Intralesional Bleomycin in Lymphangioma Circumspectum of Tongue

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Abstract

Lymphangioma circumscriptum is a congenital lymphatic malformation of superficial lymphatics. It may present at any age but is usually noted at birth or appears during childhood. The usual sites of presentation are head and neck; oral cavity is rarely involved. Very few cases of lymphangioma circumscriptum of the tongue are reported. The diagnosis is confirmed by histopathology. The usual treatment for such cases includes local excision or sclerotherapy. We present a case of symptomatic lymphangioma circumscriptum of the tongue in a 15-year-old boy who was treated by debulking of lesion, followed by intralesional injections of bleomycin.

Keywords: Intralesional bleomycin, lymphangioma circumscriptum, tongue

Introduction

Lymphatic malformations (LMs) are genetically determined structural anomalies of the lymphatic system with normal endothelial cell turnover. Lymphangioma was first described by Virchow in 1854 as a tumor of lymphatic origin. Mulliken and Glowacki in 1982 coined the currently used term, LM, in their classification of vascular anomalies. Extraoral lymphangiomas occur most commonly over the head-and-neck region. Intraoral lymphangiomas are rare. Surgical excision is the treatment of choice in most of the cases. Recurrence is reported in some cases, presumably because the lesion is interwoven between muscle fibers, preventing complete removal. We are describing a case of lymphangioma circumscriptum over the tongue treated by debulking of the lesion and intralesional bleomycin.

Case Report

A 15-year-old male presented to our department with the complaint of fluid-filled lesions over the middle of the tongue from 5 years of age which gradually progressed in size and number. There was a history of burning sensation over the lesion with off and on bleeding for the past 6 months. He also complained of coated tongue and foul breath. There was no history of slurred speech, macroglossia, associated with lesions. Family history of similar lesion was absent.

Systemic and general examination was within normal limits. Cervical lymphadenopathy was absent. On mucocutaneous examination, the tongue was indurated at the lesional site. Routine investigations, including hematology and biochemistry, were normal. Histopathology showed dilated submucosal papillae with markedly dilated lymphatic channels incompletely lined by a single layer of endothelium suggestive of lymphangioma circumscriptum. As the patient was symptomatic and in discomfort, so to hasten the response, we combined debulking of the lesion with intralesional bleomycin.

Reconstituted with 5 ml distilled water (making a solution of 3 mg/ml of bleomycin) and 1 ml of this solution were further diluted with 2 ml of 2% lignocaine to make 1 mg/ml solution.

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Using a 26G needle, multiple punctures were given. The endpoint of each injection was blanching of the site. A total of 2 ml of bleomycin solution was given. The patient is under follow-up after 2 doses of bleomycin without any side effect and more than 90% improvement [Figure 3].

**Discussion**

Vascular malformations (VMs) are progressively enlarging aberrant and ectatic vessels and may be capillary, venous, arterial, lymphatic, and combined malformations. Lymphangiomas are LM made up of variously dilated channels or cysts, lined by endothelial cells of lymphatic origin. Embryologically, they are thought to originate from the sequestration of lymphatic tissue during the development of lymphaticovenous sacs, which then fail to communicate with the remainder of the lymphatic or venous system. Later on, the sequestered lymphatic tissues dilate which results in lymphangiectasia and lymph stasis often beneath the skin. About 50% of the cases are present at birth without family history and 90% develop by 2 years of age.

LM may arise anywhere on the skin, subcutaneous tissue, or mucous membranes with predilection for the head and neck (50%–75%), proximal extremities, trunk, and buttocks. Within the oral cavity, the tongue appears to be the most common site of involvement.

Histologically, LM is classified into the macrocystic type (larger than 2 cm) and the microcystic type (smaller than 2 cm).

Lymphangioma circumscriptum is a microcystic LM that is localized to an area of the skin, subcutaneous tissue, and sometimes muscle. Superficial lesions in the oral cavity are papulovesicular lesions of normal mucosal or red-colored giving appearance of frog eggs or tapioca pudding. These lesions may lead to localized accumulation of food debris leading to halitosis, poor oral hygiene, increase salivation, secondary infection, and ulceration. The deeper lesions may not be visible but may manifest as deep-seated nodules or localized swelling. Mass effect of these lesions may lead to airway obstruction, difficulty in swallowing, macroglossia, and speech disturbances.

Treatment options include surgery and sclerotherapy. Spontaneous regression is very rare. Advancement in intralesional sclerotherapy has shown significant efficacy and reduced the need for other forms of therapy although lymphangiomas do not respond as well as to sclerosing agents as do hemangiomas. Various sclerosing agents such as picinabil (OK-432), bleomycin, doxycycline, acetic acid, alcohol, and hypertonic saline have been used for LM. Although the popularity of sclerotherapy is growing, there is no consensus regarding the type to be used.

Bleomycin was initially developed as an antitumor agent in 1966. Bleomycin has antibacterial, antineoplastic, antiviral, and antiangiogenic properties. Systemic bleomycin is the US Food and Drug Administration approved for chemotherapeutic agent. Bleomycin is used off-label in dermatology for various
indications such as recalcitrant warts, keloids, hypertrophic scars, hemangiomatas, VM, telangiectasias, cutaneous malignancies, condyloma acuminate, and cutaneous leishmaniasis.[7]

Bleomycin leads to breaks in the deoxyribose backbone of the DNA chain by generating active-free radical complexes. In addition, bleomycin has sclerosing effects on endothelial cells by inciting a mild inflammatory effect. It is used in a strength of 1 mg/ml along with local anesthetic like lignocaine.

Bleomycin is directly cytotoxic to keratinocytes and eccrine epithelium. Cysteine proteinase is an enzyme found in most tissues, except the skin, and lungs. It inactivates bleomycin through hydrolyzation. The cytotoxic effects of bleomycin are, therefore, magnified in the skin (and lungs) due to the absence of this enzyme, explaining some pulmonary and dermatologic side effects of the drug. Bleomycin is hydrophilic and does not easily cross cell membranes of vascular endothelium. Local anesthetics seemingly disrupt cell membrane structure, thus increasing bleomycin uptake and enhancing its cytotoxicity.[8] Significant dermatologic toxicities at the site of injection and oral cavity include local, pain, erythema, swelling, ulceration, hyperpigmentation, hypopigmentation fibrosis, and gangrene. At distant sites, rarely, especially in a vascular site like the oral mucosa, increased absorption of bleomycin may lead to systemic side effects such as scratch dermatitis (figurate/linear streaks induced by trauma/scratching), Raynaud’s phenomena neutrophilic eccrine hidradenitis anaphylaxis, urticaria, and very rarely pulmonary fibrosis.[8] These side effects are generally encountered during systemic therapy of bleomycin. Our patient did not develop any of the side effects except pain during injection of bleomycin.

**Conclusion**

LM, particularly intraoral, is rarely encountered. Intraoral LM can lead to various complications which can be life-threatening. Complications can also occur postoperatively or following sclerotherapy. Bleomycin injection (intralesional) is a safe and effective sclerosant for lymphangioma circumscriptum.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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