Review article

Arteriovenous malformation; a review of current concepts

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Abstract

Objectives: To further improves the ability of AVM recognition and providing the physicians with a large spectrum of valid treatment modalities and concepts.

Data source: a literature search of PubMed, Embase, and Cochrane CENTRAL from 1980 to 2014. Inclusion criteria included English language as containing original data, availability of full text article in our institution. The first author reviewed all manuscripts and performed a comprehensive assessment of current concepts around arteriovenous malformations

Methods: A review of the contemporary peer-reviewed literature as well as review articles of current diagnostic modalities and corroborated managements of facial arteriovenous malformations.

Results: imaging provides crucial informations about initial diagnosis and aids in fallow up. Specific imaging modality contributes different information to the process including anatomic extent, size, location, presence or absence of phleboliths and proximity to vital structures. An ultrasound imaging especially with gray scale is usually the first choice for pediatric patients. Standard protocol of Some institutes for vascular head and neck anomalies include tri-planar T2 weighted magnetic resonance imaging (MRI) with fat saturation, pre and post contrast axial T1 MRI, post contrast coronal and sagital T1 images with fat saturations. There have been various treatment options for AVMs consist of medical therapy, surgical removal or sclerotherapy.

Conclusion: the management of AVMs is a multifactorial decision and best determined by both patients and clinician attitudes. There is no standard recommendation for AVM treatment although there have been some suggestions about how to select your optimal sclerosing agent based upon the clinician's temporary or permanent therapeutic goals.

Key word: Arteriovenous malformation, ultrasound imaging, magnetic resonance imaging

Introduction

What encouraged us to write this article was a number of patients in our experiences which we did not know their exact vascular category and furthermore their proper management. We are not aimed to case report our patients but our mission is to illustrate how to recognize an arteriovenous malformation (AVM) from other vascular malformations and moreover how to deal with them. There is a theory of negative
vascular pattern regulation. In amnios, blood vessels develop through the embryonic disc; except for a midline region surrounding the notochord. In the embryonic midline, notochord has the main role of inhibitory signaling for vessel formation, and if it damages results in vascular-plexus formation at midline (1). Invitro, it has been established BMP (Bone morphogenetic protein) antagonists; chrodirin and Noggin inhibits vessel formation (1). The embryonic midline is defines by the notochord which signals axial patterning. Ectopic expression of BMP-4 at the embryonic midline results in an endothelial permissive zone that lacks notochords (1). A vascular anomaly most frequently presents at birth or in early childhood and craniofacial region is the most common site of involvement (2). Pediatric vascular anomalies can be divided into two broad categories: vascular tumors and vascular malformations. This biologic classification is based upon differences in natural history, cellular turnover and histology first highlighted by Mulliken and Glowacki in 1982 (3) vascular tumors (infantile Hemangioma (IH), congenital Hemangioma, kaposiform hemangioendotheliomas and tufed angiomas) are not in our discussion interest. Low flow lesions (capillary, Lymphatic and venous malformations) and high flow lesions (Arterio venous malformations (AVM), Arterio venous fistula) are two main vascular malformations subdivision (4). Mixed lesions are common.

Discussion

Imaging provides crucial information about initial diagnosis and aids in fallow-up. Each imaging study should illustrate important details such as size, location, anatomic extent, presence or absence of phleboliths, vascular anatomy and proximity to vital structures. This is not only essential for interventional and surgical planning but is also useful for classification based on ISSVA system (international society for the study of vascular anomalies) (5).

A combination of imaging modalities is useful in the evaluation of vascular anomalies. An ultrasound imaging especially with gray scale is usually the first choice for pediatric patients and it could reveal whether a lesion is cystic or Solid, compressible or not. Spectral and color Doppler are used to identify flow characteristics and to differentiate arterial from venous flow (4). According to the putten. K. study (5), some institute's standard protocol for evaluation of vascular anomalies of the head and neck includes tri-planar T2 with Fat saturation, pre and post-contrast axial T1 weighted, Post contrast coronal and sagital T1 weighted images with fat saturation (5). Angiography (and in some author's point of view CT-angiography) is the gold standard for diagnosis of high flow vascular lesions (6). On the contrary angiography is rarely needed for venous malformation's diagnosis.

