EC NEUROLOGY
Research Article

Curative Embolization of Small Brain Arteriovenous Malformation by Non-Adhesive Liquid (Ethyl Vinyl Alcohol Copolymer): A Retrospecive Study from Tertiary Care Centre

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Abstract

Background and Objective: A Randomised trial of Unruptured Brain Arteriovenous malformations (ARUBA) trial has favoured treatment of unruptured AVM by best medical management alone. However critics have generally accepted treatment of Low grade AVM by neurosurgery and deep, eloquent AVM by radiosurgery. Objective of this study is to retrospectively examine effectiveness of embolization by non adhesive liquid embolic agent (ethyl vinyl alcohol copolymer) for complete cure of small Brain AVM.

Methods: We retrospectively analyzed patients with small brain AVM treated by embolization during January 2008 to January 2020. The primary goal was to cure it completely. There were 16 patients with 9 males and 7 females. Their age was ranging from 18 to 38 years with mean of 30 years. There were 5 patients with ruptured and 11 with unruptured AVM.

Results: Twenty embolization sessions were done in 16 patients. Twelve patients had undergone single session each and 4 patients with two sessions each. Fifteen out of sixteen patients were cured completely with embolization alone (93.75% Obliteration rate). The one patient (6.25%) required SRS to achieve complete cure for the residual AVM after two sessions of embolization. Non permanent complication rate was 18.75%. There were no deaths.

Conclusion: Embolization of small brain AVM with intension to cure by non Adhesive liquid embolic agent can deliver obliteration rate of 93.75%. Complication rate associated with embolization in our small retrospective study is 18.75% with no permanent disability or deaths.

Keywords: *Curarive Embolization; Brain AVM; Non-Adhesive Embolic Liquid (EVOH)*

Abbreviations

AVM: Arteriovenous Malformation; EVOH: Ethyl Vinyl Alcohol Copolymer; DMSO: Dimethyl Sulfoxide; NBCA: N-Butyl Cyanoacrylate Glue; SRS: Stereotactic Radiosurgery

Introduction

Brain arterio-venous malformation(AVM) is tuft of abnormal vessels supplied by artery and drained by vein with arterio-venous shunting. They should be considered genetically acquired as genetic susceptibility kick starts nascent focus and environmental triggers acting as second hit, are responsible for their development and proliferation [1]. Incidence of hemorrhagic stroke as first presentation of brain AVM is low (1%) but rebleeding rate is high (up to 5%) [2,3]. Considering the life time risk of haemorrhage in brain AVM, low grade (SM grade I and II) unruptured AVM patients can be offered curative treatment [4,5]. Neurosurgery and radiosurgery are well established as curative modalities. Curative potential of embolization is still underutilized. We present retrospective study of cohort of patients with small brain AVM embolized by non adhesive liquid embolic agent (EVOH) and examine its effectiveness for complete cure. We analysed our results along with relevant literature.

Materials and Methods

We retrospectively analyzed patients with small brain AVM treated by embolization during January 2008 to January 2020. The primary intension was to cure it completely. Study spans from pre to Post ARUBA era. Small AVM was defined as any AVM with largest diameter < 3 cm. There were 16 patients with 9 males and 7 females. Their age was ranging from 18 to 38 years with mean of 30 years. There were 5 patients with ruptured and 11 with unruptured AVM. Pre procedure Glasgow coma scale was 15 /15 in all patients. All had undergone MRI brain. Size of nidus was ranging from 0.9 cm to 2.9 cm with average of 2.04 cm. Seven were at eloquent locations. Digital substraction angiogram was done in cathlab (Artis Zee, biplane or single plane DSA, Siemens, Munich, Germany) prior to embolization to determine size of nidus, feeding arteries, aneurysm associated with AVM (on the feeding arteries, at circle of Willies or intranidal), varix or stenosis of the draining vein and obliteration of dural sinus. Endovascular embolization done under general anaesthesia. Demographic, clinical and treatment details of the patients are summarised in table 1.

CN	Age in years	Sex	CP	Location	Side	Size#	VD	SM	MRS	EVOH	Adverse Events
1	36	F	UR, HA, S	MC	L	2	S	2	0	O-18	N
2	28	M	UR, HA, S	SC	L	2.9	S	2	0	O-18	N
3	32	M	UR, HA	ATC	L	2.8	D	2	0	O-18	N
4	38	M	R	PFC	L	2.7	S	2	0	O-18	TD*
5	28	F	UR, HA, S	SC	L	2.8	S	2	0	O-18	N
6	34	F	UR, HA, S	OC	L	1.8	S	1	0	O-18	N
7	32	M	UR, HA	AC	L	2.9	S	2	0	O-18	N
8	28	F	UR, HA, S	MC	R	1.8	S	2	0	S-12	TD@
9	30	M	UR, HA, S	OC	R	1	D	2	0	S-12	N
10	18	M	UR, S	SC	R	1.3	S	2	0	S-12	N
11	20	F	UR, S	AC	L	2.6	S	2	0	S-12	N
12	32	M	R	PC	L	2.8	S	1	0	0-18	N
13	28	F	R	ChLP$	L	0.9	D	2	0	O-18	N
14	30	F	R	ChLP$	L	1.2	S	1	0	S-12	N
15	22	M	UR, HA, S	OC	L	2.2	D	2	0	O-18	SAH^
16	33	M	R	CC	R	1	D	2	0	O-18	N

