Original Article

INTRALESIONAL BLEOMYCIN INJECTION A PRIMARY THERAPY FOR PERIPHERAL LYMPHANGIOMAS

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ABSTRACT

Objective: To evaluate the efficacy of intralesional Bleomycin Injection (IBI) as a primary therapy for peripheral lymphangiomas in children.

Methodology: A prospective study was conducted at NICH Karachi from January 2003 to December 2005. Patients with peripheral lymphangiomas were included in the study. Exclusion criteria included previously treated lymphangiomas, infected lesions, intra-thoracic and intra-abdominal lesions. Thirty three patients were included in the study. All were treated with Intralesional Bleomycin Injection (IBI). After aspiration of fluid from the lesion, 0.5 mg/kg of Bleomycin diluted in saline was administered at different sites into the lesion. Depending upon the size of lesion & age of patient, procedure was performed in operating theatre under local or general anesthesia.

Results: Reduction in size was seen in 90% cases (n=29), out of them 30% (n=10) showed near complete disappearance and 63% (n=21) showed good response. Two patients (6%) showed poor response and they underwent surgery. Few patients had minor complications like fever, pain, redness and increase in the size after injection. All these complications were managed conservatively with symptomatic treatment and no patient required hospitalization.

Conclusion: IBI is an effective therapy for lymphangiomas, with results comparable to surgical excision. It has the added advantage of avoiding inadvertent injury to vital structures, scarring and other complications of surgery. We recommend it as a primary therapy for all peripheral lymphangiomas.

KEY WORDS: Bleomycin, Lymphangioma, Sclerosing agents Lymphangiomas management, Intralesional Bleomycin, effective modality.

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INTRODUCTION

Lymphangiomas are common congenital lesions. About 60% are seen at birth and 80-90% manifest by the age of two years.[1] Surgical excision has been the traditional treatment however incomplete resection, recurrence, possible injury to adjacent structures and surgical scars make it a less favorable option.[2] Intralesional sclerotherapy has been used successfully to achieve these goals using a variety of sclerosing agents.[1] Bleomycin is a anti-neoplastic agent and used in a variety of malignant lesions. It also has a local effect on the endothelial cells of the lymphangioma. The main concern in using Bleomycin is pulmonary fibrosis which is seen in patients getting higher doses and underlying pulmonary conditions. The chance of developing this complication is

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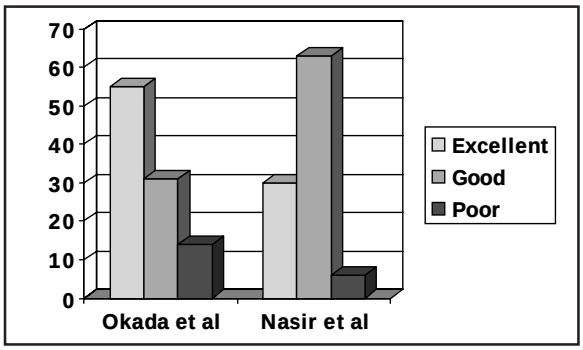

Comparison of Response to IBI in Percentage (%)

however negligible as very low dose is used for sclerotharpy.[3] This study determines the efficacy of Bleomycin aqueous solution at a lower dose as a primary therapy for peripheral lymphangioma.

PATIENTS AND METHOD

A prospective study was conducted in the department of Paediatric Surgery NICH Karachi from Jan 2003 to December 2005. A total of 33 children with lymphangiomas were included. Age ranged between one month and twelve years. Isolated peripheral lymphangiomas were included in the study. Patients having mediastinal, spinal, abdominal or visceral lymphangiomas and those with secondary infection were excluded. Operated patients and with poor follow-up (4 Cases) were also excluded from the study.

The procedure was performed on outpatient basis under local or general anesthesia in the operating theatre. Children were sedated with chloral hydrate where necessary. Using aseptic techniques, the lesion was aspirated through a hypodermic needle and Bleomycin aqueous solution was injected into the lesion with a dose not exceeding 0.5mg / kg body weight per dose.[1] Multilocular lesions were aspirated at more than one site to decompress the lesion before injection. The solution of Bleomycin was reconstituted to deliver 1mg / ml of BLM. Patients were kept in the day care ward for few hours after injection and allowed home with the instructions to come back immediately in case of any respiratory symptoms. The injection was repeated after four weeks if adequate response was not achieved. The cumulative dose of bleomycin was limited to less the 5mg / kg. The response to therapy was monitored clinically by measurement of the lesion in two dimensions and also by ultrasound at the beginning and end of the therapy. The response was graded as excellent (regression in size more than 90%), good (regression in size 50% to 90%) and poor (no response or less than 10%). The average follow up period was eight months (6-12 months).