Venous malformations

They are seen as compressible, mixed echogenic lesions with either low flow, pure monophasic flow or no flow on ultrasonography. IF a biphasic component to the vascular flow pattern is noted, a mixed vascular malformation (capillary-venous or lymphatic -capillary-venous one) should be considered (7). On MRI which is the best lesion extension identifier, venous malformations tend to appear as intermediate signal intensity on T1 and hyper intense on T2 (8). Characteristic features of venous malformations include a lobulated mass with internal surpiginous vessels, rounded signal voids representing phleboliths, and variable contrast enhancement (6). It is an aytical manifestation for venous malformations to be high flow and having flow-related enhancement. One might blame us why to describe so about non AVM malformation Such as venous types. It should be kept in mind that differentiating venous malformation from AVM is one of the most important diagnostic steps. Sometimes venous malformations have patchy hypo intense areas on T2-MRI representing blood clots and possibly fibrotic change from previous sclerotherapy (5).

Arterio-Venous malformation (AVM)

AVM of the head and neck are the most aggressive form of all the vascular malformations and can lead to dramatic deformity, functional impairment and possible mortality. They are high flow lesions characterized by direct connections between arteries and veins without an intervening capillary Bed. Their majorities are congenital and present at birth with smaller parts noted during childhood or in adult life. Among Head and neck AVMs, approximately 70% are in midface (9).

Gray Scale AVM imaging shows a heterogeneous lesion with multiple hypo echoic vascular channels without a well defined soft tissue mass (10). AVMs have two characteristic features of high flow, low resistance arteries and an arterIALIZED wave form in enlarged draining veins (4, 11). The pulsatile venous flow
is always present in AVM in contrary to hemangioma (4). Contrast enhanced CT of AVMs shows numerous enlarged feeding arteries with rapid contrast shunting in to enlarged draining veins without significant tissue enhancement usually presents within a normal capillary network (12). On spine echo images high flow vessels represent flow as flow voids, which may be distributed within small punctuate areas of high signal intensity due to hemorrhage and thrombosis with corresponding hyper intensity on flow enhanced gradient echo sequence (13). The absence of Soft tissue mass in AVM differs it from infantile hemangioma (14). Some researchers believe that angiography is essential for AVM treatment plan which shows multiple feeding arteries rapidly shunt in to enlarged veins across a nidus (6). Here before discussing about different AVM treatment Strategies it is good to be aware of one of the AVMs major differential diagnosis: VM (venous malformations) in brief. Recently common sclerosing agents for venous malformations including foam sclerosing agents: polidocanol, sodium tetradecyl sulfate, anhydrous alcohol and Bleomycin. The latest is the most popular sclerosing agent. (15) There are numerous reports regarding treatment of VM with a Single dose of anhydrous ethanol or Bleomycin (16, 17). To attain sclerosing goal usually 1(mg)/(kg) anhydrous ethanol or 8 mg of diluted Bleomycin in 4ml contrast agent (10(mg)/(m^2) Body surface)is used (15). It has been shown that the efficacy of ethanol as an sclerosing agent in venous malformations is much higher than the Bleomycin (15). Although sclerotherapy is the first line therapy for VM but it is less obvious as the first choice of AVM treatment (15). It has been demonstrated that Doxycycline could be effective in lymphatic sclerotherapy, with the concentration of 10 (mg)/(ml) and maximum dose of 20 (mg)/(kg).This finding is based on a retrospective review of 60 Doxycycline sclerotherapy procedures in 41 patients (18). As the previous study mentioned, single or intermittent injections of relatively large volumes of Doxycycline were safe with no dental staining. One should keep in mind that Doxycycline exposure to the nerves must be avoided in order to prevent one major complication; Horner's syndrome.

Arteriovenous malformations as a pathologic term confined to enlarged blood vessels separated by gliotic tissue, often with evidence of prior hemorrhage. Some vessels can be recognized as arteries with duplicated and fragmented internal elastic lamina, while others show marked thickening or partial replacement of the media by hyalinized connective tissue. Macroscopically AVM lesion appears as a tangled network of wormlike vascular channels (19).

AVM presenting symptoms can include, but are not limited to pain syndromes, neuropathy, dermatological manifestations, tissue ulcerations, hypertrophic lesions, infections, hemorrhage, pulsatile tinnitus, high-output cardiac state and even death. In neonates, AVM can presents as macular pink or red stain lesions (19). There is currently no imaging study that can diagnose an AVM at such state but special immuno - histochemical stains can be used on tissue samples to exclude an AVM. Large lesions however may be detected on routine duplex ultrasound. The symptoms of newborn AVMs usually confined to the excess regional warmth feeling which with the time results to soft tissue and bony hypertrophy (20). AVM typically shows itself as a pulsatile swelling (20). Sometimes AVMs appear as an obscure dermatological lesion which present with a cutaneous pallor in addition to a satellite pattern. It is due to a cutaneous “steal syndrome” which means rapid shunting of arterial flow to venous circulation, while bypassing the cutaneous vascular plexus (21).

