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Case Series

Bleomycin sclerotherapy in young adult females with neck lymphangioma – A case series

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Abstract

Bleomycin is a primary nonsurgical therapy option for head and neck lymphangiomas. The goal of this study is to evaluate its efficacy and look into any potential side effects. At this case series inquiry, three patients who were diagnosed with head and neck lymphangioma were seen at the ENT department. They underwent clinical and radiological evaluations before being treated with an intralesional injection of bleomycin diluted in normal saline. Full resolution and a good response were shown by all three people. There were no notable issues, except from fever. Bleomycin may be the primary treatment choice when used intralesionally.

Keywords: Bleomycin, Sclerotherapy, Lymphangioma, Surgery.

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1. Introduction

Lymphangiomas are benign tumors of lymphatic veins that develop slowly. They are often present from birth and are typically identified in early childhood (90%).[1] Any organ or soft tissue might experience them. The head and neck are the most frequent locations, followed by the mediastinum and axilla. Few instances have been documented in adults, while most cases are diagnosed in children. The two most prevalent signs are deformity and edema. Respiratory blockage and dysphagia might result from a big lesion.

Radiological and pathological evidence, clinical examination, and past history are often used to make the diagnosis. Although total surgical excision is the preferred course of treatment, invasion of tissue and neurovascular planes often makes complete removal impracticable. Radiotherapy, incision and drainage, and intralesional sclerotherapy are other alternatives.

In recent years, intralesional sclerotherapy has become a viable alternative, even as a main treatment, for lesions that were previously considered incurable. It irritates the vessel's endothelium, which results in intense inflammation and ultimately fibrosis.[2] Bleomycin, trichloroacetic acid, alcohol, and OK 432 have all been utilized in several trials with varying degrees of success.[3]

Since OK 432 is not yet accessible in India, we are sharing our experience in this research by employing bleomycin as a sclerosant.

2. Materials and Methods

Three lymphangioma cases that were reported to the ENT department of the Integral Institute of Medical Sciences and Research were investigated in this prospective investigation. Three of our patients were female, and their ages varied from 14 to 30. Our study was carried out between August 2022 and November 2023. All three patients had lymphangioma, which was diagnosed using a combination of history, clinical examination, and radiological investigations, including computed tomography (CT) and ultrasonography.

Using ultrasonography, lymphangiomas were classified as mixed, macrocystic, or microcystic. The study excluded

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lymph nodules that were less than 1 cm in size and those that spread to the axilla or mediastinum. To determine the extent of the lesion, CT scans were performed on all three patients. Following a proper diagnosis, the following information was recorded: size, weight, location, age, sex, and symptoms.

A vial containing 15 IU of bleomycin powder was diluted with normal saline to a concentration of 1.5 mg/ml after cysts were aspirated at a childcare facility while under local anesthetic. A 1-5% ml water solution containing 1.5 mg/ml bleomycin was given under USG observation. After aspiration, a first dose of 10 ml (15 mg) of bleomycin intralesional injections was given at 4-week intervals. To monitor and record issues, the patient spent 24 to 48 hours in the hospital. Following pain at the injection site, 500 mg of paracetamol was given. Every visit throughout the four-week follow-up period included a clinical examination and a measurement of the lesions. At 4 weeks, the procedure was repeated for cysts bigger than 1 cm. A second dose of bleomycin (10 milliliters) was given after a month of clinically significant edema. After three months, the patient's look improved, and all subjects provided their informed consent. (**Figure 1**)

3. Case 1

One 30-year-old woman arrived at the ENT OPD complaining of acute edema in the left submandibular area of her neck over the last two years. Single, soft, cystic in substance, non-tender, with loosely moving edges, the growth measured 4 cm by 5 cm. There was no localized increase in temperature, and there was no cervical lymphadenopathy that could be clinically identified. Shortness of breath, dysphagia, dysphonia, bodily swellings, or discomfort were not among her past medical conditions. Neither any family nor personal history that would have been relevant to the present sickness nor any references to head and neck conditions or injuries were found. Within the normal range are the blood test results. (**Figure 1**). X-ray of the chest: standard evaluation.

Several vascularity-free cystic forms may be seen on the left side of the HR-USG neck. From the submandibular area, these structures continue downward in thin, incomplete septations.

