

A Practical Guide for Diagnosis and Treatment of Arteriovenous Malformations in the Oral and Maxillofacial Region

Li Xin SU¹ Xin Dong FAN², Jia Wei ZHENG², Yan An WANG², Zhong Ping QIN³,
Xu Kai WANG⁴, Yao Wu YANG⁵, Yi Fang ZHAO⁶

Arteriovenous malformations (AVMs) are congenital vascular malformations (CVMs) resulting from birth defects of the vasculature. It is rarely seen, only accounting for 1.5% of all vascular anomalies, and 50% of the lesions are located in the oral and maxillofacial region. Regardless of the type, AVMs may ultimately lead to significant anatomical, pathophysiological and hemodynamic consequences. Therefore, despite their relative rarity, AVMs still remain the most challenging and/or life-threatening form of vascular anomalies. Transarterial coil embolisation or ligation of feeding arteries are incorrect approaches and may result in progress of the lesion. Furthermore, such procedures would prevent future endovascular access to the lesions via the arterial route, and should be abandoned. Interventional embolisation using various sclerosants is currently the mainstay of treatment for AVMs, and elimination of the nidus (if present) is the key to success. Among various embolosclectherapy agents, ethanol sclerotherapy produces the best long-term outcomes, with minimal complications. For more complex cases, multidisciplinary approaches and interventions may provide an excellent potential for a curative result.

Based on the published literature and clinical experiences, a practical treatment guideline was established in order to provide a criterion for the management of oral and maxillofacial AVMs. This protocol will be renewed and updated to reflect cutting edge knowledge, and provide the newest treatment modalities for oral and maxillofacial AVMs.

Key words: oral and maxillofacial region, arteriovenous malformations, treatment guideline

Arteriovenous malformations (AVMs) are congenital vascular anomalies featured by hypertrophied inflow arteries shunting through a primitive vascular

nidus into tortuous dilated outflow veins. No intervening capillary bed is present. The low blood resistance of the nidus makes the blood flow increase, the feeding artery becomes thicker and tortuous. Meanwhile, it steals a lot of blood from adjacent normal tissues to supply the nidus. The increased blood pressure and the accelerated blood speed make the outflow vein dilated and arterialisised¹⁻³.

The nidus of AVMs can occur anywhere in the body, such as brain, spinal cord, viscera, bone, skin and subcutaneous soft tissues. About 50% of the lesions are located in the oral and maxillofacial region, followed by the extremities and trunk. The majority of maxillofacial AVMs are located in the centre of the face – nearly 70% involve the cheek, nose, ears and upper lip, and AVM in the scalp is not rare. Among vascular anomalies, AVMs are relatively rare, accounting for about 1.5%. At present there is no accurate data regarding to the proportion of peripheral AVMs between males and females; many case reports indicate that the prevalence in females is

1 Department of Oromaxillofacial Head and Neck Surgery, Ninth People's Hospital, College of Stomatology, Shanghai Jiao Tong University School of Medicine, Shanghai, P.R. China

2 Department of Radiology, Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, P.R. China

3 Special Department of Hemangioma, Tumor Hospital of Linyi City, Linyi, Shandong Province, P.R. China

4 Department of Oral and Maxillofacial Surgery, School of Stomatology, China Medical University, Shenyang, P.R. China

5 Department of Oral and Maxillofacial Surgery, School of Stomatology, Fourth Military Medical University, Xi'an, P.R. China

6 Department of Oral and Maxillofacial Surgery, School of Stomatology, Wuhan University, Wuhan, P.R. China

Corresponding author: Dr. Xin Dong FAN, Department of Radiology, Ninth People's Hospital, College of Stomatology, Shanghai Jiao Tong University School of Medicine, #639, Zhi Zao Ju Road, Shanghai 200011, P.R. China. Tel: 86-21-23271063; Fax:86-21-63121780. E-mail: fanxindong@aliyun.com

slightly higher than males, with a 1.5:1 ratio in some case reports. Besides the common regions, AVMs can rarely involve organs such as the iris, tongue, and mandible^{4,5}.

