Intravascular approach to the treatment of cerebral arteriovenous malformations and dural arteriovenous fistulae

Figure 1:Magnetic resonance imaging can be used as a useful tool in the diagnostic approach to AVMs. The anatomical location, size, venous drainage and condition of the surrounding brain can be demonstrated.(Arrow)

The gold standard as a diagnostic tool is however angiography. Digital subtraction angiography is of great value especially when one of the newer generation X-ray machines is used with a high pixel rating, magnification and good road mapping abilities. (Figures 2a & b)

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Treatment options for AVMs and fistulae are explored and results are presented from this South African centre.

Introduction

Cerebral arteriovenous malformations (AVMs) may pose as one of the more formidable challenges to a neurosurgeon.[1]

A multi-disciplinary approach including the neurosurgeon, interventional neuroradiologists and radiosurgeon and neurologists, seems to be the ideal modern day treatment of these lesions.

Complications due to AVMs include haemorrhage, mass effects, epilepsy and bruit.

Diagnosis

With the advent of computed tomography (CT) and magnetic resonance imaging (MRI) as well as three dimensional MRI and spiral CT, the anatomical information such as nidus size, functional location and venous drainage and surrounding state of the brain can become readily known (Figure 1).
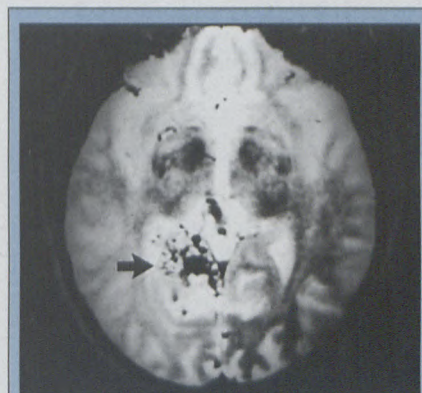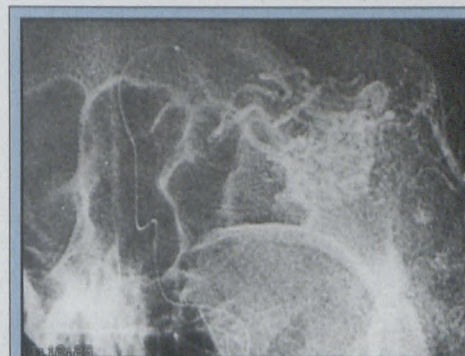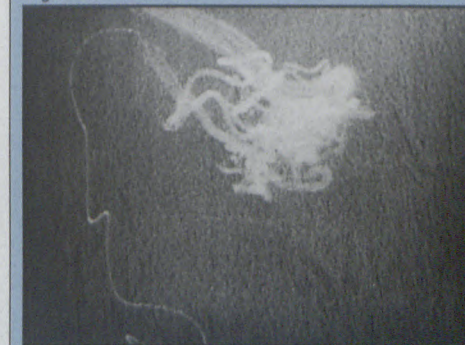

Figure 2a:

Figure 2b:

Subtraction angiography is of great value as can be seen on the views with the subtracted image, on (b)of the same patient at the same time.

History and development

The intravascular treatment of AVMs has its origin with Zuessen-hop *et al*.[2] They used silastic spheres injected via a direct surgical approach in the internal carotid and vertebral arteries. The spheres were then flow directed to the lesion. It was however non-selective and occluded mostly the proximal feeding vessels. The nidus often recanalised through lepto-meningeal, transmedullary and transdural collateral vessels. It was of little value where small arteries supplied the lesion e.g. perforating arteries.

Serbinenko[3] in 1974 described safe selective intracranial catheterisation beyond the circle of Willis, using detachable balloons to occlude the larger feeding arteries of the AVMs and fistulae. The use of a calibrated leak balloon on a micro-catheter was reported by Kerber[4] in 1976. Distal navigation became possible and the use of acrylic agents was introduced for the occlusion of the nidus. These catheters needed to be inflated for the advance into the arterial system but caused complications like rupture and haemorrhage.[5] Only fluids could be injected through it precluding the use of particles, because of its small lumen diameter.