Acro Angiodermatitis
This is one of particular cutaneous manifestations of AVMs which sometimes called pseudo- Kaposi sarcoma. On the contrary it has no association with Human herpes virus-8 [HHV-8]. It appears as a circumscribed pigmented, violaceous or dusky macules, plaques or nodules of the skin overlying or distal to the arteriovenous anomaly. Some lesions may have chronic changes such as ulcerations and lichenification (21). Although most of the AVMs appear as a single lesion, the pretreatment workups should rule out the co-existence of other congenital vascular malformation (22, 23).

AVM diagnostic evaluation
The initial diagnostic evaluation of an AVM should includes a non-invasive investigation such as Doppler or Duplex ultrasonography, MRI with T1 & T2 weighted images, MRA( Magnetic resonance angiography ), CTangiography or super selective catheter arteriography as Gold Standard (24, 25). By DUS (Duplex ultrasound sonography) we can differentiate venous malformations(VM) from
AVMs and lymphatic ones. VM has the characteristics of cystic components and compressibility. It is considered as an operator-dependant method (19). MRI remains the major diagnostic study for AVM lesions (26). Only when dealing with a specific AVM in a vital area difficult to treat, CT is indicated though extremely rare. Basic diagnosis of AVM is generally based upon the previously described non invasive investigations (19). The final diagnosis of the AVM should be confirmed by angiography. To minimize radiation exposure, these techniques are usually performed simultaneously with the treatment in young patient (19).

These studies include:
- Selective arteriography
- Percutaneous direct puncture arteriography
- Percutaneous direct puncture phlebography (27)

An ill planned and improper treatment such as incomplete surgical excision, ligation or proximal embolization of the feeding arteries could transform AVMs in to a proliferative state (20).

**AVM treatment options**

**Laser therapy:**
It has been reported that pulsed dye laser can be a useful treatment in port wine stain (PWS) and also facial vascular malformations. It has been also mentioned about PWS that the laser responsiveness depends upon the anatomical site. In adults and children the centrofacial regions (medial aspects of the check, upper lip and nose) response less favorably than the other regions (periorbital, forehead, temple, lateral chin, cheek and neck)(28).

What we discuss about till now were mainly around PWS. Experiences for photocagulation of AVMs have been also reported with satisfactory responses including three different laser types:
- Nd - YAG laser
- Pulse- dye laser
- Diod - laser

Per cutaneous approach with the laser fiber guided to the nidus fluoroscopically and an intra operative approach in to dilated afferent arteries and efferent veins in a previously resected malformation are two more recent techniques (25, 29).

The endovascular laser remains to be further proven for the efficacy in the treatment of AVM lesions (25, 29).

**Embolization / sclerotherapy**

The main goal of AVM treatment should be targeting the AVM nidus. Post operative supplemental endovascular therapy (embolization) has been shown to be effective in the surgical treatment of AVM (30). Precise delivery of the emboli/sclerosants directly in to the nidus of the extratruncular AVM lesion is essential. The most appropriate embolic agents for AVM includes; absolute ethanol, onyx, N-butyl cyanoacrylate (NBCA) and venous coils. The use of NBCA or Onyx alone is generally inadequate to cure or long term control of AVM (20, 25).

**NBCA (N-Butyl cyanoacrylate)**

NBCA is a clear free flowing adhesive liquid that will polymerize on contact with any ironic material. Its combination with ethiodized oil improves the liquids' polymerization time and its radio opacity. Imposing an acute inflammatory effect associated with heat generated during polymerization in addition to chronic chemical inflammatory response, a long term vascular occlusion achieved. Only very tiny AVMs (therefore also resectable types) are responsive to this method as in larger lesions the chemical material assumed to be resorbed (31-33).