At present, it has not yet been found that AVMs have transmissibility and there is no proof that food, medicines, or X-rays may lead to the deformity. However, AVMs can be hereditary, for example, hereditary hemorrhagic telangiectasia (HHT), also known as Rendu-Osler-Weber Syndrome. This is an autosomal dominant inherited disease, usually appearing as telangiectasis in the skin and mucosa, with nasal and gastrointestinal bleeding, and AVMs of the brain, lung, and liver. Again, capillary malformation-arteriovenous malformation (CM-AVM), a newly discovered vascular lesion named and mainly described by Eerola, appears as a familial orbicular-ovate blood capillary red spot, and includes 10% of family members with AVM or AVF. Moreover, AVM is also a kind of appearance in other complex symptoms such as Parke-Weber syndrome and Wyburn-Mason syndrome. Among these complex symptoms, AVMs may be located in the brain, spinal cord, gastrointestinal tract, head and neck and extremities^{5,6}.

Clinical manifestation

Symptoms are usually referable to the anatomic location of the AVMs. The larger and the more anatomically central AVMs are, the greater the likelihood of high-output cardiac consequences will be. Other presenting symptoms can include pain, a disfiguring mass, tissue ulceration and haemorrhage⁸.

The superficial area of the head and neck is about 14% in surface area, but 50% AVMs of soft tissue happen in this area. Although AVMs are a kind of congenital disease, only 60% are discovered after birth, the rest are seen in childhood or adulthood. The development of the nidus is proportional to the physical development. It can remain stable over a long period or expand rapidly in a short time. This situation usually happens after a trauma, during pubescence or following the change of estrogenic hormones when pregnant and improper treatment, such as the partial resection of the lesion, occlusion or ligation of the feeding artery¹.

Most patients with AVMs of maxillofacial soft tissue present with a facial deformity with an unclear boundary, telangiectasia or kermesinus. The temperature of the involved area is higher than the surrounding normal skin, and the thrill and pulsation can be detected. These objective signs remind us of the existence of AVMs and the character of high blood flow. The volume of the ears, nose, lip, and extremities enlarges gradually and

the appearances are totally destroyed. In the later stage, the surface of AVMs turns into an ulcer and bleeding as blood steal, distension of jugular vein and an increase of pressure in the superior vena canal cause widen heart boundary and heart failure^{1,7,8}.

The clinical manifestation of AVMs is similar to AVF, but the physiological characteristics and clinical course are completely different. AVF is mostly postnatal, it originates from trauma and chronic involvement, and there is a singular fistulous tract between the arteries and veins, so the arterial blood flows into the vein directly and makes the backflow vein high blood pressure. AVM is a congenital disease and has multiple fistulous communications between the arteries and veins. They both have dilated and tortuous feeding arteries and backflow veins⁹.

Intraosseous AVMs are usually called central hemangioma of the jaw. The hazard is uncontrolled acute bleeding. Acute bleeding usually occurs in the exchange of the primary and secondary teeth in children, especially at about 10 years old. Most emergent bleeding episodes happen after a tooth extraction. The intraosseous AVMs are mainly located in the molar areas, with or without involving the adjacent soft tissue. Some patients with mandibular AVMs may report numbness around the lower lip¹⁰⁻¹².

Diagnosis of AVMs

The AVMs of soft tissue in the maxillofacial region are mostly located on the surface of the body, which can be noted according to clinical symptoms and signs. Lesions located deeper within the body often need the aid of imaging machines to discover the nature and extent of the nidus; enhanced CT and MRI machines are commonly used. AVMs of the soft tissue on CT scans often appear as an abnormal soft tissue bulge of isodensity. After injecting contrast, the abnormal soft tissue bulge can be obviously enhanced to similar to the density of blood vessel. The drainage vein expands and is seen sooner. AVMs of the soft tissue is demonstrated as abnormal soft tissue mass with moderate signal both at T1-weighted and T2-weighted images of MRI, and flow voids is noted. After injecting contrast, the signal of the abnormal soft tissue can be enhanced. An angiogram is the "golden standard" to diagnose AVMs, but is not often an independent diagnosis modality and usually combines with interventional therapy. The vascular architecture of AVMs in the maxillofacial soft tissue includes nidus formation, earlier appearance of drainage vein and the expanded, manifold feeding artery. The origin of the feeding artery depends on the location of the lesion.

The internal carotid artery provides the blood for the AVMs located at the upper one-third of the maxillofacial region and the back of nose, the remaining two-thirds often come from the external carotid artery. The drainage veins become expanded and appear with the nidus in the arterial phase simultaneously. High flow AVMs with obvious A-V fistula, much blood flood into the nidus and which results in the distal end of artery invisible, that is named after “steal of blood phenomenon”.