During 1988-89 new micro-catheters were developed that made super selective catheterization deep into the distal arterial tree possible. The new over the wire
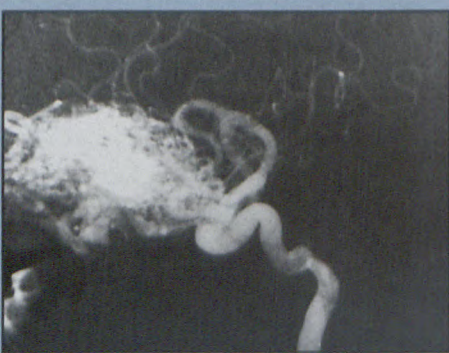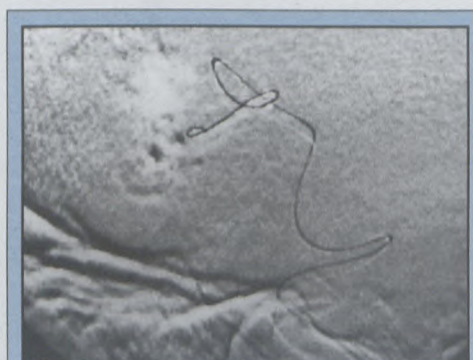

Figure 3(b): The catheter on the right has to follow suit to the nidus.

catheters made it possible to introduce a wide variety of particles into the nidus and supplying pedicles(Figures 3a & b). The flow-guided catheters allowed only fluids and very small particles, but could be negotiated into very small tortuous and distal vessels.

Anatomy of AVMs

A cerebral AVM usually consists of a nidus or central part, supplied by arterial feeders and draining vein or veins (Figures 4a & b).
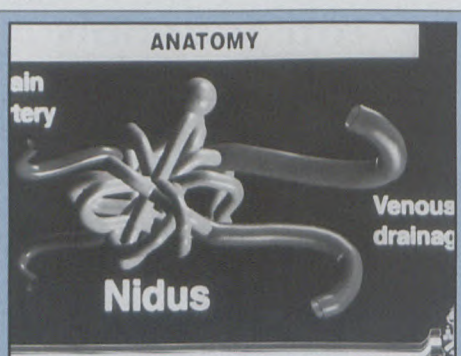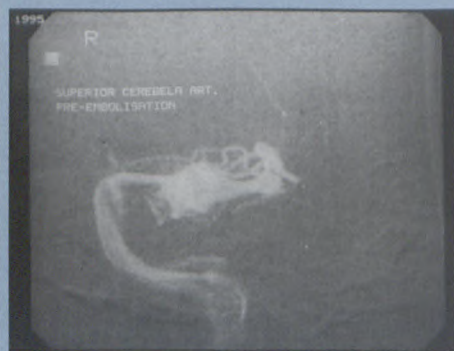

Figure 4a:

Figure 4b:The nidus, arterial supply and venous drainage are seen (a) in this model and demonstrated (b) in a patient.

Figure 3(a): The tortuousness of the afferent vessels is clearly demonstrated in this patient.

Each nidus is composed of a series of compartments which could be in contact with one another. The compartments are fed by different arterial pedicles. Because of the high flow (from 150-900 ml/min with an average of 490 ml/min)[6] these pedicles are quite large. According to the Hagen-Poiseville equation the flow in the feeding artery is directly related to the feeding artery's blood pressure and the fourth power of its radius. It is inversely related to the length of the pedicle.

$$Q = \frac{\Delta P \times \pi r^4}{8 \times L \times \eta}$$

η is the viscosity of the blood.

P is the intraluminal pressure

L is the length of the vessel

It is generally accepted that large AVMs with high flow usually have a low arterial pressure and less chance of haemorrhage than the smaller slow flow but high pressure lesions. The larger lesions present more often with seizures.[7] Miyasaka *et al*[8] concluded that fewer draining veins increased the risk of haemorrhage.

During embolisation intra-arterial pressure would rise significantly.[9] It is also clear that the intraluminal pressure of the feeding arteries is much less than that of the carotid or vertebral arteries in the neck.[10] Gradients of up to 75 mm Hg have been reported. This gradient however subsides after nidal embolisation.

The high flow state in the feeders, nidus and draining veins causes histological changes that enhance the preponderance of local trauma during catheterisation and manipulation.[11]

Grading of AVMs

The surgical grading system devised by Spetzler and Maartin[12] correlates the risk following surgical removal of AVMs. We find it an excellent way of entrée to the

treatment of these lesions. Where embolisation is concerned the difficulty in approaching the lesions via the intraluminal paths, the tortuousness and length and number of vessels, as well as the presence of large fistulae in the nidus play important roles concerning the outcome of the procedure and should be taken into account.

Embolic agents

The ideal material for endovascular embolization of AVMs has yet to be discovered. Ideally, an embolic agent should be non-biodegradable, non-toxic, and non-mutagenic. It should be easily delivered through a microcatheter, be easily seen on fluoroscopy, and adhere to the walls of the vessels without extravasation or recanalization. Finally, the ideal embolic material should be soft enough to allow retraction of the lesion from surrounding normal tissues during surgical excision.