At levels 2 and 3, the left side of the neck exhibits a clear, non-enhancing hypodense region of 7.8 * 5.2 * 3.4 cm, with no discernible mass impact. **Figure 2** shows the FNAC neck, a proteinaceous backdrop with a high number of lymphocytes and a low quantity of macrophages. There were no strange cells found.(**Figure 3**) 3-month follow-up neck HRUSG: There was a noticeable cystic lesion measuring 1.8*0.3 cm in the rear of the left upper cervical area. The anterior cervical area has an extra cystic lesion measuring 2.0*0.8 cm. When the third bleomycin dosage was administered in the anterior and posterior edema zones while USG monitoring was in place, the treatment was effective. A total of five milliliters of bleomycin were administered.

Upon follow-up HRUSG, two cystic lesions measuring 0.6 cm by 0.3 cm and 0.3 cm by 0.3 cm were discovered. Normal study, WNL follow-up blood test, and chest X-ray. Following three months of monitoring, the patient's appearance improves (**Figure 4**).

4. Case 2

In the submandibular region on the left side of her neck, a 14-year-old girl complained of a large swelling that had persisted for a year. There was no clinically noticeable cervical lymphadenopathy, and the enlargement was 5 x 6 cm, was single, soft, cystic in substance, non-tender, with ill-defined boundaries, and easily movable. She had never had any pain, shortness of breath, dysphagia, dysphonia, or physical swellings. There was no family or personal history of relevance related to the current condition, nor was there a history of head and neck infections or trauma.

Blood test findings are within the typical range. A chest X-ray is a routine measurement.

HR-USG neck: a distinct multilobulated multiseptated anechoic cystic lesion (measuring 36*12*37 mm and vol - 8cc) resulting from lymphangioma is seen in the left upper cervical region, deep to the sternocleidomastoid muscle.

The internal jugular vein, common carotid artery, and sternocleidomastoid are laterally displaced by the large, well-defined, oblong cystic lesion in the last cervical region known as the CECT neck. A noticeable improvement was not seen.

Cellular in nature, FNAC neck smears have a background of mostly lymphocytes and red blood cells. There is no evidence of granuloma or malignancy.

Complete resolution for the follow-up HRUSG in the fourth month is observed.

WNL blood test follow-up, normal chest X-ray investigation.

Three months have passed, and the patient looks better.(**Figure 5**)

5. Case 3

A 16-year-old girl reported having minor neck edema that had lasted for a decade. It was a single 3 x 3 cm enlargement that was readily movable, soft, cystic, and non-tender. There was no evidence of cervical lymphadenopathy. She did not have any history of pain, dysphagia, dysphonia, dyspnea, or any swellings. Neither personal nor family history was significant in relation to the current disease, and there was no indication of a history of neck trauma or infection.

Findings from blood tests fall within the typical range. An ordinary chest X-ray.

HR-USG neck: multiloculated cystic lesion, 45*25*45 mm, with one small cyst with internal septations and the largest cyst, about 14*8 mm, situated just above the mouth's left mandibular angle. Internal vascularity does not exist. In the CECT neck, a distinct, lobulated, solid cystic lesion that affects the superficial and deep lobes of the left parotid gland measures 45*49*23 mm and has peripheral enhancement. The lesion lies anterior to the masseter muscle, and the subcutaneous tissue is protruding laterally.

Using a cytocentrifuged deposit of fluid aspirated from left preauricular swelling, a richly cellular FNAC neck smear reveals a polymorphous population of lymphoid cells, mainly mature lymphocytes, along with a large number of histiocytes, a few neutrophils, and degenerated cells on a proteinacious background. Analysis of the smears revealed no anomalous cells.

5.1. Follow up

The left parotid area gland on the fourth month's HRUSG has a few lymph nodes and a few cystic spaces, the biggest of which is around 11*10*10 mm (0.5 ml).

Follow up WNL blood test, chest X-ray: normal examination.

Following a three-month follow-up, the patient has improved cosmetically. (**Figure 6**)

6. Results

The ages of three male and three female patients varied from 14 to 30. The maximum diameters were 1.5 to 8 cm. The edema affected all three individuals. Discomfort (n = 2), difficulty chewing (n = 0), fever (n = 1), and skin erythema (n = 0). Each comprised the neck and head (n = 3). Just the cheek (n = 1), and only the neck (n = 2). Body weights ranged from 25 to 68 kg.