Table 1: *Summary of demographic, clinical and endovascular treatment details of patients.*

Abbreviations: *CN: Case Number; F: Female; M: Male; UR: Unruptured; R: Ruptured; HA: Headaches; S: Seizures; MC: Motor Cortex; SC: Sensory Cortex; ATC: Anterior Temporal Cortex; PFC: Prefrontal Cortex; AC: Angular Cortex; OC: Occipital Cortex; PC: Parietal cortex; CC: Corpus Callosum (Splenium); ChLP: Choroidal AVM Supplied by Lateral Posterior Choroidal Artery ($- Location of AVM is Temporal Horn of Lateral Ventricle); #: Size of Nidus in Centimeters; L: Left Hemisphere of Brain; R: Right Hemisphere of Brain; SM: Spetzler Martin Grade; MRS: Modified Rankin Score at One Month; VD: Venous Drainage; S: Superficial; D:Deep; O-18: Onyx-18; S-12: Squid -12; TD: Transient Deficit (*-Transient Naming Difficulty, @-Transient Motor Weakness); SAH^: Sulcal Subarachnoid Hemorrhage in the Vicinity of Arterial Rupture; N: Nil Deficit.*

Embolization technique

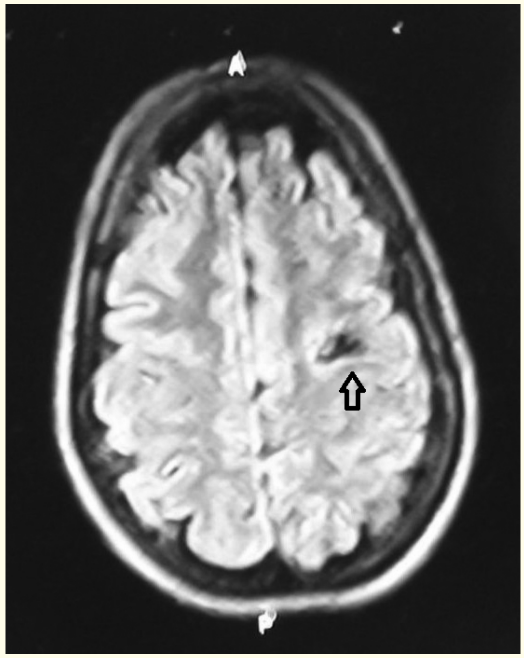
Written informed consent was taken after explaining the need for treatment, procedure and complications including neurological deficits and potential chance of death. Unilateral 6F Transfemoral access gained under ultrasound (USG) guidance. Systemic heparinization was given 3000 IU as loading and 1000 IU as maintenance per hour thereafter. 6F Guiding catheter (Envoy, Codman Neuro, Raynham, MA) was navigated and parked in the target artery. Supple flow guided microcatheters (Ultraflow or Apollo ev3, Medtronic, Cork, Ireland or Sonic, Balt, Montmorency, France) navigated into the feeding artery (in case of two feeders wherever it goes first) with tip is placed as close to the nidus as possible preferably at the entrance of the nidus. Super selective angiogram taken to further characterise angioarchitexture. Microcatheter is fushed with normal saline. It is filled with Dimethyl sulfoxide (DMSO) up to the dead space typically 0.3 ml over 45 seconds. EVOH (Onyx-18 :Medtronic, Cork, Ireland and Squid 12 or 18 : Balt, Montmorency, France) Embolizing agent is slowly injected over blank roadmap slowly at the speed of 0.1 ml over 1 - 2 minutes. Total Volume of Liquid embolic agent injected was 2 - 3 vials. Duration of Injection was ranging from 40 minutes to 60 minutes. The Target was intension to cure. The EVOH should spread from feeder towards vein and centrifugally. Care was taken to reach footsteps of veins at the end and finally occluding the venous drainage completely along with complete exclusion of the nidus from the circulation. Heparin was reversed. Then with Gentle Pull catheter was snapped out. Detachable tip micro catheters were always preferred whenever available. Post Procedure patients were extubated in the cathlab while taking care of not to cause hypertension during extubation. Patients were kept in ICU under strict observation with target BP maintained below 110 - 120 systolic and below 70 - 80 diastolic. Lower ranges of blood pressures were preferred. Outcomes were evaluated by Digital substraction Angiography (DSA) immediate post embolization, any time between one to three years of follow up period and modified rankin Scale (MRS) before discharge and subsequent follow ups. Clinical Follow up was at one month, six months and every year thereafter. All patients were put on adequate antiepileptic drugs prior to procedure.

