

Management of Venous Malformation using Injection of Bleomycin Intralesional: Cases Report

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Abstract: Introduction: Vascular anomalies are among the most common form of congenital and neonatal dysmorphogenesis, which can occur in various areas throughout the body with 60% located in the head and neck. Percutaneous sclerotherapy developed as a minimally invasive treatment modality for this lesion. Bleomycin is known to have a sclerosing effect on endothelial cells, so it can be used to treat vascular malformations. Objective: This case report aims to analyze the management of venous malformation therapy in the oromaxillofacial region using intralesional Bleomycin injection. Case Report: A 39-year-old female patient diagnosed with simple venous malformations which carried out bleomycin injection at RSUP Dr. Hasan Sadikin Bandung. After three sessions of injection, the lesion was significantly reduced from volume and size by more than 51% but still could look at different colours (score 3). The patient was satisfied with the results of the treatment, and the lesion was known to show no symptoms of recurrence after control three months postoperatively in the third session. Discussion: The results from the treatment in this case report are similar to the treatment results from several case reports that use Bleomycin as a sclerotherapy agent to treat vascular malformations. The high success and minimal risk of treatment with Bleomycin make it the first choice sclerotherapy agent. Conclusion: Treatment of this case shows that Bleomycin Intralesional Injection of venous malformations is an effective non-invasive treatment and has no side effects. Bleomycin sclerosant can be an effective and safe way for nonsurgical treatment options for head and neck vein malformations. Bleomycin is also considered safe with minimal risk in the treatment of venous malformations.

Keywords: Venous malformations, Bleomycin, Intralesion injection

1. Introduction

Vascular anomalies are among the most common form of congenital and neonatal dysmorphogenesis, which can occur in various areas throughout the body with 60% located in the head and neck.¹ That lesions are a challenging, complex group of the injury for oral and maxillofacial clinicians. Those lesions described as a board spectrum of pathologies in vascular structures, ranging from simple capillary irregularities to complex abnormalities involving arteries, veins and lymphatics. These lesions also have different clinical characteristics, natural evolution, and therapeutic approaches.¹⁻³ Vascular anomalies frequently misdiagnose as Hemangioma. Still, Hemangioma lesion is one of the vascular anomalies but, not all of the vascular anomalies have tumour characteristics like Hemangioma.^{4,5}

The complexity in diagnosing and managing of the vascular anomalies has been mainly due to its varied spectrum of presentation. Several classifications have been developed to describe vascular anomalies and to facilitate the selection of treatment plans by clinicians.^{2,4} Those classifications form based on the gross appearance, histological appearance, treatment, and even flow rates.^{2,4,5} The most commonly used classification in use today comes from the International Society for the Study of Vascular Anomalies (ISSVA), which has been reviewed and modified several times since first conduct in 1988 (revised in 1992, 2014 and 2018).^{2,4,6} The last version of the ISSVA classification can be seen in Table 1 and also can be found online (<http://www.issva.org/classification>) as an interactive format.⁶

There are many treatment options for vascular anomalies, including laser therapy, sclerotherapy, embolization,

electrochemical therapy, copper needle treatment, surgical resection, and a combination of these options.^{1,7} The choice of treatment modality depends on the type, location, and size of the lesion, patient status, and available techniques. Percutaneous sclerotherapy developed as a minimally invasive treatment modality for this lesion. It is usually safe and effective for small and medium malformations. It has also shown to be helpful as an additional preoperative treatment of large lesions to reduce blood loss due to surgery. Agents such as Bleomycin, Ethibloc, and OK-432 have now been used for percutaneous sclerotherapy.^{1,2,7}

Table 1: International Society for the Study of Vascular Anomalies (ISSVA) Classification (revised 2018)⁶

Vascular Anomalies				
Vascular tumours	Vascular Malformations			
	Simple	Combined	Major named Vessels	Associated with other anomalies
Benign	Capillary malformations	CVM, CLM	Depending on the structure affected	Associated with other syndrome or anomalies condition
Locally aggressive or borderline	Lymphatic malformations	LVM, CLVM		
Malignant	Venous malformations	CAVM*	Depending on the Anomalies	
	Arteriovenous malformations	CLAVM*		
	Arteriovenous fistula	others		

This case report discussed regarding cases of simple venous malformations which carried out bleomycin injection at RSUP Dr. Hasan Sadikin Bandung in 2019.

