BRIEF COMMUNICATION

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Late side effects of bleomycin injection into the lower lip mucosa of a nine-year-old patient with venous malformation

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Abstract (J Korean Assoc Oral Maxillofac Surg 2023;49:304-307)

Venous malformation (VM) is a benign lesion of blood vessels caused by an error in vascular morphogenesis during the embryologic phase. This entity mostly affects the head and neck region, including the lips, tongue, buccal mucosa, gingiva, or palate. VM may cause functional and aesthetic impairments. The anatomical structure and shape of the lips provide an important aesthetic accent for an individual. Therefore, management of VM in the lip area without postoperative defects or scarring is challenging. In this brief communication article, we present a conservative approach to lip VM in a nine-year-old boy using a bleomycin injection that had good aesthetic and functional outcomes. Injection of 2 mL of 1/10 of 15 mg bleomycin in a saline dilution into the lip mucosa may present a drug reaction as a white plaque and reddish owl eye lesion that takes up to three weeks to resolve without a scar. It is important to recognize the characteristics and self-limiting nature of postoperative bleomycin complications to avoid unnecessary treatment.

Key words: Arteriovenous malformation, Bleomycin, Drug side effects, Pediatrics, Sclerotherapy

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I. Introduction

Venous malformation (VM) is a benign lesion of blood vessels caused by an error in vascular morphogenesis during the embryologic phase. This entity mostly affects the head and neck region, including the lips, tongue, buccal mucosa, gingiva, or palate. Most VMs are venous and demonstrate slow flow[1,2]. VM may be present at birth but not show signs or symptoms, and a lesion may be triggered by infection, pregnancy hormones, or trauma. The presentation typically is a soft, poorly defined swelling that readily blanches with compression[1,3].

VM may cause functional and aesthetic impairment. The anatomical structure and shape of the lips provide an important aesthetic accent for an individual. Therefore, management of VM in the lip area without postoperative defects or scarring is challenging. In this brief communication article, we present a conservative approach to lip VM in a nine-year-old patient using bleomycin injections that produced good aesthetic and functional outcomes. We also describe the characteristics and management of postoperative complications of bleomycin injection into the lip mucosa.

II. Brief Communication

A nine-year-old patient presented to the Oral and Maxillofacial Surgery Department of Seoul National University Dental Hospital with a lump on his lower lip. Based on the history provided by his parents, the lump had appeared when the patient's lip hit the corner of a desk when he was three years old. Previously, the patient had been diagnosed with mucocele and had undergone mucocele removal twice in another department.

The patient was prescribed vitamin B once per day for four weeks, and massage of the lower lip was emphasized. At the one-month follow-up, the size of the lesion had decreased, so a six-month follow-up appointment was set. After six months, the size of the lesion had increased, and mass excision with biopsy was planned. Under local anesthesia, aspiration was

