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International Journal of Cranio-Maxillofacial Surgery & Rehabilitation

Review Article

Medical Management of Vascular Lesions of the Head and Neck: Review of Literature

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How to cite: *Christopher P, Medical Management of Vascular Lesions of the Head and Neck – Review. Int J Cranio Maxillofac Surg Rehab Volume 2022, Article ID 22054381, 7 pages.*

Received:02/02/22 *Accepted:18/02/22* *Web Published:02/03/22*

Abstract

Head and neck vascular abnormalities are a diverse set of lesions that pose a challenge to head and neck surgeons. Hemangiomas and vascular malformations remain perplexing in terms of understanding the differences between their two unique forms and their therapy. The goal of this article is to provide a review of vascular malformations with respect to their subtypes and characteristic features. This review also aims to provide a clear understanding of the available treatment options with the proposed treatment algorithm and an elaboration on medical management for vascular lesions in an evidence-based manner.

Keywords: *Bleomycin, Hemangioma, Vascular Malformation, Intralesional Steroid, Vascular Lesions*

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INTRODUCTION

The vascular lesion signifies 2 entities of anomalies: hemangioma and vascular malformations. The credit goes to Wardrop (1818) for recognizing that these two entities, though mimicking each other, in fact, were two different pathologies [1]. Interestingly, the first public demonstration of ether anesthesia by Mortan was for the surgical removal of a venous malformation. Though Karl Virchow was the first to classify vascular anomalies in 1863 based on microarchitecture into angioma simplex, cavernosum, and racemosum, it has little clinical and surgical significance. The classification proposed by C.S. Nair in 2011 which is based on anatomy and provides useful information for surgical management [2].

Type I- cutaneous or mucosal
Type II- subcutaneous or submucosal
Type III- glandular
Type IV- intraosseous
Type V- deep visceral

It was ISSA that classified vascular lesions into vascular malformation and vascular tumor (consisting of hemangiomas) in 2014 [3]. Hemangiomas and vascular malformation present strikingly different clinical features and have inherently different behavior. The salient features are as follows:

Hemangioma	**Vascular malformation**
Present at birth and diagnosed by one year of age	Present at birth but not diagnosed until the second decade
Rapid growth until 6 to 8 months, involutes by 5 to 9 years.	Slow-growing, no involution, increases during trauma or infection
Osseous involvement rare	Osseous Involvement 35%
Low flow	Maybe the low or high flow
Usually, treatment is not required	Usually requires treatment
Neoplastic – increased endothelial cell turnover	Growth due to change in flow dynamics to the lesion and collateral blood supply

MANAGEMENT OF VASCULAR LESIONS

Due to their inherent difference in behavior and presenting features, the treatment for hemangiomas and vascular malformation is also different. C. S. Nair's Algorithm for management of vascular lesions proposed in 2018 is simple and coherent with his classification proposed in 2011 (Figure 1) [4].

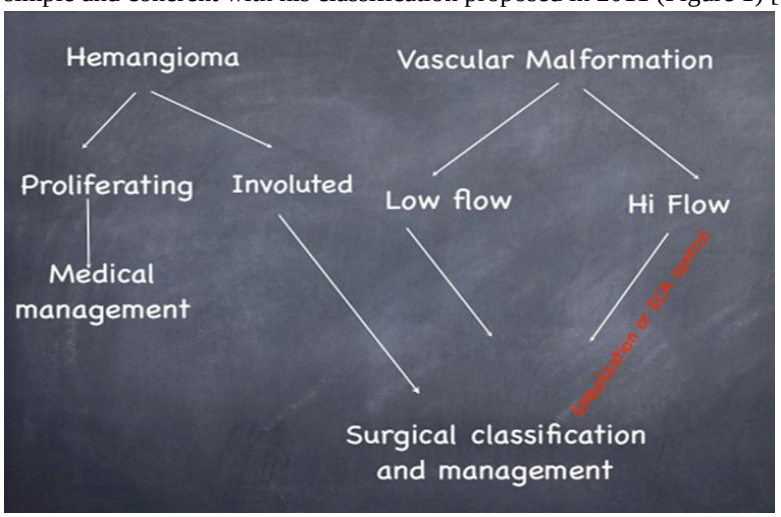

Figure 1: C. S. Nair's Algorithm for management of vascular lesions (2018)

