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Response Rate of Cervicofacial Lymphangioma to Sclerotherapy (Bleomycin Injection): Case-Series from Single Institution

Alonazi M, Alsinan T, Alonazi N, Sulaiman A, Alotaibi A and Almohaidly M*

Prince Sultan Military Medical City, Riyadh City, Saudi Arabia

Abstract

Background: Lymphangiomas, arising from developmental anomalies in lymphatic tissue, pose challenges in treatment due to their infiltrative nature. Sclerotherapy, particularly with bleomycin, has emerged as an alternative to surgery, showcasing promising results in prior studies.

Objective: This retrospective study aimed to assess the response rates of cervicofacial lymphatic malformations to intralesional bleomycin therapy.

Methods: A retrospective case series was conducted on pediatric patients (0-12 years) diagnosed with cervicofacial lymphangiomas who underwent intralesional bleomycin therapy at our institution between 2005 and 2012. Data including demographics, lesion characteristics, treatment details, complications, and response rates were collected and analyzed.

Results: The study comprised seven patients (5 males, 2 females) with cervicofacial lymphangiomas, predominantly on the left side. Following intralesional bleomycin therapy, response rates were categorized as excellent (57.1%), good (28.6%), and poor (14.2%), with no major complications observed.

Conclusion: Intralesional bleomycin emerges as a safe and effective therapeutic option for cervicofacial lymphangiomas. Despite variations in treatment response, its commendable safety profile and promising efficacy advocate for its consideration in managing these challenging malformations.

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Correspondence:
Mohammad Alonazi, Prince Sultan Military Medical City, Riyadh City, Saudi Arabia, Tel: 505466625;

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Introduction

Lymphangiomas are believed to originate from a complex interplay of factors, including the failure of lymphatics to establish connections with the venous system, abnormal budding of lymphatic tissue, and the persistence of sequestered embryonic lymphatic rests [1]. These residual lymphatic rests may infiltrate nearby structures, dissect along fascial planes, and ultimately canalize. Due to the absence of venous outflow tracts, these spaces retain their secretions, forming cystic components. The classification of lymphangiomas–capillary, cavernous, or cystic–depends on the nature of the surrounding tissue. Notably, cystic lymphangiomas localized in the cervical area are commonly referred to as Cystic Hygromas [2].

Microcytic lymphangiomas comprise cysts, each measuring less than 2 cm^3, while macrocystic lymphangiomas contain cysts larger than 2 cm^3. Mixed-type lymphangiomas encompass both microcystic and macrocystic components [3]. Typically congenital, lymphatic malformations manifest usually before the age of 2. Clinical indications for intervention include respiratory distress, recurrent infections, or concerns related to aesthetics [4]. While complete surgical excision remains the gold standard treatment, sclerosant therapy, particularly sclerotherapy with agents such as OK-432, Bleomycin, Doxycycline, or Alcohol, has gained prominence due to the infiltrative nature of these lesions and their associations with vital structures [5]. Furthermore, sclerotherapy is advocated as an adjunct to surgery, facilitating lesion regression, thereby easing subsequent resection [6].

This study specifically examines the response rates of cervicofacial lymphatic malformation patients to bleomycin injection at our institution. Bleomycin, recognized primarily as an antineoplastic drug, has found application as a local sclerosing agent, particularly in cases of congenital lymphatic malformations [7]. Its efficacy lies in inducing fibrotic transformation of vascular endothelium. Intralesional bleomycin therapy offers an effective non-surgical option, especially when surgery

Table 1: The cases demographics and lymphangioma information listed.

Case No.	Gender	Presentation Age	Site	Size	Type	Discharge
1	M	Since birth	Left chest, anterior superior	Increased	Macrocystic	Bluish with distended veins
2	F	Since day 15	Left submandibular	Increased	Macrocystic	None
3	M	4 years	Left neck	Fixed	Microcystic	None
4	M	Since birth	Left neck, posterior supraclavicular	Fixed	Macrocystic	None
5	M	7 months	Right neck, anterior supraclavicular	Increased	Macrocystic	None
6	M	1 year	Right neck	NA	Macrocystic	None
7	F	3 months	Left neck, submandibular	Increased	Mixed	None

Table 2: Summarized the procedure findings and outcomes.

