Unruptured Aneurysms with Cranial Nerve Symptoms: Efficacy of Endosaccular Guglielmi Detachable Coil Treatment

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Objective: To evaluate the efficacy of endosaccular Guglielmi detachable coil (GDC) treatment of unruptured aneurysms causing cranial nerve (CN) symptoms.

Materials and Methods: Among a database of 218 patients whose aneurysms were treated using GDC, seven patients met the criteria for unruptured aneurysms presenting with symptoms and signs of CN palsy. Changes in CN symptoms before and after GDC treatment were reviewed.

Results: Aneurysms were located in the internal carotid-posterior communicating artery (n=3), the basilar bifurcation (n=1) and the cavernous internal carotid artery (n=3). CN symptoms included ptosis (n=6), mydriasis (n=2), and extraocular muscle (EOM) disorder (CN III: n=4; CN VI: n=3). Overall, improvement or resolution of CN symptoms after treatment was noted in five patients. CN symptoms in cases involving small ($\leq$10 mm) and intradural aneurysms tended to respond better to GDC treatment. Ptosis was the initial symptom to show improvement, while EOM dysfunction responded least favourably.

Conclusion: GDC coil packing appears to be an appropriate treatment method for the relief of CN symptoms associated with intracranial aneurysms.

Index terms:
Aneurysm, cerebral
Aneurysm, therapy
Nerves, cranial
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Embolization with Guglielmi detachable coils (GDC) has recently been advocated as a safe and less traumatic alternative for the treatment of intracranial aneurysms, and is accepted as an effective and safe method for preventing rehemorrhage of ruptured cerebral aneurysms (1). However, only a limited number of reports have described the effects and outcome of endosaccular coiling of aneurysms causing mass effects on cranial nerves (CN), and even less attention has been given to the respective symptoms of CN dysfunction and its outcome after endosaccular coil-packing treatment (2–4). The purpose of this article is to evaluate the effect of intra-aneurysmal GDC coil packing on CN symptoms and signs, and also to evaluate the responses of these to GDC treatment.

MATERIALS AND METHODS

Between March 1996 and August 2002, 218 patients with intracranial aneurysms were treated by means of endosaccular GDC packing (Boston Scientific, Fremont, Cal., U.S.A.) at our institution. Eighty of these patients had been treated for unruptured aneurysms (including those found incidentally), for coincidental unruptured aneurysms [in patients with aneurysmal subarachnoid hemorrhage (SAH)], or for those in which mass effect had occurred. Among patients with unruptured aneurysms, seven fulfilled the following criteria: 1) they had shown specific CN symptoms and

signs consistent with the location of the aneurysm, and 2) they had undergone endosaccular packing of aneurysms, using GDC coils. Their medical records were analysed retrospectively, and they were interviewed by telephone.

The following CN symptoms and signs were evaluated: ptosis; diplopia, arising from oculomotor external ocular muscle (EOM) dysfunction; mydriasis, in patients with oculomotor CN neuropathy; and lateral rectus EOM dysfunction in those with abducens CN neuropathy. The duration of respective symptoms and signs prior to endovascular treatment and the outcome of the respective signs were evaluated, and the outcome was classified as improved, resolved, unchanged, or worsened. The time taken for CN signs to show initial improvement after endovascular treatment was determined, and clinical evaluations were performed at preembolization, immediate post embolization, monthly outpatient follow-up after embolization, and then bimonthly and at the final outcome.

Aneurysms were assessed in terms of their location, size (longest diameter), and the results of GDC treatment. Location was classified as intradural or extradural, and size as small (≤10 mm) or large (> 10 mm). GDC treatment outcomes were categorized as complete, small neck remnant, small aneurysmal remnant, or incomplete.