The surgical and medical management options for hemangiomas are as follows [5]:

Medical
-Beta-blockers
-Steroids
-Vincristine
- Interferon alpha
-Sclerosants

Non-medical
-LASER

Surgical
-Excision of residual a lesion in involuntary face

MEDICAL MANAGEMENT

Medical management is usually the first choice of treatment for low-flow lesions as they are less morbid and in most cases, it is sufficient in reducing or eliminating the lesions. Over the last few decades, several pieces of evidence were published regarding the effectiveness of medical management for vascular lesions. A literature search has surfaced six systematic reviews published over the last 12 years in this area of interest. The medical management options available in the literature are sequenced as follows:

Intralesional Alcohol

It destroys endothelial cells. Ethanol is the most popular sclerosing agent due to its ready availability, low cost, and ease of use. But the procedure is quite painful and may require general anesthesia. Absolute ethanol (95 to 98%) works on the principle of destroying endothelial cells thereby preventing recurrence (Berenguer et al,1999). Prasetyono et al (2009) evaluated the effectiveness of intralesional alcohol injection in vascular malformation and categorized complete resolution as excellent results decrease in size or symptoms as a good result and little or no improvement as a poor result from a total of 30 prospective and retrospective studies which were included, only 14 studies comprising 332 patients had evaluated the clinical result post-treatment [6]. The authors concluded that 10.2% of cases resulted in poor results, 22.3% of cases resulted in excellent results, and 67.5% of cases resulted in good results. The most common complication faced with the use of intralesional alcohol is necrosis of a chastened tissue secondary to extra-lesional extravasation. Prasetyono et al (2009) identified skin damage (21.1%) and tissue fibrosis (1.9%) as the most commonly recorded complications. Intralesional alcohol injection as a solitary treatment was assessed by Prasetyono et al (2009) where excellent results were obtained in 89% of cases (a total of 28 patients). Horbach et al (2015) reviewed 36 prospective and retrospective studies to evaluate the effectiveness and safety of the most frequently used sclerotic agents for vascular malformation. Of the 36 studies, only six studies (with a total of 327 patients) evaluated the effectiveness of absolute ethanol as monotherapy. Of the six studies, only two were prospective in nature. The authors found that overall response varied from 84% to a hundred percent but the complication rates were a whopping 22 to 68% which predominantly included nerve injury and local skin complications [7].
Standardization of intralesional alcohol: There is a lack of standardization with respect to those, volume, and number of cycles. The maximum recommended dose is one ML per KG, the lack of information provided in the included studies regarding protocols followed may make interpretation of complication rate and success rate difficult and unreliable. This is evident in the review by Horbach et al (2015) and Prasetyono et al (2009). While the latter considers intralesional alcohol as reasonably safe, the former warns us to use it with caution due to the higher complication rate. The lack of standardization of included studies may serve as a major factor influencing the authors' contradicting results [6,7].

Intralesional Steroid

Steroids used for vascular malformation were an incidental finding in 1963. Theoretically, the local introduction of high-dose steroids decreases systemic absorption and hence is a safe option. Prasetyono et al (2011) evaluated the effectiveness of intralesional steroids in reducing head and neck hemangiomas. The most commonly used steroids were in the following order – only triamcinolone (83.1%, 10 to 50 MG per ML) and triamcinolone combinations (8.4%). The combinations were usually with betamethasone (6MG per ML). The dosage, volume, number of sites, intra or perilesional injection, gauge of needle used, and number of sessions varied among the 22 including prospective, retrospective, and case series studies. The authors identified excellent results in 71% of cases and good results in 23.4% of cases. Of the 22 studies only five studies evaluated the solitary use of intralesional steroids (with a total of 238 patients) showing excellent results in 22.9% cases, good results in 62.1% cases and would result in 7.9% cases. Surgical debulking was done on patients in whom the lesion failed to involute (2.8%). 96.8% of patients underwent surgery for cosmetic purposes to eliminate residue will defects or scars. In their study, the authors noted the overall complication rate to be 5.9%. No cases of retinal artery occlusion (dreaded complication) were noted in their systematic review [8]. The authors think that an intralesional steroid is a good option in treating head and neck hemangiomas at proliferative face with relatively low complications.

