Absolute Ethanol Embolization of Infiltrating-diffuse Extracranial Arteriovenous Malformations in the Head and Neck

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WHAT THIS PAPER ADDS
Ethanol embolotherapy has proved to be curative for the treatment of arteriovenous malformations (AVMs). However, the sole use of absolute ethanol embolization is not suitable for all types of AVMs. This study reports a single center experience and evaluates technical and clinical safety, and effectiveness of the sole use of absolute ethanol embolization for infiltrating-diffuse extracranial AVMs in the head and neck.

Objective: Extracranial arteriovenous malformations (AVMs) of an infiltrative type in the head and neck can cause cosmetic, functional, and psychological problems. This study reports a single center experience and evaluates the clinical safety and effectiveness of the sole use of absolute ethanol embolotherapy for infiltrative extracranial AVMs in the head and neck.

Method: From June 2011 to June 2013, 168 consecutive patients with extracranial AVMs in the head and neck underwent staged ethanol or other methods of embolization, of whom 66 patients had infiltrating-diffuse extracranial AVMs of type III in the head and neck. Absolute ethanol embolization was solely used and retrospectively evaluated. All patients were assessed at clinical follow up (mean 16.8 months; range 12–38 months). Therapeutic outcomes were determined by evaluating the clinical outcome of symptoms and signs, as well as the degree of devascularization by follow up angiography.

Results: For the 96 sessions, the mean amount of ethanol used in a single embolization session was 13.6 mL and range was from 2 to 25 mL. Fifty-six of the 66 patients were effectively controlled with 100% of the AVMs devascularized, and the remaining 10 patients had partial remission with various degrees of AVM devascularization (50–99%). Transient hemoglobinuria occurred in five of the 66 patients for a total 16 out of 96 procedures. There were no major complications.

Conclusions: The sole use of ethanol embolotherapy appears to be efficacious and safe in the management of infiltrating-diffuse extracranial AVMs in the head and neck.

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INTRODUCTION
Arteriovenous malformations (AVMs) of the extracranial head and neck can cause tremendous cosmetic, functional, and psychological problems. Small and superficial AVMs can be cured by surgical resection; however, most AVMs are inoperable as they are large and diffuse in nature and they involve important normal adjacent structures. With improvements in catheter technology, superselective techniques, and the use of liquid embolic agents, embolotherapy has emerged as the primary mode of treatment for the management of peripheral AVMs.1–4

Ethanol embolotherapy has proved to be effective, even in complex AVMs, by a combination of the direct denuding effect on the vascular wall and clumping of damaged erythrocytes and denatured proteins, which result in complete and permanent obliteration of the vessel lumen.5–7 However, the sole use of absolute ethanol embolization is not suitable for all types of AVMs. AVMs were categorized by Cho et al.8 according to the angiographic morphology of the nidus: type I (larger arteriovenous fistulae with no more than three separate arteries shunting to the initial single venous outflow component), type II (smaller arteriovenous fistulae with multiple arterioles shunting to the initial part of a plexiform appearance into a single venous component), type IIIa (arteriovenous fistulae with non-dilated fistulae with multiple fine shunts present between arterioles and arteriovenous fistulae with non-dilated fistulae with multiple fine shunts present between arterioles and arteriovenous fistulae with non-dilated fistulae with multiple fine shunts present between arterioles and arteriovenous fistulae with non-dilated fistulae with multiple fine shunts present between arterioles and arteriovenous fistulae with non-dilated fistulae with multiple fine shunts present between arterioles and arteriovenous fistulae with non-dilated fistulae with multiple fine shunts present between arterioles and arteriovenous fistulae with non-dilated fistulae with multiple fine shunts present between arterioles and arteriovenous fistulae with non-dilated fistulae with multiple fine shunts present between arterioles and arteriovenous fistulae with non-dilated fistulae with multiple fine shunts present between arterioles and arteriovenous fistulae with non-dilated fistulae with multiple fine shunts present between arterioles and arteriovenous fistulae with non-dilated fistulae with multiple fine shunts present between arterioles and arteriovenous fistulae with non-dilated fistulae with multiple fine shunts present between arterioles and arteriovenous fistulae with non-dilated fistulae with multiple fine shunts present between arterioles and arteriovenous fistulae with non-dilated fistulae with multiple fine shunts present between arterioles and arteriovenous fistulae with non-dilated fistulae with multiple fine shunts present between arterioles and arteriovenous fistulae with non-dilated fistulae with multiple fine shunts present between arterioles and arteriovenous fistulae with non-dilated fistulae with multiple fine shunts present between arterioles and arteriovenous fistulae with non-dilated fistulae with multiple fine shunts present between arterioles and arteriovenous fistulae with non-dilated fistulae with multiple fine shunts present between arterioles and arteriovenous
the venous component), and type IIIb (arteriovenous fistulae with dilated fistulae with multiple shunts present between arterioles and the venous component). Similar angiographic morphology was found in the head and neck in the present study, although the Cho et al. classification focuses mainly on the trunk and extremities. The present work benefits from this classification, especially for the absolute ethanol embolization procedure. As a result of the augmented flow with the increased volume rate of types I and II arteriovenous fistulae, most of the ethanol was flushed away by the circulation. Intravascular occlusion coils within the venous component of the nidus must be used to reduce the rate and volume of blood flow. Sole absolute ethanol embolization was not as effective as seen with type III AVMs. Herein, these are referred to as "infiltrating-diffuse" AVMs.

