Case Reports & Case Series

Rare cases of multiple unruptured intracranial aneurysms: Illustrative report and review on management options

Niranjana Rajagopal (DNB)[a,*], Yasuhiro Yamada (M.D., PhD.)[b], Arun Balaji (M M.S., Mch.)[c], Tsukasa Kawase (M.D., Ph.D.)[b], Yoko Kato (M.D., PhD.)[b]

[a] Department of Neurosurgery, Sri Sathya Sai Institute of Higher Medical Sciences, Bangalore, India
[b] Department of Neurosurgery, Fujita Health University, Banbuntane Hotokukai Hospital, Nagoya, Japan
[c] Department of Neurosurgery, Kovai Medical Center and Hospital, Coimbatore, Tamil, Nadu, India

ARTICLE INFO

ABSTRACT

Introduction: Multiple intracranial aneurysms [MIA] occur in 7% to 34% of patients with intracranial aneurysms. They can be treated with both surgical and endovascular techniques. Here we report 2 cases of multiple intracranial aneurysms with 6 and 7 aneurysms respectively who were treated at our institute by surgery followed by a discussion on incidence, conditions associated with multiple aneurysms, ethnicity and management strategies.
Methods: A retrospective analysis of 2 patients with incidentally detected aneurysms with 6 and 7 aneurysms respectively, who were treated with microsurgical clipping was conducted. A systematic search was performed using the PUBMED database and relevant articles were reviewed with particular attention to incidence, associated conditions, risk factors and management strategies.
Results: Both the patients were females with incidental detection of the aneurysms. One had 6 and the other had 8 aneurysms respectively. Both patients underwent bilateral pterional craniotomy and clipping of all the aneurysms except for one aneurysm in the cavernous ICA, for which the patient is planned for an endovascular procedure. Both had an uneventful postoperative course with the CT angiogram showing obliteration of all the aneurysms except one.
Conclusions: There is a lack of prospective randomized controlled trials to analyse management options, particularly in comparing intervention with conservative management. Most of the available data is retrospective in nature and lacks objective short and long-term outcome analysis. Furthermore, we need randomized trials to directly compare clipping and coiling of multiple unruptured aneurysms to decide the best intervention strategy of this pathology.

1. Introduction

One third of intracranial aneurysms are multiple. They can be managed surgically or by endovascular coiling. The reported number of aneurysms vary between 2 and 13 [1,2]. Several authors have described the treatment of unruptured multiple intracranial aneurysms in various combinations such as single or multi stage surgical clipping/coiling or a combination of both. However, the decision of when to treat and which modality best suits the situation is yet not clear from the available literature. Thus the decision to provide the best option for the patient requires a multidisciplinary approach between the endovascular and surgical team [3,4]. We report 2 cases of multiple intracranial aneurysms with 6 and 7 aneurysms respectively, who were treated at our institute by surgery followed by a discussion on incidence, conditions associated with multiple aneurysms, ethnicity and management strategies.

2. Illustrative case 1

A 57 years old lady, who was a known case of hypertension on medications, was incidentally detected to have multiple aneurysms when she was screened for the same as she had a family history of
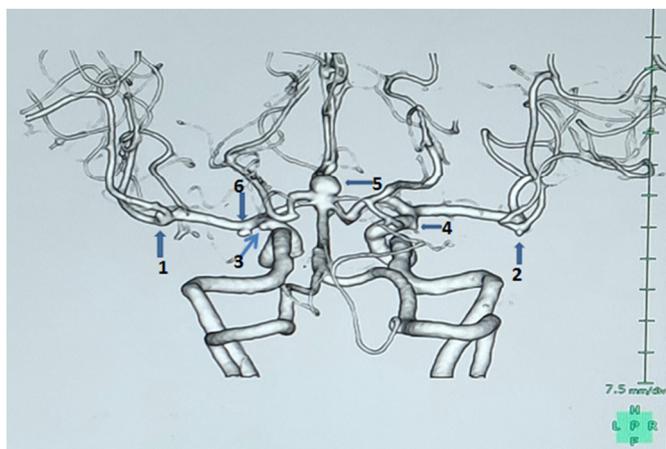