Case No.	Injections No.	Aspiration	Bleomycin Doses	Complications	Response	Total Days of Admissions
1	3	Clear with yellowish	6.5 mg	Infection	Excellent	19 days
2	8	Darkish brown with blood	22 mg	Infection	Good	38 days
3	4	Clear with yellowish	14.5 mg	None	Excellent	6 days
4	3	Clear yellow	11 mg	None	Excellent	8 days
5	4	Dark blood	6 mg	None	Excellent	32 days
6	2	NA	3 mg	Infection	Good	14 days
7	5	NA	15 mg	Infection	Poor	48 days

may pose risks to vital structures or result in poor cosmetic outcomes due to neural involvement. Encouragingly, long-term results have demonstrated satisfaction. Minor post-injection complications such as transient fever or local skin inflammation have been reported; however, literature also records severe complications, including instances of pulmonary fibrosis-associated mortality [8].

Patients and Methods

A retrospective case series encompassed all pediatric patients aged 0 to 12 years diagnosed with cervicofacial lymphangiomas who received intralesional bleomycin therapy at our hospital between 2005 and 2012. Medical records of patients diagnosed with cervicofacial lymphangioma and treated *via* intralesional bleomycin injection were collected for analysis. Informed consent was obtained from the parents or legal guardians of the children who underwent intralesional bleomycin therapy.

A standardized data collection sheet was employed to systematically gather information from each patient. The collated data included the time of initial presentation, anatomical site of the lymphangioma, lesion dimensions, details of any radiological investigations conducted, doses of bleomycin administered, encountered complications, duration of hospital admission, and subsequent response rates.

The evaluation of response rates was conducted through clinical and radiological assessments, involving measurements of the lesion's dimensions. The regression response of the swelling was graded as follows:

- Excellent: Reduction in size more than 90%
- Good: Reduction in size ranging between 50% and 90%.
- Poor: Less than 50% reduction in size.

Results

The study comprised seven pediatric patients diagnosed with cervicofacial lymphangiomas, all of whom underwent primary treatment *via* bleomycin injection.

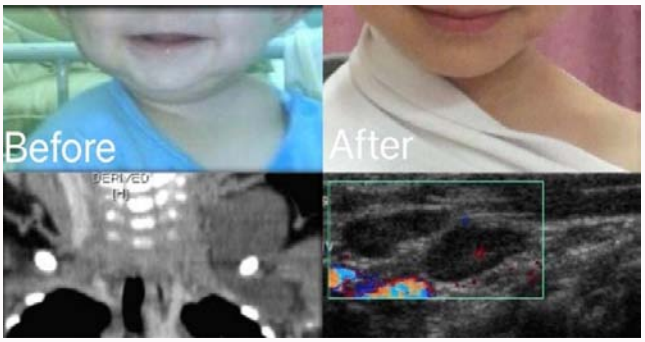

Figure 1: Case 4. A 4-year-old boy who was born with left neck lymphangioma and managed with Bleomycin injections (Three sessions over 1 year), results before and after injections are shown in the images.

Procedure technique

Admission for Bleomycin injection involved sedation under the supervision of an anesthetist. Interventional radiologists conducted the aspiration of fluid samples under ultrasound guidance. Samples obtained were subjected to analysis. A 22G spinal needle, along with a 10cc or 25cc syringe, was utilized for both aspiration and injection procedures. Contrast-enhanced injections were administered in two cases where the fluid sample exhibited signs of blood staining. This precautionary measure aimed to verify the absence of vascular connections before initiating the injection. Subsequently, one case was identified with suspected vascular involvement, leading to the abortion of the injection. The average duration of admission, excluding patients with complications, was three days. Patients were observed in the Intensive Care Unit (ICU) post-injection, but none necessitated intubation.

