

Efficacy of endovascular intervention in patients with unruptured posterior communicating artery aneurysm-related oculomotor nerve palsy

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Abstract

OBJECTIVES: Oculomotor nerve palsy (ONP) is commonly encountered in daily neurosurgical activities. The ONP secondary to un-ruptured PComA aneurysm might be a unique entity that was different in diagnosis, treatment and prognosis from its ruptured counterparts. Perhaps as a result of the limitation in sample size, studies that solely focused on factors affecting recovery of ONP in patients with unruptured corresponding PComA aneurysms were scarce.

METHODS: In this study, we would like to report a relatively larger case series of patients with un-ruptured PComA aneurysm-related ONP. A retrospective review of medical records of 39 patients with un-ruptured PComA aneurysm-related ONP was performed with endovascular coiling.

RESULTS: All 39 consecutive patients underwent endovascular coiling. Eighteen (46%) patients had a complete resolution of ONP, 14 (36%) patients had a partial resolution. Time interval from onset of ONP to endovascular intervention ($P=0.004$), degree of ONP ($P=0.015$) and age ($P=0.016$) were predictors of ONP recovery with statistical significance. Sex, aneurysm size and risk factor exposure (smoking, alcohol abuse and hypertension) were not associated with ONP outcomes.

CONCLUSION: ONP secondary to un-ruptured aneurysm should be treated as a unique entity from its ruptured counterparts. A prospective study that contains surgical clipping and endovascular coiling, and comparison between two treatment modalities would be more convincing and is anticipated.

INTRODUCTION

Oculomotor nerve palsy (ONP) is commonly encountered in daily neurosurgical activities (Amano *et al.* 2018; Zu *et al.* 2017; Hall *et al.* 2017). The concomitant existence of a posterior communicating artery (PCoA) aneurysm should be considered in the differential diagnosis of ONP (Zu *et al.* 2017; Gao *et al.* 2017), because the incidence of ONP in patients with PCoA aneurysms can be as high as 56% (Giombini *et al.* 1991; Kassis *et al.* 2010). The sudden onset of ONP may reflect the rapid growth of an unruptured aneurysm and should be considered a warning sign of an impending rupture (Hu *et al.* 2015; Bederson *et al.* 2000). Although surgical clipping and endovascular coiling are treated as the two standard treatment modalities, many studies including systematic reviews support the viewpoint that endovascular coiling was superior (Mino *et al.* 2015; Khan *et al.* 2013). Most of the published case series and reviews mainly focused on the difference in efficacy between the two treatment modalities or factors associated with ONP recovery. Perhaps as a result of the limitation in sample size, studies that solely focused on the factors affecting the recovery of ONP in patients with unruptured corresponding PCoA aneurysms were scarce (Hu *et al.* 2015). So ONP secondary to ruptured or unruptured PCoA aneurysms were always mixed together in these studies (Giombini *et al.* 1991; Kassis *et al.* 2010; Güresir *et al.* 2011; Brigui *et al.* 2014). In this study we would like to perform a retrospective review of the medical records of 39 patients with unruptured PCoA aneurysm-related ONP. All of the 39 consecutive patients underwent endovascular coiling. To our knowledge, this is the largest cases series on this specific topic so far.

EXPERIMENTAL

Study protocol

A retrospective review of the medical records of patients admitted to our institution for ONP between January 2001 and March 2013 was made under the approval of institutional ethics committee. Among the 845 consecutive patients with ONP, 48 (5.7%) were identified with corresponding unruptured ipsilateral PCoA aneurysms according to the set criteria, of whom 39 underwent endovascular coiling according to the International Study of Unruptured Intracranial Aneurysms criteria (Wiebers *et al.* 2003) and the willingness of the patients. All the surgeries were performed by 2 surgeons in the same medical team. Clinical data including sex, age, degree of ONP on admission, time interval from symptom onset to surgery, size, risk factors as smoking, alcohol abuse and hypertension and outcome were extracted from the data base (Table 1). The degree of ONP was assessed by one ophthalmologist on admission, while the degree of recovery was assessed by the same staff according to the follow-up questionnaires or inspection in outpatient clinic.

Diagnosis of unruptured PCoA aneurysm-related ONP

Unruptured PCoA aneurysm was deemed as the corresponding cause of ONP when all of the criteria were met.

ONP as the sole complaint on admission. Radiological examination after the onset of ONP revealed no subarachnoid hemorrhage. Ipsilateral PCoA aneurysm was identified on CT angiography (CTA) or digital subtraction angiography (DSA). No other risk factor that might contribute to ONP could be identified.