Fig 1:. Case 1 aneurysms with their sizes:- **1,2** – bilateral MCA bifurcation aneurysms (right- 2 mm, left- 0.4 mm); **3,4** – bilateral anterior choroidal artery aneurysms (right-3 mm, left- 2 mm); **5** - basilar top (6.4 mm); **6** - left M1 aneurysm (3 mm).
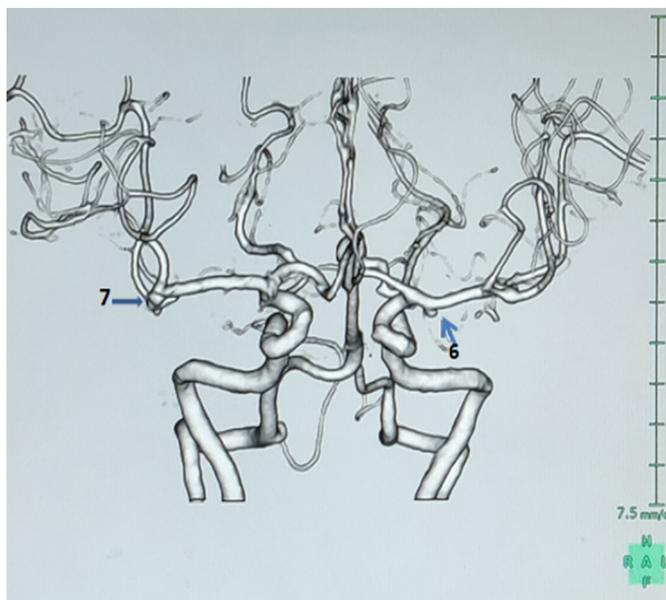

Fig 2:. Case 1 aneurysms with their sizes:- **6** - left M1 aneurysm (3 mm); **7** – Right M1 aneurysm (3 mm).

subarachnoid haemorrhage but not of any detected aneurysms. She had no history of smoking, alcohol abuse or history of any syndromes. On examination, she did not have any neurological deficits. She underwent CT angiogram of the brain with three-dimensional reconstructions and a 4-vessel DSA which demonstrated the following aneurysms:- basilar top, bilateral M1, bilateral MCA bifurcation and bilateral anterior choroidal artery aneurysms (Figs. 1 and 2). There were a total of 7 aneurysms in the patient. After careful evaluation of the radiologic images, we decided to attempt a 2 stage surgical procedure and clipping of all the aneurysms. She initially underwent a left pterional craniotomy and clipping of the basilar top, left anterior choroidal, M1 and MCA bifurcation aneurysms. She underwent the second surgery after 1 month, which was a right pterional and trans-sylvian approach, similar to the first one and clipping of right anterior choroidal, M1 and MCA bifurcation aneurysms. The postoperative course after both the procedures was uneventful. The postoperative CT angiogram showed complete exclusion of all the aneurysms while preserving the normal flow.
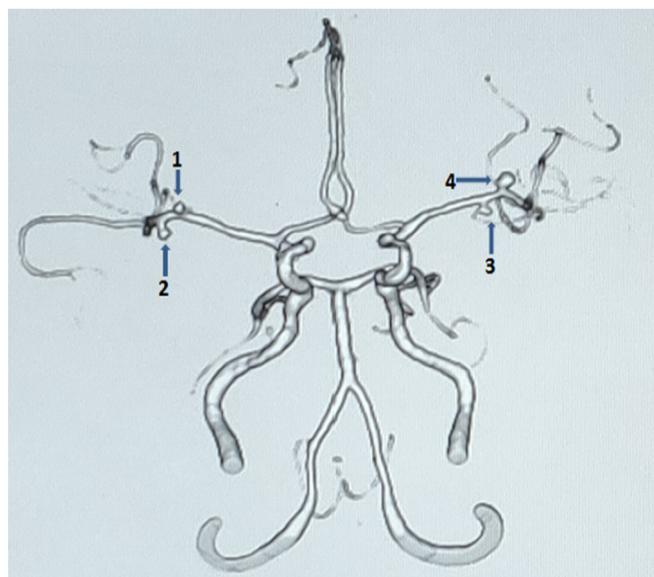

Fig 3:. Case 2 aneurysms with their sizes:-bilateral MCA aneurysms (**1**-2.3 mm, **2**- 2.6 mm, **3**- 2.4 mm, **4** – 3.2 mm).

3. Illustrative case 2

A 63 years old lady, who was a known case of hypertension on medications, was incidentally detected to have multiple aneurysms when she was evaluated for a nonspecific type of a headache. She had no family history of SAH or aneurysms. She had no past history of smoking, alcohol abuse or any syndromes. On examination, she did not have any neurological deficits. She underwent CT angiogram of the brain with three-dimensional reconstructions and a 4-vessel DSA which demonstrated the following aneurysms:- Acom, 2 sets of bilateral M1 and a right cavernous ICA aneurysms (Figs. 3 and 4). There were a total of 6 aneurysms in the patient. We decided to attempt a 2 stage surgical procedure and clipping similar to the previous case. She initially underwent a right pterional craniotomy and clipping of both the MCA and Acom artery aneurysms. The right cavernous ICA aneurysm was wrapped. She underwent the second surgery after 1 month, which was a left pterional approach and clipping of the left MCA aneurysms. The postoperative course after both the procedures was uneventful. The postoperative CT angiogram showed complete exclusion of all the aneurysms except the right cavernous ICA aneurysm while preserving the
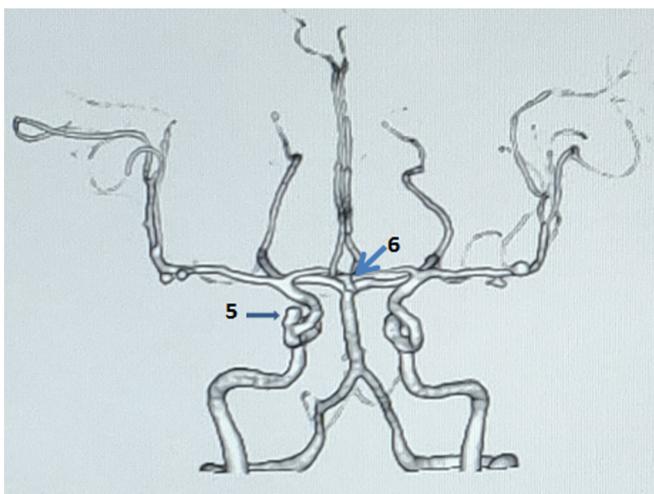