Many different embolic agents were used like silk, coils, microspheres (metal, polyvinyl alcohol, Spongistan) and liquid adhesive polymers.

Of the liquid adhesive polymers, alkyl cyanoacrylate monomers have been most widely used. Two kinds are used these days *viz*. isobutyl 2-cyanoacrylate (IBCA) and n-Butyl cyanoacrylate (NBCA). Once the monomer is exposed to an ionic fluid (like blood) it polymerizes immediately. A tight bond between tissue and the polymer exists that is used to bond tissues together in surgery[13] (Figure 5).
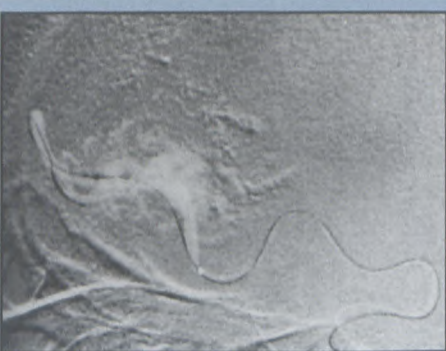

Figure 5: The polymer moulds can be seen after embolisation in the nidus of the same patient.

Vinters *et al* reported on the long term follow-up of cerebral AVMs treated by embolization with bucrylate.[14] They found bucrylate in the extra-vascular space 41 days after embolization and occasionally earlier. Although the nidus can be fully embolised with these materials, re-canalization does occur up to 12-20 months later.[15]

It is a good embolic agent, but by no means permanent. IBCA is quite brittle and therefore difficult to handle at surgery, without traumatizing the brain. Carcinogenicity is also a concern. IBCA has been replaced by n-Butyl cyanoacrylate.[16] Bucrylates have been used for the treatment of AVMs for the last 15 years without any report in the literature of the proposed mutagenicity having occurred.[17] However, NBCA is less brittle than IBCA and has a slightly shorter polymerization time.

Other liquids in the offing are ethylene vinyl alcohol copolymer introduced by Taki *et al*[18] and estrogon alcohol and polyvinyl acetate.[19]

Patho-histological changes after embolization with polymers include a foreign body response followed by an inflammatory response[20] and vessel wall necrosis followed by either aneurysms and/or extra-vascular appearance of the polymer. Haemorrhage may occur due to the secondary formed aneurysms after embolisation.

Haemorrhage associated with AVM embolisation ranges from 3-11%.[21] We administer Nimodipine and steroids intravenously during and after the procedure. Nimodipine is usually administered before the procedure.

Particulate materials

The most commonly used particulate is polyvinyl alcohol. Sizes from 75 to 1250µm are available. The particles are suspended in diluted contrast and injected at small non-laminar flow boluses. Starting from the smaller particles enhances the possible blocking of the smaller intra-nidal vessels followed by the larger ones to occlude larger vessels and fistulae. The main pedicle can be occluded with silk or fibred coils. When fistulae are present pulmonary embolism may occur.

It is reported that collagen (avitene) may enhance the thrombo-genecity of the mixture.[22]

Tissue response to PVA is well described by Germano *et al*[23] in the brain. They investigated 66 consecutive excised AVMs histologically, that were embolised with PVA before surgery. They found an inflammatory response in the vessels, including angionecrosis of the wall, even as soon as two weeks post-procedurally. Foreign material was found in 63% of cases. Recanalization occurred in 18% of lesions within four weeks.

Pulmonary embolism during the treatment is a well known complication. Venous outlet obstruction can pose a high risk if the inflow to the AVM is still prevalent and extremely high.[24]

Technique

Grading according to Spetzler and Maartin is done on MR or CT, followed by an angiogram for further assessment of velocity, pedicle, nidus size and appearance, draining veins and anterior and/or posterior cerebral supply.

The clinical judgement for possible way of treatment resides mostly with the referring neurosurgeon.

In some centres general anaesthesia is administered and in others neurolept analgesia. Purdy *et al*[25] say that unless the feeding pedicle is fully embolised sodium Amytal testing is not needed.

Nowadays we tend to embolise our patients while they are awake and resort to provocative testing.

Our patients are heparinised (5000 units) where the pedicles are not easily

negotiable. We prefer not to use heparin when the lesion is easily approachable and where arterial spasm of pedicles is less of a problem. Once the patient is heparinised we prefer not to administer protamine sulphate but allow the activated clotting time (ACT) to come down to 150 seconds before we remove the sheath from the femoral artery.

All our patients are placed in the intensive care unit for a 24-48 hour observation period after treatment. They are discharged as soon as their condition allows it.

