Original Article

Intralesional Bleomycin for Orbital Vascular Malformations at a Tertiary Care Centre

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ABSTRACT

Purpose: To report the outcomes of intralesional bleomycin injections for orbital venous malformations (OVMs) in a tertiary care setting.

Study Design: Interventional case series.

Place and Duration of Study: Jinnah postgraduate medical Centre Karachi from January 2020 to April 2022.

Methods: This case series included 24 consecutive cases presenting with orbital vascular malformations, including orbital capillary hemangiomas, lymphangiomas, and orbital varices. The location, dimensions, extent of involvement, signal characteristics, and enhancement pattern following contrast administration of the lesion were determined. Intralesional bleomycin injections were given at a dose of 0.5 mg/kg body weight diluted in lidocaine. Retreatment, if needed was done at an interval of 4 weeks. Follow up included measurement of proptosis and radiological measurements of tumor volume.

Results: Proptosis and lid swelling were the most common presentations. An average of 2.27±1.3 injections of bleomycin were given. The mean pretreatment volume was 3.61±1.14 $cm^3$and the post-treatment volume was1.41±1.06 cm^3 with a mean reduction in tumour volume of 2.20±1.13 cm^3 (t=9.52, p<0.001). There was marked improvement in clinical symptoms and the proptosis reduction averaged 7.22±2.80 mm (t= 10.95, p<0.001). Side-effects included conjunctival swelling, skin hyperpigmentation around the lesion, and madarosis.

Conclusion: Intralesional bleomycin injection proved to be an effective and minimally invasive treatment modality for orbital venous malformations, resulting in significant reduction in lesion volume and proptosis, along with marked symptomatic improvement. It is a valuable therapeutic option for orbital vascular malformations, particularly in cases where surgical excision is challenging.

Keywords: Intralesional bleomycin, capillary hemangioma, lymphangioma, Orbital vascular malformations, proptosis, sclerotherapy.

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INTRODUCTION

Orbital vascular malformations (OVMs) are a common diverse spectrum of orbital lesions causing proptosis, motility dysfunction, pain, and visual impairment.[1] The International Society for the Study of Vascular Anomalies classification system has categorized these vascular malformations into fast-flow and slow-flow.[2] Arterial and arteriovenous malformations are categorized as fast flow and venous or lymphatic malformations are slow flow.[3] Lymphatic malformations can be found in any part of the human body. However, it has been estimated that up to 45% of the lymphatic malformations are present in the head and neck region and 4% of all orbital masses are lymphatic malformations.[4,5]

Most of these lesions are benign and localized, however, a few can be locally aggressive and recurrent. Rarely, these can be malignant with a risk of metastasis and poor prognosis. Non-invasive imaging with MRI and CT scans and Doppler ultrasound aids in delineating the size and the extent of the lesions and any bony involvement.[6]

Surgical debulking is not an option for most of these lesions as it has been associated with lesion expansion, retrobulbar hemorrhage, iatrogenic damage to adherent orbital structures, and a risk of recurrence due to the friable and infiltrative behavior of the lesions. Recently, orbital vascular malformations have been treated using an interdisciplinary approach, which includes surgical excision, selective embolization, CO^2 laser therapy, and sclerotherapy.[7,8] The therapeutic choice for each patient depends upon the site and size of lesions, hemodynamics, type of abnormality, and surgeon preference.

Bleomycin is an anti-neoplastic, antibiotic cytotoxin. It has a sclerosing effect on venous malformations in several areas, including the orbital and periorbital regions. Bleomycin sclerotherapy works by damaging endothelial cells, triggering inflammation, and promoting thrombus and fibrotic tissue development, which ultimately obstructs the affected vessels.[9]

With encouraging outcomes, percutaneous sclerotherapy is being utilized more frequently as a less invasive option for the treatment of OVMs. Bleomycin has shown to be a well-tolerated and efficient therapy for vascular malformations of the head and neck among the sclerosing drugs now on the market.[10] In this study, we report the outcomes of treating OVMs with intralesional bleomycin injections at a tertiary care center.