**ONYX**

In 2013 paramasivam.S and colleagues introduced ONYX embolization as a new technique for vascular malformation management. They used dimethyl-sulphoxide (BMSO) compatible double lumen catheters for this embolization method. Among different arteriovenous malformations they could cure facial, mandibular and lingual AVMs. They have claimed this method as "a safe and effective technique". It consists of a catheter with good navigability and a stable, penetrable balloon(30). Onyx consists of two active components: Ethyl and vinyl alcohol (EVOH) dissolved in dimethyl sulfoxide (DMSO). Although there are some cases of onyx extensive arterial occlusion without nidus penetration, this agent is known as an effective agent in targeting a large part of the nidus with macro shunting (34). Sometimes ONYX and NBCA could impose neo-vascular stimulation on the treated lesions leading to symptom recurrence and also makes other endovascular or surgical options impossible for the patient (20, 34).

**Sodium tetradecyle sulfate (STS)**
STS is another effective sclerosing agent which is a long –chain fatty acid salt with detergent characteristics. By altering the surface tension of the vessels, it imposes a vascular injury to the lesion. Its patency is not as much as ethanol. This agent's popularity is basically for venous malformations. Regarding to occurrence of some cases of extensive vascular thrombosis occasionally beyond the injected site in intra-arterial use of STS, its administration in AVM treatment is not a routine treatment (20).

Poly methyl metacrilate (PMMA)

PMMA is a dual component substance composed of aluminum hydroxide and an acrylic polymer. These two agents in combination transform in to a solid material. Primarily it has been innovated for percutaneous vertebroplasty. Recently, it has been reported to be effectively useful in the treatment of intraossous AVMs (35).

There is a common misconception that there is only one "gold standard" embolic agent in AVM treatment. Selecting an appropriate agent depends upon three main stones; clinical circumstances, morphology and lesion location. The later is the most important factor. For instance, using ethanol is contraindicated when the lesion is located near neurologic structures. In these situations NBCA or ONYX may be suitable substitutes.(36) If the primary goal of our treatment is aimed to surgically resolve the lesion, this entire destruction (37). Considering significant probability of cardiopulmonary complications during ethanol injection, this procedure should be undertaken under general anesthesia and close cardiac monitoring. Using a pulmonary artery catheter during the ethanol administration will be a complementary monitoring technique (38).

A total dose of ethanol which is less than 1 ml/kg is the maximum convenient safe volume (39). It has been advocated that if ethanol injection rate limits up to 0/14 ml ethanol / kg ideal body weight every 10 minutes, pulmonary artery catheter necessity could be obviated (40). The success rate of this method depends on the precise AVM nidus injection that is non nutritive and without capillaries (20, 29).

Alcohol is not used directly to the vascular lesions without mixing with the contrast agents because alcohol itself can not be visualized on fluoroscopy science the usage of this material in the head and neck, some authors realized that its application could be without using fluoroscopy. They mean alcohol sclerotherapy outside of c-arm so that alcohol could comfortably been injected without any obstacle around the patient but there is still the conflict of how we follow the pathway of our injections. These researchers have solved this problem with intermittent venograms between the injections to detect whether there is any dangerous venous outflow drainage such as superior ophthalmic vein to the cavernous sinus. The volume of alcohol usage in each session was by mean of 815ml(41). In other studies sometimes the mean alcohol usage did not exceeds 3/4ml. in these studies it has been proved that usage of Bleomycin (with a mean of 3/7 mg) after the embolization of the drainage vein with ethanol as a safe and effective treatment method(42, 43). In Beak HJ and colleagues study the maximum anhydrous ethanol was 1mg/kg with a single dose ≤ 50ml. When they assume the ethanol exceeds 0/5 ml/kg they used pulmonary artery monitoring.

Surgical

Before surgical en-block resection it is much better to use silicon balloon expanders for promoting future defect reconstructions. It does not seem that scarifying peripheral healthy tissue to be beneficial in security margin resection (31, 32). Again we should emphasis on post operatively embolization as a supplemental method for surgical effectiveness (20).

Pharmacologic treatment

Pharmacologic treatment of AVM is in infancy and includes matrix me talloproteinase inhibitors such as Doxycycline in brain AVMs, Thalidomide, Avastin / bevacizumab or Sorafeinbla (multi kinas inhibitor). Unfortunately administration of the vast majority of these drugs has been stopped due to either their side effects or their clinically insignificant changes.(24, 25, 44, 45)

Conclusion
To conclude, nowadays there are numerous imaging and therapeutic modalities for arteriovenous malformation. It is not surprising that we encountered a variety of different therapies in the same vascular situations; in fact choosing the best modality is based upon whether you need a permanent effect or not. It is also depends on the location of the lesion and the burden of disease it might cause. There is no standard recommendation for AVM treatment although there have been some suggestions.

References


