Transcatheter Embolo-sclerotherapy of High Flow Arteriovenous Malformations

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ABSTRACT

Background: Vascular malformations can be classified according to endothelial characteristics and flow dynamics of the lesions, on which the principles of treatment are based. Percutaneous injection of sclerosing agents such as ethanol or sodium tetradecyl sulfate is the mainstay treatment for the more prevalent low-flow or venous vascular malformations. In contrast, symptomatic high-flow arteriovenous malformation (AVM) generally requires transcatheter embolo-sclerotherapy with or without surgery to control the disease process.

Objective: To evaluate the safety and efficacy of endovascular management of high flow arteriovenous malformation by embolization and sclerotherapy.

Patients and methods: This study was conducted at Mansoura University Hospitals, we included a total of 18 cases diagnosed with high flow AVM. All cases were subjected to complete history taking, thorough physical examination, and routine laboratory investigations. Also, duplex ultrasound (US) and computed tomography (CT) angiography were ordered for all cases.

Results: The mean age of the included cases was (26.73 years (range, 8 – 60 years). Males represented 61.11% of these cases, while the remaining patients were females. As regard the clinical result, success was achieved in 16 cases (61.11%). Only two cases had poor clinical result (11.11%). Transient ischemia was encountered in 2 cases (11.11%). Other complications included ulceration (5.56%), foot gangrene (5.56%), hand ischemia with amputation (5.56%), contracture scar (5.56%), and necrosis with transient PE (6.7%). With a mean follow up period of 26 months (range, 6 – 36 months), 16 cases showed very good outcome (88.89%), one case had good outcome (5.56%), while the remaining case had poor outcome (5.56%).

Conclusion: Embolo-sclerotherapy appears to be safe and effective intervention for high flow arteriovenous malformations.

Keywords: Arteriovenous Malformations, Embolo-sclerotherapy, Transcatheter.

INTRODUCTION

AVMs are one of various congenital vascular malformations (CVMs) that result from birth defects involving the vessels of both arterial and venous origins resulting in direct communications between the different size vessels or via a meshwork of abnormal vessels termed a "nidus". These lesions are defined by shunting of high velocity, low resistance flow from the arterial vasculature into the venous system in a variety of fistulous conditions [(1)].

Irrespective of the presence or absence of a nidus, all AVMs demonstrate high flow through micro- or macro-fistulous communications between the arterial and venous systems. Due to this unique condition of AV shunting, AVMs have vastly different clinical presentations compared to VMs and other CVMs, with a wide range of presentations, unpredictable clinical course, complicated anatomical, pathophysiological, and hemodynamic status [(2)].

Vascular malformations at the histologic level demonstrate no endothelial cell proliferation, contain large vascular channels lined by flat endothelium, have a unilamellar basement membrane, do not incorporate tritiated thymidine into endothelial cells, and have normal mast cell counts. They may be formed from any combination of arterial, capillary, venous, or lymphatic elements with or without direct arterial venous shunts. Vascular malformations are true structural anomalies resulting from incomplete resorption of primitive blood vessels [(3)].

Ultrasonography is the method of choice for initial evaluation and demonstrates anechoic tubular structures, without well-defined soft tissues mass. At Doppler ultrasonography, the lesion presents with areas of arteriovenous shunt with increased peak systolic velocity and ectatic veins with arterialized flow. Magnetic resonance imaging demonstrates several areas with signal absence (signal-void) on T1- and T2-weighted sequences, corresponding to the supplying arteries and to the malformation nidus. Generally no mass is observed adjacent to the pathological vessels, which facilitates the differentiation between AVMs and hypervascular tumors [(3)]. At computed tomography the aspect of multiple ecstatic supplying arteries is also observed, with early contrast-enhancement of the drainage veins, with no significant interposed mass. Computerized tomography angiography (CTA) is the gold standard for the diagnosis of AVMs, characterized by early contrast-enhancement of venous structures and by the presence of malformative nidus [(4)].

High-flow lesions include congenital arterial vascular malformations, arteriovenous fistulae, and acquired vascular lesions as well. Low-flow lesions

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include venous malformations, lymphatic malformations, capillary venous malformations, and mixed lesions [5].

Endovascular therapy with various embolization and sclerotherapy modalities, is now fully accepted as the 'preferred' therapeutic option in the majority of "extratruncular" high flow AVM lesions [6]. Endovascular/Embolo-sclerotherapy alone as an independent therapy is the treatment of choice for surgically "inaccessible" lesions or the lesion with prohibitive surgical risks as independent therapy, such as AVM lesions that extend beyond the deep fascia and involve muscle, tendon and bone – the diffuse infiltrating type of extratruncular form of AVMs in particular. Precise delivery of the embolo/sclerosants directly into the nidus of the extratruncular AVM lesion is required for successful endovascular therapy. The outdated approach with the coil embolization or proximal ligation of AVM feeding arteries should be abandoned [7].