Fig 4:. Case 2 aneurysms with their sizes:- **6** – Acom aneurysm (3 mm); **7** – right cavernous ICA aneurysm (3.2 mm).
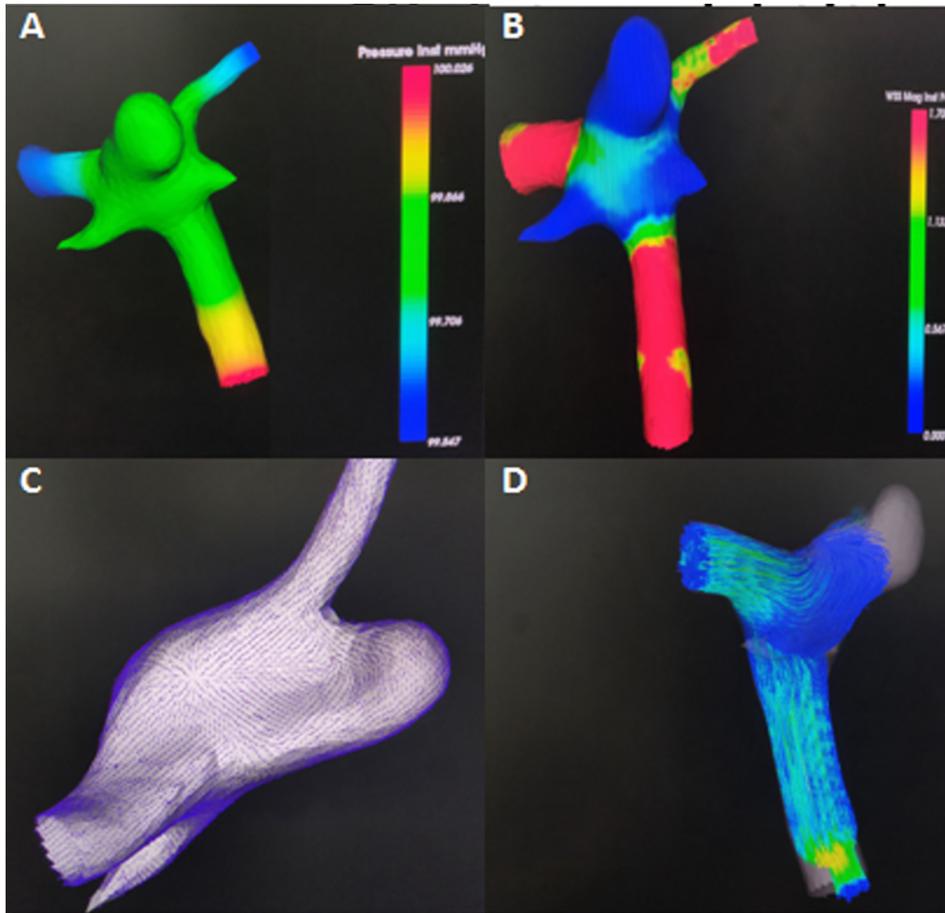
Fig 5:. Preoperative CFD:- A) shows wall pressure; B) shows wall shear stress pressure; C) shows the vector which is divergent; D) shows the flow within the vessel and the aneurysm.

normal flow. She is planned for an endovascular procedure for the cavernous ICA aneurysm.

Although only one patient had a positive family history of SAH with no proven aneurysms, both of them were recommended to undergo genetic counselling along with a screening of family members. For both the patients preoperative CFD was done to analyse the hemodynamics of the aneurysms (Fig. 5).

Intraoperatively, we used electrophysiological monitoring like MEP, indocyanine green video angiography with DIVA for an intraoperative assessment of the occlusion of the aneurysms and the preservation of the blood flow in parent/branching vessels (Fig. 6) and Doppler. There

was no intraoperative rupture in any of the procedures.