2. Case Report

A 39-year-old female patient came with a lump in the left cheek since four years ago. The lump was initially only a point and then enlarged slowly since one year ago. The patient has never taken medication or gone to the doctor to check his condition. History of systemic diseases and family ailments is denied.



Figure 1: (A) Preoperative profile, (B) Intraoral photos of the lesions, bluish-purple lump measuring 5x1x0.5 cm in the left buccal region.

On clinical examination, there is a bluish-purple lump measuring 5x1x0.5 cm in the left buccal region with a soft consistency and negative tenderness (Figure 1.B). The patient was diagnosed with venous malformations in the left buccal area.

After giving informed consent to the patient and family, treatment using Bleomycin injection was decided as the first treatment option. Bleomycin injection was carried out in three sessions at three-month intervals per session.



Figure 2: (A) Intraoperative images of first Bleomycin Injection. (B) Post-operation images of the first Bleomycin Injection operation

Bleomycin injection is performed under general anaesthesia. The dose of Bleomycin used is 15 mg per session (Figure 4A and B). Patients were prescribed ibuprofen analgesics 400 mg / 8 hours after surgery and recommended a soft diet. Control and evaluation of treatment results were carried out one week postoperatively.

The results of treatment are evaluated using photos taken before surgery and after surgery. After the first session of Bleomycin injection surgery, the lesion has not changed much (Figure 2B). Changes can only be seen in the photo after the second session injection surgery, where the lesions look smaller and fade (Figure B).



Figure 4: (A) Intraoperative images of second Bleomycin Injection. (B) Post-operation images of the second Bleomycin Injection operation



Figure 2: Intra operative photos of the second Bleomycin Injection

The results of the new treatment series can be assessed after the third injection operation. The results were scored according to a 4-point scale modified after Achauer et al. based on improvement in volume, colour, and texture after treatment (Table 2).¹ It was seen that the lesion was significantly reduced from volume and size by more than 51% but still could look at different colours (score 3). The patient was satisfied with the results of the treatment, and the lesion was known to show no symptoms of recurrence after control three months postoperatively in the third session.



Figure 5: (A) Intraoperative images of third Bleomycin Injection. (B) Post-operation images of the third Bleomycin Injection operation

Table 2: Result score of the treatment based on improvement in volume, colour, and texture after treatment.¹

Score	Result of the Treatment
1	No response, that is, no change in the size or continued to enlarge
2	Mild improvement, that is, the lesions decreased in size, but less than 50% with an increase in appearance.
3	Marked improvement, that is, the lesions decreased in size more than 51%, but less than 100% with remarkable improvement in appearance.
4	Cured, that is, the lesions disappeared completely without recurrence at least six months after treatment.

3. Discussion

According to ISSVA classification, simple vascular malformations divided into five different sub-classification depends on the type of affected vascular; capillary malformations, lymphatic malformations, venous malformations, arteriovenous malformations, and arteriovenous fistula (Figure 1).⁶ Venous malformations are the most common type of vascular malformation with an incidence of 1 to 2 in 10,000 with the prevalence of 1%.⁸

Venous malformations are the lesions that arise due to venous dysmorphogenesis and exhibit normal endothelial turnover.⁹ Venous malformations feature shows a stagnant appearance of blood flow, which can spontaneously cause thrombosis, and clinically presents with symptoms of pain and swelling, discolouration of the skin, and excessive tissue growth. However, the exact symptomatic clinical presentation tends to depend on location.⁸

The patient that was reported in this case was diagnosed with a venous malformation in the left buccal region. The diagnosis is made based on the results of the history taking and clinical examination. The patient complained of a lump that felt enlarged slowly since four years ago. The patient has never taken medication or gone to the doctor to check her condition. On clinical examination, it was found a bluish-purple lesion measuring 5x1x0.5 cm with soft consistency on palpation. From these signs and symptoms, it can be ascertained that the patient was diagnosed with venous malformations and not hemangiomas.^{2,8} The difference in signs and symptoms between the two diseases can be seen in Table 3.