A combination approach utilizing all three routes of delivery (transarterial, transvenous, and direct puncture) should be considered to destroy the AVM lesion nidus as much as possible. Multi-session endovascular therapy is preferred and every effort should be exercised to minimize the risks of embolo-sclerotherapy during each session. The most appropriate embolic agents for primary control of AVM include: absolute ethanol, onyx and N-butyl cyanoacrylate (NBCA). The use of NBCA or onyx alone is generally inadequate to "cure" or provide long-term control for AVM [8].

The aim of the current study was to evaluate the safety and efficacy of endovascular management of high flow arteriovenous malformation by embolization and sclerotherapy.

PATIENTS AND METHODS

This prospective cross-sectional study was conducted at Vascular Surgery Department, Mansoura University and Emergency Hospitals, Mansoura, during the period between December 2015 and November 2020. It was performed aiming to evaluate the efficacy of transcatheter embolo-sclerotherapy in patients presenting with high flow AVM during the study period.

Ethical consideration:

An informed written consent was obtained from all cases prior to the procedure after complete explanation of the benefits and drawbacks of the intervention planned. **Also, the study was approved by the Institutional Review Board of Faculty of Medicine, Mansoura University.**

Inclusion criteria: All patients presented to our hospital with high flow arteriovenous malformations as assessed by clinical examination, ultrasound, and preoperative MRI or CTA, and can afford high treatment cost.

Exclusion criteria: Intracranial AVM, hypersensitivity for angiographic dye, renal impairment, poor cases who cannot afford treatment cost.

Patient preparation:

All cases were evaluated and performed by the same surgical and radiological team with the standard procedure.

History: Personal history, present history, the symptoms varied according to the site and size of the lesion, medical history and surgical history.

Examination: General examination, local examination: for the detected lesion including inspection, palpation, and auscultation.

Laboratory investigations: Renal function was evaluated prior to embolization procedure, prothrombin time and concentration (International Normalized ratio or INR), partial thromboplastin time, and platelet count were also ordered and virological markers (including HCV Ab, HBV HBs Ag, and HIV Ab).

Radiological investigations: Ultrasound with duplex to assess the tumour size, vascularity, nature, and depth of the tested lesion, computerized tomography angiography (CTA) to assess the relation of the mass to the surrounding blood vessels and magnetic resonance imaging (MRI) was ordered in some doubtful cases for further assessment of lesion size, shape, extent, along with its relation to surrounding soft tissues.

Anesthesia: Either local or general anesthesia was used based on lesion site and anesthesiologist's preference.

Access: Either of the transfemoral or trans-brachial approaches was used according to pre-procedure imaging. Single or double access techniques were used. Double access technique was approached via femoral artery and vein, or femoral artery and internal jugular vein. Duplex was used to facilitate access.

Angiography: Initial flush arteriogram was performed to map out arterial anatomy. When stable selective catheter position was achieved, a microcatheter was usually used to select the arteries directly supplying the lesion.

Angiographic appearance: The number and origin of the feeding vessels were evaluated. Collateralization to or from adjacent healthy tissue was also assessed.

Post-procedural care: Analgesia and anti-inflammatory medications were needed for control of post procedure pain. Pain was usually controlled via IV paracetamol or NSAIDs. Post-embolization syndrome (fever, abdominal pain and leukocytosis after embolization) was best managed by supportive

therapy. Anti-emetics, anti-inflammatory, and oral pain medications were commenced when needed.

Statistical Analysis

Recorded data were analyzed using the statistical package for the social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean± standard deviation (SD), median, and range. Qualitative data were expressed as frequency and percentage.

RESULTS

We collect a total of 18 cases with high flow AVM in the current study. The mean age of the included cases was 26.73 years. Males represented 61.11% of these cases (Table 1).

Table (1): Demographic data of cases included in study

Variable	Study cases (N = 18)	
Age		
Mean ± SD	26.73 ± 16.38	
Median (Min-Max)	23 (8-60)	
Gender		
	Number	Percentage
Male	11	61.11 %
Female	7	38.89 %

Regarding the site of AVM, left mandible was affected in 3 cases (20%), while right hand was affected in the same number of cases. Other sites included lower lip, lower lip and right mandible, right mandible, right ear and mandible, posterior neck triangle, right cheek, right lumbar region, right and left foot (Table 2).

Table (2): Site of the lesions of cases included in study

	Number	Percent
Lower lip	2	11.11%
Lower lip and right mandible	1	5.56%
Right mandible	1	5.56%
Left mandible	3	16.67%
Right ear and mandible	1	5.56%
Posterior triangle of neck	1	5.56%
Right cheek	1	5.56%
Right forearm	2	11.11%
Right lumbar	1	5.56%
Right hand	3	16.67%
Right foot	1	5.56%
Left foot	1	5.56%

Painful swelling was reported by all cases, whereas bleeding was experienced in 8 cases. In addition, ten cases complained of disfigurement caused by the lesion (Table 3).