Definition of the degree of ONP on admission and recovery outcome

Patients presenting with all of the symptoms above were deemed as with complete ONP, while those presenting with one or two or incomplete presentation of the symptoms were deemed as with incomplete ONP. Complete resolution was defined as complete recovery of the symptoms above. Partial resolution was defined as one or more of the symptoms partially recovered.

Surgical procedure

Endovascular treatment was performed under general anesthesia with systemic heparinization on a biplane angiographic unit (Philips Integra V3000 Neuro; Philips Medical Systems, Best, the Netherlands). Heparinization was continued for 48 hours after treatment, followed by 80 mg aspirin daily for 3 months. Aneurysm occlusion was performed with Guglielmi detachable coils (Boston Scientific, Fremont, Calif), and one giant PCA aneurysm was occluded with very long mechanically detachable coils (Detach 18; Cook, Copenhagen, Denmark). Aneurysms with a well-defined neck were selectively occluded with coils and aneurysms without a defined neck were occluded together with the parent PCA.

Statistical analysis

Six independent variables according to the literature and our medical records were obtained. They were sex, age, degree of ONP, time interval from ONP onset to surgery, risk factor exposure and aneurysm size. Continuous variables as age, symptom interval and aneurysm size were expressed as mean \pm SD and assessed with a two-tailed student t-test. Categorical variables were assessed by chi-squared or Fisher exact test. SPSS 17.0 was used in the statistical analysis and $p < 0.05$ was considered with statistical significance.

RESULTS

This study consisted of 39 (15 males) patients and 32 patients (82%) enjoyed ONP recovery in different degrees. Eighteen (46%) patients had a complete resolution of ONP, 14 (36%) patients had a partial resolution. The time interval from onset of ONP to endovascular coiling ranged from one day to one year. Clinical

Tab. 1. Clinical and demographic data of the patients

Patient	Sex	Age	Risk factor	State on admission	Size	Interval	Outcome	Follow-up
1	M	45	P	PP	8mm	8d	CR	12m
2	F	42	N	CP	5mm	31d	PR	9m
3	F	52	P	PP	10mm	22d	CR	15m
4	F	65	P	CP	9mm	45d	NR	28m
5	M	32	N	CP	13mm	3d	PR	24m
6	M	47	N	CP	11mm	17d	PR	32m
7	F	38	N	PP	10mm	4d	CR	6m
8	F	71	P	CP	8mm	49d	NR	40m
9	F	64	P	CP	12mm	27d	PR	40m
10	M	51	P	CP	8mm	1y	NR	40m
11	F	28	N	PP	14mm	2d	CR	6m
12	M	74	N	PP	12mm	15d	CR	20m
13	F	47	N	PP	5mm	4d	CR	8m
14	M	55	P	CP	8mm	3d	PR	24m
15	F	21	N	PP	16mm	1d	PR	24m
16	F	73	N	CP	9mm	10d	PR	24m
17	M	60	P	CP	6mm	4d	PR	19m
18	F	42	P	PP	9mm	7d	CR	12m
19	F	32	N	CP	12mm	2d	PR	24m
20	M	54	N	CP	14mm	29d	NR	24m
21	M	47	N	CP	13mm	3d	CR	15m
22	F	54	N	PP	7mm	9d	CR	20m
23	F	35	N	CP	10mm	15d	PR	24m
24	M	54	P	PP	7mm	8d	CR	12m
25	F	60	P	PP	11mm	9d	PR	24m
26	F	35	N	PP	7mm	3d	CR	12m
27	F	45	P	CP	7mm	48d	NR	24m
28	F	55	P	PP	10mm	5d	CR	12m
29	M	48	P	CP	5mm	7d	CR	12m
30	M	53	P	PP	8mm	9d	CR	14m
31	F	73	N	CP	12mm	35d	NR	24m
32	F	35	P	PP	8mm	3d	CR	12m
33	F	56	N	CP	7mm	14d	NR	24m
34	F	43	N	PP	8mm	10d	CR	12m
35	M	46	P	CP	11mm	18d	PR	27m
36	M	56	P	PP	5mm	21d	PR	24m
37	F	44	N	PP	7mm	5d	CR	12m
38	M	34	N	CP	6mm	4d	CR	12m
39	F	43	N	PP	11mm	3d	PR	24m

F: Female, M: Male, P: Positive, N: Negative, CP: Complete palsy, PP: Partial palsy, CR: Complete resolution, PR: Partial resolution, NR: Non-resolution

follow-up ranged from 6 to 40 months. The outcome was assessed as ONP resolution (partial or complete) or non-resolution. The details of statistical analysis are summarized in Table 2 and the relationship between the demographic and clinical data and ONP recovery would be illustrated separately.

