe, and is therefore not a clinically useful sign.

Category 1, elevation of the lid on adduction, was not noted in any patient to any reliable extent, and Category 5 was not noted at all. Category 6 was not looked for.

The obvious drawback to these arguments is the small number of patients (only eleven cases of acknowledged aberrant regeneration). From other published series, as well as this paper, it is obvious that there is a need for more cooperation between the ophthalmologist and neurosurgeon in the management and assessment of these cases. Case 8, wearing her patch quite unnecessarily, is an apt illustration of this point. Subjective recovery is accepted by all workers as being very common. It is rare for such patients to need surgical correction or even prisms for their diplopia, as compared with the much more demanding patient with endocrine ophthalmopathy. The presence of aberrant regeneration may indicate the need for more definitive action by an ophthalmologist, whereas before it appears, one may prefer to wait for recovery.

Conclusion

Aberrant regeneration of the third cranial nerve is most commonly seen as adduction on attempted elevation of the globe. Once present, further recovery of third nerve function is unlikely. Complete recovery is possible and may take up to 3 years if surgery (direct intracranial approach) is undertaken within 10 days of the onset of the third nerve palsy.

In this series, however, there was a 29 per cent. mortality of those patients who had a preoperative third nerve palsy, and the fate of the third nerve after operation is only one of a number of factors that the neurosurgeon must evaluate. None the less, the authors feel that greater awareness of aneurysm as a cause of third nerve palsy would lead to quicker treatment, which would reduce morbidity.

Summary

Orthoptic analysis confirms that full recovery of a third nerve palsy associated with a posterior communicating aneurysm is possible but may take well over 2 years. It occurred only if the aneurysm was treated by direct intracranial surgery within 10 days of the onset of the paresis.

Those patients who did not recover completely and had been followed for over 3 years all showed aberrant regeneration. The commonest single sign of this was adduction of

the eye on attempted elevation (91 per cent.; the more classical pseudo-Graefe sign occurred in only 27 per cent.).

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