Results

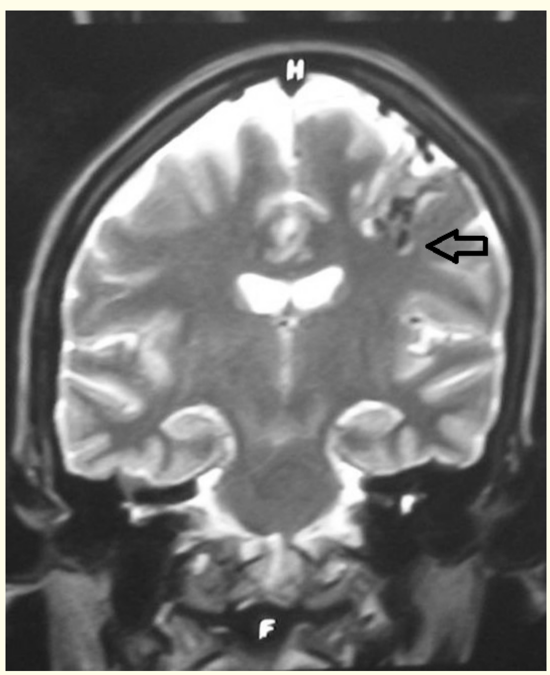
Primary target was to cure AVM completely. Complete cure was defined as non opacification of the Nidus and draining vein on DSA. Twenty embolization sessions were done in 16 patients. Twelve patients had undergone single session each and 4 patients with two sessions each. Fifteen out sixteen patients were cured completely with embolization alone (Obliteration rate 93.75%).The complications were seen in 3/16 patients (18.75%). Case number 8 (Table 1) patient with Motor cortex AVM had transient hemiparesis which recovered with anticoagulation over 48 hours. Case number 4 (Table 1) patient with AVM in prefrontal cortex area had transient naming difficulty and non fluent speech recovered completely after one month of speech therapy. Case number 15 (Table 1) patient had subarachnoid haemorrhage due to rupture of the artery while retrieving the microcatheter. The active leak of contrast stopped spontaneously after reversal of the heparin. He had headache for a week which settled gradually. Non permanent complication rate was 18.75%. There were no life disabling complications or deaths. MRS at three months follow up was 0 in all patients. Twelve patients were completely cured angiographically in one session each and four patients with two sessions each. The one patient (6.25%) required SRS to achieve complete cure for the residual AVM after two sessions of embolization.

Illustrative case number 1 (Table 1)

36 years house wife presented with convulsions involving right side of body. EEG confirmed epilepsy with MRI showing small AVM in Left motor cortex. Feeders were from Left MCA pre central hypertrophied two branches. It was drained by cortical vein into mid-superior sagittal sinus. Complete embolization with no neuro deficit with MRS-0 at one month follow up. DSA showed complete obliteration of the AVM as shown immediately post and 2 years after embolization. She was seizure free on last follow up after 6 years without medications (Figure 1A-1H).



A



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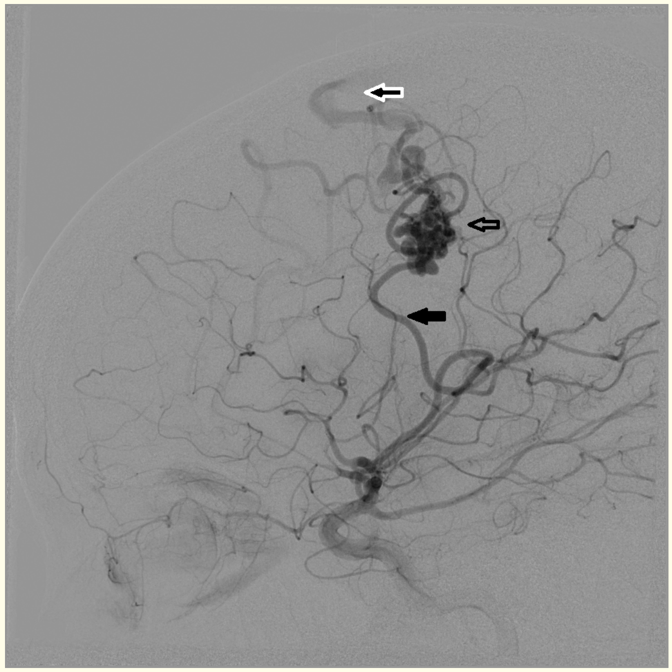