Gender and age

The overall efficacy of endovascular coiling in male and female was 87% and 79%, respectively. No statistical significance ($P=0.869$) was noted (Table 2). Patients with no resolution of ONP (59.29 ± 10.56 year) were older than those with resolution (46.69 ± 12.26 year) with statistical significance (Table 2, $P=0.016$).

Exposure to risk factors

We treated smoking, alcohol abuse and hypertension as the risk factors. Because diabetes has long been demonstrated to be an independent cause of ONP by some studies, it was excluded from our risk factor family. If one or more of the three risk factors were present, the patient would be treated as risk factor exposure positive, negative otherwise. Seventy-six percent of patients with risk exposure and 86% patients without enjoyed ONP resolution (complete or partial). Statistical significance was not reached (Table 2, $P=0.706$).

Degree of ONP on admission

ONP recovered in 19 (95%) of 20 patients with partial ONP and in 13 (68%) of 19 patients with complete ONP and the difference was statistically significant (Table 2, $P=0.015$).

Time interval from ONP onset to endovascular coiling

Patient 10 had suffered from ONP for one year before admission and he experienced no remission of the symptom during a follow-up of 40 months. As his symptom of ONP was extremely longer compared with

his counterparts, he was excluded from the statistical analysis of the relationship between time interval from ONP onset to endovascular coiling and ONP recovery. The time interval in the patients with resolution (9.13 ± 7.74 day) was significantly shorter than those without (36.67 ± 13.60 day) (Table 2, $P=0.004$).

Size of the aneurysm

Aneurysm sizes were 9.19 ± 2.87 mm and 9.29 ± 2.69 mm in patients with resolution and without, respectively. No statistical significance (Table 2, $P=0.934$) was noted.

DISCUSSION

The incidence of ONP in patients with PComA aneurysms can be as high as 56%^[5, 6]. A sudden onset of ONP may reflect the rapid growth of an unruptured aneurysm and should be considered a warning sign of an impending rupture (Hu et al. 2015; Bederson et al. 2000). Historically, surgical clipping was considered as standard or even sole treatment modality for ONP recovery and prevention of aneurysm rupture, until the publication of Birchall's report of three patients successfully embolized in 1999 (Birchall et al. 1999). Although some authors have enthusiastically demonstrated the successful application of endovascular coiling in a relatively larger population (Santillan et al. 2010; Ko & Kim 2011; Chalouhi et al. 2013), up to date studies including some meta-analyses still supported the superiority of surgical clipping vs endovascular coiling (Güresir et al. 2011; Tan et al. 2015; Brigui et al. 2014; Chen et al. 2006).

The difference between two the treatment modalities in efficacy on ONP recovery might be partly due to the mechanism of ONP. Generally speaking, a combination of the compressive mass effect of the aneurysm and irritation caused by its pulsation is the preferred pathophys-

Tab. 2. Relationships between variables and ONP recovery.

Clinical data	Outcome			P value	
	Resolved				
	CR (N, %)	PR (N, %)	NR (N, %)		
Sex	Male	7, 47%	6, 40%	2, 13%	0.869
	Female	11, 46%	8, 33%	5, 21%	
Risk factor	P	7, 41%	6, 35%	4, 24%	0.706
	N	11, 50%	8, 36%	3, 14%	
Degree of ONP	CP	3, 16%	10, 53%	6, 31%	0.015
	PP	15, 75%	4, 20%	1, 5%	
Age (y, mean ± SD)		46.69 ± 12.26		59.29 ± 10.56	0.016
Interval (d, mean ± SD)		9.13 ± 7.74		36.67 ± 13.60	0.004
Size (mm, mean ± SD)		9.19 ± 2.87		9.29 ± 2.69	0.934

P: Positive, N: Negative, CR: Complete resolution, PR: Partial resolution, NR: Non-resolution

iological mechanism of ONP in the setting of PComA aneurysm (Güresir *et al.* 2011). It is believed that coiling relieves irritation caused by aneurysm pulsatility, while surgery resolves both pulsatility and the mass effect (Brigui *et al.* 2014; Chen *et al.* 2006). Furthermore, the coil mass itself could contribute to mass effect. In the present study, all the 39 consecutive patients underwent endovascular coiling, intraoperative decompression was also applied if needed. But as our study showed, the rates of complete resolution and partial resolution were 46% and 36%, respectively. No superiority in efficacy was observed compared with the previous studies on surgical clipping vs endovascular coiling (Kassis *et al.* 2010; Güresir *et al.* 2011; Chen *et al.* 2006; Nam *et al.* 2010). However, this study solely focused on unruptured aneurysms with endovascular coiling, which might have perplexed the interpretation of results.