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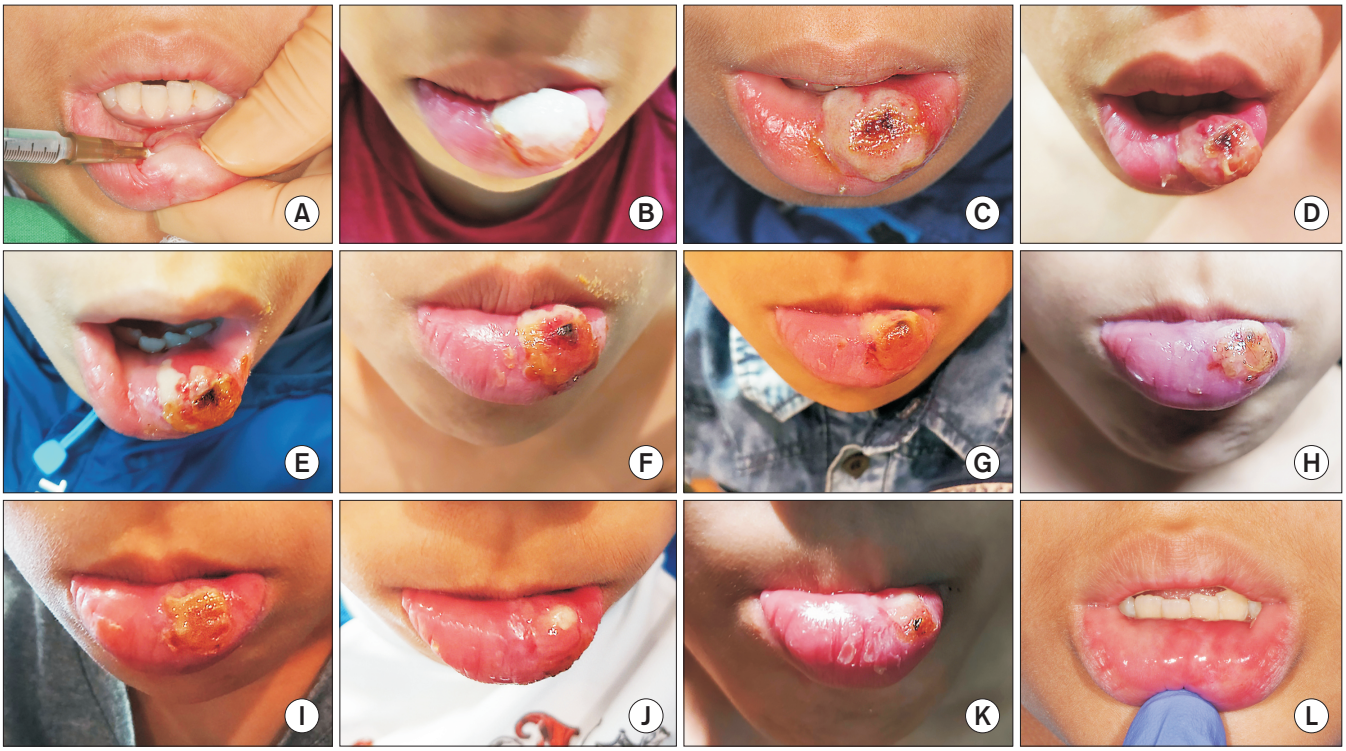

Fig. 1. Post-injection/operative day (PID) clinical appearance. Immediate PID appearance (A). A well-demarcated, smooth white plaque was observed on PID 3 (B). A reddish owl eye lesion was noticed on PID 6 and was characterized by indurated swelling with a red scab surrounded by a whitish plaque (C, D). On PID 7 (E), PID 8 (F), and PID 9 (G), the swelling was reduced. At PID 10, the reddish owl eye lesion had resolved (H). Uneventful healing took place on PID 11 (I), PID 12 (J), and PID 13 (K), and the scab was gradually replaced by re-generated mucosa. The lip was fully healed after three weeks (L).
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performed, and 0.6 mL of blood was withdrawn. The mass was excised and sent for biopsy, which revealed fibrous scar tissue with VM. Sclerotherapy using bleomycin (Bleocin; DongA ST Co.) injections was performed two months later using a minimum dosage of 15 mg bleomycin at a ratio of 1/10 diluted with normal saline into two 1-mL syringes. Prior to the injections, a topical anesthetic was applied to the lower lip, and the two injections were administered on the lingual side of the lesion. Following the injections, digital pressure was applied to the injection site for about 5 minutes, and the patient was asked to wait for 30 minutes for observation of any postoperative complications, such as fever or a hypersensitivity reaction. No postoperative complications were observed on the day of the injections, and the patient was discharged uneventfully.

On post injection day (PID) 3, the patient woke up with a well-demarcated, smooth white plaque at the injection site that had burst by the next morning. The parents were asked to take pictures of the lesion every day to monitor wound healing and were informed of possible complications and adverse effects of the injection. On PID 6, a reddish owl eye lesion characterized by indurated swelling with a red scab surrounded by whitish plaque was observed. Wound dressing using a chlorhexidine ball was performed, and the patient was prescribed Augmentin 375 mg and a half tablet of Ibuprofen three times per day for five days. The parents were guided on wound dressing using chlorhexidine balls twice per day at home. The swelling had decreased by PID 9, and the reddish owl eye lesion resolved by PID 10, followed by uneventful healing. At the three-week follow-up, the wound had fully healed without any swelling or blister, and the lip showed a normal appearance.(Fig. 1)

III. Discussion

Many options for VM treatment are available, including surgical procedures, embolization via interventional radiology, sclerosing therapy, cryotherapy, or laser therapy[3]. Sclerosing therapy is considered a simple and easy treatment[4]. Most of the time, sclerosing therapy is performed prior to surgical

excision[5]. However, in our case, we successfully managed the patient with surgical excision first for confirmation of disease through positive blood aspiration and biopsy as the lesion resembled a mucocele, which originated from the minor salivary gland. Sclerosing therapy was performed later after VM was confirmed by biopsy.