Table (3): Symptoms and signs of cases included in study

Variable	Study cases (N = 18)	
Pain		
Absent	0	0 %
Present	18	100 %
Swelling		
Absent	0	0 %
Present	18	100 %
Bleeding		
Absent	10	55.56 %
Present	8	44.44 %
Disfigurement		
Absent	8	44.44 %
Present	10	55.56 %

Table 4 shows the clinical stage of the included cases, previous intervention, other embolic materials used, technical results and clinical results included in study.

Table (4): Clinical stage of cases, previous intervention, other embolic materials used, technical results and clinical results included in study

Parameters	Study cases (N = 18)	
Clinical stage: Stage II	10	55.56 %
Stage III	8	44.44 %
Previous intervention: No	11	61.11 %
Surgical	4	22.22 %
Embolization	2	11.11 %
Surgical + Embolization	1	5.56 %
Other embolic materials: Alcohol	10	55.56 %
Alcohol + Coils	5	27.78 %
Alcohol + Histoacryl	3	16.67 %
Technical results: Complete	16	88.89 %
Partial	2	11.11 %
Clinical results: Poor	2	11.11 %
Success	16	88.89 %

No complications were encountered in 11 cases. Complications in other cases included in study are shown in table 5.

Table (5): Complications in the cases included in study

Complications	Study cases (N = 18)	
No	11	61.11%
Transient ischemia	2	11.11%
Ulceration	1	5.56%
Foot gangrene	1	5.56%
Hand ischemia and amputation	1	5.56%
Contracture scar	1	5.56%
Necrosis and transient PE	1	5.56%

With a mean follow up period of 26 months, 16 cases showed very good outcome (Table 6).

Table (6): Follow up duration and final outcomes of cases included in study

Variable	Study cases (N = 18)	
Duration of follow up (months)		
Mean ± SD	26 ± 11.71	
Median (Min-Max)	24 (6 - 36)	
Final outcome		
	Number	**Percentage**
Poor	1	5.56 %
Good	1	5.56%
Very good	16	88.89 %

DISCUSSION

This study was conducted at Mansoura University Hospitals aiming to evaluate the safety and efficacy of endovascular management of high flow arteriovenous malformation by embolization and sclerotherapy. We included a total of 18 cases diagnosed with high flow AVM whose mean age was 26.73 years. Another study handling the same perspective included a total of 16 cases, whose mean age was 38.9 years, and that age was higher than the one reported by ours [9]. The difference between results regarding age could be attributed to the small sample size and the characteristics of the included population in every study.

In the current study, males represented 61.11% of these cases, while the remaining patients were females. In line with our findings, **Kilani *et al.*** [10] also reported that males had higher prevalence compared to females in their study that included 19 cases with AVM. The authors included 10 males in addition to 9 females.

Regarding the site of AVM in the current study, left mandible was affected in 3 cases (20%), while right hand was affected in the same number of cases. Other sites included lower lip, lower lip and right mandible, right mandible, right ear and mandible, posterior neck triangle, right cheek, right lumbar region, right and left foot. In another study, AVMs were located in the head and neck (6), extremities (5), chest (2), kidney (2), uterus (2), pelvis (1) and parietal (1) [10]. Of course, the site of AVM will be different between different studies. Due to the variability in the location of the lesion and small sample size, it is reasonable to find a heterogenicity of locations in each study, and that represents one of the current study limitations.

In our study, we either used the single way technique through the femoral or brachial arteries. However, double access technique was used in some cases to approach both of the feeding artery and vein to obtain better results.

As regard the previous interventions for AVM included, four cases had previous surgical intervention (22.22%), while embolization was performed in two cases (11.11%). Only one case had both surgery and embolization (5.56%). **Kilani and his associates** [10] reported that 6 out of the included 19 cases had previous intervention for their AVM. One case (5.26%) had previous embolization with surgery, while two cases (10.63%) had previous coil embolization. In addition, another 2 cases had previous gelatin sponge embolization, whereas one case had amputation of the little finger as a partial management of his AVM. This denotes the variability of interventions proposed for AVM according to the treatment protocol in every surgical center. Also, the previous findings indicate that some cases may not benefit the previous interventions and were seeking for another one.