This study reports outcomes and complications seen in a series of 66 cases of infiltrating-diffuse type III extracranial AVMs, according to the Cho et al. classification, located in the head and neck which were solely treated with absolute ethanol embolization.

**METHODS**

**Patients**

Approval from the institutional review board of the study hospital was obtained for a retrospective review of patients’ medical and imaging records, and informed patient consent for the study was also obtained. From June 2011 to June 2013, 168 consecutive patients with extracranial AVMs in the head and neck underwent staged ethanol embolization or other methods of embolization, of whom 66 patients with type III extracranial AVMs were identified by angiography and treated. The study group consisted of 66 patients (28 males, 38 females) with a mean age of 26.8 years (age range 16—46 years) at the time of treatment. Diagnosis of AVMs was made by the referring center on the basis of clinical and imaging findings. Eight patients had undergone previous partial resection or n-Butyl cyanoacrylate embolization at other hospitals before undergoing ethanol embolotherapy.

Selective and superselective angiograms were performed before embolization in all patients to accurately define the feeding arteries, draining veins, and nidus of the AVM.

**Angiographic and embolization techniques**

All procedures were performed by two experienced interventional radiologists. Sixty-six patients with 96 embolization procedures received general anesthesia after nasal intubation. Blood pressure, electrocardiogram, oxygen saturation, and end tidal carbon dioxide levels were constantly monitored during the procedures.

To determine the detailed angio-architecture of the AVMs, selective angiograms of the feeding artery including facial artery, superficial temporal artery, posterior auricular artery, or the occipital artery were performed to further identify the main feeding artery. It was also necessary to identify any abnormal extracranial and intracranial communications. The major compartments of the AVMs and endovascular accesses to those compartments were delineated. All angiograms of these AVMs showed tortuous arteriolar components of the nidus, and arteriovenous fistulae without obvious dilated outflow vein formation.

For the patients whose external carotid arteries were ligated during prior therapies, angiograms of the common carotid artery, the vertebral artery, and the thyrocervical trunk were performed on the same side of the lesions, as well as the external carotid artery on the opposite side. Once the feeding vessels of the lesions were identified, a microcatheter (Powler10, Cordis Endovascular, Miami Lakes, FL, USA) was inserted into the nidus. In cases in which these complex maneuvers failed, a direct puncture of the nidus was performed. The area of percutaneous puncture was prepped and draped. A 21 gauge butterfly needle was advanced under the guidance of repeated contrast injections. Super-selective placement of the catheter tip or the needle tip was a requirement, only then could ethanol be injected into the nidus with sparing of all normal vascular structures. Absolute ethanol (99.7%) was used as the embolization agent. The intention was to direct ethanol towards the nidus itself and not towards the vascular feeders. Repeated angiograms through the needle were used to ensure that there was no retrograde flow of contrast to the proximal part of ophthalmic artery or other feeding arteries before ethanol injections. The contrast medium could only be seen in the nidus and outflow vein. The goal was to embolize all or part of the nidus until the desired clinical results were achieved. For the 96 sessions of ethanol embolization performed, a solitary transarterial approach was used in 28 sessions, solitary direct puncture in 26 sessions, and a combination of both in 42 sessions.

