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Mini Review

Intralesional Bleomycin Sclerotherapy in Childhood Lymphangioma: A Review Article

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Abstract

Being one of the most common benign lesions of childhood lymphangioma manifests frequently before 2 years of age. Although surgical excision has been considered the treatment of choice, intralesional injection of bleomycine is noninvasive and effective means of therapy. This clinical review aims to evaluate the efficacy of intralesional bleomycin sclerotherapy (IBS) in children with lymphangioma. There are not so many major adverse effects. In the case of occurence these complications should be kept in mind and in occurrence be treated immediately. With regard to treatment modalities in lymphangioma, IBS is effective.

Keywords: *Lymphangioma; Sclerotherapy; Bleomycin*

Introductıon

Believed to originated from lymphatic vessels Lymphangioma is a benign tumour with varying size. It is mostly seen in the head and neck, comprising 75% of all cases [1,2]. It is usually seen at birth in up to 65% and 90% of cases presents during the first 2 years of life [1,3,4]. The incidence range of lymphangioma is between 1.5 - 2.8 per 1000 and there is no predilection for either sex [5]. The most common symptoms are swelling and cosmetic deformity.

The traditional management is surgical excision and its goal is the removal of involved tissue without sacrificing vital structures but this is not always achievable. This lesion has a propensity to infiltrate tissue planes and encircle important neurovascular structures so complete excision may sometimes be impossible [3]. There are multiple nonsurgical therapies regarding the treatment options in lymphangiomas. These are namely diathermy, cryotherapy, radiotherapy, fibrin glue and percutaneous sclerotherapy. Intralesional sclerotherapy is another choice in the treatment of lymphangiomas in children. There are various sclerosing agents compatible for usage in the treatment of childhood lymphangiomas.

In the management of lymphangioma which manifests frequently before 2 years of age surgical excision is a treatment of choice. The lesion has a propensity of infiltrating adjacent structures so during surgical excision incomplete resection or inadvertent nerve injury may result. Recurrence rates following surgical excision are between 15 - 40% [8].

In 1933 the first case of lymphangioma was reported to be treated by sclerotherapy with sodium morrhuate [9]. Following this intervention various sclerosing agents have been used in the management of lymphangiomas. As an antitumor agent bleomycine was discovered in 1965. Along with its antineoplastic effect, regarding bleomycine, there is an irritant effect on endothelial cells of the cyst wall of lymphangioma. It is probable that bleomycine causes non-specific inflammatory reaction which leads to fibrosis of the cysts. First report

of intralesional bleomycine therapy dates back to 1977 with good results [9]. Following this various studies depicted promising results [9-13]. In a recent series reported by Erikci., *et al.* it was found that bleomycine was effective in most of the patients and their results were found to be similar to previously published series [14]. The response rates of bleomycine therapy in lymphangiomas are between 36 - 63% for complete tumor regression, significant lesion involution up to 88%, and 12 - 18% of poor response [5,9,10-13].

Injection of bleomycine is recommended to be performed to children under general anesthesia. According to Yura method, after aspiration of the cyst content, bleomycin aqueous solution with a dosage of 1 mg/kg [7] is injected directly into a cyst. Maximum alloved total dose is 15 mg. With regard to previous reported series n this subjecti there is no concensus about the dose of this drug. Doses between 0.3 and 0.6 mg/kg for each injection, with a total amount of bleomycin injected up of to 50 mg or 5 mg/kg, and up to 16 injections with intervals of between 2 weeks and 2 months have been reported [4,9,12,15,16].

Most of the patients with lymphangioma consisting of macrocysts respond well to local injection therapy and the response has been reported to be lower in microcystic lymphangioma [17-19]. The response to bleomycine injection in patients with mixed type of lymphangioma including both macrocystic and microcystic lesions is variable but should be kept in mind as a first choice of therapy although poor response to IBS may be observed. In the patients with servico-thoracic involvement with lesions which extend into the anterior mediastinum and it is recommended that only the neck components is aspirated and injected with bleomycin hoping that after the neck component reduces in size, the mediastinal lesion would easily be detected in the neck. It is dangerous for the mediastinal component to be directly aspirated and injected because it may cause mediastinitis compromising adjacent vital structures. Repeat injection may be planned for future resolution in patients with partial esponse to IBS.

If the complications in IBS are regarded, most common ones are skin erythema, local swelling, induration. Fortunately these symptoms do not prolong the patients' stay in hospital. Fever has been reported to be the most common side effect noted with an incidence of 30% [20] it was not observed in any of the patients in a recent series reported by Erikci [14]. Pulmonary toxicity is the primary concern in IBT. The risk depends on dose of agent administrated and life-threatening pulmonary toxicity at total doses of below 150 mg or 450 U is rare [21,22]. On the other hand it has been previously reported that two children undergoing bleomycin therapy died post-treatment from pulmonary complications, but no definitive link to bleomycin therapy was established [3]. Clinical studies from different centers comprising 104 patients revealed that there was no report pulmonary fibrosis as a complication [9-13].