METHODS

This was an interventional case series conducted at the Jinnah postgraduate medical Centre Karachi, from January 2020to April 2022. This study included a total of 24 patients with orbital vascular malformations, including orbital capillary hemangiomas, lymphangiomas, and orbital varices, who were given an intralesional bleomycin injection. Of the cohort, 15 were female (62.5%) with ages ranging from 2 to 77 years, while 9 were male (37.5%), aged 11 to 25 years. Exclusion criteria comprised of known hypersensitivity to bleomycin, impaired renal or pulmonary function, and failure to complete follow-up. The study was conducted after obtaining consent from the patients or their legal guardians and approval from the local institutional review board **(IRB number F.2-81/2019/GENL/35480/JPMC).**

The preprocedural evaluation included a full ophthalmic assessment including refraction, fundus examination, intraocular pressure, extraocular motility, degree of proptosis, and dystopia. Adjunctive contrast-enhanced computed tomography (CT) or magnetic resonance imaging (MRI) scans were performed in all cases and were evaluated by experienced radiologists. The location, dimensions, extent of involvement, signal characteristics, and enhancement pattern following contrast administration of the lesion were recorded. Sclerotherapy with bleomycin was performed by an experienced ophthalmologist under general or local anesthesia. The periocular region was prepared using a 5% povidone-iodine solution and partial aspiration of the cyst was performed using a 23-gauge needle.

General anesthesia was administered in children under 7-8 years, and a dose of 0.5 mg/kg (range 0.2–0.9 mg/kg per injection) was injected after diluting 15 IU in 15 ml of normal saline and 1% lignocaine. A multi-puncture technique was used, and the injection volume did not go above the predicted volume of the tumor. After the injection, pressure was administered for ten minutes. Oral analgesics were prescribed, with retreatments and reviews scheduled every four weeks.

Patients were observed for 24 hours and received an ophthalmic evaluation prior to discharge. Patients were followed every 4-6 weeks. Assessments included quantification of proptosis, evaluation of dystopia, and visual acuity. The patients were also monitored for any complications. Repeat MRI scans were used to determine the local response to therapy. Bleomycin injections were repeated at 6-8 weeks based on the clinical and radiological response to treatment. Statistical analyses were performed using SPSS version 23. Proptosis and tumor volume were compared before and after therapy using the paired t-test.

RESULTS

Twenty-four patients were given intralesional bleomycin injection between January 2022 and April 2024. Their ages ranged between 2 and 77 years (mean: 23.9±23.0 years). There were nine (37.5%)

Table 1: *Initial and post treatment clinical and radiological results.*

Clinical Feature	Mean±SD	Range	p-value
Proptosis pretreatment (mm)	23.56±3.22	18.00 – 29.00	
Proptosis post-treatment(mm)	16.33±3.83	10.00 - 22.00	<0.001
Reduction in proptosis post-treatment (mm)	7.22±2.8	2.00 – 13.00	
Volume of lesion pretreatment (cm^3)	3.61±1.14	1.70 – 6.00	
Volume of lesion post-treatment (cm^3)	1.41±1.06	0.00 – 3.20	<0.001
Reduction in volume post-treatment (cm^3)	2.20±1.13	0.50 – 5.00	
Number of bleomycin injections	2.17±1.3	1.00 – 6.00	

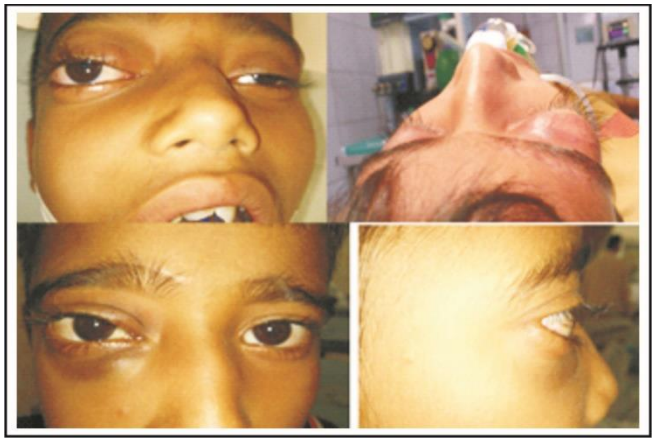

Figure 1: Orbital giant intraconal venous malformation in an 11-year-old boy (top preoperative images and bottom postoperative images).