The ethanol was manually injected after several test injections with the contrast medium to determine the pressure required and the amount of ethanol to inject based on the exact flow characteristics of the AVMs. The amount of ethanol used during embolization was based on the amount of contrast medium required to fill the portion of the AVM being treated. Arteriography was performed 5–10 minutes after each ethanol injection to determine whether blood flow stasis had been achieved. Meticulous repetition of the above described technique was required until complete embolization of at least one compartment of the AVM was achieved. Ethanol should not be injected again when the outflow vein disappears and the feeding artery appears refilled in retrograde fashion. When the direct puncture embolization was performed, if the injected contrast was seen out of the vascular nidus and staining normal tissues, no more ethanol was injected so as to avoid any possible necrosis. The total amount of absolute ethanol used per session was less than 1 mL/kg of body weight.

To minimize local soft tissue swelling and accompanying pain, all patients received an intravenous injection of dexamethasone prior to the procedure, usually 5—10 mg, depending on their body weight. Post-operative management included an intravenous infusion of dexamethasone.
Further medications usually included a tapering dose of corticosteroids over 7 days and Zantac (Sanofi, Hangzhou, China). Any hemoglobinuria that occurred during the procedure was managed by means of hydration with an intravenously administered crystalloid solution. To evaluate renal function, serum creatinine and urea levels were measured at least once during the hospital stay.

In some cases with almost 100% devascularization of abnormal arteriovenous communications as seen on angiograms, but which still presented with some degree of cosmetic problems left by the AVM, further operation was necessary to correct the contour or function.

**Evaluation of clinical data and follow up results**

Follow up evaluation was obtained on the basis of physical examination at 3 month intervals and telephone questionnaire at 1 month intervals in all patients (follow up range 12–38 months; mean 16.8 months) after the initial procedure. Additional embolization was recommended if the symptoms and signs remained or if the AVMs were still present on follow up imaging. The results were graded on a four point scale: worse (AVMs became larger); no change (AVMs ≤49% resolved); improved (AVMs were 50–99% resolved); and effective control (AVMs were 100% resolved). One oral and maxillofacial surgeon and one interventional radiologist evaluated the clinical outcome of symptoms and signs by consensus. Cure was defined as complete resolution of the clinical symptoms and signs, with 100% devascularization of AVMs as seen on angiography. Partial remission was defined as complete resolution or improvement of the clinical symptoms and signs, with 50–99% devascularization of AVMs as seen on angiography. No remission was defined as no improvement or no change of the clinical symptoms and signs, with less than 50% devascularization of AVMs as seen on angiography. Aggravation was defined as an aggravation of the clinical symptoms and signs, regardless of the degree of AVM devascularization as seen on angiography. Cure and partial remission were considered effective therapeutic outcomes of ethanol embolization of AVMs.

Complications were classified into major and minor according to standards reported by the Society of Interventional Radiology. Minor complications were defined as those that required no management and resulted in no consequences. Major complications included those that required therapy or caused permanent adverse sequelae or death. When complications were observed, the angiograms were reviewed again to detect the possible cause of the complications.

**RESULTS**

**Clinical outcomes**

The post-operative recovery in all the patients was uneventful. There was no significant bleeding. After the needle was removed, manual pressure on the puncture site was performed for 5 minutes until there was no more oozing. After the procedure, patients exhibited focal swelling in the area of the AVMs, which was resolved within 1–2 weeks.