4. Discussion

4.1. Epidemiology

The prevalence of intracranial aneurysms in the general adult population is 1 to 3.2%. Amongst these, the reported cases of multiple intracranial aneurysms range from 2% and 45% [3,5–10]. The incidence of mirror aneurysms accounts for nearly 5% of all intracranial aneurysms and approximately 40% of all multiple aneurysms [11–14].
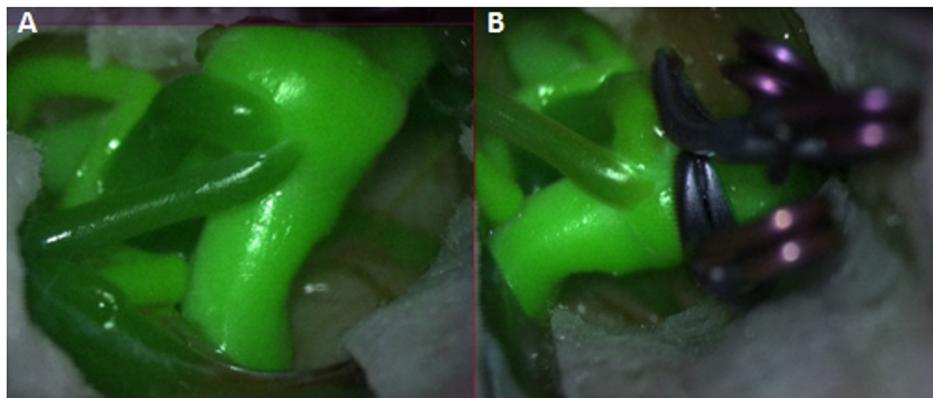

Fig 6:. A) Pre clipping DIVA showing the aneurysm and the adjacent vessels.
B) Post clipping DIVA shows no residual aneurysms with intact adjacent vessels.

In The 2 illustrative cases presented in this report, we had 5 sets of mirror aneurysms. Literature shows that MCA is the commonest site followed by ICA and Pcom for these type of aneurysms [12–15]. It has been postulated that mirror aneurysms have an underlying embryological evolution. Anterior circulation aneurysms originate from the embryologic prosencephalic region. Thus any insult prior to the cephalic segmentation phase might trigger the formation of this pathology [12,14,16–18]. The mere presence of mirror aneurysms is not a predictor of SAH or poor outcome. There are no clear consensus on the management protocol of these lesions and remain similar to the management of other MIAs.

4.2. Etiopathogenesis and natural history

The risk factors for MIAs remain similar to the known predictors of intracranial aneurysm formation such as, female sex, hypertension, smoking and alcohol abuse [5,9,18–21]. Non-modifiable risk factors include old age, female sex, Japanese or Finnish descent and genetic factors whereas the modifiable ones are cigarette smoking and hypertension [18,19,21,22]. Jabbarali et al. [5] in his meta-analysis on MIAs opined that higher age and family history along with the other mentioned predictors are major risk factors for MIAs.

Size and location have been identified as the most important aneurysm-specific predictors of rupture in both single and multiple aneurysms [6,9,23,24]. Lu et al. [23] in his retrospective analysis of 294 aneurysms and other authors [9,20,22,25] have concluded that Acom artery aneurysms and the ones larger in size were more prone to rupture. The ISUIA trial and the meta-analysis by Wermer et al. [22] concluded that significantly higher rupture rates were noted for aneurysms located in the posterior circulation, basilar top aneurysms and the ones in posterior communicating arteries. In addition to this, the position of an aneurysm on the parent vessel also predicts rupture i.e. midline aneurysms have a higher risk of rupture than the ones on the lateral aspect of the vessel [23]. Kleinloog et al. [26] in his retrospective analysis of 102 studies, identified that the irregular shape of an aneurysm was an independent predictor of risk of rupture. The last meta-analysis on the risk of rupture (which included MIAs too) was published in 2007 and found that age > 60 years, female gender, Japanese or Finnish descent, size > 5 mm, posterior circulation location, and symptoms were all risk factors for rupture [9,22]. Amenta et al. [27] in their retrospective review of over 2000 patients, identified Aspect Ratio > 1.6, dome diameter > 10 mm, a deviated neck, and right-sidedness as independent risk factors for rupture.