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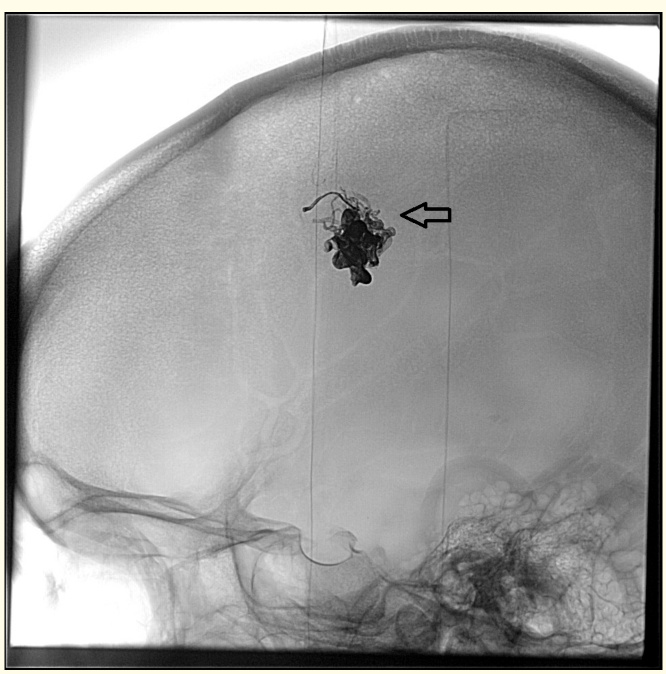


F

G

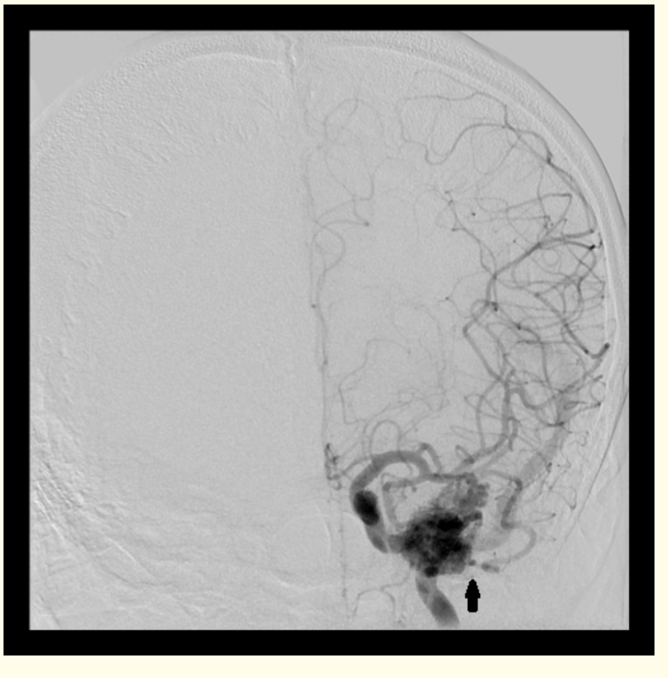
H

Figure 1: *MRI in Axial (A) and Coronal (B) planes showing small AVM in left motor cortex. DSA in Antero-posterior (C) and Lateral (D) views show Feeding artery (Solid black arrow), nidus (Empty black arrow)draining Vein (White bordered black arrow). Images E and F show EVOH cast In Antero-posterior and lateral Views respectively (Empty black arrow). Images G and H showed complete exclusion of the AVM from circulation at immediate post embolization DSA. DSA at 2 years follow up confirmed complete cure (Not shown here).*

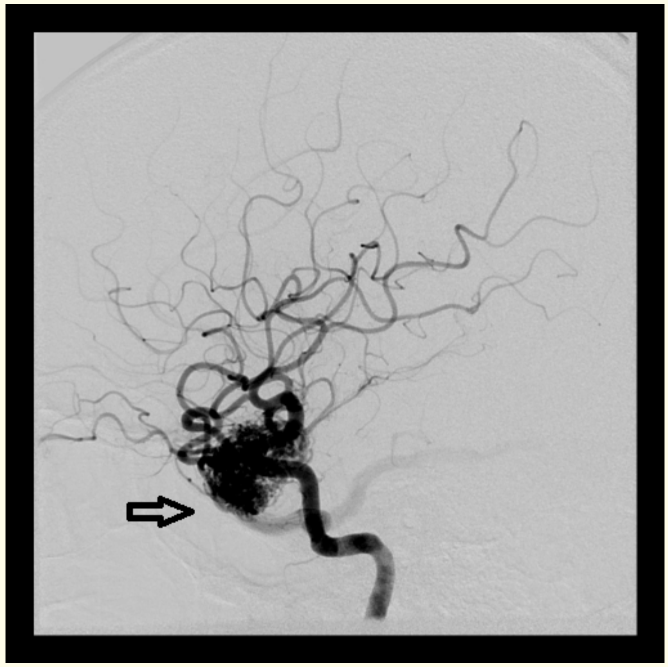
Illustartive case number 3 (Table 1)

32 years old male farmer. He had presented with episodes of forgetfulness followed by sudden loss of consciousness. MRI showed left temporal AVM. ECG confirmed epileptic focus in left temporal lobe DSA showed nidus with deep drainage via basal vein of Rosenthal along with vein of labbe draining into transverse sinus. Complete obliteration of nidus was achieved by embolization. 3 years follow up DSA confirmed obliteration. He is seizure free without any medications after 12 years of clinical follow up (Figure 2A-2H).