RESULTS

A total of 33 patients were studied, out of them 60% were less than one year of age. There were 14 male and 19 females. The most common site was neck in 78% (26) cases, followed by chest wall 15% (5) and trunk 6% (2). The total dose of BLM ranged from 4 mg to 25 mg and the mean dose per kg of body weight was 1.4 mg after completion of the treatment. Reduction in the size of the swelling was noted from two weeks to 6 months and the requirement of sclerotherapy for each patient varied from one to four injections.

Reduction in size was seen in 90% cases (n=29), out of these 30% (n=10) showed near complete disappearance and 63% (n=21) had good response. Only in two patients (6%) response was poor and they underwent surgery. Most patients with excellent or good response were satisfied with the outcome. Complication included fever in 78% (n=26) cases, transient increase in size in 63% (n=20), cellulitis in 6% (n=2), discoloration of skin 6% (n=2). None of these patients developed serious systemic complication or pulmonary symptoms.

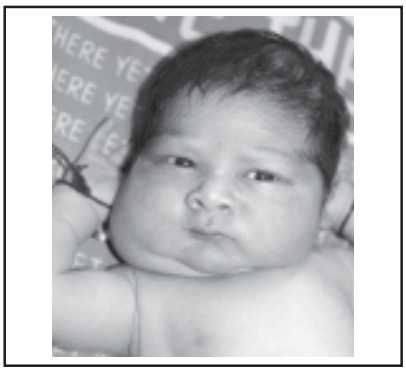

Fig-1: Right Cervical Lymphangioma (Pre-Injection appearance)

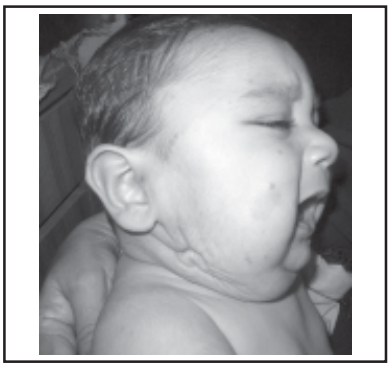

Fig-2: Post Injection regression of the lesion

DISCUSSION

Intralesional BMI was described by Yura et al in 1977 as an effective sclerosing agent for lymphangiomas.[4] Since then other studies also proved its efficacy in congenital lymphatic and vascular hamartomas. It is used as aqueous solution or oil emulsion. Its activity is enhanced when used in the form of micro sphere-in-oil emulsion and thus is retained in the lesion for a longer period of time.[5] Bleomycin has also been shown to be more effective for cystic type as compared with the capillary or cavernous lymphangioma.[6] Cervical, facial and axillary lymphangiomas are mostly of cystic variety. These are cosmetically important areas. Surgical excision may cause complications like nerve palsy, wound infections and residual scars. Therefore non- surgical option is a preferred method of treatment.

Intralesional Bleomycin solution has been effective in resolution of lymphangioma in 80% of the children in the present study and the results are comparable with those described by others.[1,2,5] The dose of Bleomycin used is much less than that likely to cause pulmonary toxicity. The summated dose with Bleomycin solution for lymphangioma has been described to be 5mg / kg and minimum dose per injection is 0.5mg per kg.[1-5] A proper dose after aspiration may have given better results. Our study showed good results after aqueous BMI; However comparing with better response in Okada et al study, we feel that we injected lesser dose due to fear of complications.

The incidence of complications with use of BMI has been minimal. Fever, redness and pain subside rapidly and do not cause long term sequel. This is also supported by other studies. Pulmonary toxicity is a potential serious side effect of Bleomycin therapy. Interestingly not even a single case has been reported after use of BMI for lymphangiomas. This risk is dose related. Complications are seen when total dose exceeds 400 mgs or a single dose exceeding 30mg / m^2 of body surface area. Elderly patients and those with underlying pulmonary disease are at increased risk.[6] Close monitoring is required for lesions of the anterior neck and floor of the mouth, for airway compromise after BLM injection in this area.[1-3]

Other sclerosing agents have also been used with variable success rates. Promising results have been reported with the use of OK-432, a low virulence group-A Streptococcus pyogenes cultured with penicillin. Ogita et al reported favorable results without recurrence or significant side effects.[7,8] But the availability and cost of OK-432 is a limiting factor in our setup.[7]

In Summary intralesional BLM is an effective and safe therapy for peripheral lymphangiomas. The incidence of complications is low and can further be reduced by using BLM in proper dosage. Transient fever and local pain are common but subside rapidly.

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