RESULTS

Table 1 summarizes the features observed at clinical presentation and the aneurysmal characteristics. All patients were female, and their mean age was 63 years. The aneurysms were located intradurally in four patients [internal carotid-posterior communicating artery (IC-Pcom) (n=3); basilar bifurcation (n=1)], and extradurally [cavernous internal carotid artery (ICA)] in three. Their mean size was 11.5 mm and the mean follow-up period was 23 months.

Overall, two patients (29%) showed complete resolution of all CN symptoms, three (43%) showed some improvement, and in two (29%), symptoms were unchanged or worsened.

The incidence of the respective CN signs according to the location of the aneurysm is shown in Fig. 1. For IC-Pcom aneurysms (n=3), ptosis and EOM dysfunction was present in all patients, and mydriasis occurred in two. The basilar bifurcation aneurysm (n=1) gave rise only to symptoms of ptosis, while for cavernous ICA aneurysms (n=3), ab-

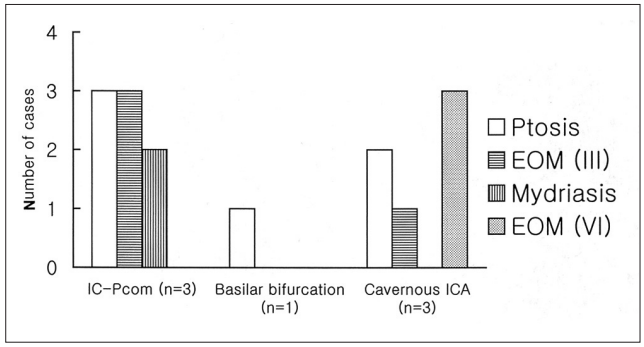

Fig. 1. Incidence of cranial nerve signs according to aneurysm location.
Note.— EOM(III): extraocular muscle dysfunction, cranial nerve III, IC-Pcom: internal carotid-posterior communicating artery

Table 1. Findings in Seven Patients with GDC-treated Unruptured Aneurysms Presenting with Cranial Nerve Signs

Patient	Age/Sex	Location	Size (mm)	GDC Result	Symptom Duration	F/U	Presenting Signs	Improvement Noted at:	Outcome
1	79/F	IC-Pcom	9	neck	6 d	48 m	Pt	2 m	R
							EOM (III)	2 m	I
							Myd	N/A	R
2	55/F	IC-Pcom	9	neck	64 m	6 m	Pt	4 m	R
							EOM (III)	6 m	I
							Myd	5 m	I
3*	74/F	IC-Pcom	7	neck	6 d	3 m	Pt	1 m	I
							EOM (III)	–	U
4	71/F	BABif	16	Inc	4 d	48 m	Pt	1 m	R
5	60/F	C4-5	17	An	14 d	10 m	Pt	–	W
							EOM (III)	–	U
							EOM (VI)	–	U
6	62/F	C4	10	Com	24 m	36 m	EOM (VI)	–	U
							Pt†	–	
7	42/F	C5-PTA	13	An	1 m	1 m	EOM (VI)	1 m	R

Note.— F/U: follow up, IC-Pcom: internal carotid-posterior communicating artery, BABif: basilar artery bifurcation, C: cavernous ICA, PTA: persistent trigeminal artery, Com: complete, An: small aneurysmal remnant, Neck: small neck remnant, Inc: incomplete, D: days, M: months, Pt: ptosis, Myd: mydriasis, EOM: extraocular muscle dysfunction, N/A: not available, R: resolved, I: improved, U: unchanged, W: worsened
*Transient development of mydriasis after treatment, †Newly developed after GDC treatment

ducens EOM dysfunction was present in all patients and ptosis and oculomotor EOM dysfunction in two and one, respectively.

For CN signs, the final outcomes after GDC treatment are indicated in Fig. 2. Both patients with mydriasis showed clinical improvement or complete resolution, and in four of six who presented with ptosis, the symptoms improved or were resolved. The improvement or resolution of oculomotor dysfunction was noted in two of four patients, and of abducens EOM dysfunction, in one of three.