Bleomycin

Bleomycin is cytotoxic and induces sclerosis or fibrosis. Cytotoxic agents like bleomycin are used to treat vascular and lymphatic lesions in recent times due to their ability to induce sclerosis or fibrosis and their cytotoxic properties [9]. Horbach et al (2016) systematically reviewed the available literature to investigate the effectiveness of intralesional injection of bleomycin for vascular malformation. Only articles published after 1995 with follow-up of at least six months were included in their review. Studies including bleomycin as part of combination therapy were excluded, thereby eliminating a confounding factor. But the authors noted the dosage, the number of sessions required and several injections per session varied among the included 27 studies overall, with at least 50% of lesions reduced in size among the included studies. But the assessment of size reduction was highly diverse among studies ranging from clinical assessment or radiograph to Doppler imaging or CT. However, a meta-analysis performed for four of the 27 included studies revealed no statistically significant difference between bleomycin and ethanol or sodium morrhuate injection for venous malformation. Among 1406 patients Treated with bleomycin only 14% reported complications ranging from flu (5%) and wound infection (1%) to hyperpigmentation (0.8%). Pulmonary fibrosis and acute pulmonary toxicity were not reported in any of the included studies [10]. The authors state that the use of intralesional injection of bleomycin is comparable in effectiveness to other sclerosis but superior in safety compared to sclerosants like ethanol. But effectiveness with respect to size reduction alone may not always correspond to the relief of symptoms. Horbach et al evaluated the effectiveness of various sclerosis in 2015 in an attempt to identify the optimal agent. Though they failed to identify such an optimal agent, they identified the overall response rate of bleomycin to be more than 95%. With complete responses between 46% and 100% and a remarkably low level of adverse events (less than 2%) [10].

DISCUSSION

Though a good number of systematic reviews are available for medical management of vascular malformation, most of them have included level four evidence making them quality studies. Interestingly, only one RCT was included among all the systematic reviews each containing at least 20 studies. And there is no standardization of dosage, site of injection, number of sites, number of sessions, and technique of injection for any of the available drugs. In addition, almost all of them suffered from four search strategies as none of the authors had conducted a manual search for articles. Prasetyono et al (2009 &2011) restricted their search to the English language only with publication restricted the absence of independent search. Quality assessment, risk of bias, publication bias, heterogeneity of included studies, characteristics of the included study, and PRISMA flowchart were also not given in their studies (both in 2009 and 2011). This makes both the systematic reviews by Prasetyono et al poor quality and unreliable evidence [6,8]. Horbach et al (2015) Was the only author who performed a meta-analysis and assessed the risk of bias, quality of included studies, and heterogenicity and followed Prisma guidelines. Hence, only this study is relatively reliable. With the available evidence, it can be concluded that absolute ethanol, though having a good cure rate, has less safety profile. The effectiveness (concerning cure rate) of bleomycin is comparable to other potent sclerosants like ethanol with the added benefit of a superior safety index when compared to ethanol. Also, bleomycin was the only sclerosant that was most often used solitarily compared to other sclerosants in the study by Horbach et al (2016) [7,10]. The confounding factors and possibility of bias are lesser for studies evaluating the effectiveness of bleomycin compared to other sclerosants making the results obtained from these studies more reliable.

CONCLUSION

Based on the evidence, bleomycin can be safely and effectively used to treat vascular malformations of the head and neck as part of medical management. Future research should concentrate on designing studies with sound methodology with proper standardization of drug dosage and administration protocol that will help us to arrive at a more concrete and reliable consensus.

Financial support and sponsorship - Nil

Conflicts of interest - There are no conflicts of interest

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