In our study, onyx ampoules (type 18 – 1.5 ml) were used in 12 cases (66.67%). Together with onyx, alcohol was injected in 10 cases (55.56%), while it was used along with coil embolization in 5 cases (27.78%). Combined alcohol and histoacryl injection were performed in 3 cases (16.67%). As regard cases for whom onyx was not applied, 3 cases had histoacryl and alcohol, while two cases had coil embolization and alcohol injection. Additionally, one case had alcohol injection only. Onyx was the main embolic agent in our study due to its advantages, while the use of other agents was based on operator preference. Additional agents should be considered to occlude vessels not suitable for onyx®, as occurred in 31.2% of cases in this series; comparable additional agents usage rates were reported by both **Kilani *et al.*** [10] **and De Beule *et al.*** [11] (41% and 31.5%, respectively). These studies reported lower rates compared to ours, as the included cases in the previous studies did not necessarily had high flow AVM, which might need additional embolic or sclerosing agents along with onyx to obtain optimum technical result. Different embolic agents can be used for endovascular transcatheter embolization. Coils and detachable balloons cause proximal occlusion with no distal penetration into the nidus. When used, even in preoperative setting, coils may

preclude further endovascular access especially in case of recurrence after surgery [12].

In the current study, 13 cases had only one embolization session, whereas the remaining five cases had two sessions (27.78%). It is frequent that multiple embolization sessions are necessary [13-15]. In another study conducted in 2017, only one embolization session was performed in 14 cases (73.68%); two sessions in three cases (15.78%); three sessions in one (5.26%) and five sessions in one case (5.26%) [10].

As regard outcomes in the current study, complete embolization was achieved in most cases (88.89%), while only one case had partial embolization. As regard the clinical result, success was achieved in 16 cases (61.11%). Only two cases had poor clinical result (11.11%). Regarding outcomes reported in other studies, in an initial case series published in 2004, **Numan *et al.*** [16] referred to 15 procedures of 9 patients affected by upper or lower extremity AVM; they described complete embolization in 2 patients and significantly reduced flow in other 4 cases with relatively low clinical success (33.3%). The reason of this low success rate may be explained by the uncomplete knowledge of onyx® properties at that time and since handling of this material has improved thanks to the experience acquired in neurovascular interventions.

De Beule *et al.* [11] performed 25 procedures on 22 patients and described complete radiological success in 8 cases and near-complete nidus embolization in the remaining 14 patients; nevertheless, they reported clinical success in 18 patients (82%), but at follow-up they found 32% of recurrence, resulting in quite accordance with this experience (43.7% recurrence rate). **Kilani *et al.*** [10] reported that completion angiogram revealed total occlusion in 12 patients (63%). Embolizations were incomplete but achieved marked flow reduction (>80 %) through the malformation in 5 patients (26%). This was due to non-embolized feeders originating from ICA, or due to very tiny feeders that were difficult to catheterize with important risk of reflux. In 16 patients (84.21%), clinical symptoms completely disappeared after embolization and/or surgery. **Barral *et al.*** [17] also evaluated the outcomes of onyx embolization in uterine malformations. Sixteen arterial embolization procedures were performed. Angiographically, 6 women had high flow AVM and 6 had low flow AVM. The rate of technical and clinical success was 91.6% (11/12 patients).

As regard the encountered complications in the current study, transient ischemia was encountered in 2 cases (11.11%). Other complications included ulceration (5.56%), foot gangrene (5.56%), hand ischemia with amputation (5.56%), contracture scar (5.56%), and necrosis with transient PE (6.7%). The two cases who had finger and foot amputation had previous brachial and posterior tibial ligation respectively. Also, histoacryl was used in these cases, and it was associated with reflux, that exaggerated the ischemic condition.

Park *et al.* [18] reported that skin necrosis was encountered in 11.4% of cases, while gangrene occurred in 2 cases (0.2%). In addition, contracture occurred in only one case (0.1%). Other complications included discoloration, distal embolism, rhabdomyolysis, bladder rupture, compartmental syndrome, and focal renal infraction. Another study reported that complications following the procedure were as follows; one patient developed stroke. 1 case had microcatheter fracture. 1 patient presented severe pain and bradycardia during the procedure that disappeared shortly after. One patient had persistent but less frequent epistaxis. Another patient had persistent pain without improvement [10].

In the study conducted by **Giurazza and his associates** [9], one episode of nontarget embolization due to ethylene-vinyl alcohol copolymer (EVOH) reflux occurred, with consequent peroneal artery definitive embolization; however, no long-term ischemic clinical sequelae were seen (6.25%). In three patients, groin swelling and hematoma, self-limiting without additional therapies, were registered (13.75%); 4 patients (25%) showed post-embolization syndrome up to 5 days after the procedure and they were managed with anti-inflammatory medications and antibiotics.

CONCLUSION

Embolo-sclerotherapy appears to be safe and effective intervention for high flow arteriovenous malformations. Onyx seems to provide controlled embolization due to slow polymerization which enables deep penetration in the nidus with less risk of catheter gluing due to its non-adhesive nature.

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