The outcome of CN signs according to the size, duration of symptoms and location of an aneurysm is summarized in Table 2. For small aneurysms measuring 10 mm or less, three of four patients with ptosis, two of three with oculomotor EOM dysfunction, and both with mydriasis showed improvement or resolution of the respective CN signs, with an overall incidence of improvement or resolution of 7/10 (70%). For aneurysms larger than 10 mm, however, improvement or resolution was noted in only one of two ptosis patients and one of two with abducens EOM dysfunction; the overall incidence of improvement or resolution was 2/5 (40%).

Regarding the duration of pre-treatment symptoms, a shorter duration (1 month or less) led to improvement or resolution in three of four patients with ptosis, one of three with oculomotor EOM dysfunction, the one with mydriasis, and one of two with abducens EOM dysfunction. The overall incidence of improvement or resolution was 6/10 (60%). Where the duration of symptoms was longer (more than 1 month), there was improvement or resolution in one of two patients with ptosis, the ones with oculomotor EOM dysfunction and mydriasis, but not in the one with abducens EOM dysfunction. Three of five patients (60%), in other words, experienced improvement or resolution of their CN symptoms.

The improvement or resolution of symptoms also varied according to location. Intradural aneurysms showed improvement or resolution in all four patients with ptosis, in two of three with oculomotor EOM dysfunction, and in both with mydriasis, an overall incidence of 8/9 (89%). For extradural aneurysms, however, improvement or resolution was noted in only one of three patients with abducens EOM dysfunction, an overall incidence of 1/6 (17%).

Among the oculomotor CN signs showing improvement, ptosis seemed to show the earliest response, with improvement beginning at a mean of two months after endovascular treatment (Fig. 3).

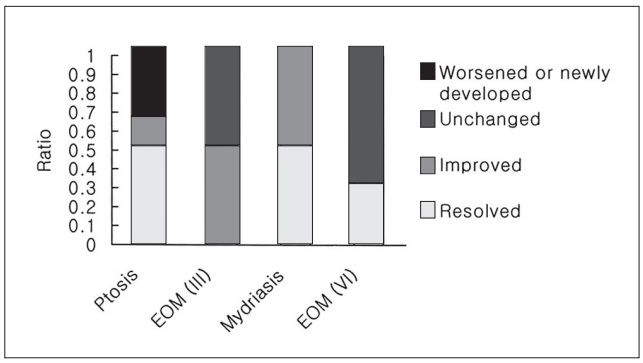

Fig. 2. Outcome of cranial nerve signs after GDC treatment.
Note.—EOM(III): extraocular muscle dysfunction, cranial nerve III

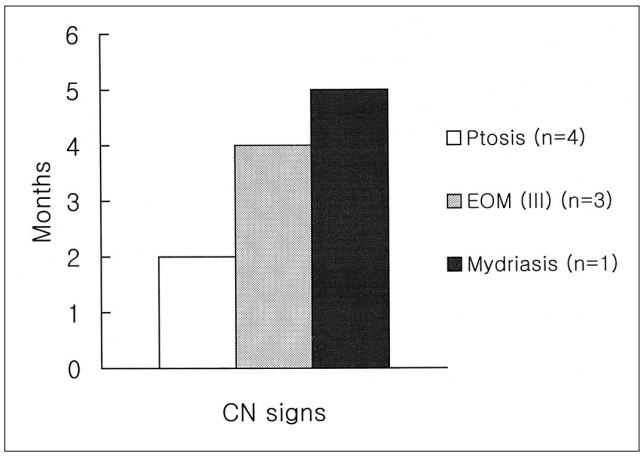

Fig. 3. Time taken for improvement of oculomotor cranial nerve signs. Patient totals include only those in whom the time taken for improvement or resolution was definite.
Note.—EOM(III): extraocular muscle dysfunction, cranial nerve III