A



B



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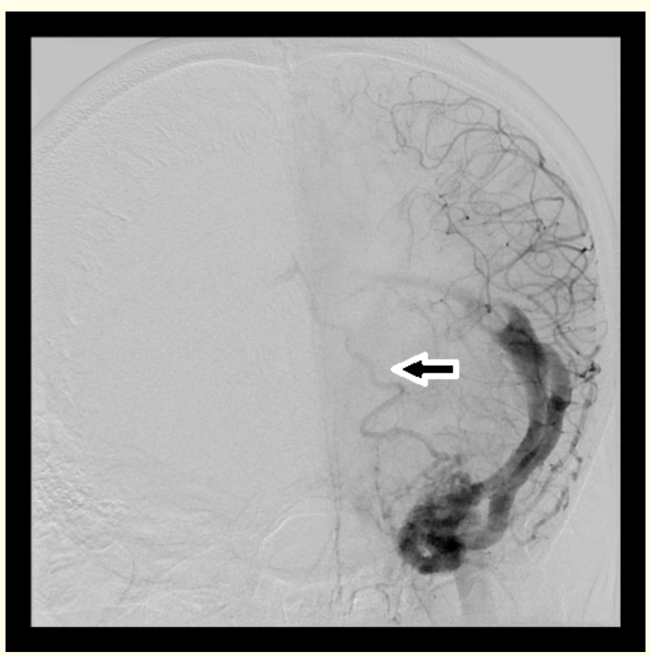

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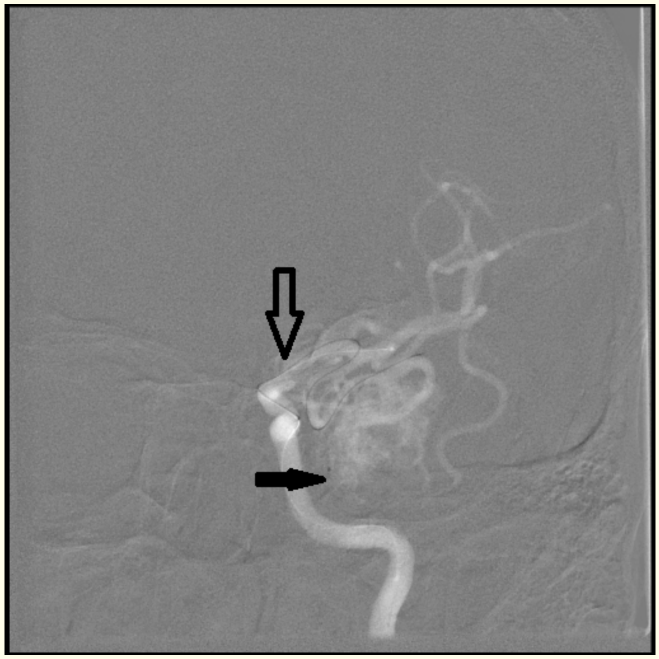

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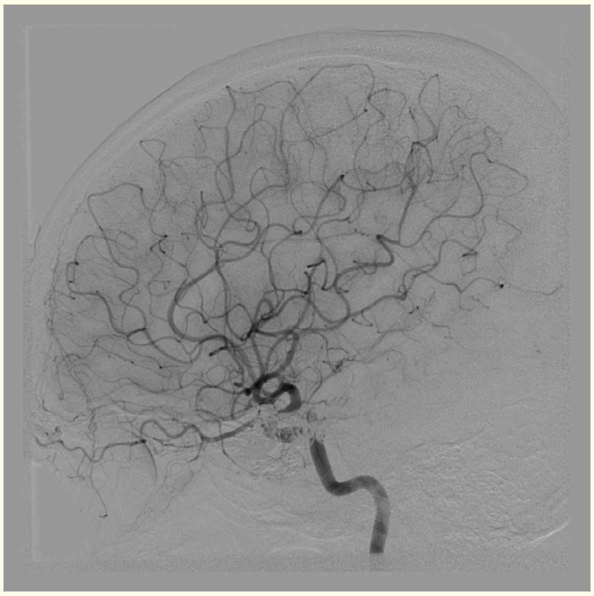