The familial forms of aneurysms have been associated with conditions such as autosomal dominant polycystic kidney disease, Marfan's syndrome, Ehlers–Danlos syndrome type IV, fibromuscular dysplasia, Moyamoya disease, sickle cell disease and arteriovenous malformations of the brain. Patients with one affected family member have approximately a 4% risk and ones with 2 or more affected first-degree family members have an 8–10% risk of developing an aneurysm [9,18,19]. In addition to the aforementioned genetic disorders, there are less obvious variations in the genetic code, which may also play a role in the development and rupture of cerebral aneurysms. Increased familial risk indicates a possible genetic risk. Aneurysm multiplicity is probably more common in those with a familial aneurysm than in those without, and there seems to be some predilection for aneurysms in the middle cerebral artery. Multiple studies have shown a statistically significant association between intracranial aneurysms formation, SAH and variants of the genes CDKN2 (chromosome 90), SOX17 (chromosome 8), and EDNRA (chromosome 4) [9,19,28–30]. Abnormalities in the CDKN2 gene leads to heterogenous wall thickness thus leading to aneurysm formation. The polymorphisms of the EDNRA gene may result in the inability of the vascular smooth muscle to compensate against the shearing forces and the SOX17 gene polymorphism contributes to the disruption of the endothelial homeostasis thus leading to the formation and rupture of aneurysms. The commonest histological finding is a decrease in the tunica media, the middle muscular layer of the artery, causing structural defects. These defects, in combination with the hemodynamic factors, lead to the formation of aneurysms. Further research is required to elucidate the genetic factors responsible for structural remodelling. While the contributions of the other factors can't be ignored, it is also required to determine these genetic factors to help identify patients at risk and develop novel gene based therapies [9,19,28–30].

Hemodynamics of the lesion with its impact on aneurysm initiation, remodelling, degradation of the wall structure and its mechanical strength, plays a fundamental role in its rupture [6,7]. Furthermore, hemodynamic assessment by CFD study could give us details about wall shear stress, oscillatory stress and flow patterns which could help us detect lesions with high probability of future rupture [31]. This information can aid in the staged management of MIAs. Meng et al. [32] postulated two different hypothesis on aneurysmal rupture, in CFD depending on the aneurysm type. One with low WSS in combination with high OSI can lead to an inflammatory-cell-mediated pathway in large, atherosclerotic aneurysm phenotypes. However, abnormally high WSS combined with a positive WSS gradient might initiate a mural-cell-mediated pathway for small or secondary bleb aneurysms. However, further studies in CFD are required to clarify the risk profile in patients with unruptured MIAs.

4.3. Management strategies

Several studies showed that MIAs are associated with a less favourable outcome than are single aneurysm cases after SAH, thus necessitating intervention on diagnosis [7,20]. On detection of unruptured aneurysms, the risk of rupture has to be balanced against the risk of surgery. The predictors of rupture according to the pooled data from 6 prospective cohorts [PHASES score] were geographical region, hypertension, age, history of SAH from another aneurysm, aneurysm size and location, aneurysms with large diameter (> 7 mm) and aneurysms in the vertebrobasilar, anterior communicating, and posterior communicating arteries [33]. Along with these, the aneurysmal factors such as morphology, potentiality of a thrombus within the aneurysm, presence of a daughter sac or multiple lobes and other individual risk factors such as smoking, MIA and family history should be taken into account for decision making [9,19].

The optimal management strategy of unruptured intracranial multiple aneurysms is yet a highly controversial topic. There are no randomised controlled trials to analyse management options such as intervention versus conservative management or clipping versus coiling. The primary question to be addressed is whether patients with MIAs are at a higher risk of aneurysm rupture compared to the ones with single aneurysms? Till date, there is no conclusive scientific evidence about this [2,9,34,35]. However, many authors have opined MIAs are an additional risk factor warranting treatment [5,7,25]. Thus till future evidence-based protocols are in place, treatment by an interdisciplinary approach, based on the availability of both surgical and interventional expertise, tailoring individual therapeutic approaches based on lesion and patient characteristics is probably the best form of management in MIAs which is what we also followed in both our patients, though both of them were asymptomatic. Surgery is recommended for MIAs, if not amenable to coiling [36]. Literature search also revealed that the majority of neurosurgeons trend towards operating on all the detected aneurysms [37].

A single-stage procedure is indicated by multiple intracranial aneurysms on the same side of the anterior circulation. However, if the aneurysms are located bilaterally in the anterior circulation or if they are in both the anterior and the posterior circulations, a two-stage procedure is suitable. However, bilateral Anterior cerebral artery A1 segmental aneurysms, A1-A2 junctional aneurysms, posterior cerebral artery P1 segment aneurysms, superior cerebellar artery aneurysms, internal cerebral artery bifurcation aneurysms and paramedian

aneurysms have been successfully treated with a unilateral craniotomy [2,38,39]. Several authors have stated that a single stage surgery for bilateral multiple aneurysms increases the neurovascular manipulation, surgical time, morbidity and mortality. Many state that a multistage approach has a better outcome [4,11,37,40]. However, multistaged treatment does have disadvantages like increase in the risk of rupture of the unclipped aneurysms, increased hospital stay, high costs and aggravation of psychological burden. Postoperative hyper dynamic therapy is also not possible in multistaged approach as it carries an increased risk of rupture of the unclipped aneurysms [11,40,41].

Microsurgical clipping of small aneurysms is specifically demanding and requires the deployment of techniques like double clip technique, not only for complete occlusion but to prevent slipping of clips as well [42]. In both our cases, we used bilateral multistage approach. We used intraoperative monitoring like MEP, indocyanine green video angiography with DIVA for an intra-operative assessment of the occlusion of the aneurysms and the preservation of the blood flow in parent and branching arteries and Doppler. Postoperative imaging showed complete exclusion of all the aneurysms from the circulation while preserving normal flow except for the cavernous ICA aneurysm, which was wrapped.