For the 96 sessions, the mean volume of ethanol used was 13.6 mL and ranged from 2 mL to 25 mL for a single embolization session. Even when the maximum amount of ethanol was used, the total dose did not exceed 1 mL/kg of body weight. No patient experienced ethanol induced side effects on the liver and kidneys (measured by appropriate lab tests). Hemoglobinuria occurred in five of the 66 patients for a total of 16 out of 96 sessions, which disappeared at 5–6 hours after continuous intravenous infusion; no patient showed elevation in creatinine or urea levels.

As a therapeutic outcome of ethanol embolization, there was an obvious reduction in redness, swelling, and warmth in all of the patients. Fifty-six of the 66 patients were cured with 100% of AVM devascularization, with the remaining 10 having partial remission with various degrees of AVM devascularization (50–99%).

The required number of embolization procedures in patients varied depending on the volume and behavior of the lesion and the adjacent tissues involved. A single embolization procedure was usually sufficient to achieve cure of localized AVMs, but diffuse cases involving adjacent soft tissue required multiple sessions. In patients who needed two or more procedures, the time interval between the procedures ranged from 1 to 2 months. The amount of ethanol used and results of treatment in 66 patients are summarized in Table 1. Thirteen of the 66 patients had further operations to correct persisting deformity after the embolization.

| Table 1. Demographic data of treatment, results, and complications in 66 patients with 99 procedures. |
|---------------------------------|-------------------------------------------------|
| **Parameter**                  | **Value**                                       |
| Approach                        |                                                 |
| Transarterial                   | 28 (29.2%)                                      |
| Direct puncture                 | 26 (27.1%)                                      |
| Combined                        | 42 (43.7%)                                      |
| Total                           | 96 (100%)                                       |
| No. of embolization procedures  |                                                 |
| Total                           | 96                                              |
| Mean                            | 1.44                                            |
| Amount of injected ethanol (mL) |                                                 |
| Mean (range)                    | 13.6 (2–25)                                     |
| Degree of devascularization     |                                                 |
| 100%                            | 56 (84.8%)                                      |
| 76–99%                          | 10 (15.2%)                                      |
| Total                           | 66 (100%)                                       |
| Complications (SIR classification)|                                               |
| No complication                 | 50 (75.8%)                                      |
| B                               | 16 (24.2%)                                      |
| Follow up (mo) (range)          | 16.8 (12–38)                                    |
| Complications:                  |                                                 |
| Minor Complications: A. No therapy, no consequence | |
| B. Nominal therapy, no consequence |                                   |
| C. Require therapy, minor, hospitalization (48 hours) | |
| D. Require major therapy, unplanned increase in level of care, prolonged hospitalization (48 hours) | |
| E. Permanent adverse sequelae, F. Death | |
Complications

There was no procedure related mortality. Sixteen of the 66 patients had minor complications classified as B using the SIR (Society of Interventional Radiology) classification. Minor complications included skin blistering or superficial skin necrosis. Skin blisters, superficial skin necrosis, and pyogenic granulomas from puncture points were healed with wound dressing, and skin grafting was not required. One case with AVMs in the chin had ethanol backflow to the distal part of the facial artery causing superficial skin necrosis of the buccal area and an obvious but acceptable scar (Table 1).

Case illustrations

Case 1: A 26 year old male presenting with a red pulsating mass at the left buccal region was treated successfully with 5 mL absolute ethanol embolization by percutaneous direct puncture (Fig. 1). The pre-embolization angiogram demonstrated that the AVMs were supplied mainly by a tortuous facial artery, and that these were type III (Fig. 2A). A lateral view of the vein phase of the pre-embolization angiogram shows an infiltrating-diffuse nidus of AVMs and outflow vein (Fig. 2B). Because of the tortuous facial artery, the microcatheter failed to reach the center of the nidus of AVMs. A 21 gauge butterfly needle was used to directly puncture the nidus. Contrast medium was injected to make sure that there was no backflow to the feeding arteries before ethanol injection, and then followed by a total of 5.0 mL absolute ethanol given in increments (2.0 mL + 2.0 mL + 1.0 mL) (Fig. 2C). Arteriography was performed 5 minutes after each ethanol injection to determine whether thrombosis had occurred. Ethanol should not be injected again when the outflow vein disappears and the feeding artery appears (Fig. 2D). A lateral view of the angiogram of the facial artery shows complete obliteration of AVMs and the outflow veins (Fig. 3).