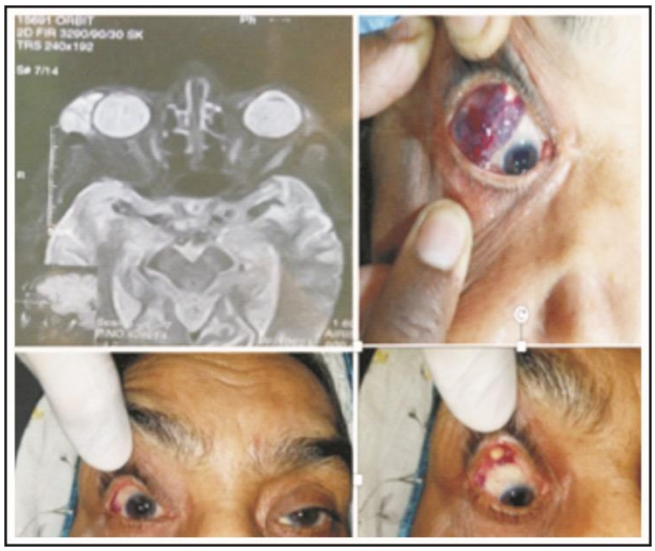

Figure 2: Upper lid venous malformation in a 77-year-old female (above) and four weeks after one dose of intralesional bleomycin (below).

males and 15 (62.5%) females. Venous malformations were confined to the periorbital or orbital region in all patients, with 11 lesions (45.8%) on the right and 13 (54.2%) on the left. Lid swelling was noted in 6 (25%) and proptosis in 18 (75%) patients. The mean number of injections administered were 2.27±1.30 (range: 1.0–6.0).

Post treatment conjunctival swelling was noted in 3 patients (12.5%) which was noted 1-2 days following sclerotherapy which resolved spontaneously over weeks. Hyperpigmentation of the perilesional skin was noted in two patients (8.3%) with eventual good cosmetic outcome. Two patients (8.3%) had madarosis following the fourth dose of bleomycin. Few patients with larger lesions experienced mild to moderate pain during the injection which was resolved with oral acetaminophen. None of the patients experienced systemic or ocular functional adverse effects such as visual loss, neural damage, scarring, tissue necrosis, pulmonary fibrosis, hematologic cytopenia, or anaphylactic reaction.

All the cases showed decrease in volume of the lesions. The average preoperative tumour volume was 3.61±1.14 cm^3 (1.70-6.00 cm^3) and the average postoperative tumour volume was 1.41±1.06 cm^3 (0.00-3.20 cm^3). The mean reduction in tumour volume was 2.20±1.13 cm^3 ($t=9.52$, $p<0.001$). Table 1 summarises the post-treatment clinical and radiological results.

DISCUSSION

Benign congenital abnormalities known as orbital vascular malformations account for 1-3 percent of all orbital masses that present to tertiary orbital centres.[11] OVMs can either be localized or extensive and due to their cosmetic or functional ocular morbidities they often necessitate an intervention. Because of the decreased blood flow, there is also a risk of debilitating pain, thrombosis, or hemorrhage.[12]

Several treatment modalities such as carbon dioxide laser ablation, intralesional /oral steroids, intralesional sclerosing therapy, surgical excision, or a combination of these are available to treat OVMs with

variable results.[13,14] However, laser therapy and surgical excision are only beneficial for superficial lesions. Complete removal is sometimes not feasible without causing major structural damage, or it carries a high risk of serious morbidity. Sclerotherapy, therefore, could be a desirable substitute for treating complicated and refractory OVMs.

Bleomycin is a sclerosing agent that is less likely to result in side effects such as subcutaneous atrophy, venous blockage, and inflammation-related pain. Prior research has demonstrated that bleomycin is effective in treating vascular abnormalities in the maxillary region.[15] It has been seen that bleomycin administered as a single agent can considerably reduce the amount of orbital cavernous hemangiomas.[1] More importantly, using bleomycin combined with fibrin glue or lipiodol emulsion can virtually eliminate the pain and swelling associated with proptosis in high-flow OVMs. These substances might lengthen bleomycin's local effect, improving the effectiveness of the treatment.[16]

Intralesional administration of bleomycin has achieved a success rate of 72.3%, while adverse effects such as erythema, localized swelling, and injection-site discomfort have been documented.[17] In another study by Gooding C., et al, four patients with orbital lymphangioma received intralesional bleomycin therapy, resulting in encouraging clinical responses and no observed systemic or ocular adverse effects.[18]

We observed a significant reduction in proptosis, lid or conjunctival swelling, and pain after bleomycin injection without any long-term complications. Figure 1 shows an example of a giant intraconal venous malformation in an 11-year-old boy that led to a proptosis of 22 mm on Hertel's exophthalmometer in the right eye. An eighty percent reduction in volume was shown by magnetic resonance imaging, and the proptosis resolved after two doses of intralesional injection of bleomycin. Figure 2 shows an upper lid venous malformation in a 77-year-old woman that showed a significant reduction in the volume of the lesion after a single dose of bleomycin. The complications included eyelid muscle atrophy or deformation resulting in ptosis, occlusion of the visual axis, and, in certain patients, eyelid retraction.