Provocative testing

The so-called Wada Test was first done by Wada and Rasmussen.[26] They injected sodium amobarbital (Amytal) within the internal carotid artery (ICA) to evaluate cerebral dominance before epilepsy surgery. When Amytal is injected into a feeding pedicle of an AVM reversible changes to normal brain can be elicited according to Ranch et al.[27]

We now administer ±35mg Amytal before embolisation in two distinct boluses. The first bolus is given slowly to flush the normal distal brain. The second bolus is given as fast as possible to cause, if possible, slight retrograde reflux into the feeding pedicle. Once polymer is injected the flow state of the AVM changes and may cause stasis of blood flow with possible untoward embolisation of the pedicle. Immediately after the administration of the Amytal a neurologist in theatre tests areas of eloquence close to the lesion. When a negative response is elicited embolisation is commenced. Brevital may also be used.[28] It has a shorter half life than Amytal and is more readily available in South Africa(Figure 6).
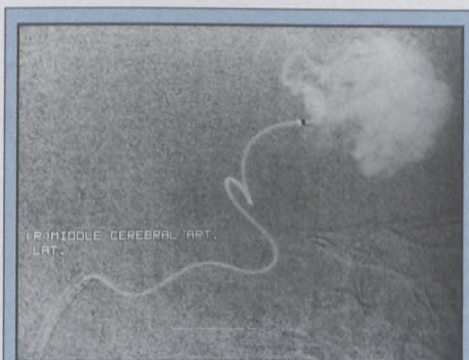

Figure 6:The catheter tip should be as close as possible to the nidus before provocative testing is done and treatment commenced.

Ten therapeutic options exist for AVMs:

1 No therapy
2 Microsurgery
3 Radiosurgery
4 Embolisation
5 Embolisation plus microsurgery
6 Embolisation plus radiotherapy
7 Staged surgical procedure
8 Conventional surgery followed by radiosurgery
9 Radiosurgery followed by conventional surgery
10 Various triple therapy combinations[29]

Clinical materials and methods

Between April 1995 and May 1996 13 patients with AVMs were treated in our unit by means of the endovascular route.

The indications for treatment were:

· Palliation in non-resectable AVMs.

· Pre-surgical devascularization.

· Diminution of nidus size in combination with radiosurgery.

· Total obliteration.

Two patients were treated with PVA as a presurgical adjunct. The rest of the cases were embolised with polymer, of which two were operated on later. Twelve patients were male and 1 female. Their ages varied from 19 to 53 with the average age of 37.3 years. Seven cases were graded as Hunt & Hess I and four cases as Hunt and Hess II and two as Hunt and Hess III. The first two

cases were done under general anaesthesia and last 11 under local anaesthetics.

Four patients' AVMs were graded as Spetzler and Maartin Grade IV and the rest as Grade II and I. The last 11 patients were subjected to sodium Amytal provocative testing. Staged procedures were done in three patients.
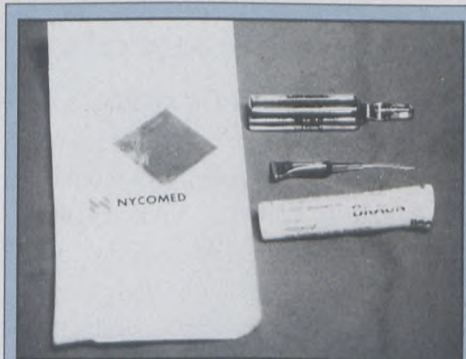

Figure 7:From top to bottom, Lipiodol in a glass vial, then the polymer in a small plastic vial. Tungsten powder is supplied in sterile plastic sachets.

We use a mixture of Lipiodol, Tungsten powder and NBCA (Figure 7). The faster the flow, the faster polymerization is needed and the less Lipiodol is added and vice visa. The idea is to completely fill the nidus with the polymer without venous occlusion.

Results

All patients has a diminution in size of the AVMs(Figures 8a & b).

All the presurgical patients were successfully operated on, one of which was followed up and showed no recurrence. The others are due for follow-up MRI and angiography.

One patient was completely cured on the one year follow-up angiogram.

One epileptic patient has had no seizures since the procedure but remains on anti-epileptic treatment.

One patient with a massive frontal AVM had a personality change for the better.

Complications

Two patients with lesions in their dominant hemispheres had temporary speech deficits post procedure.