There were between one and three surgeries with a total bleomycin dose of 1–15 mg. The aspirate was 1–12 ml in volume and had a rich chocolate hue. Every patient reacted favorably and had complete resolution. Fever (n = 1) and discomfort were the two most common early issues. There were no allergic reactions or respiratory problems brought on by bleomycin.

Table 1: [a]Complete resolution 100% resolution, good response > 50% resolution, poor response < 50%

Results	Complete resolution[a]	Good response[a]	Poor response[a]
Age 1–15 years	1/3	0	0
Age 16–54	2/3	0	0
Total	3/3	0	0

Table 2: Complications

Complications	Total %
Erythema, pain	1/3
Fever	1/3
Restricted neck movement	0/3
Abscess	0/3

Figure 1: Preoperative

Figure 2: CECT neck

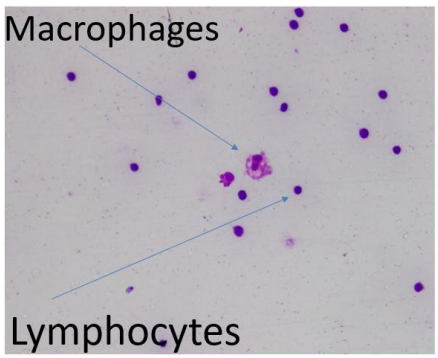

Figure 3: FNAC neck

Figure 4: Follow up HRUSG

Table 3: Previous studies on intralesional bleomycin

Study	No. of patients	Complete resolution[a] (%)	Significant response[a] (%)	Poor response[a] (%)
Tanigawa[9]	33	39.4	82	18
Zulfiqar[10]	11	36	82	18
Rozman[6]	24	63	84	16
India (uttar Pradesh -this study)	3	100	0	0

Figure 5: First visit and after treatment

Figure 6: First visit and after treatment

7. Discussion

Congenital abnormalities of the lymphatic veins, known as lymphphangiomas, are often seen in children and develop gradually. In the first known instance of sclerotherapy for lymphangiomas, sodium morrhuate was employed in 1933. Six weeks after an intralesional injection, the tumor had completely shrunk in size.[4]

Sclerosing was first employed to treat lymphangiomas because lymphatic malformations naturally involutate when infected and resolve, resulting in fibrosis. Although iodine, ethanolamine oleate, alcohol, ethibloc, tetracycline, cyclophosphamide, and bleomycin are sclerosing medications, OK-432 is the primary treatment for lymphangiomas.[5]

US, CT, and MRI should be utilized to see how the lesion is related to the surrounding structures and to help plan surgical or non-surgical methods. Cystic hemorrhage, either spontaneous or traumatic, is the most common outcome of an untreated lesion.

Bleomycin is an anti-neoplastic antibiotic produced by the streptomyces verticillus bacterium. It was found in 1965 that this drug caused single-strand and double-strand DNA breaks and reduced the creation of DNA and RNA.[4] Due to its anti-neoplastic qualities, bleomycin has been utilized to treat cancer ever since. By producing severe scarring and fibrosis, bleomycin has been shown to be an effective treatment for malignant pleural effusion. In 1977, this sclerosing capacity was initially used to treat lymphatic malformation. In that trial, bleomycin was utilized to treat eight individuals with tumors that were either inoperable, recurrent, or not surgically removed enough. Positive results were seen for these individuals.[4]

Bleomycin has been used in many trials with encouraging outcomes.[4,6-8] Our investigation's results were consistent with those of other published series and demonstrated the effectiveness of intralesional bleomycin treatment as a primary treatment for lymphangiomas. Similar to our study, a number of articles have shown success rates of up to 88% significant lesion shrinking, 36% to 63% entire tumor regression, and 12–23% poor response with either bleomycin or OK432.[8] (**Table 3**)

The investigation found no significant side effects from intralesional bleomycin treatment, with most patients reporting fever, discomfort, moderate soreness, local swelling, and skin erythema, lasting only a day or two.

8. Conclusion

The research suggests that bleomycin may be the first line of therapy for macrocystic lymphangioma, with no significant side effects.[4,6,9] recommends intralesional bleomycin as the main therapeutic option, with surgical procedures reserved for difficult or failed patients. The study's small sample size and limited resources may limit its applicability.[10-18]

9. Informed Consent

Informed Consent was taken from each of the participants. Additional informed consent was obtained from all individual participants for whom identifying information (pictures) is included in this article.

10. Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of Integral institute of medical sciences and research Lucknow.

11. Source of Funding

None.

12. Conflict of Interest

None.

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