H

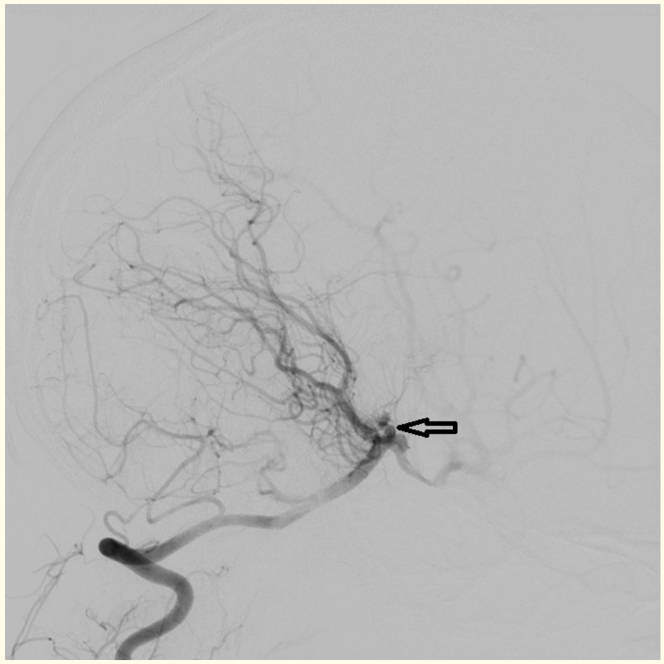
Figure 2: *MRI axial plane (A) showed Left Anterior Temporal AVM. DSA Images Antero-posterior view (B) and Lateral view (C) showed AVM nidus (Empty Black arrow). Image (D) antero-posterior view showed deep sylvian vein draining into basal vein of Rosenthal (White bordered black arrow). Image (E) showed microcatheter taking multiple acute curves (Empty black arrow) and Tip of microcatheter just at the entrance of nidus (solid black arrow). Image (F) antero-posterior view showed EVOH cast. DSA antero-posterior view (G) and Lateral View (H) showed complete obliteration of AVM at Immediate post embolization. DSA after 3 years confirmed complete cure (Not shown here).*

Illustrative case number 14 (Table 1)

30 years old housewife presented with sudden onset headache followed by loss of consciousness. On examination she was GCS 15/15 with no neuro-deficit. CT scan showed intraventricular haemorrhage in temporal horn of left lateral ventricle. DSA showed small Choroidal AVM supplied by left lateral posterior choroidal artery which was embolized with squid-12. She was completely cured with MRS-0 and remained so on one year follow up (Figure 3A-3J).

A

B



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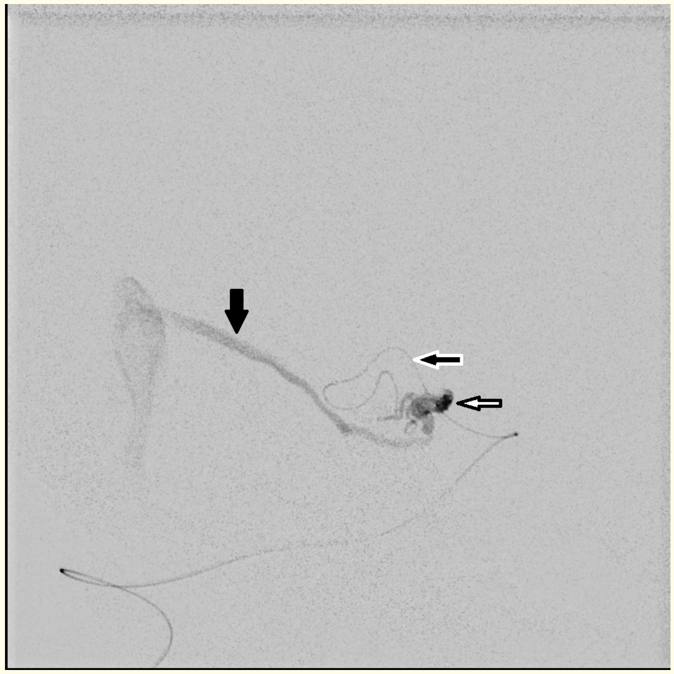
D



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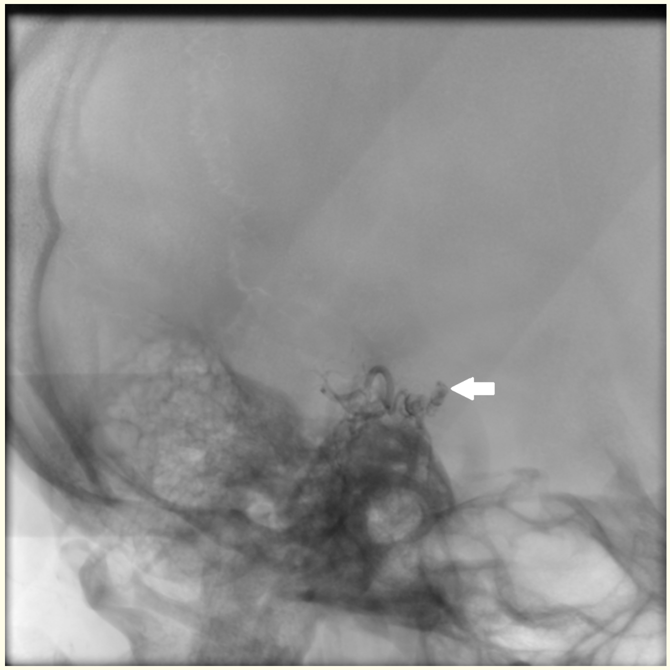

