NON SURGICAL MANAGEMENT OF CYSTIC LYMPHANGIOMA

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Abstract: *Aim/Purpose:* To evaluate our experience of 19 patients of lymphangioma who were treated by intralesional Bleomycin. **Materials and Methods:** Nineteen patients of lymphangioma aged between 16 days to 11 years were managed in the department. The male-female ratio was of 2:1. Commonest sites were in the neck (58%) followed by axilla (21%). The patients were treated by intralesional bleomycin injection. Bleomycin was given at a dose not exceeding 0.5 unit/kg/dose at interval of 2 weeks. Reduction in size of the mass was noted in between 2 weeks to 16 weeks and number of injections required for each patient varied from 1 to 6. Follow up ranged from 1-7 years. **Result:** In injection group, significant reduction of mass was noted in 84% (n=16) and 57% (n=11) of them showed complete disappearance. No serious complications were noted in any patient. **Conclusion:** Our experience showed that Bleomycin in aqueous solution is a good sclerosing agent in the management of lymphangioma.

Keywords: Lymphangioma, Bleomycin, Sclerosant

INTRODUCTION

Cystic lymphangioma is a congenital lymphatic malformation. It can lead to morbidity because of cosmesis, compression of adjacent organs (*i.e.* respiratory obstruction, dysphagia, nerve compression and malocclusion) or can result in local inflammation, infection, sinus formation and hemorrhage. Spontaneous resolution occurs infrequently. Surgical excision is a treatment option but it has unacceptable rate of complications and recurrences. Various alternative approaches had been tried. Recently local injection of bleomycin has drawn attention as an efficacious non-surgical measure against primary moderately sized, residual and recurrent lymphangioma. We present our experience with this modality of treatment.

MATERIALS AND METHODS

Nineteen cases of Lymphangioma were admitted and treated between 1997 to 2000 in the Department of Pediatric Surgery, King George Medical University, Lucknow, India. Diagnosis was made mainly on clinical finding. Doppler ultrasound was done in mixed lesions to exclude hemangiomatous components. CT scan was needed in few. Fine Needle Aspiration Cytology (FNAC) was done in doubtful cases. Serial clinical photographs and size measurements were done before and after Bleomycin injection and in follow up. Procedure was performed on outpatient basis without local or regional anesthesia after taking consent from parent. After local part preparation, cyst was aspirated and maintaining intra cystic position of needle (20-24 gauge) diluted bleomycin was injected with a dose of 0.1 to 0.5 unit/kg/dose. One unit of bleomycin was diluted in 10 ml of 0.9% saline. If the cysts were not communicating with each other they were aspirated at multiple sites and Bleomycin was injected at multiple sites. Repeat dose were offered after 2-3 week interval depending on clinical response. Total numbers of injections needed were noted and total dose was limited to less than 5 unit/kg. The response to treatment were monitored by clinical (length, breadth and area)

and radiological (ultrasound) method. The response was graded as excellent when complete disappearance, Good (>50% reduction) and poor (<50% reduction).

Mean follow up period was 3.5 years (range 1 year to 7 years).

OBSERVATIONS AND RESULTS

Nineteen patients of lymphangiomas were treated. 13 were male and 6 were female. Commonest site of cystic hygroma was neck (posterior triangle of neck 58%) followed by axilla (21%) (Table I). The size of the lesion varied from 4 cm to 15 cm.

Majority of patients were less than 6 months of age. Youngest patient was 16 days old, weighted 3 kg and had right axillary cystic hygroma. Oldest patient was 11 years old female who had lesion on the right side of the neck (Table-II).

Nineteen patients were given intralesional chemotherapy. One patient showed complete disappearance after single dose, 10 patients showed complete disappearance of mass after 3 - 5 doses of Bleomycin therapy (Figure I & II) and remaining showing marked reduction. No patient developed recurrence. Reduction of mass was usually seen between 2 weeks to 16 weeks. For cystic lesion good response were noted even after single injection. Out of 19 cases, 11 patients showed an excellent response, 5 patients showed good response and 3 patients poor response. There were no serious side effects. Most of side effects appear within 24-48 hours after injection and subsided without much treatment. One patient with chest wall lymphangioma developed infection after first dose of Bleomycin and was managed by Intravenous antibiotics. (Table III).

Three patients had to undergo surgical resection because of poor response. Histopathology of resected specimen showed dense fibrosis, loss of endothelium lining of cyst and infiltration

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Fig 1: Cystic hygroma in a 16 days male baby before Bleomycin injection

by lymphocytes, and macrophages. Extension of fibrosis was also noted in surrounding few centimeter of normal tissue.