Pain, erythema, and edema are the adverse effects of intralesional bleomycin that are most frequently noted and documented. With analgesics, the pain is normally alleviated within 48 to 72 hours. Reports of patients developing pigmentation of the skin after treatment with bleomycin in our study were 8.3%, which resolved spontaneously over a few weeks. A similar percentage of patients developed madarosis which has not been reported in other studies. Twelve percent of patients also developed conjunctival swelling that also resolved spontaneously. None of our cases developed fever, gastrointestinal symptoms, symptoms of pulmonary fibrosis, or any other systemic complications. MacIntosh PW et al, have reported transient fever as the most common systemic adverse effect in patients receiving large doses of intralesional bleomycin. They also reported diarrhea, local infection, and vomiting in descending order.[19]

Although there have been rare, reported cases of pulmonary injury observed in children after bleomycin intralesional administration, our series no such complication was noted.[20]

The small sample size, usage of a single centre, and varied patient population are our study's limitations. Even though three separate investigators completed the scoring, measurement bias could have been an issue. Furthermore, due mostly to their poor adherence, we could notretrieve follow-up outcomes from part of the cohort for longer than 3 months. Although the possibility of recurrence was stressed and patients were urged to return to the clinic, some did not believe that recurrence was likely. Lastly, the lack of detrimental side effects in this trial involving a small number of participants does not indicate safety, and a risk of optic nerve damage and central retinal artery occlusion remains.

CONCLUSION

Intralesional bleomycin injections could be taken into consideration as an alternative therapy option for refractory cases or as a first-line drug in situations of untreated deep and superficial orbital venous malformations.

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Patient's Consent: Researchers followed the guidelines set forth in the Declaration of Helsinki.

Conflict of Interest: Authors declared no conflict of interest.

Ethical Approval: The study was approved by the Institutional review board/Ethical review board **(F.2-81/2019/GENL/35480/JPMC)**.

