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Research Article

Treatment of Intracranial Superficial Micro-AVMs: A Single Center Experience

Abstract

Background: Surgery and embolization may both be considered in ruptured superficial micro-AVMs. However, surgery may be challenged by poor recognition of the lesion and embolization by difficulty in achieving complete obliteration and avoiding *en passage* feeders. Recent developments in AVM surgery and embolization techniques call for a reevaluation of these treatment options.

Methods: Eight consecutive patients with superficial micro-AVMs are presented. All patients received an initial embolization attempt with either nBCA or ONYX. If complete obliteration was not obtained, either a second embolization or surgical resection was offered. At surgery, indocyanine green video angiography (ICG-VA) was used in all cases. Effectiveness and safety of all procedures were evaluated retrospectively. Functional outcome at 6 months was assessed by the modified Ranking Score (mRS).

Results: Patients had a mean age of 52±17 years and all presented with hemorrhage. The mean nidus size was 4 mm, and was localized supratentorially in 5 cases and infratentorially in 3. Initial embolization was successful in 2 patients (25%). One patient underwent a second, unsuccessful, embolization attempt and 1 patient did not receive further treatment. Consequently, five patients underwent surgery, which was successful in four (80%). The unsuccessful case was successfully reoperated. The only two procedural complications were related to superselective embolization, but neither caused clinical sequelae. Mean clinical follow-up was 29 months (range, 4–75mo), with mRS 0 in 2, mRS 1 in 4 and mRS 3 in 2 cases.

Conclusions: In a current case series, embolization of superficial micro-AVMs was associated with a lower success rate (25% vs 80%) than microsurgery and a higher procedural complication rate (minor complications: 22% vs 0%).

Introduction

Micro-arteriovenous malformations (AVMs) are defined as brain AVMs with a nidus smaller than 1 cm in diameter [1]. Micro-AVMs are rare and account for approximately 8–11% of all cerebral AVMs [2–4]. Patients with these small AVMs almost always present with intracranial hemorrhage and are most frequently young adults. Anatomic characteristics can be made visible with intra-arterial digital subtraction angiography (DSA), but at times the only finding is an early draining vein. Diagnosis can be difficult as the hemorrhage can obscure the micro-avm by direct compression or post hemorrhagic thrombosis and vasospasms [5]. Second (late) angiographic evaluation and selective angiography have been reported to increase the diagnostic yield in patients with a high suspicion of an underlying AVM [2,6,7]. Part of the clinical challenge is the choice from multiple treatment modalities, represented by microsurgical resection, endovascular embolization and

stereotactic radiosurgery. Although ruptured micro-AVMs which are not suitable for either endovascular treatment or surgery, due to their angioarchitectural details and/or location, may be treated by stereotactic radiosurgery, endovascular treatment and surgery are the first choice of treatment since they offer the advantage of immediate obliteration of the AVM and subsequent protection from recurrent hemorrhage. Recent microsurgical advantages regarding the use of intraoperative indocyanine green video angiography (ICG-VA) and endovascular advantages regarding the introduction of cellulose acetate polymers (ONYX) for embolization and continuing improvements of (micro)catheters and guide wires call for a reevaluation of the choice between these treatment modalities [8–10].

Methods

A retrospective analysis of intracranial micro-AVMs treated at the Leiden University Medical Center between

December 2007 and November 2013 was performed. Patients were included if DSA demonstrated an AVM with a nidus size smaller than 1 centimeter or without a clearly definable nidus, but demonstrating early venous drainage. Only superficial micro AVM were included, defined by a cortical and/or subcortical localization, as these were equally amenable to both endovascular and surgical treatment. Patients who had undergone prior treatment of their AVM were excluded.

DSA was performed with standard biplane fluoroscopy equipment (Infinix, Toshiba Medical Systems, Japan). Diagnostic workup consisted of bilateral injections of the internal carotid arteries, external carotid arteries and at least one vertebral artery. During each injection anterior-posterior and lateral projections were obtained at 6 fps.

Following evaluation by a multidisciplinary team, the treatment protocol for (sub) cortical micro-AVMs typically included an initial embolization attempt. If complete obliteration was not obtained, either a second embolization or surgical resection was offered, depending on the procedural findings and patient preference.

Endovascular treatment was performed under general anesthesia. A 6 French (F) guiding catheter was positioned in the internal carotid or vertebral artery that supplied the AVM. Systemic heparin was administered with an initial dose of 3000 IU, followed by an hourly dose of 2000 IU. A 1.2 / 1.8F microcatheter (Marathon; Covidien, Ireland, Sonic; Balt, France or Ultraflow; Covidien, Ireland) was placed in the feeding artery as close as possible to the AVM nidus. Embolization agents used were either N-butyl-cyanoacrylate (nBCA) or ONYX (Covidien, Ireland), and depended on the interventionalist's preference.