DISCUSSION

Lymphangioma is a common developmental anomaly of the lymphatic system. It is characterized by the formation of a multilocular cystic mass of variable size. Majority of lymphangiomas occur in the head and neck area.¹ Other site includes the mediastinum, axilla, arm, chest wall, abdomen, inguinal region and leg. About 50% present at birth and 80-90% are detected before the age of two years². Few cases manifest in adulthood³. Lymphangioma has been classified into three varieties: (a) Lymphangioma simplex, composed of capillary sized thin walled lymphatic channels, (b) Cavernous lymphangioma and (c) Cystic lymphangioma, composed of cysts of few millimeters to several centimeters in diameter. Different varieties frequently co-exists.⁴ Usually lymphangioma are found to contain a clear lymphatic fluid unless there is infection or hemorrhage inside.

Surgery had been the mainstay of treatment of lymphangioma. But even in the most expert hands, it still carries a complication rate as high as 12-33%, and a recurrence rate of 15-53%.^{4, 5, 6, 7} Because of surgical complications, multiple non-surgical strategies have been attempted in order to cure the lesion with minimal complications.⁷ They include radiotherapy, combined radio-chemotherapeutic approach and lasers. CO₂ and Nd-YAG lasers are more extensively used for localized laryngeal lymphangiomas⁸. Use of an argon beam coagulator has been reported in a 13 year old girl with life threatening total abdominal lymphangiomatosis.⁹ However, none of these treatments are sufficiently effective.

The use of sclerosing agents in treatment of lymphangiomas is an old one. After spontaneous infection, lymphangiomas were noted to shrink or even completely regress. The epithelium lining the cystic spaces is destroyed, with subsequent decrease in lymph fluid production and collapse of the cysts. Many different drugs were used to mimic what may occur spontaneously. The drugs included alcoholic solution of zein (Ethibloc)¹⁰, acetic

acid¹¹, fibrin sealant¹², triamcinolone¹³ but none worked as expected. One of the main problems with sclerosing drugs is their tendency to spread outside the lesion once injected. This can cause unpredictable damage to surrounding structures and make subsequent surgery more difficult. Hence surgical treatment remained the first option.

Fig 2: Same patient after 2 cycles of Bleomycin showing complete disappearance of swelling.

In 1977 bleomycin, was proposed as a new sclerosing agent for cystic hygroma.^{14,15} After that several trials have been reported using bleomycin with good or excellent results in up to 88% of cases.^{16,17} Bleomycin is an antibiotic known to have some antitumoral activity and also have local sclerosing effect on endothelial cells of cysts wall of lymphangioma. Intralesional Bleomycin microsphere in oil-emulsion has reported good response because it is retained for longer period of time.^{17,18} Report of intralesional aqueous solution of Bleomycin is limited^{16,19}. In our study, intralesional aqueous solution of Bleomycin has good response in cystic type of lymphangioma as compared to cavernous and other complex lymphangioma¹⁹. One patient showed complete disappearance after single dose of Bleomycin. This was a complete cystic lesion. 10 patients showed complete disappearance after 3 to 5 doses of Bleomycin. They were cystic and cavernous lesions (mixed lesions). Therefore, case selection for this mode of therapy is important. Intralesional bleomycin has been effective in complete disappearance of cystic hygroma in 61% of patient in the present study and results are comparable with those described by others^{16, 17, 19}. Pulmonary toxicity is a potential side effect of bleomycin therapy. This risk is related to dose. If total dose exceeds more than 400 units or single dose exceeds 30 units/m² of body surface area, the risk increases. Elderly patients and those with underlying pulmonary disease also are at risk.⁷

Recently favorable results have been reported by use of OK-432 (a low virulence strain of *Streptococcus pyogenes* cultured with penicillin-G) without recurrence or significant side effects. But its availability and cost factor limits its use²⁰.

CONCLUSION

The role of sclerosing agents in the treatment of cystic hygroma and lymphangioma are quite encouraging, more so with bleomycin. Our study concludes that intra-lesional aqueous solution of Bleomycin, as sclerosant, appears to be a safe and effective alternative to surgery in the treatment of cystic lymphangioma. More centres should undertake the study and come with optimum therapies.

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Table-I: Site of Lesion

Site of lesion	Total
Neck	11
Axilla	4
Parotid	1
Chest wall	1
Buttock	1
Abdomen & Upper thigh	1

Table-II: Age of Patients

Age of admission	Total
0-6 months	8
6-12 months	2
12-24 months	3
24-36 months	1
> 36 months	5

Table-III: Complications after Bleomycin Injection

Complications	Number
Fever	2
Local pain	8
Erythema	4
Hematoma and cellulitis	1

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