The AVMs of the mandible is much more common than the maxilla. The different manifestations are demonstrated on the X-ray film, such as unilocular radiolucency, multilocular radiolucency, coarse trabecular, soap bubble and honeycomb. Expansion of the mandibular canal is often noted in the case of AVMs of the mandible. Expanded marrow space and obliteration of trabeculae are depicted on the CT scan, which shows a single capsule or capsule-like low-density lesions. The cortical bone is perforated if the adjacent soft tissue is involved; if not, the cortical bone is intact. After the injection of the contrast, the AVMs of jaws are enhanced to the same density as the surrounding vessels, and the earlier demonstration of drainage vein is also found. The features of the CT make it the most important imaging modality in the diagnosis of AVMs of the jaw. Angiograms show the AVMs of the jaw as varix in the posterior part of alveolar bone, which lasts to venous phase and communicated to the drainage vein. The feeding arteries of the AVMs of the maxilla are the superior alveolar artery and the descending palatine artery, and the inferior alveolar artery feeds the AVMs of the mandible. The supplement of the multiple fine branches to the AVMs' nidus is demonstrated in the super selective angiogram of the feeding artery. AVMs of the jaw are demonstrated on MRI scans as a lower signal in both T1- and T2-weighted images and the obliteration of fat signals in the marrow. If the soft tissue involvement occurred, flow voids was noted around the adjacent the jaw^{13,14}.

Once an AVM of the jaws is clinically suspected, a biopsy should be prohibited. The panorama and enhanced CT scans are the primary methods to detect the lesion. Usually enhanced CT scans will make the final diagnosis of an AVM of the jaw, and the panorama may depict the relationship between the teeth and the lesion. When the interventional therapy is selected, the angiogram will be indicated.

Treatment of AVMs

After the diagnosis is established, the next hurdle is to determine which therapy is warranted. A vascular

malformation team should be in place even though the international radiologist primarily plans and directs a patient's care. There are many therapies to treat AVMs, embolisation has been the mainstay to treat AVMs so far, surgery is used to correct appearance after embolisation debridement of the postoperative infection and tracheotomy. Although small nidus can be resected, sometimes complete excision of the lesion is impossible as its boundary is unclear, and partial resection may make the AVMs worsen. The target of the embolisation is to eradicate the nidus. The ligation or occlusion of the feeding artery should be forbidden^{15,16}.

There are now many endovascular ablative therapy agents that are used in various clinical scenarios. The choice of agent depends upon several factors: the vascular territory to be treated, the type of abnormality being treated, the possibility of superselective delivery of occlusive agents, the goal of the procedure, and the permanence of the occlusion required. Polyvinyl alcohol foam (PVA) is formed by the reaction of polyvinyl alcohol foam with formaldehyde. It is biologically inert and provokes a mild inflammatory reaction. Initially thought to be a permanently occluding agent, PVA is now known to recanalise when used to treat vascular malformations. PVA is usually supplied in suspension in size of 150–300 μm for AVMs of the soft tissue in the maxillofacial region. N-butylcyanoacrylate (NBCA) belongs to a class of tissue adhesive that are used for endosurgical vascular ablation. NBCA is used to treat AVMs and AVF. This glue remains in the liquid state until contact occurs with blood, whereby it polymerises from its monomeric form to polymeric form. In this polymerisation process, the cyanoacrylates generate heat, which may contribute to some level of histotoxicity in the adjacent area and angioneclerosis. Coils with or without attached cotton or Dacron fibers have long been used to induce vascular occlusion. Many coils have been developed that will pass through standard 5F and mini 2.2 F catheter systems. These occluding spring coils emboli function similarly to an arterial ligation in that they occlude the artery where the coils is released and do nothing to the capillary bed distally. A newer development in coils technology is the detachable coil device. This is a platinum coil that is very soft and radiopaque on fluoroscopy. This is a distinct advantage in that perfect control can always be maintained. If the operator does not like a particular coil positioning, it can be totally retracted. Further, once in position and ready for detachment, it will detach without any pulling force. The objectives of embolisation of maxillofacial AVMs should be a curative fashion, not a palliative fashion. As has been reported by several practitioners, the use of

PVA, NBCA and coils had not only gotten incomplete treatment, but also recanalisation. The main reason recanalisation and neovascular recruitment phenomenon occur in AVMs management is that all embolic agents do not completely destroy the endothelial cells of the AVMs. The endothelial cell, when it is intact during thrombosis, senses decreased oxygen tension and sends out an angiogenesis factor, which stimulates neovascular formation. Further, it sends out chemotactic factors that cause a cellular infiltration to carry debris from the vascular channels. Once it occurs, the endothelial cell re-endothelialises and recanalisation occurs. With the use of ethanol, the endothelial cell is denuded from the vascular wall, its protoplasm is precipitated, and there is a fracture in the vascular wall to the level of the internal elastic lamina. Because of this destruction of the endothelial cell, the permanence encountered by ethanol in treating AVMs is almost routine^{17,18}.