In case of surgical removal of the micro-AVM we routinely used MRI neuronavigation to plan the craniotomy and to localize the nidus. ICG-VA was used to map the angioarchitecture of the AVM before resection and to rule out the presence of residual early venous drainage post resection in all cases. A bolus of 25 mg ICG in 5 mL of saline was administered intravenously by the anesthesiologist. We used the IR800 module provided with the Zeiss Pentero operating microscope (Zeiss, Germany).

Effectiveness and safety of all procedures were evaluated retrospectively. Follow-up evaluations of the patients consisted of clinical examinations performed by a neurosurgeon during hospital admission and outpatient clinic visits. To confirm complete obliteration or surgical removal all patients underwent a post procedural DSA, at least 6 months after treatment. Final outcome after at least 6 months was classified according to the Modified Rankin Scale (mRS). The evaluation was performed by the treating physician during follow-up at the outpatient clinic.

Results

Between December 2007 and November 2013, 8 consecutive patients with superficial micro-AVMs were included. Patients had a mean age of 52±17 (SD) years and included 3 males and 5 females. Table 1 lists a summary of patient demographic

data and angiographic characteristics. All patients presented with hemorrhage. None required immediate evacuation of the hematoma. Six patients had a mRS 4, 1 mRS 3 and 1 mRS 2 during admission. All patients underwent a diagnostic DSA. In two patients delayed angiography was required to detect the micro-AVM. The mean nidus size was 4 mm (range 2 – 9). Superficial micro-AVMs were localized supratentorially in 5 patients and infratentorially in 3 patients. Initial embolization was successful in 2 patients (1 treated with ONYX and one treated with nBCA). Of the unsuccessful attempts, 3 patients demonstrated only *en passage* feeders and no embolization was attempted; embolization was performed in the other 3 patients without achieving complete obliteration due to incomplete nidal opacification and persistent early venous drainage. Liquid embolic agents used were ONYX in 2 patients and nBCA in 1 patient. Subsequently, one patient refused further treatment, one insisted on a second embolization attempt which was deemed feasible by the interventionalist and 4 patients underwent microsurgical resection. The second embolization attempt using ONYX was, again, unsuccessful due to incomplete nidal opacification. Follow-up DSA demonstrated persistent early venous drainage and was followed by surgery. Surgery resulted in complete removal of the micro-AVM in 4 of 5 cases. Repeat surgery was performed in the one case with a residual shunt, and was followed by a DSA demonstrating complete removal. Figure 1 demonstrates these treatments in a flow-chart.

Intraoperative ICG-VA allowed for quick and accurate recognition of the angioarchitecture (Figure 2). Negative ICG-VA following the removal of the micro-AVMs was in agreement with conventional follow-up DSA in 5 out of 6 procedures (Figure 3). Initial post-operative DSA was performed after a mean of 4 (0–7) months and the 3 patients who had their initial DSA within 0–3 months underwent a second late postoperative DSA after 17–27 months. Two complications related to the attempt of superselective embolization occurred (dissection of an MCA branch during catheter retrieval and a feeder perforation), but neither caused clinical sequelae. No

Table 1: Patient characteristics

Sex	Age	Initial neurological condition	AVM localization	Feeding artery	Nidus size
M	40	hemiparesis	fronto-parietal cortex	distal callosal marginal artery	2 mm
F	59	hemiparesis	parietal cortex	distal superior MCA branch	3 mm
M	64	hemiparesis, seizures	fronto-parietal cortex	distal callosal marginal artery	3 mm
F	29	afasia, hemiparesis	fronto-parietal cortex	distal MCA branch	3 mm
F	59	gait instability	cerebellar cortex	distal SCA branch	5 mm
F	77	gait instability, dysarthria	cerebellar vermis	distal SCA branch	9 mm
F	29	hemianopia	occipital cortex	calcarine branch of medial occipital artery	4 mm
M	56	obtunded, ataxia, diplopia	cerebellar vermis	distal SCA branch	5 mm

MCA: middle cerebral artery; SCA: superior cerebellar artery

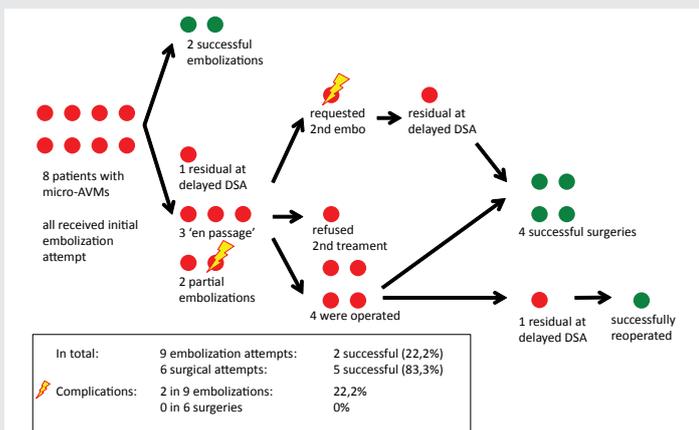


Figure 1: Flow-chart of treatments, micro-AVM obliteration rate and complication incidence.