Among the seven cases, there were five males and two females, with ages ranging from 0 to 4 years. All identified lymphangiomas

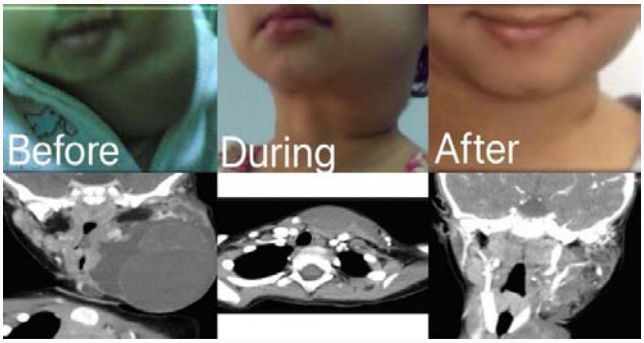

Figure 2: Case 2. A 6-year-old baby girl who was born with left submandibular lymphangioma and managed with multiple Bleomycin injections (8 injections over 6 years), course of bleomycin injection results are shown in the images.

were localized in the cervicofacial region, with five occurring on the left side (71.4%) and two on the right side (28.6%). Assessment of response rates revealed an excellent response in four patients (57.1%), a good response in two patients (28.6%), and a poor response in one patient (14.2%). Table 1 and 2 summarize demographics, symptoms, and procedural findings (Figure 1, 2).

Discussion

Despite the limited scope of our study, confined to cervicofacial lymphangiomas, our aim was to review and assess the outcomes of employing bleomycin as a primary treatment for lymphatic malformations, focusing on our observations and experiences.

The inception of intralesional bleomycin as a sclerosing agent was credited to Yura et al. [4]. Since then, subsequent studies and literature have continually reinforced the idea that sclerosant therapy, including Bleomycin injections, stands as a viable alternative to surgery. This therapeutic avenue often demonstrates promising outcomes while minimizing the inherent risks associated with surgical interventions. Notably, while advocating the efficacy of bleomycin, it is crucial to acknowledge its potential hazards as a chemotherapeutic agent, primarily the rare yet severe complication of pulmonary fibrosis [8]. In our study, thankfully, no patients suffered major complications attributable to bleomycin therapy. We did observe minor complications in a subset of patients (57.1%), primarily manifested as fever in three cases and infections in two cases. Our findings corroborate existing literature, highlighting that lymphangiomas of the macrocystic and mixed types exhibited more favorable responses to the sclerosing treatment. However, when dealing with predominantly microcystic compositions or mixed types where larger cysts had been aspirated, further intervention became challenging. This challenge stemmed from the remaining presence of smaller cysts and microscopic lymphatic channels, limiting the feasibility of additional aspirations [3,9].

The success observed in treating lymphangiomas with bleomycin injection aligns with the growing body of evidence advocating for sclerosant therapy as a frontline option. This approach not only demonstrates effectiveness in reducing the size and symptoms of lymphatic malformations but also offers a non-invasive alternative, particularly in cases where surgery poses significant risks or challenges.

Our study underscores the importance of considering sclerosant therapies, particularly bleomycin, as a viable primary treatment for cervicofacial lymphangiomas. Further research encompassing larger patient cohorts and more diverse lymphatic malformation types could provide deeper insights into the efficacy, safety, and long-term outcomes of bleomycin therapy for this condition.

Conclusion

Intralesional Bleomycin therapy proves safe and effective in treating lymphangiomas. Our findings align with previous studies, highlighting its reliability and safety. Notably, no severe side effects were observed. However, responsiveness to this therapy may vary based on the lymphatic malformation type. Overall, intralesional bleomycin stands as a valuable treatment option, necessitating further research for broader understanding and long-term outcomes.

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