In treating AVMs, super selective catheter placement is absolutely essential. When this is not possible, then direct percutaneous puncture techniques should be used to circumvent any catheterisation obstacles. If super selective placement at the AVM nidus is not possible, then the use of ethanol must be avoided. Frequently, outflow occlusion is required to decrease the flow of the lesion in those cases with obvious expansion of drainage vein to maximise the thrombogenic properties of ethanol. This can be achieved through the use of detachable coils. The amount of ethanol used in each endovascular ablative procedure is up to the flow-volume characteristics of the individual lesion. No predetermined volume of ethanol is ever considered.

Endovascular ablation of AVMs with ethanol has ushered in a new era in the therapy of these problematic anomalies. Cure and permanent partial ablation have been documented in patient series resulting in symptomatic improvement. Because neovascular recruitment and recanalisation have not been observed, permanent partial ablations have led to long-term symptomatic improvement, obviating the need for further treatment^{19,20}.

The partial resection of the jaw is used as treatment of AVMs of the jaw. Not only can facial deformity occur after this operation, but this procedure is also hazardous. Even if after this radical resection, AVMs of the soft tissue around the jaws still keep progressing and cause ulcer formation and bleeding. The curative embolisation of AVMs of the jaws include filling coils into the nidus, and then destroying the lesion with ethanol^{20,21}.

The complications of ethanol embolization of AVMs

Despite the success that is possible with ethanol, it must be remembered that it is an extremely dangerous intravascular sclerosant that can cause tissue necrosis and cardiopulmonary collapse.

Nontarget embolisation with ethanol will lead to tissue necrosis as capillary beds are entirely destroyed. Being a fluid agent, ethanol penetrates to the capillary level, devitalising normal tissue. The following improper operations will cause necrosis:

- Injection of ethanol into normal tissues.
- Less than 10~15 min waiting between injections of ethanol, and the excessive ethanol flow to normal tissue.
- Ethanol overflow when digital pressure of the drainage vein.

Once tissue necrosis is found, the colour of the involved area turns dark, then black and finally necrotic tissue is lost. A hot compress and vasodilating agent may help to relieve the progress of necrosis. The following debridement and surgical correction is sometimes necessary.

Cardiovascular collapse is a rare and serious complication of ethanol-related treatment. When ethanol is injected into the nidus of AVMs, some outflow of ethanol makes the precapillary of the pulmonary artery (PA) spasm, causing increased PA pressure, leading to increased right ventricular (RV) after-load, decreasing RV contractility, and decreasing RV cardiac output. This leads to decreased left heart filling, decreased left heart cardiac output, systemic hypotension, and decreased coronary perfusion. If severe enough, it leads to cardiac arrhythmia and cardiopulmonary collapse. If high doses of ethanol are used during embolisation, a Swan-Ganz catheter induced to monitor pulmonary artery pressure is an effective method to control this complication. Once an obvious rise in PA pressure is noted, the ethanol injections should be stopped immediately. If PA hypertension cannot be recovered, nitroglycerin is indicated to be drip fed^{18,22}.

Temporary haemoglobinuria commonly occurs during high doses of ethanol embolisation. This is because erythrocyte, platelet and haemoglobin are destroyed as they come into contact ethanol, then are excreted by the kidneys. When the injection dosage of ethanol is more than 0.8ml/kg, the probability of haemoglobinuria occurs in nearly 100% of patients, but there are no reports of kidney impairment so far^{23,24}.

Conclusion

At long-term follow up, the cure of AVMs with ethanol embolisation is a distinct possibility. Acceptable complication rates can occur with the use of ethanol. In the endovascular management of AVMs, ethanol demonstrates a level of permanence that is seldom encountered by other agents. Surgical procedures are just as an adjunctive method for correcting facial deformity, debridement of necrotic tissue and tracheotomy.