Coiling was also considered in both the patients and they were given a detailed explanation of the risk-benefit ratio about both coiling and clipping prior to the decision of surgery. Coiling involves no manipulation of cerebral arteries or brain tissue [4,10]. As such, when multiple aneurysms are located either on both sides or in both the posterior and anterior circulations, a single-stage treatment with coiling may be more practical than one with clipping. However, coiling for very small aneurysms is technically challenging and frequently requires adjunctive techniques such as balloon-assisted or stent-assisted coiling, which may require subsequent antiplatelets and anticoagulation for many months after the procedure. Additionally, coiling is associated with higher intraprocedural rupture rates in small aneurysms compared with larger ones [42–45]. Patients undergoing coiling are prone to thromboembolic events and prolonged treatment time along with contrast-induced nephropathy [12]. Both the International Study of Intracranial Aneurysms (ISUIA) and the International Subarachnoid Aneurysm Trial (ISAT) have reported better outcomes with endovascular coiling when compared with microsurgical clipping [36,46]. However, these conclusions are significant and clinically applicable only for aneurysms whose anatomy, infrastructure, cost and available expertise is suitable for the technique and this is not the case in many instances.

The management of multiple aneurysms should be customised to each case according to the various factors such as preoperative clinical picture, multiplicity, location, size and projection of aneurysms. The experience of the operating surgeon, detailed imaging, meticulous planning, intraoperative adjuncts [IOM, neuronavigation, DIVA etc.] and judicious microsurgical techniques are imperative for a good clinical outcome [11,14].

5. Conclusions

Asymptomatic multiple unruptured intracranial aneurysms are being incidentally detected at a higher rate because of the increased availability of imaging modalities. Once detected, we need to compare the aneurysm's natural history to the risk of intervention while considering the aneurysm location, size, morphology, age, clinical presentation, and medical co-morbidities. These factors will also determine the type of interventional technique to pursue. After an exhaustive review of the literature, the optimum management of this pathology yet remains unclear. The recommendations are based mainly on expert opinion and guidelines, but no high-level evidence is available from clinical trials. Currently, we do not have well defined data about risk of rupture specific to aneurysmal size or location. There is a lack of prospective randomized controlled trials to analyse management options, particularly in comparing intervention with conservative management.

Most of the available data is retrospective in nature and lacks objective short and long-term outcome analysis. Furthermore, we need randomized trials to directly compare clipping and coiling of multiple unruptured aneurysms to decide the best intervention strategy of this pathology.

Declaration of Competing Interest

We have no conflict of interest.

References

[1] S Takeuchi, Y. Takasato, Report of a patient with 13 intracranial aneurysms, Neurol India 59 (5) (2011) 790.

[2] S Guo, Y. Xing, Surgical treatment of multiple intracranial aneurysms, Turk Neurosurg 24 (2) (2014) 208–213.

[3] O Ahmed, P Kalakoti, M Hefner, H Cuellar, B. Guthikonda, Seven Intracranial Aneurysms in One Patient: treatment and review of literature case report introduction, J Cerebrovasc Endovasc Neurosurg 17 (2) (2015) 113–119.

[4] E. Akgul, H.B. Onan, H.T. Balli, N.E. Cetinalp, A patient with eight intracranial aneurysms: endovascular treatment in two sessions, Case Rep Neurol Med 2016 (2016) 1–7 Sep 7.

[5] R. Jabbarli, T.F. Dinger, M. Darkwah Oppong, D. Pierscianek, P. Dammann, K.H. Wrede, et al., Risk factors for and clinical consequences of multiple intracranial aneurysms, Stroke 49 (4) (2018) 848–855. Apr.

[6] Doddasomayajula R, Chung BJ, Mut F, Jimenez CM, Hamzei-Sichani F, Putman CM, et al. Hemodynamic Characteristics of Ruptured and Unruptured Multiple Aneurysms at Mirror and Ipsilateral Locations.

[7] M. Asiltürk, A. Abdallah, Clinical outcomes of multiple aneurysms microsurgical clipping: evaluation of 90 patients, Neurol. Neurochir. Pol. 52 (1) (2018) 15–24 Jan.

[8] C.B. Theodotou, B.M. Snelling, S. Sur, D.C. Haussen, E.C. Peterson, M.S. Elhammady, Genetic associations of intracranial aneurysm formation and subarachnoid hemorrhage, Asian J Neurosurg 12 (3) (2017) 374–381.

[9] N. Ajiboye, N. Chalouhi, R.M. Starke, M. Zanaty, R. Bell, Unruptured cerebral aneurysms: evaluation and management, Sci. World J. 2015 (2015) 1–10.