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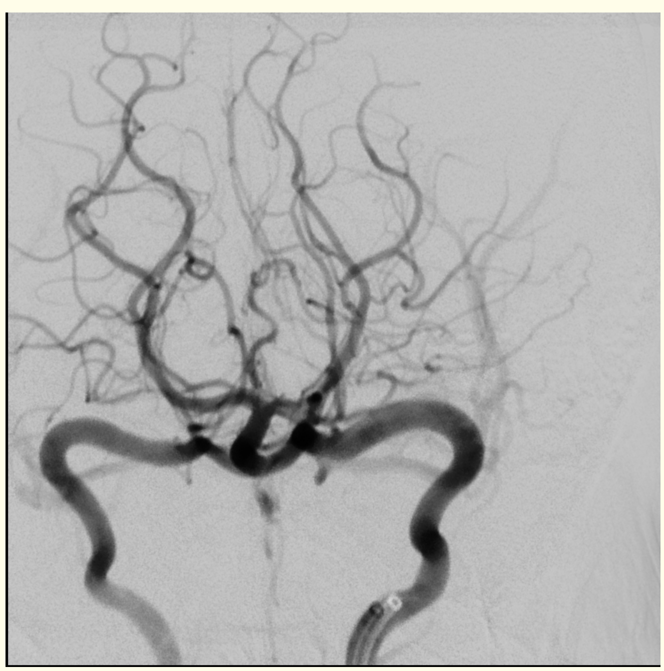

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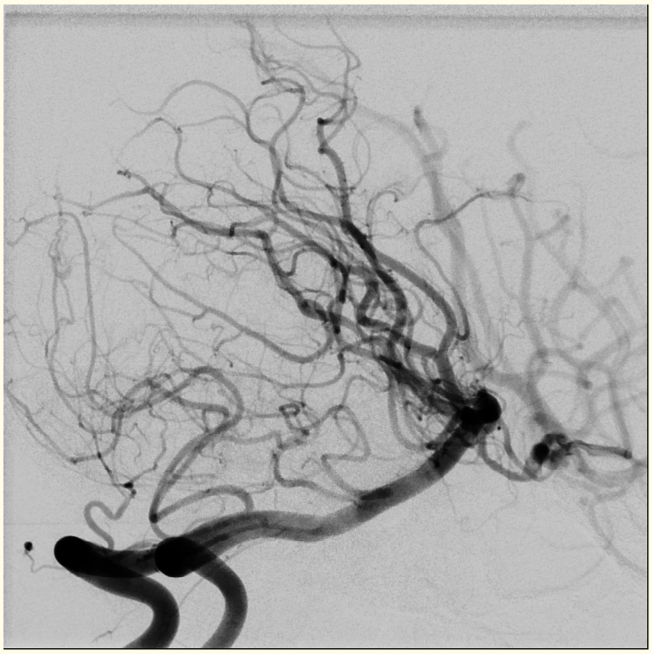
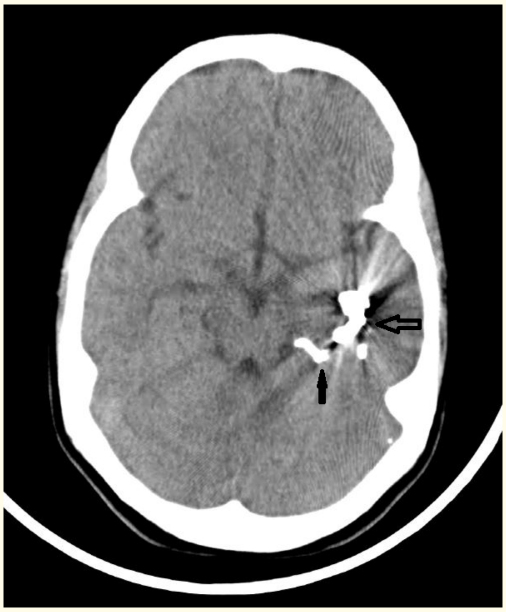


I



J

Figure 3: *Image A shows axial NECT showing blood in temporal horn of left lateral ventricle. DSA images B (AP) and C (Lateral) views showed small AVM marked empty black arrow. Images D (AP) and E (Lateral) showed microcatheter marked by white bordered black arrow, nidus with bunch of tiny aneurysms (Black bordered white arrow) and drained by petrosal vein into superior petrosal sinus (solid black arrow). Images F (AP) and G (Lateral) showed EVOH cast marked by solid white arrow. Images H and I showed post embolization DSA images with complete exclusion of the AVM from circulation. Image J showed axial CT showing EVOH cast near temporal horn (site of bleed) marked by empty black arrow. Note EVOH cast in Lateral Posterior choroidal artery (solid black arrow).*

Discussion

Critiques of ARUBA trial are not ready to accept the conservative management and believe in curative treatment in selected cases of unruptured brain. Blanket application of the ARUBA results to AVM across all Spetzler Martin the grades, varied angioarchitexture, and superficial to deep locations is unreasonable [4-6]. It is observed that if unruptured AVM are followed for 10 - 20 years, much more longer than ARUBA, the risk of development of permanent deficit or death increased up to 42% with annualized rupture rate of 1.8% and re-rupture rate of 4.8% [7]. Treatment of Ruptured AVM is universally accepted and justifiable to prevent recurrent hemorrhage.