Case 2: A 36 year old female presenting with an AVM in the buccal region was treated successfully with two procedures of absolute ethanol embolization (15.0 mL + 3.0 mL) (Fig. 4A and B).

Case 3: A 22 year old male presenting with AVM at the lower lip and buccal area was treated successfully with one procedure of absolute ethanol embolization (8.0 mL) (Fig. 5A and B).

DISCUSSION

AVMs in the extracranial head and neck regions are rare and challenging entities. Surgical treatment is the classic...
method for treating vascular malformations; either by ligation of the feeding arteries or by attempted excision after embolization, but such procedures have not been very successful.

With the development of interventional radiology, embolotherapy is playing an ever increasing role in the management of AVMs. There are many embolic agents for use in various clinical scenarios, with the choice of agent depending on several factors: the vascular territory to be treated, the type of abnormality being treated, the possibility of superselective delivery of an occlusive agent, the goal of the procedure, and the permanence of the occlusion required. With regards to vascular malformations, permanent treatment is a significant issue. It has already been documented in the literature that embolization with materials such as polyvinyl alcohol (PVA), tissue adhesives, and coils is rarely curative and provides only temporary palliation. The main reason for recanalization and neovascular recruitment is that none of the aforementioned embolic agents completely destroys the endothelial cells in the nidus of the AVMs. These may sense decreased oxygen tension, resulting in the release of angiogenesis factors that stimulate neovascular formation and release of chemotactic substances that cause cellular infiltration contributing to the removal of debris from the vascular channels. Once this happens recanalization occurs and previously embolized vessels re-endothelialize.

With the use of absolute ethanol, the endothelial cells are denuded from the vascular wall, its protoplasm is precipitated, and a fracture in the vascular wall at the level of the internal elastic lamina is formed, followed by shrinking of the lesion. In AVMs, these changes are desirable and responsible for the curative effects and permanence of ethanol embolization. This is quite important for AVMs of the face, considering the aesthetic aspects. The judicious use of ethanol as an embolic agent has revolutionized the ability to permanently cure these lesions in soft tissues, organs, bone, and brain as described in 1994 by Coldwell, Yakes, and multiple other authors.

Figure 2. (A) Lateral view of the pre-embolization angiogram showed AVMs mainly supplied by a tortuous facial artery (arrow). (B) Lateral view of the venous phase of the pre-embolization angiogram showed infiltrating-diffuse nidus (short arrow) of AVMs and outflow vein (long arrow). (C) Direct puncture of the nidus was performed. The area of percutaneous puncture was prepped and draped. A 21 gauge butterfly needle was used for puncture (arrow). The contrast medium was injected through a needle to make sure that there was no backflow of contrast to the proximal part of facial arteries before ethanol injection, followed by absolute ethanol injection three times in increments (2.0 mL + 2.0 mL + 1.0 mL). (D) Arteriography through the 21 gauge butterfly needle was performed 5 minutes after each ethanol injection to determine whether thrombosis had occurred. Ethanol should not be injected again when the outflow vein disappears and the feeding artery appears (arrow).
Even if ethanol, the most powerful embolizing agent, is used, sole absolute ethanol embolization cannot achieve good results in all extracranial AVMs in the head and neck. In some high flow cases with a dominant outflow vein (DOV), the injected ethanol may become diluted with blood and may be swept away from the nidus before it causes nidus occlusion. Thus, flow occlusion techniques, including external pneumatic pressure cuffs and intravascular occlusion balloon catheter or coil embolization of the DOV, are sometimes required to achieve effective ethanol embolization of this subset of peripheral AVMs, as described by Jackson, Cho, and Yakes.18

Angiographic classification of AVMs as described by Cho et al. provides a useful classification for AVM treatment, especially for absolute ethanol embolization. Although their classification mainly focuses on the trunk and extremities, this classification is useful in the study of AVMs in face and neck, with similar findings on angiographic morphology. Based on this classification system, most of the AVM cases in the present study were mixed types and good results were obtained with ethanol embolization.