Most of the published case series and reviews on PComA aneurysm-related ONP mainly focused on the difference in efficacy between the two treatment modalities or factors affecting ONP recovery (Kassis *et al.* 2010; Güresir *et al.* 2011; Chalouhi *et al.* 2013; Gu *et al.* 2012). But ONP secondary to unruptured PComA aneurysm might be a unique entity that was different in diagnosis, treatment and prognosis from its ruptured counterparts. A prospective study that contains ruptured and unruptured aneurysms, surgical clipping and endovascular coiling and statistical analysis of the two treatment modalities in different circumstances is more convincing. A relative large case series of unruptured PComA aneurysm-related ONP before this study was described by Yanaka K and colleagues in 2003^[22]. This study consisted of 16 patients with ONP (13 due to PComA aneurysm). Among the 13 patients, one died from aneurysm rupture before endovascular coiling was performed, one underwent endovascular coiling with no change to ONP, the remained 11 underwent endovascular coiling with 10 (91%) enjoyed ONP recovery (4 incomplete, 6 complete).

According to the past studies and our medical records, we chose 6 independent variables (sex, age, exposure to risk factors, time interval from ONP onset to endovascular coiling, degree of ONP on admission and aneurysm size) for statistical analysis. Consistent with the past studies (Giombini *et al.* 1991; Hu *et al.* 2015; Güresir *et al.* 2011), timely endovascular coiling was still the most potent factor affecting ONP recovery ($P=0.004$). Sex ($P=0.869$) and exposure to risk factors (smoking, alcohol abuse and hypertension) ($P=0.706$) were not indicative of ONP resolution. Contrary to our common intuitive but consistent with the previous studies (Hu *et al.* 2015; Güresir *et al.* 2011; Tan *et al.* 2015; Chen *et al.* 2006), aneurysm size was not related to nerve function recovery ($P=0.934$). This might be explained by a recently published article which concluded that a shorter distance between internal carotid artery (ICA) and anterior-posterior clinoid process may be related to the occurrence of PCoA aneurysm-related ONP (Anan

et al. 2014). Even relatively small unruptured PCoA aneurysms can cause third nerve palsy if the ICA runs adequately close to the skull base, this means that the PCoA aneurysm should be closer to the third nerve when the ICA runs closer to the skull base (Anan *et al.* 2014). Degree of ONP on admission was another factor accounting for the prognosis of recovery. This study indicated that patients with partial ONP (95%) was more likely to have a better oculomotor nerve recovery than those with complete palsy (68%) ($P=0.015$). But the relationship between degree of ONP and recovery varied according to different reports (Kassis *et al.* 2010; Hu *et al.* 2015; Chen *et al.* 2006; Nam *et al.* 2010). In previous reports age was not associated with ONP recovery (Kassis *et al.* 2010; Hu *et al.* 2015; Güresir *et al.* 2011; Chen *et al.* 2006; Nam *et al.* 2010). But contrary to previous reports, our study showed that younger patients enjoyed a better recovery than the older ($P=0.016$). This might be explained by the cultural and economical circumstance in China. As China is a developing country, the economic reality makes people pay less attention to seemingly nonfatal health problems, especially in the older people.

There are some deficiencies in our study. First of all, the sample size of this study is relatively small, and the promotion of the research results requires the verification of a larger sample. Secondly, due to the improvement of living standards, the rapid development of interventional materials, and the increasing maturity of intravascular treatment technologies, endovascular treatment of OMNPs caused by unruptured PComA is more effective, faster to restore the function of oculomotor nerve, and ultimately to improve the patient life quality.

CONCLUSIONS

This study indicates that endovascular coiling could achieve encouraging neural recovery in patients with unruptured PComA aneurysm-related ONP. Time interval from onset of ONP to endovascular intervention is a potent predictor of ONP resolution. Degree of ONP on admission and age also affect outcome with statistical significance. Sex, aneurysm size, exposure of risk factors as smoking, alcohol abuse and hypertension are not associated with ONP recovery. ONP secondary to unruptured aneurysm should be treated as a unique entity from its ruptured counterparts. But this study has its own shortcomings. Firstly, it is retrospective in its nature. And then it only focuses on the efficacy of endovascular intervention. A prospective study that contains endovascular coiling and surgical clipping, and comparison between the two treatment modalities would be more convincing and is anticipated.

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