Endovascular treatments for venous malformations (VMs) and arteriovenous malformations (AVMs)

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Introduction

Vascular malformations are developmental errors of vascular morphogenesis, and can be divided into subtypes based on the dominant vascular component and flow characteristics. Low-flow vascular malformations include capillary (CM), lymphatic (LM), and venous (VM) malformations, and high-flow malformations include arteriovenous malformations (AVM) or arteriovenous fistula (AVF). Combined variants of these malformations are occasionally associated with the bone and soft tissue abnormality of the affected limbs like often seen in Klippel-Trenaunay syndrome (KTS) and Parkes Weber syndrome (PWS). In this lecture, endovascular treatments of VMs and AVMs are mainly reviewed, as these lesions are most often treated by interventional radiologists.

Pretreatment Evaluation

VMs and AVMs can occur in any part of the body, and generally progress or enlarge proportionally to age. Puberty, trauma, pregnancy, and surgical procedures are known risk factor for aggravation. In most cases, the diagnosis of VMs and AVMs can be made by careful medical interview and physical examinations. At outpatient clinic, ultrasound examination is helpful to assess the morphology and flow characteristics. MRI is essential for further evaluation of the lesion extent and the deep tissue involvement. Worsening in symptoms, functions, and cosmetics are considered for treatment, but it is important to weigh the balance between the risk of procedure-related complications and symptom severity in each patient. Both VMs and AVMs are often difficult to "cure", and require multiple treatment sessions to control the symptoms.

Sclerotherapy of VMs

VMs consist of dysmorphic ectatic veins, and the morphology is variable from a focal cavernous mass to a diffuse or extensive form. Sclerotherapy aims to expose sclerosing agents to the malformed veins to induce endothelial damage and subsequent thrombosis and fibrosis[1)]. The lesion is accessed with direct needle puncture under ultrasound guidance. Then, angiography is taken by contrast injection to confirm the needle tip within the venous cavity, and estimate the dose of sclerosing agent to fill the cavity before entering the drainage vein. Isolated VMs without visualization of drainage vein will respond well to sclerotherapy, whereas diffuse VMs with early venous drainage are more difficult to treat, because the sclerosing agent easily escapes into

the circulation[2]. Blood flow control with manual compression or tourniquet may reduce the escape of sclerosing agent and help the contact with the lesion vessel wall.

Various sclerosing agents are used to treat VMs. Ethanol is the most aggressive agent that causes instant endothelial cell damage and rapid thrombosis. However, ethanol carries the risk of serious complications such as tissue necrosis, nerve injury, and systemic side effects including CNS depression, hypoglycemia, hemolysis, and cardiopulmonary collapse[3]. Ethanol sclerotherapy usually requires general anesthesia, because careful monitoring is necessary and ethanol injection is very painful. Detergent sclerosing agents such as sodium tetradecyl sulfate, polidocanol, and ethanolamine oleate are another common agents for VMs. Like ethanol, these agents induce endothelial damage, but the effect is milder, and they can be used under local anesthesia. Foam sclerotherapy has become popular by mixing these detergents with air or carbon oxide. Theoretical advantage of foam sclerotherapy is that the foam may displace the blood, prolong contact with the endothelium, give bight echogenicity for ultrasound monitoring, and reduce the net amount of drug. As an example of creating foam, we usually mix 2 mL of 3% polidocanol with 8 mL of air through a three-way stopcock (so-called the Tessari method). Recently, there has been increased interest to apply bleomycin to treat VMs, because of fewer side effects than other agents despite the concern of pulmonary fibrosis. In malignancy treatment, the recommended lifetime dose is <400 mg or <5 mg/kg to reduce risk of pulmonary fibrosis. Bleomycin foam has been proposed to allow treatment of larger lesions while reducing the total dose of bleomycin[4]. The recent meta-analysis did not provide evidence that pulmonary fibrosis occurred after intralesional bleomycin injection[5]. However, there is a case report of transient acute pulmonary toxicity in an 8 month-old girl (body weight 5.5kg) with the upper extremity LM treated by intralesional injection of 7 mg (1.2 mg/kg) of bleomycin[6].

Embolization of AVMs

AVMs form the "nidus" consisting of the abnormal fistulous connections between arteries and veins. The goal of embolization is symptom improvement by reducing the shunt flow. It is essential to occlude the nidus, although it is technically challenging with the risk of normal tissue ischemia and systemic escape of embolic agents through the shunt. Therefore, it is important to analyze the angioarchitecture of the nidus to apply a suitable approach and embolic agents. Cho's classification[7] has been widely applied to assess the nidus of peripheral AVMs: type 1, direct fistulae between large arteries and veins; type 2, fistula between multiple arteries and the dominant outflow veins (DOV); and type 3a and 3b, non-dilated and dilated fistula between multiple arteries and multiple veins, respectively.

Various embolic agents are used to treat AVMs and should be chosen based on vascular anatomy and flow condition. Liquid agents such as n-butyl cyanoacrylate

(NBCA) glue and ethanol are often used as primary agents to occlude the nidus. NBCA is difficult to adjust the occlusion level precisely. The foreign body remnant of NBCA limits its use in the superficial lesions, and catheter occlusion or gluing is also problematic. Onyx is increasingly used in Western countries despite off-label, which allows more controlled delivery into the nidus without risk of catheter occlusion or gluing. Ethanol induces acute thrombosis with endothelial damage, but it requires extreme caution to avoid tissue necrosis and nerve injury. The maximum total dose of 0.5-1mL/kg per session and <0.1mL/kg per bolus with 5-10 minutes interval are advocated by experts to minimize the risk of systemic toxicity[8]. Coils can be used to occupy a large venous cavity, but should not be used to occlude the proximal feeding artery, because it will recruit new collaterals to the nidus. Particles or microspheres are seldom used, because they may pass through the shunt, but sometimes helpful to reduce the small shunts. Blood flow control (compression, tourniquet, and balloon) may help the action of embolic agents, however, there is a risk of reflux of embolic agents into arteries by complete blood flow cessation. In addition, release of blood flow control after long stasis can cause rapid escape of sludge that may affect cardiopulmonary function. Recently, direct puncture or transvenous retrograde approach has become a more preferred access to occlude the DOV in the type-2 AVM with favorable outcomes[9]. In contrast, type-3 AVMs with diffuse fistulae is generally difficult to access and occlude. We often apply direct puncture if the nidus is accessible by needle.

Post-procedural Care

Acute inflammatory swelling usually occur for several days after the procedure, but usually manageable by local cooling, steroids or non-steroid anti-inflammatory drugs. Prophylactic antibiotic is used, when local infection is concerned. Hemoglobinuria due to hemolysis is expected after large amount of sclerosing agent is used. Gross hemoglobinuria is managed by intensive hydration and urine alkalization with sodium bicarbonate.

Complications

Local complications include skin necrosis, nerve injury, infection and muscle contracture. Thromboembolic events such as deep venous thrombosis and pulmonary embolism and worsening of coagulopathy and bleeding may occur in patients with large VMs or AVMs. Drug-induced events include systemic drug toxicity, renal damage by hemoglobinuria, and cardiopulmonary collapse. These complications can be prevented by careful assessment of vascular anatomy and flow dynamics as well as separate sessions with limited dose of sclerosing agents.

Summary

Endovascular treatment for VMs and AVMs are always challenging with risks of severe adverse events. As these lesions are a kind of rare disease, no standardized practice has been established regarding techniques and choice of agents. Therefore, patients should be managed by the dedicated multidisciplinary team to apply appropriate therapeutic options on the case-by-case basis.

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