Table 2. Number of Patients Showing Improvement or Resolution of Respective Cranial Nerve Signs after GDC Treatment

	Size		Duration of Symptoms		Location		Total
	Small (≤10 mm)	Large (> 10 mm)	Short (≤1 month)	Long (> 1 month)	Intradural	Extradural	
Ptosis	3/4	1/2	3/4	1/2	4/4	0/2	4/6
EOM III	2/3	0/1	1/3	1/1	2/3	0/1	2/4
Mydriasis	2/2	0	1/1	1/1	2/2	0	2/2
EOM VI	0/1	1/2	1/2	0/1	0	1/3	1/3
Total	7/10	2/5	6/10	3/5	8/9	1/6	

Note.—EOM III: extraocular muscle dysfunction, cranial nerve III

DISCUSSION

The surgical clipping of aneurysms causing CN symptoms is known to be effective in relieving mass effect (5–8). In a published report, analysis of the outcome of surgical management in unruptured aneurysms causing CN dysfunction revealed that 41% of patients showed resolution or improvement, symptoms remained stable in 24%, and symptoms worsened or complications arose in 25% (4). Similar or better results have been reported in endovascular treatment using balloons or aneurysm coils in which CN dysfunction arose (2–4, 9). Unlike surgical clipping, endovascular treatment does not immediately resolve the mass effect of an aneurysm; the loss or reduction of aneurysmal pulsatility afforded by GDC embolization may, however, be more important in the resolution of CN palsy caused by cerebral aneurysms than in anatomic detachment of the CN from an adjacent and adherent cerebral aneurysm by clipping. In a series of 19 patients with CN dysfunction who underwent treatment, Malisch et al. (4) reported complete resolution in 32% of cases, improvement in 42%, and no significant change or worsening in 26%, and our results (29%, 43%, and 29%, respectively) and theirs were comparable.

With regard to the various CN symptoms and signs occurring among our patients, ptosis was the most frequent symptom, present in all patients with IC-Pcom and basilar tip aneurysms, and two of three with a cavernous ICA aneurysm. Mydriasis occurred in two of the three with IC-Pcom aneurysms; its absence is considered an important differential point between diabetic and aneurysm-related oculomotor nerve neuropathy, and its absence in one patient in our series was unusual. An IC-Pcom aneurysm that compresses the oculomotor nerve superomedially exerts pressure on the dorsomedially-located irido-constrictor fibers, causing mydriasis. In diabetic neuropathy, however, impairment of the vasa vasorum leads to ischemic damage to the central portion of the nerve, thus sparing pupillary movement. The absence of mydriasis in oculomotor neuropathies caused by IC-Pcom aneurysms, such as in our patient 3, has, however, been previously reported. The existence of a supplementary bundle of parasympathetic nerve fibers coursing laterally through the nerve has been demonstrated and it is these that sustain pupillary tone after the damage to dorsomedially-located fibers (5). In our patient 3, ptosis improved after GDC treatment, indicating that an aneurysm was the cause of the neuropathy.

Aneurysms located in the cavernous ICA are known to cause a variety of CN III, IV, V, and VI dysfunctions (10, 11), and in some instances, the presenting symptoms may vary according to the location and direction of the aneurysm in relation to the course of the CN within the sinus.

Within the anterior cavernous sinus, superior orbital fissure or posterior orbit, the oculomotor CN divides into a superior ramus, which supplies the superior rectus muscle and the levator muscle of the eyelid, and an inferior ramus, which supplies the medial and inferior rectus muscles, the inferior oblique muscle, and the ciliary ganglion (parasympathetic fibers to pupillary constrictors). In the posterior cavernous sinus, sympathetic nerve fibers send filaments to the abducens CN, which traverses the lateral aspect of the ICA. Compressive lesions in these respective areas may lead to localized oculomotor or abducens CN dysfunction, and Horner's syndrome (12). In our series, abducens CN dysfunction occurred in all cavernous aneurysms, while oculomotor CN dysfunction was noted in patient 5 and after embolization in patient 6. Both these aneurysms had anterior cavernous components, but in patient 7, the aneurysm was located at the posterior genu of the cavernous ICA, showing only abducens CN dysfunction.