[10] X. Shen, T. Xu, X. Ding, W. Wang, Z. Liu, H. Qin, Multiple intracranial aneurysms: endovascular treatment and complications, Interv. Neuroradiol. 20 (2014) 442–447.

[11] Choque-Velasquez J, Colasanti R, Fotakopoulos G, Elera-Florez H, Hernesniemi J. A challenging case from the Andean slopes managed with 1-stage surgery. World Neurosurg. 97:565–70.

[12] A. Mehrotra, P. Sharma, K.K. Das, K.S. Bhaisora, J. Sardhara, S. Gupta, et al., Mirror aneurysms among multiple aneurysms: lesser of the two evils, World Neurosurg 92 (2016) 126–132. Aug.

[13] A. Sharma, N. Gupta, M. Gupta, S. Sharma, Dreadful twins: twin unruptured aneurysms of bilateral intracranial arteries, Saudi J Med Med Sci | Publ by Wolters Kluwer-Medknow (2016) 215–217.

[14] T.K. Maiti, S. Konar, A. Nanda, Multiple mirror aneurysms: does the embryological perspective merit a special mention? Neurol. India 63 (5) (2015) 784.

[15] J. Zhao, R. Wang, D. Zhang, S. Wang, Y. Zhao, H. Niu, A comparative study of 43 patients with mirror-like intracranial aneurysms: risk factors, treatment, and prognosis, Neuropsychiatr. Dis. Treat. 10 (2014) 2231 Nov 19.

[16] C.E. Baccin, T. Krings, H. Alvarez, A. Ozanne, P. Lasjaunias, Case report multiple mirror-like intracranial aneurysms. Report of a case and review of the literature, Acta Neurochir. 148 (2006) 1091–1095.

[17] I. Meissner, J. Torner, J. Huston, M.L. Rajput, D.O. Wiebers, L.K. Jones, et al., Mirror aneurysms: a reflection on natural history, J. Neurosurg. 116 (6) (2012) 1238–1241 Jun.

[18] H.E. Ellamushi, J.P. Grieve, H.R. Jäger, N.D. Kitchen, Risk factors for the formation of multiple intracranial aneurysms, J. Neurosurg. 94 (2001).

[19] R.D. Brown, J.P. Broderick, Review Unruptured Intracranial Aneurysms: Epidemiology, Natural History, Management Options, and Familial Screening, vol. 13, (2014).

[20] M. Kaminogo, M. Yonekura, S. Shibata, Incidence and outcome of multiple intracranial aneurysms in a defined population, Stroke 34 (1) (2003) 16–21.

[21] S. Juvela, Risk factors for multiple intracranial aneurysms, Stroke 31 (2) (2000) 392–397 Feb.

[22] M.J.H. Wermer, I.C. Van Der Schaaf, A. Algra, Rinkel J.E. Gabriël, Risk of Rupture of Unruptured Intracranial Aneurysms in Relation to Patient and Aneurysm Characteristics an Updated Meta-analysis, (2007).

[23] H.-T.T. Lu, H.-Q.Q. Tan, B.-X.X. Gu, Li M.-H.H. Wu-Wang, Risk factors for multiple intracranial aneurysms rupture: a retrospective study, Clin. Neurol. Neurosurg. 115 (6) (2013) 690–694 Jun 1.

[24] M. Shojima, A. Morita, H. Nakatomi, S. Tominari, Size is the most important predictor of aneurysm rupture among multiple cerebral aneurysms: post hoc subgroup analysis of unruptured cerebral aneurysm study Japan, Neurosurgery 82 (6) (2018) 864–869 Jun 1.

[25] B. Weir, L. Disney, T. Karrison, Sizes of ruptured and unruptured aneurysms in relation to their sites and the ages of patients, J. Neurosurg. 96 (1) (2002) 64–70.

[26] R. Kleinloog, N. de Mul, B.H. Verweij, J.A. Post, G.J.E. Rinkel, Y.M. Ruigrok, Risk factors for intracranial aneurysm rupture: a systematic review, [E-published ahead

of print], Neurosurgery 82 (4) (2018) 431–440. Apr 1.

[27] P.S. Amenta, S. Yadla, P.G. Campbell, M.G. Maltenfort, S. Dey, S. Ghosh, et al., Analysis of nonmodifiable risk factors for intracranial aneurysm rupture in a large, retrospective cohort, Neurosurgery 70 (3) (2012) 693–701 Mar 1.

[28] D.H. Kim, G. Van Ginhoven, D.M. Milewicz, Familial aggregation of both aortic and cerebral aneurysms: evidence for a common genetic basis in a subset of families, Neurosurgery 56 (4) (2005) 655–661. Apr. (discussion 655-61).

[29] J.E.C. Bromberg, G.J.E. Rinkel, A. Algra, C.M. van Duyn, P. Greebe, L.M.P. Ramos, et al., Familial subarachnoid hemorrhage: distinctive features and patterns of inheritance, Ann. Neurol. 38 (6) (1995) 929–934 Dec.