Endovascular embolization

Endovascular embolisation of brain AVM has evolved significantly in last decade with availability of non-adhesive ethyl vinyl alcohol copolymer (EVOH). Advantage of EVOH is non adhesive nature as against n-butyl cyanoacrylate glue (NBCA). Prolonged injection is possible without microcatheter getting stuck which facilitates complete obliteration of nidus in single session. Detachable tip microcatheter adds further safety over non detachable tip if catheter gets stuck in EVOH cast. It can still be pulled out with less chances of vessel injury. We should take upmost precaution that EVOH should spread from catheter tip towards to footsteps of veins and centrifugally. If EVOH is reaching veins before completely obliterating nidus, we can either stop and plan for second session at later date or try injecting from other feeder. But premature closure of draining vein should be avoided. If it happens then surgical excision should be considered as soon as possible to safeguard from delayed hemorrhage.

Complications of embolization

Complications can be ischemic or hemorrhagic. Ischemic damage to normal brain parenchyma in immediate vicinity of nidus or compression by onyx cast (as in our case number 8, Table 1). Unintentional, excessive reflux of EVOH resulting into occlusion of normal branches or toxicity of DMSO due high volume should be avoided. Hemorrhage can be due perforation of artery from protruding microwire, avulsion of cortical branch (as in our case number 15, Table 1) during withdrawal of catheter after embolization or delayed hemorrhage due to venous occlusion. Avoiding protrusion of microwire beyond catheter tip during navigation as much as possible and use of detachable tip catheter might help in reducing hemorrhagic complications. Our complication rate of non-permanent deficit was 18.75% with no disability or mortality.

Obliteration rate of embolization

In our series obliteration rate by embolization alone was 93.75.1% with no permanent disability. The reported curative Obliteration rate for SM Grade 1 - 2 by embolization alone is up to 98% in large series [8,9]. Various studies involving treatment of AVM by onyx quotes complication rate ranging from 4 to 12.2% [10]. These studies' and our complication rates are significantly lower than the intervention arm of ARUBA.

Contemporary philosophy of AVM treatment

As partial treatment of AVM has been proved futile or dangerous, primary objective of any intervention should be complete cure. We strongly believe this can be achieved in single or at the most two session of embolization. Complete embolization of AVM with nidus size less than 2 cm in single session is proposed by Mosimann., *et al* [11]. The AVM inaccessible by surgery are navigable and treatable by embolization. The delayed obliteration and interval risk of haemorrhage associated with radiosurgery can be avoided by single session of curative embolization in small AVM. We need close cooperation and extensive discussion with neurosurgeons and radiotherapists when choosing the appropriate treatment modality. Availability of biplane cathlab, neurological ICU, expertise and experience of interventional team are prerequisites for better outcome. Alternative approaches within the endovascular treatment milieu are worth discussing at this point. Transvenous approach is novel alterative when all other ways of embolisation are closed [11]. Although this approach is still evolving and needs further validation in large prospective randomized trials. We had one case where all arterial feeders were not navigable with tiny residual AVM after two sessions of embolization. However, we didn't consider transvenous approach back in 2014 and we referred it for SRS which resulted in complete angiographic cure.

What is to choose? Embolization or neurosurgery and or radiosurgery

Neurosurgery is safe, effective, durable and is considered the standard of care for Smaller grade AVM (SM grade 1-2). However, Eloquent and deep locations pose challenge to Neurosurgery [11-14]. Hence alternative modalities of treatment should be advocated for these cases. Traditionally these lesions are subjected to stereotactic radiosurgery (SRS) [15-18]. It is reported that there is shifts of brain function in eloquent area to ipsilateral surrounding brain particularly in younger population [19,20]. Treatment of motor cortex AVM by radiosurgery have reported complications rate ranging from 5.3 to 18.4% [20]. Recent advances in Endovascular techniques can be viable option with equal if not less complication rates in selected cases as compared to SRS. Hence it is reasonable to offer embolization to this cohort of patients with small nidus and favorable angioarchitexture after multidisciplinary discussion.

Drawbacks of Our Study

Our Study has small cohort. It is retrospective analysis from tertiary care centre.. However it gives insight into the efficacy and safety of embolization armed with recent advances. Till date it is considered adjuvant to neurosurgery and SRS. But it has curative potential too if used judiciously.

Conclusion

Embolization of small brain AVM with intension to cure by non adhesive Liquid Embolic agent can deliver obliteration rate of 93.75%. Complication rate associated with embolization in our small retrospective study is 18.75% with no permanent disability or death However Prospective registries and randomized control trial involving embolization versus neurosurgery and/or SRS will validate role of embolization of small Brain AVM as curative treatment.

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Conflict of Interest

Nil.

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