Sclerosing agents may damage the local vascular endothelium, leading to thrombosis, endothelial exfoliation, collagen fiber shrinkage, and blood vessel occlusion[6]. Bleomycin is a sclerosing agent known as an antineoplastic antibiotic. It is active against gram-positive and gram-negative bacteria and fungi. However, its precise mechanism on VM is not fully understood. The use of intralesional injections of bleomycin has been recommended, especially in moderate-sized, low-flow VM of the head and neck, with a high success rate and without systemic or pulmonary complications[3]. Several local side effects may occur, including erythema, a stretching sensation, blistering, ulceration, swelling, and pain. However, these complications are self-limiting and require no clinical intervention[2,3,5,6]. In cases where necrotic tissue appears following injection, debridement is required and can result in complete healing[2]. In our case, a well-demarcated, smooth white plaque was the earliest sign of a postoperative complication at the local site. Following bursting of the white plaque, a reddish owl eye lesion remained for approximately nine days. During this period, only supportive management for pain and wound hygiene maintenance were required due to its self-limiting characteristics. With careful maintenance, uneventful healing occurred, and the VM lesion completely resolved. The surface color of the lip mucosa returned to normal, and no pigmentation was observed on the lip skin three weeks after first injection. At one-year follow up, no sign of recurrence was observed.

In conclusion, bleomycin as a sclerotherapy agent is a safe option for conservatively managing lip VM, especially in children. The injection of 2 mL of 1/10 of 15 mg bleomycin in a saline dilution into the lip mucosa may present a drug reaction as a white plaque and reddish owl eye lesion that takes up to three weeks to resolve without a scar. It is important to recognize the characteristics and self-limiting nature of postoperative bleomycin complications to avoid unnecessary additional management strategies. Providing the patient or guardian with precautions on possible complications and ways of management will not only build the patient's trust in the clinician, but will also accelerate the patient's healing process.

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Authors' Contributions

All authors read and approved the final manuscript. K.R.M. and S.M.K. collected the data and wrote the manuscript. S.M.K. revised, designed, and wrote the manuscript.

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Ethics Approval and Consent to Participate

The study procedures received ethics approval from the Institutional Review Board of School of Dentistry, Seoul National University (S-D20220019) and were in accordance with the 1964 Helsinki Declaration and its later amendments (2013) or comparable ethical standards. Written informed consent was obtained from the patient's guardian.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

References

1. Couto DAF, Ito FA, Lima HG, Novais JD, Novais JB, Dallazen E, et al. Sclerotherapy for extensive vascular malformation in the tongue. J Craniofac Surg 2019;30:e796-9. https://doi.org/10.1097/scs.0000000000005788
2. Zeevi I, Chaushu G, Alterman M, Chaushu L. Sclerotherapy of vascular malformations in the oral cavity-minimizing postoperative morbidity. Medicina (Kaunas) 2020;56:254. https://doi.org/10.3390/medicina56050254
3. Bajpai H, Bajpai S. Comparative analysis of intralesional sclerotherapy with sodium tetradecyl sulfate versus bleomycin in the management of low flow craniofacial soft tissue vascular lesions. J Maxillofac Oral Surg 2012;11:13-20. https://doi.org/10.1007/s12663-011-0325-7
4. Min HG, Kim SG, Oh JS, You JS. Sclerotherapy using 1% sodium tetradecyl sulfate to treat a vascular malformation: a report of two cases. J Korean Assoc Oral Maxillofac Surg 2015;41:322-6. https://doi.org/10.5125/jkaoms.2015.41.6.322
5. Berenguer B, Burrows PE, Zurakowski D, Mulliken JB. Sclero-

therapy of craniofacial venous malformations: complications and results. Plast Reconstr Surg 1999;104:1-11; discussion 12-5.
6. Song D, Guo L, Sheng H, Li J, Wang L, Wu C, et al. DSA-guided percutaneous sclerotherapy for children with oropharyngeal low-flow venous malformation. Exp Ther Med 2020;19:3405-10. https://doi.org/10.3892/etm.2020.8581

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