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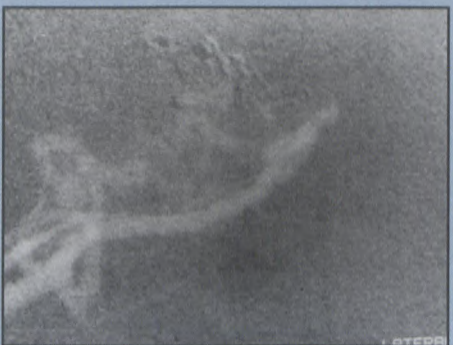
Figure 8a

Figure 8b
Angiographic appearance (a) before and (b) after embolization of this posterior cerebral artery AVM.

One had a writing deficit that resolved after a few weeks.

One patient developed slow retrograde thrombosis of the calloso-marginal artery and subsequently developed hemiplegia.

No deaths occurred and no haemorrhages occurred.

One patient developed severe vascular spasm causing us to terminate the initial procedure. The endovascular therapy for vasospasm due to haemorrhage or catheter manipulation includes papaverine hydrochloride. Up to 300mg can be infused at a time over a period of one hour.[30]

Pre-surgical embolisation was achieved step by step using PVA until the proper results had been achieved. These patients were operated on 48-72 hours later (Figure 9).

A mixture of polymer and PVA can be helpful with the latter occluding small or even larger parts of the residual lesion after initial embolisation with polymer(Figure. 10).

Radiosurgery with the gamma knife or other modes of radiation can be important adjuncts to the treatment of these lesions, but is beyond the scope of this article.

Three of these patients had dural arteriovenous fistulas which were treated with polymer. In the follow-up angiograms

two of these patients had recurrence of different arteries supplying the fistulae. It is now a known fact that these lesions are acquired usually secondary to venous thrombosis[31] or hypertension[32]. In many cases the pathogenesis is unknown. Normal microarteriovenous shunts exist between the arterial and venous systems. Due to abnormal pressures in the venous side caused by

IBCA vs PVA	
IBCA	**PVA**
1. More inflammatory response	Less inflammatory response
2. Extra vasation	No or very little extravasation
3. Pulmonary embolisation	Pulmonary embolisation
4. Recanalization little	Recanalization 18-30%
5. Less collaterals	New collaterals form rapidly when totally occluded
6. Mutaganicity Ames test + NBVA IBCA not proven.(Berenstein A et al, J Neurosurg. 67:318-319,1987)	Ames test- but Oppenheimer BS showed + mutagenicity (Cancer Res 15:333-340,1955)
Comparison: Valavanis uses both	

Figure 10:The histological response to these two agents in the use of AVM treatment is compared.

either thrombosis or trauma to the endothelium angiogenesis factor is released that may enhance the development of these fistula. Djindjian *et al*[33] classifies these lesions in three grades.The detailed discussion of this very interesting and extensive condition is beyond the scope of this publication.

Discussion

The venous drainage pattern must be well demonstrated in all cases[34] due to the fact that the risk involved with treatment is directly related to it.

According to Halbach *et al*[35] dural fistulas involving the cavernous, inferior petrosal, and marginal sinuses can usually be effectively managed by endovascular techniques exclusively. The fistulae in the ethmoidal region can be treated by surgery alone. The remaining dural fistulae require a combination of endovascular and surgical

Patient	♂ / ♀	Age	H & H	Place	Glue	PVA	Results	%
1. B	♂	28	1	Mid & ant cerebral art	+		Temporary writing & speech	95
2. D	♂	43	11	Post cerebral	+		No deficit	70
3. P	♀	19	111	Superior cerebral	+		Slight	95
4. M	♂	42	1	Mild, post external carotis	+		No deficit	90
5. S	♂	38	11	Middle cerebral	+		No deficit	95
6. K	♂	43	11	Post cerebral	+		No deficit	80
7. N	♂	41	1	Dural & external carotis	+		No deficit	90
8. B	♂	31	111	Anterior cerebral	+		Hemiplegia	90
9. D	♂	42	1	Anterior cerebral	+		No deficit	90
10. G	♂	32	1	Ext carotid vertebralis		+	No deficit	90
11. V	♂	29		Middle cerebral	+		No deficit	80
12. M	♂	53	11	Middle cerebral	+		Slight speech deficit	90
13. S	♂	44	1	Middle cerebral		+	No deficit	95

Figure 9: Patients treated with AVMs and dural fistulae with ages, gender and Hunt & Hess (H&H) grading tabulated. Outcomes are demostrated on the right.

techniques. Close cooperation between all the clinicians involved is essential.

Conclusion

The endovascular approach to the treatment of arteriovenous malformations of the brain and dural arteriovenous fistulae is an adjunct to surgery and radiation therapy in these very important conditions. Close co-operation between the specialists involved is of utmost importance. The therapeutic vision should be that of total therapy using a multi-disciplinary approach.

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