Table 3: Difference between Hemangiomas and Vascular Malformations²

Hemangioma	Vascular malformation
Present at birth, most diagnosed by 1 year old	Present at birth but often not diagnosed until second decade
Rapid growth until age 6–8 months, then slows and involutes by 5–9 years	Slow growth throughout life with an increase in response to infection, trauma or hormonal fluctuation; does not involute
Neoplastic growth with increased endothelial cell turnover	Growth due to flow dynamics through the lesion and recruitment of collateral supply
Osseous involvement rare	Osseous involvement 35%
Female-to-male ratio 5:1	Female-to-male ratio 2:1
Usually, low flow Frequently does not need treatment	May be low flow (capillary, venous, lymphatic) or high flow (arterial or arteriovenous) Often requires treatment

Before starting treatment, it is essential to review the pathophysiology of the lesion, aetiology, and consequences of the procedure. There may be instances when it is wise to postpone an intervention for the sake of observation or to avoid interference if there are no significant symptoms and risks.⁸ The selection of the treatment modalities depends on the type, location, and size of the lesions, the patients' status, and techniques available.^{2,5,8} Sclerotherapy is a sclerosing agent directly through the skin that is used for vascular malformations, especially for venous and lymphatic abnormalities in the head and neck region.⁸⁻

¹¹ Various sclerotherapy agents are used for venous malformations. Agents commonly used as first-line therapy with satisfying results are Bleomycin, acetic acid, OK-432, and Doxycycline.^{10,12,13}

Bleomycin is a cytotoxic glycoprotein antibiotic isolated from strains of *Streptomyces verticillus*, which was discovered by Umezawa as an antitumor agent in 1966.¹² Bleomycin is known to have a sclerosing effect on endothelial cells, so it can be used to treat vascular malformations and hemangiomas.^{1,9,10,12,13} Bleomycin acts by inhibiting DNA synthesis.¹² One of the benefits of treatment using Bleomycin is the results of treatments that do not leave scar tissue with a high success rate, besides the risk of minimal toxicity when the treatment dose <1 mg/kg per session and is used for no more than one interval for three weeks.¹ The dosage of Bleomycin depends on the patient's body weight and the size of the lesion. The amount injected should not widen the lesion and trigger inflammation. The total dose of injection should not be more than 10 mg per complete injection because there can be a risk of pulmonary interstitial fibrosis.^{9,10,14}

Bleomycin is used as a sclerotherapy agent in patients in this case with consideration of its effectiveness in treating venous malformation lesions and cosmetic concerns where the results of treatment tend not to leave scars. The Bleomycin dose used in this case is 15 mg per session. This dose is similar to the dose used in 75 patients diagnosed with venous malformations and hemangiomas in the Hassan et al. case report in 2013.¹

In this case report, Bleomycin injection was carried out in three sessions, with three-month intervals between sessions. Advances in treatment were seen at the end of the second and third sessions, where the lesions appeared smaller and faded. The results were scored according to a 4-point scale that was modified after Achauer et al.¹ based on increasing volume, colour, and texture after treatment. In the patients in this case report, the results of the treatment of three Bleomycin injection sessions were a scale of 4 (Marked improvement, that is, the lesions decreased in size more than 51%, but less than 100% with remarkable improvement in appearance). The patient was satisfied with the results of the treatment, and the lesion did not recur after control three months after the injection of the third session.

The results from the treatment in this case report are similar to the treatment results from several case reports that use Bleomycin as a sclerotherapy agent to treat vascular malformations.^{1,10,13} The high success and minimal risk of treatment with Bleomycin make it the first choice sclerotherapy agent.

4. Conclusion

Treatment of this case shows that Bleomycin Intralio Injection of venous malformations is an effective non-invasive treatment and has no side effects. Bleomycin sclerosant can be an effective and safe way for nonsurgical treatment options for head and neck vein malformations. Bleomycin is also considered safe with minimal risk in the treatment of venous malformations.

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