REFERENCES

1. **Kamil Z, Qurban Q, Hassan Khan MT.** The Experience of Intralesional Bleomycin For Orbital Vascular Anomalies. J Ayub Med Coll Abbottabad. 2021;**33(2):**240-243. PMID: 34137537.
2. **Wassef M, Blei F, Adams D, Alomari A, Baselga E, Berenstein A, et al.** ISSVA Board and Scientific Committee. Vascular Anomalies Classification: Recommendations From the International Society for the Study of Vascular Anomalies. Pediatrics. 2015;**136(1):**e203-214. Doi: 10.1542/peds.2014-3673.
3. **Das A, Goyal A, Sangwan A, Bhalla AS, Kumar A, Kandasamy D, et al.** Vascular anomalies: nomenclature, classification, and imaging algorithms. Acta Radiol. 2023;**64(2):**837-849. Doi: 10.1177/02841851221082241.
4. **Nassiri N, Rootman J, Rootman DB, Goldberg RA.** Orbital lymphaticovenous malformations: current and future treatments. Surv Ophthalmol. 2015;**60:**383–405. Doi: 10.1016/j.survophthal.2015.03.001.
5. **Dave TV, Madhuri BK, Laghmisetty S, Tripathy D, Kaliki S, Rath S, et al.** Long-term outcomes of transcutaneous non-image guided bleomycin sclerotherapy in orbital/adnexal lymphatic malformations: a protocol-based management in 69 eyes. Eye (Lond). 2022;**36(4):**789-799. Doi: 10.1038/s41433-021-01527-9.
6. **Teplisky D, Szhafir I, Mansilla MC, Torres N, Tellería R, Affranchino N, et al.** Update on orbital vascular anomalies in pediatrics: imaging studies and management. Arch Argent Pediatr. 2023;**121(2):**e202202692. English, Spanish. Doi: 10.5546/aap.2022-02692.eng.
7. **Lam SC, Yuen HKL.** Medical and sclerosing agents in the treatment of orbital lymphatic malformations: what's new? Curr Opin Ophthalmol. 2019;**30:**380–385. Doi: 10.1097/ICU.0000000000000585.
8. **Patel SR, Rosenberg JB, Barmettler A.** Interventions for orbital lymphangioma. Cochrane Database Syst Rev. 2019;**5(5):**CD013000. Doi: 10.1002/14651858.CD013000.pub2.
9. **Hanif AM, Saunders JA, Hawkins CM, Wojno TH, Kim HJ.** Use of percutaneous bleomycin sclerotherapy for orbital lymphatic malformations. Orbit. 2019;**38(1):**30-36. Doi: 10.1080/01676830.2018.1480636.
10. **Rootman DB, Diniz SB, Cohen LM.** Clinical Assessment and Lesion-Specific Management of Orbital Vascular Malformations. J Neurol Surg B Skull Base. 2021;**82(1):**116-128. Doi: 10.1055/s-0040-1722702.
11. **Khan AA, Latif S, Khan MIA, Ahmad I.** Orbital Lesions: A bird's eye view of series of 2068 cases in 27 years in a tertiary care hospital in Pakistan. Pak J Med Sci. 2024;**40(8):**1625-1631. Doi: 10.12669/pjms.40.8.9843.
12. **Tawfik HA, Dutton JJ.** Orbital Vascular Anomalies: A Nomenclatorial, Etiological, and Nosologic Conundrum. Ophthalmic Plast Reconstr Surg. 2022;**38(2):**108-121. Doi: 10.1097/IOP.0000000000002029.
13. **Spector JA, Zide BM.** Carbon dioxide laser ablation for treatment of lymphangioma of the conjunctiva. Plast Reconstr Surg. 2006;**117(2):**609-612. Doi: 10.1097/01.prs.0000200872.78741.9a.
14. **Patel SR, Rosenberg JB, Barmettler A.** Interventions for orbital lymphangioma. Cochrane Database Syst Rev. 2019;**5(5):**CD013000. Doi: 10.1002/14651858.CD013000.pub2.
15. **Mazhar A, Shazlee MK, Mallick YA, Muhammad AA, Samad L.** Assessment of outcomes after intralesional bleomycin sclerotherapy of lymphatic malformations in children. J Pak Med Assoc. 2023;**73(2):**290-293. Doi: 10.47391/JPMA.5623.
16. **Li YY, Qu XL, Ma R, Hu J, Hei Y, Xu WQ, et al.** [Treatment of orbital vascular malformations with intralesional bleomycin injection and N-butyl-2-cyanoacrylate glue embolization]. Zhonghua Yan Ke Za Zhi. 2023;**59(1):**37-43. Chinese. Doi: 10.3760/cma.j.cn112142-20220424-00207.
17. **Acevedo JL, Shah RK, Brietzke SE.** Nonsurgical therapies for lymphangiomas: a systematic review. Otolaryngol Head Neck Surg. 2008;**138(4):**418-424. Doi: 10.1016/j.otohns.2007.11.018.
18. **Gooding C, Meyer D.** Intralesional bleomycin: a potential treatment for refractory orbital lymphangiomas. Ophthalmic Plast Reconstr Surg. 2014;**30(3):**e65-67. Doi: 10.1097/IOP.0b013e31829bb4a9.
19. **MacIntosh PW, Yoon MK, Fay A.** Complications of intralesional bleomycin in the treatment of orbital lymphatic malformations. Semin Ophthalmol. 2014;**29(5-6):**450-455. Doi: 10.3109/08820538.2014.959617.
20. **Sheng L, Yu Z, Li S, Cao W, Jiang Z.** Bleomycin sclerotherapy for large diffuse microcystic lymphatic malformations. Gland Surg. 2021;**10(6):**1865-1873. Doi: 10.21037/gs-21-70.

Authors Designation and Contribution

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Rabia Khawar Chaudhry; Consultant Ophthalmologist: *Design, Statistical Analysis,*

Manuscript Preparation, Manuscript Editing, Manuscript Review.

Arifa Farooq; FCPS Trainee: *Statistical Analysis.*

Amna Hanif; FCPS Trainee: *Literature Search, Manuscript Preparation.*