[30] C.J. Kim, S.S. Park, H.S. Lee, H.J. Chung, W. Choi, J.H. Chung, et al., Identification of an autosomal dominant locus for intracranial aneurysm through a model-based family collection in a geographically limited area, J. Hum. Genet. 56 (6) (2011) 464–466.

[31] P. Berg, O. Beuing, Multiple intracranial aneurysms: a direct hemodynamic comparison between ruptured and unruptured vessel malformations, Int. J. Comput. Assist. Radiol. Surg. 13 (1) (2018) 83–93 Jan 21.

[32] H. Meng, V.M. Tutino, J. Xiang, A. Siddiqui, High WSS or low WSS? Complex interactions of hemodynamics with intracranial aneurysm initiation, growth, and rupture: toward a unifying hypothesis, Am. J. Neuroradiol. 35 (2014) 1254–1262.

[33] J.P. Greving, J.H. Wermer, R.D. Brown, A. Morita, S. Juvela, M. Yonekura, et al., Development of the PHASES score for prediction of risk of rupture of intracranial aneurysms: a pooled analysis of six prospective cohort studies, The Lancet Neurology 13 (2014).

[34] M. Bruneau, M. Rynkowski, K. Smida-Rynkowska, J. Brotchi, O. De Witte, B. Lubicz, Long-term follow-up survey reveals a high yield, up to 30% of patients presenting newly detected aneurysms more than 10 years after ruptured intracranial aneurysms clipping, Neurosurg. Rev. 34 (4) (2011) 485–496 Oct 4.

[35] S.D. Carstairs, D.A. Tanen, T.D. Duncan, O.B. Nordling, J.E. Wanebo, T.R. Paluska, et al., Computed tomographic angiography for the evaluation of aneurysmal subarachnoid hemorrhage, Acad. Emerg. Med. 13 (5) (2006) 486–492 May.

[36] M. Koźba-Gosztyła, B. Czapiga, W. Jarmundowicz, Aneurismal subarachnoid

hemorrhage: who remains for surgical treatment in the post-ISAT era? Arch. Med. Sci. 3 (3) (2015) 536–543.

[37] D. Murrone, B. Romanelli, A. Ierardi, Surgical case series of multiple aneurysms: a single-centre experience of 16 years, Int. J. Surg. Case Rep. 42 (2018) 191–195.

[38] V. Acik, G. Cavus, E. Bilgin, A. Arslan, Y. Gezercan, A.İ. Okten, Surgical treatment of mirror middle cerebral artery aneurysms: bilateral and unilateral approach, World Neurosurg 108 (2017) 774–782 Dec.

[39] C. Kakucs, I.St. Florian, X. Shen, T. Xu, X. Ding, W. Wang, et al., Multiple cerebral aneurysm - case report, Rom Neurosurg 21 (3) (2014) 279–282 Jun.

[40] Y. Xu, S. Chen, B. Lei, W.-H. Zhang, W.-Y. Wang, One-stage operation for rare multiple mirror intracranial aneurysms: a case report and literature review, Turk Neurosurg 24 (4) (2014) 598–601.

[41] D. Wachter, I. Kreitschmann-Andermahr, J.M. Gilsbach, V. Rohde, Early surgery of multiple versus single aneurysms after subarachnoid hemorrhage: an increased risk for cerebral vasospasm? J. Neurosurg. 114 (4) (2011) 935–941. Apr.

[42] N.A. Sai Kiran, B.R. Jahromi, J.C. Velasquez, F. Hijazy, F. Goehre, R. Kivisaari, et al., Double-clip technique for the microneurosurgical management of very small (< 3 mm) intracranial aneurysms, Neurosurgery 11 (Suppl. 2) (2015 Jan) 1.

[43] R. Mohammadian, M. Asgari, N. Sattarnezhad, R. Mansourizadeh, F. Mohammadian, M. Shimia, et al., Endovascular treatment of very small and very large ruptured aneurysms of the anterior cerebral circulation: a single-center experience, Cerebrovasc. Dis. 35 (3) (2013) 235–240.

[44] J. Zhang, X. Lv, C. Jiang, Y. Li, X. Yang, Z. Wu, Endovascular treatment of cerebral aneurysms with the use of stents in small cerebral vessels, Neurol. Res. 32 (2) (2010) 119–122 Mar 19.

[45] P. Jeon, B.M. Kim, D.J. Kim, D.I. Kim, S.H. Suh, Treatment of multiple intracranial aneurysms with 1-stage coiling, AJNR Am. J. Neuroradiol. 35 (6) (2014) 1170–1173.

[46] J. Raymond, F. Guillemin, F. Proust, A.J. Molyneux, A.J. Fox, J.S. Claiborne, et al., Unruptured intracranial aneurysms, Interv. Neuroradiol. 14 (1) (2008) 85–96 Mar 1.