References

- Zheng LZ, Fan XD, Zheng JW, Su LX. Ethanol embolization of auricular arteriovenous malformations: preliminary results of 17 cases. *AJNR Am J Neuroradiol* 2009;30:1679–1684.
- Yang CH, Ohara K. Acquired digital arteriovenous malformation: a report of three cases and study with epiluminescence microscopy. *Br J Dermatol* 2002;147:1007–1011.
- Kohout MP, Hansen M, Pribaz JJ, Mulliken JB. Arteriovenous malformations of the head and neck: natural history and management. *Plast Reconstr Surg* 1998;102:643–654.
- Tille JC, Pepper MS. Hereditary vascular anomalies: new insights into their pathogenesis. *Arterioscler Thromb Vasc Biol* 2004;24:1578–1590.
- Leon-Villapalos J, Wolfe K, Kangesu L. GLUT-1: an extra diagnostic tool to differentiate between haemangiomas and vascular malformations. *Br J Plast Surg* 2005;58:348–352.
- Krebs LT, Shutter JR, Tanigaki K, et al. Haploinsufficient lethality and formation of arteriovenous malformations in Notch pathway mutants. *Genes Dev* 2004;18:2469–2473.
- Yakes WF, Haas DK, Parker SH et al. Symptomatic vascular malformations: ethanol embolotherapy. *Radiology* 1989;170:1059–1066.
- Do YS, Yakes WF, Shin SW et al. Ethanol embolization of arteriovenous malformations: interim results. *Radiology* 2005;235:674–682.
- Persky MS. Congenital vascular lesions of the head and neck. *Laryngoscope* 1986;96:1002–1015.
- Kiyosue H, Mori H, Hori Y, et al. Treatment of mandibular arteriovenous malformation by transvenous embolization: A case report. *Head Neck* 1999;21:574–577.
- Beek FJ, ten Broek Fw, van Schaik JP, Mali WP. Transvenous embolization of an arteriovenous malformation of the mandible via a femoral approach. *Pediatr Radiol* 1997;27:855–857.
- Benndorf G, Kim DM, Menneking H, Klein M. Endovascular management of a mandibular arteriovenous malformation in a patient with severe hemophilia a. *AJNR Am J Neuroradiol* 2004;25:614–617.
- Fan X, Zhang Z, Zhang C, et al. Direct-puncture embolization of intraosseous arteriovenous malformation of jaws. *J Oral Maxillofac Surg* 2002;60:890–896.
- Fan X, Qiu W, Zhang Z, Mao Q. Comparative study of clinical manifestation, plain-film radiography, and computed tomographic scan in arteriovenous malformations of the jaws. *Oral Surg Oral Med Oral Pathol Oral Radio Endod* 2002;94:503–507.
- Yakes WF, Pevsner P, Reed M, et al. Serial embolization of an extremity arteriovenous malformation with alcohol via direct percutaneous puncture. *AJR Am J Roentgenol* 1986;146:1038–1040.
- Lee BB, Baumgartner I, Berlien HP, et al. Consensus Document of the International Union of Angiology (IUA)-2013. Current concept on the management of arterio-venous management. *Int Angiol* 2013;32:9–36.
- Yakes WF, Luethke JM, Parker SH. Ethanol embolization of vascular malformations. *Radio Graphics* 1990;10:787–796.
- Yakes WF, Krauth L, Ecklund J et al. Ethanol endovascular management of brain arteriovenous malformations: initial results. *Neurosurgery* 1997;40:1145–1152.
- White RI Jr, Pollak J, Persing J, et al. Long-term outcome of embolotherapy and surgery for high-flow extremity arteriovenous malformations. *J Vasc Interv Radiol* 2000;11:1285–1295.
- Fan XD, Su LX, Zheng JW, et al. Ethanol embolization of arteriovenous malformation of the mandible. *AJNR Am J Neuroradiol* 2009;30:1178–1183.
- Fan X, Zhu L, Zhang C. Treatment of mandibular arteriovenous malformation by transvenous embolization through the mental foramen. *J Oral Maxillofac Surg* 2008; 66:139–143.
- Stefanutto TB, Halbach V. Bronchospasm precipitated by ethanol injection in arteriovenous malformation. *AJNR Am J Neuroradiol* 2003;24:2050–2051.
- Lee JJ, Do YS, Kim JA. Serum ethanol levels after alcohol sclerotherapy of arteriovenous malformations. *J Korean Med Sci* 2004;19:51–54.
- Jeong HS, Baek CH, Son YI et al. Treatment for extracranial arteriovenous malformations of the head and neck. *Acta Otolaryngol* 2006;126:29–300.