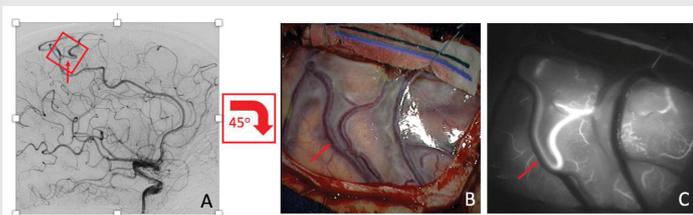


Figure 2: Correspondence of angioarchitecture of a micro-AVM at DSA, intraoperative inspection and ICG-VA. (A) Diagnostic DSA demonstrating an early draining vein (arrow), draining towards the superior sagittal sinus. (B) Intraoperative photograph, taken through the operating microscope, demonstrating the area where the micro-AVM is expected to be. (C) Image from the ICG-VA video, prior to resection, demonstrating the early filling of the vein in the arterial phase (arrow), comparable to image A.

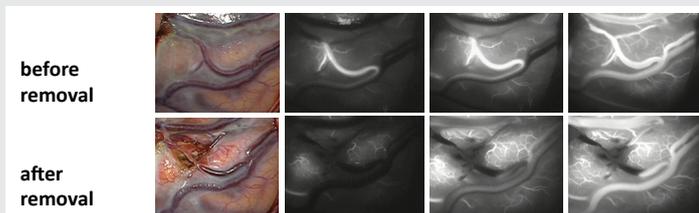


Figure 3: Intraoperative ICG-VA. Same case as Figure 2. Surgical photograph and three images from the ICG-VA video (early arterial, late arterial and venous phases) before resection of the micro-AVM demonstrating early venous drainage (top row) and after complete resection of the micro-AVM (bottom row).

complications of microsurgery were observed. Mean clinical follow-up was 29 months (range, 4–75mo), with mRS 0 in 2, mRS 1 in 4 and mRS 3 in 2 cases. These mRS scores depended primarily on the effects of the initial hemorrhage, rather than the treatment.

Discussion

This study presents a retrospective analysis of a consecutive series of 8 patients with a hemorrhage due to a superficially located micro-AVM, all of which were subjected to an initial endovascular treatment attempt. If only the first endovascular or surgical treatment attempt is considered for each case, the success rates were respectively 2 out of 8 (25%) and 4 out of 5 (80%). The only two procedural complications occurred in endovascular procedures, fortunately without clinical sequelae.

Since patients were of middle age and presented with hemorrhage, the risk of recurrent hemorrhage was expected to outweigh the potential risk for complications of treatment [11,12]. To ensure immediate protection from recurrent hemorrhage we did not offer stereotactic radiosurgery. For the remaining treatment options, endovascular or surgical, these lesions would appear to be perfectly amenable to both, since small nidus size is a favorable characteristic for both surgery and endovascular treatment [3,4,10,13,15]. We expected the primary endovascular challenge to be microcatheterization sufficiently close to the lesion and the primary surgical challenge to be identification of the small nidus. Recent developments bear on both challenges, e.g. new endovascular materials, new embolic agents and intraoperative video angiography. Therefore, we opted to offer all patients an endovascular treatment attempt, followed by surgery if necessary and analyzed the treatment results, retrospectively.

In literature, we identified 8 previous studies that reported on the treatment results of surgery, endovascular treatment or both for micro-AVMs (Table 2). Overall, these reports favor surgical treatment, with obliteration rates of surgery ranging from 88–100% and those of endovascular treatment ranging from 0–100%. However, a reliable comparison of surgery and endovascular treatment from these studies is hampered by the fact that in each case a choice was made for one treatment modality or the other. Even in those studies reporting on both treatment modalities, patients were not randomly assigned to one or the other modality, rendering the two subgroups incomparable. Generally, superficial micro-AVMs embedded in non-eloquent brain area generally received surgical treatment and micro-AVMs in an eloquent area or with deep venous drainage were offered endovascular treatment [4,14,15]. Although our study is also a retrospective analysis, it does allow for a more reliable comparison of treatment results, since we included only cortical and subcortical AVMs (<1cm) equally amenable to endovascular and surgical treatment and all patients underwent an initial embolization attempt.