Conclusion

Most studies concerning the IBS have have limitations due to the retrospective design and relative short follow up periods which may undermine the strength of these studies. Relative short durations of surveillance in these series should prevent the clinician dealing with these children from drawing clear conclusions concerning the recurrence. More fundamental information on this matter may be obtained with prospective studies having more patients with longer follow up periods.

As first-line therapy, local injection of bleomycin is recommended and surgical excision should be reserved for cases with refractory lesions untreatable with any other treatment modality and for patients with lymphangioma that present a diagnostic difficulty. However with regard to level of evidence in IBT, it is low. With the help of randomized clinical trials using local bleomycin therapy and standardized protocols with reliable outcome reporting, it is possible that the heterogeneity of the literature may be decreased and future treatment guidelines on the IBT will be possible. In conclusion, although there are a few major adverse effects and complications during IBS, local bleomycine injection is effective in the treatment of lymphangioma.

Bibliography

1. Ravitch MM and Rush Jr BF. "Cystic hygroma". In: Welch KJ, Randolph MM, Ravitch MM, *et al* (eds). Pediatric Surgery. Chicago (III): Year Book Medical (1986): 533-539.

2. Emery PJ., *et al*. "Cystic hygroma of the head and neck: a review of 37 cases". *Journal of Laryngology and Otology* 98.6 (1984): 613-619.

3. Acevedo JL., *et al*. "Nonsurgical therapies for lymphangiomas: a systematic review". *Otolaryngology–Head and Neck Surgery* 138.4 (2008): 418-424.

4. Sanlialp I., *et al*. "Sclerotherapy for lymphangioma in children". *International Journal of Pediatric Otorhinolaryngology* 67.7 (2003): 795-800.

5. Rozman Z., *et al*. "Lymphangioma: is intralesional bleomycine sclerotherapy effective?" *Biomedical Imaging and Intervention Journal* 7.3 (2011): e18.

6. Ogita S., *et al*. "OK-432 therapy for unresectable lymphangioma in children". *Journal of Pediatric Surgery* 26.3 (1991): 263-270.

7. Yura J., *et al*. "Bleomycine treatment for cystic hygroma in children". *Nippon geka hokan. Archiv für japanische Chirurgie* 46.5 (1977): 607-614.

8. Alqahtani A., *et al*. "25 years' experience with lymphangiomas in children". *Journal of Pediatric Surgery* 34.7 (1999): 1164-1168.

9. Okada A., *et al*. "Injection of bleomycin as a primary therapy of cystic lymphangioma". *Journal of Pediatric Surgery* 27.4 (1992): 440-443.

10. Zulfiqar MA., *et al*. "The treatment of neck lymphangioma with intralesional injection of bleomycin". *Medical Journal of Malaysia* 54.4 (1999): 478-480.

11. Tanigawa N., *et al*. "Treatment of cystic lymphangioma with the use of bleomycin fat emulsion". *Cancer* 60.4 (1987): 741-749.

12. Orford J., *et al*. "Bleomycin therapy for cystic hygroma". *Journal of Pediatric Surgery* 30.9 (1995): 1282-1287.

13. Mahajan JK., *et al*. "Bleomycin as intralesional sclerosant for cystic hygromas". *Journal of Indian Association of Pediatric Surgeons* 9.1 (2004): 3-7.

14. Erikci V., *et al*. "Intralesional bleomycin sclerotherapy in childhood lymphangioma". *Turkish Journal of Pediatrics* 55.4 (2013): 396-400.

15. Jiang JP. "Local injection of bleomycinin lymphangioma in children: Analysis of 100 cases". *Chung Hua Wai Ko Tsa Chih* 27.12 (1989): 741-744.

16. Stringel G. "Hemangiomas and lymphangiomas". In: Ashcraft KW (ed) Pediatric Surgery, 3rd edition. Philadelphia, London, New York, St. Louis, Sydney, Toronto: W.B. Saunders Company (2000): 965-986.

17. Ogita S., *et al*. "OK-432 therapy in 64 patients with lymphangioma". *Journal of Pediatric Surgery* 29.6 (1994): 784-785.

18. Luzzatto C., *et al*. "Sclerosing treatment of lymphangiomas with OK-432". *Archives of Disease in Childhood* 82.4 (2000): 316-318.

19. Sichel JY., *et al*. "OK-432 therapy for cervical lymphangioma". *Laryngoscope* 114.10 (2004): 1805-1809.

20. Churchill P., *et al*. "Sclerotherapy for lymphatic malformations in children: a scoping review". *Journal of Pediatric Surgery* 46.5 (2011): 912-922.

21. Balis FM., *et al*. "General principles of chemotherapy". In: Pizzo PA, Poplack DG (eds). Principles and Practice of Pediatric Oncology. 4th edition. Philadelphia, Baltimore, New York, London, Buenos Aires, Hong Kong, Sydney, Tokyo: Lippincott Williams and Wilkins (2001): 274-275.

22. Dorr RT and von Hoff DD. "Drug monographs, bleomycin sulfate". In: Dorr RT, von Hoff (eds). Cancer Chemotherapy Handbook. 2nd edition. Norwalk, Connecticut: Appleton and Lange (1994): 227-235.

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