Another reason for the sole use of ethanol to embolize the type III infiltrating-diffuse extracranial AVMs in the head and neck, is that cosmetic corrections should be considered. Most infiltrating-diffuse AVMs in this region present as facial masses with superficial skin involvement. Obvious shrinkage of the AVM mass and cosmetic improvement can be achieved after absolute ethanol embolization. Polymerizing liquid agents such as nBCA and ONYX have commonly been used; however, they cannot cause shrinkage of the AVM’s mass like that caused by ethanol. Meanwhile, most infiltrating-diffuse AVMs in this region are superficial and skin is involved in the lesion. When coils lie very superficially, they can erode through the overlying skin and cause ulceration, and in addition, patients can feel some discomfort because of the mass effect. In some cases of AVMs with DOV, if coils have to be used to reduce the flow speed and volume of DOV, extraction of these coils is required during the follow up period.

Complications are one of the most important issues for interventional radiologists when treating AVMs with absolute ethanol, and cardiovascular collapse is the most severe complication related to it. There was a case of cardiovascular collapse during ethanol embolization for a type I AVM of the upper lip, not in this group, and the patient died with DIC 2 days after cardio-pulmonary resuscitation was successfully performed. No relationship was found between cardiovascular collapse and the dosage or method of injection of ethanol.21 To avoid such complications it is critical that the dose per kilogram and per 10 minutes is no more than 0.14 mL/kg. This is well documented in previous publications by Young So Do.22

Figure 3. Lateral view of the angigram of the facial artery showed complete obliteration of AVMs and the outflow veins.

Figure 4. (A) Lateral view of the venous phase of the pre-embolization angiogram showed infiltrating-diffuse nidus in the buccal area (short arrow) of AVMs and outflow vein (long arrow). (B) Lateral view of angiogram of the facial artery showed complete obliteration of AVMs and the outflow veins.
Because of the comparatively low flow, ethanol embolization for type III AVMs has a lower incidence of cardiovascular collapse than for type I or type II. The main complication that should be considered when using ethanol to treat infiltrating-diffuse extracranial AVMs in the head and neck is local skin necrosis and ectopic embolism of a normal artery. Non-target embolization with ethanol will lead to tissue necrosis as capillary beds are entirely destroyed. Being a fluid agent, ethanol penetrates to the capillary level, devitalizing normal tissues. Skin blisters, superficial skin necrosis, and pyogenic granulomas were the most common complications in the present study, but these healed well with wound dressings and no scars were left. Only one case with AVMs in the chin had ethanol backflow to the distal part of the facial artery causing skin necrosis of buccal area and an obvious but acceptable scar.

Although ethanol is one of the strongest embolization agents known, it must be remembered that ethanol is also an extremely dangerous intravascular sclerosant that can cause total tissue devitalization and neuropathy. In the face and neck area it is important to be aware of all communications that exist between the internal and external carotid artery domains. The internal carotid artery, which supplies the supraorbital area, nasal dorsum, and forehead, communicates with the external carotid artery along the suborbital area and paranasal skin. These communications are of clinical importance, as they may open and lead to non-target embolization of the ophthalmic artery, with possible visual dysfunction or blindness. The backflow of ethanol from the occipital artery to the spinal artery should be monitored when treating AVMs in the occipital scalp region.

CONCLUSION

Ethanol is one of the strongest embolization agents and can cause severe complications if not properly used. The present study demonstrated that the sole use of ethanol for embolization is efficacious and safe in the management of infiltrating-diffuse extracranial AVMs in the head and neck. Through transarterial embolization or direct puncture embolization, the nidus within the AVMs can be reached and completely obliterated in one or more sessions by the controlled delivery of absolute ethanol.

CONFLICT OF INTEREST
None.

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