The outcome of the various CN symptoms after embolization varied according to the size of the aneurysm. Where these were smaller ($\leq$10 mm), the overall result tended to be better than where they were larger (> 10 mm); the respective incidences of improvement or resolution were 7 of 10 (70%) and 2 of 5 (40%). Malisch et al. (4) also reported better results for smaller aneurysms, though the difference was statistically insignificant.

Outcome also varied according to location, tending to be better for intradural aneurysms than extradural: the respective incidences of improvement or resolution were 8/9 (89%) and 1/6 (17%). As far as we are aware, differences of this kind have not previously been reported for GDC-treated aneurysms. In the cases of extradural aneurysms reported by Malisch et al. (4) (n=3; mean size, 18 mm; mean duration of signs, 6 months; mean follow-up period, 33 months), and Halbach et al. (9) (n=14; mean size, 17 mm; mean duration of signs, 12 months; mean follow-up period, 67 months), endosaccular treatment lead to improvement or resolution of CN symptoms in all cases. In our series, however, the mean size of extradural aneurysms was 13.3 mm (n=3; mean duration of signs, 8.5 months; mean follow-up period, 16 months), only slightly larger than that of intradural aneurysms (10.3 mm). This poorer outcome is difficult to explain but may in part be due to our shorter duration of follow-up (33 months and 67 months, versus 16 months). Compared to the intradural aneurysms in our series, intradrual aneurysms located in the subarachnoid space may be more mobile and more vulnerable to pulsations than extradural cavernous

aneurysms, which are trapped in an enclosed space, the cavernous sinus, thus resulting in a better outcome after endosaccular embolization.

In both surgical and endovascular series, a shorter duration of CN symptoms prior to embolization is generally accepted as a factor for good prognosis (4, 5, 9), but in the literature, definitions of 'short' and 'long' durations of symptoms vary between 14 days and 12 months (4, 5). When symptom durations were collapsed into '$\leq$ 1 month' and '> 1 month', the authors could find no difference between the groups.

The recovery of oculomotor CN function after surgical treatment follows a predictable course: ptosis is frequently the first ocular sign to subside, with recovery generally beginning within the first month of surgery, and full recovery taking several months. In our series, ptosis was the initial symptom to show improvement, at about the second month. Published reports have described more rapid resolution of CN symptoms in ruptured aneurysms treated by GDC coils (2, 3), and complete recovery of CN symptoms as early as between one and three weeks has been claimed. In our series, however, the outcome was neither as prompt as this, nor as complete, findings which might be explained in part by the fact that in the patients those reports described, aneurysms were mostly intradural or small.

In patients with CN dysfunction who are recovering from aneurysmal mass effect, the resolution of ptosis is usually complete, whereas extraocular muscle function frequently remains impaired (3); aberrant regeneration of the oculomotor nerve has been suggested as a possible cause (3, 12). In accordance with the findings of previous reports, less than 50% of the patients with EOM dysfunction in our series showed improvement or resolution.

An important limitation of our study is the small number of patients included. Few earlier studies, however, have investigated the outcome of the various symptoms of each CN sign, and to our knowledge, the series involved in this current study is the largest to date to report these outcomes in patients with unruptured aneurysms presenting with CN deficits and treated with GDCs.

In conclusion, endosaccular GDC coil packing for aneurysms which cause CN dysfunction is effective for the treatment of CN symptoms. In our series, smaller ($\leq$10 mm) or intradural aneurysms tended to show better results. Among the various CN signs, ptosis seems to be the first to respond to endovascular therapy, while EOM dysfunction showed a slower and less favorable response.

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