Compared to results of previous studies reporting embolization results of micro-AVMs, our success rate of embolization is relatively low. One explanation for this difference is that we performed superselective catheterization in all cases, under general anesthesia, considering this an embolization attempt. Safe and complete occlusion of a nidus can only be achieved with superselective access to distal feeding arteries, which are not of an *en passage* nature. Consequently, three embolization attempts were aborted in this study due to the presence of only *en passage* feeding arteries. Such angioarchitectural details are generally not recognized on diagnostic (non-superselective) angiography. The remaining four unsuccessful attempts failed to achieve complete obliteration of the micro-AVM. Liquid embolic agents used in our series were ONYX in 4 procedures (1 successful) and nBCA in 2 (1 successful). All previous studies reporting embolization results of micro-AVMs used nBCA [13–15]. The safety and effectiveness of both agents in preoperative adjunct treatments, have been compared in a single randomized controlled trial including larger AVMs [16], but they have not

Table 2: Previously published (retrospective) series of micro-AVMs

Study	Oya et al. 2015	Alen et al. 2013	Andreou et al. 2008	Perrini et al. 2004	Cellerini et al. 2002	Stiver et al. 1999	Willinsky et al. 1992	Willinsky et al. 1988
Size / location	N=8 2 deep, 6 superficial	N=28 19 cortical, 9 deep	N=26	N=14 12 cortical, 2 deep	N=10 9 cortical, 1 deep	N=12 10 cortical, 2 deep	N=5	N=13 13 superficial
Endovascular obliteration rate	NA	2/2	20/26	7/9	5/7	0/2	0/3	NA
Surgical obliteration rate	8/8	16/16 (4/6 radiosurgery)	NA	7/8	5/5	12/12	1/1	13/13
Endovascular complications	NA	no morbidity	3 (12%) haemorrhagic	2 (22%) haemorrhagic	no neurological	none*	0/3	NA
Surgical complications	no neurological	no morbidity	NA	0	no neurological	2 (17%) neurological, 1 (8%) infection	NA	0
Endovascular method	NA	nBCA	25 nBCA, 1 ONYX	nBCA	nBCA	nBCA *no safe catheter positioning	nBCA	NA

NA: not available

been compared directly in achieving successful obliteration to date. Unfortunately, the number of patients in our study is too small to draw any conclusions regarding the choice of embolic agent.

Our endovascular complication rate is comparable with the 12–22% hemorrhagic complications reported by Andreou et al. and Perrini et al. [13,15]. Others have merely reported the absence of neurological complications [4,14], which is also similar to our results. Neurologic deficits were attributable to the initial hemorrhage and depended on the size and location of the hematoma.

All patients underwent delayed postoperative DSA to confirm complete micro-AVM obliteration after at least 6 months. Although recurrence of AVM generally does not occur among adults after complete resection [17], we believe that early postoperative angiographic evaluation may yield false negative results due to low-flow AVM remnants of a micro-AVM that was already barely visible during the initial DSA. Furthermore, in cases of AVM's treated with endovascular embolization proximal occlusion of feeding arteries with incomplete embolic nidal opacification is associated with AVM recurrence [18].

The use of ICG-VA in AVM surgery has been previously reported to be a useful adjunct in micro-AVM surgery [10]. In our experience ICG-VA was particularly useful to identify the vascular anatomy as demonstrated by the pre-operative DSA. However, the technique has limitations regarding deep seated lesions and AVM with deep venous drainage as only exposed vessels are visualized with ICG-VA [19]. Moreover, we do not consider post-resection ICG-VA a substitute for postoperative follow-up DSA. Despite negative ICG-VA following removal of the micro-AVM, 1 out of 6 postoperative DSAs demonstrated persistence of the micro-AVM. Similarly, other authors have reported cases with residual AVM despite negative postoperative ICG-VA [19,20]. Adverse reactions to ICG-VA are rare [21] and we did not encounter any.

Conclusion

Although microsurgical resection and endovascular embolization may both be considered in ruptured superficial micro-AVMs, our results – although based on a small series – showed that endovascular treatment was associated with a lower success rate (25% vs 80%) and a higher procedural complication rate (22% vs 0%) than microsurgical resection. In our experience the higher success rate of microsurgery benefits from the use of intra operative ICG-VA. Our results suggest that microsurgery, using ICG-VA, should be considered the primary choice for the treatment of superficial micro-AVMs. In case an initial endovascular treatment attempt is offered, procedural risks should be kept at a minimum, as subsequent microsurgery can be performed safely and effectively.

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