INTRALESIONAL BLEOMYCIN SCLEROTHERAPY: AN EFFECTIVE TREATMENT OF CYSTIC HYGROMA IN CHILDREN

Naima Rasool, Mushahid Aslam, Zafar Iqbal Gondal, Shehla Kanwal, Farzeen Sharaf, Hashim Zaidi, Asrar Ahmad, Javed ur Rehman, Habib ur Rehman, Chaudhry Aqeel Safdar

Military Hospital Rawalpindi

ABSTRACT

Objective: To study the outcome of intralesional sclerotherapy with injection Bleomycin in cystic hygroma in children.

Study Design: A case series.

Place and Duration of Study: The department of Pediatric Surgery at Military Hospital, Rawalpindi, Pakistan from Jan 2011 to Dec 2012.

Patients and Methods: All patients with peripheral cystic hygroma (CH) presenting to us, were enrolled in the study. The cyst was aspirated in the operation theater under sedation. Injection bleomycin 0.5 mg /kg diluted in 10-15 cc of distilled water was injected in the cyst at multiple sites. Injection was repeated after every month depending upon the response.

Results: A total of 30 patients reported to the department with superficial cystic hygroma, 12 were males (40%) and 18 were females (60%), age ranged from 15 days to 8 years. Cervico-facial was the most common site. Results were assessed in terms of excellent (complete resolution), good (> 50% reduction in size) and poor (< 50% reduction in size). In 2 patients, complete resolution was achieved after maximum seven shots of intra-lesional bleomycin injections (IBI), while 18/30 (60%) resolved after single dose. Twenty seven patients (90%) resolved completely, 2 (6.6%) had good response, 1 (3.3%) showed poor response. Minor complications were noted which were treated by symptomatic treatment. No major side effects or recurrence were noted in maximum 2 years follow up.

Conclusion: Intralesional bleomycin sclerotherapy is safe and effective as primary treatment in cystic hygroma.

Keywords: Cystic Hygroma, Intralesional Bleomycin Injection, Peripheral lymphangiomas, Sclerotherapy.

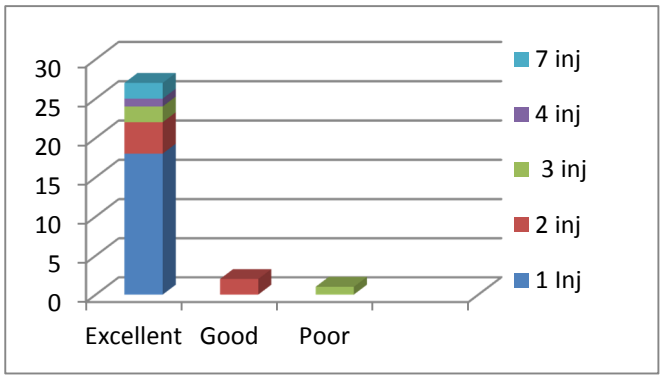
INTRODUCTION

Peripheral lymphangiomas are congenital, hamartomatous malformations of lymphatic system involving skin and subcutaneous tissues. It is classified into three sub types: which are capillary, cavernous lymphangioma and cystic hygroma (CH)[1]. CHs are cystic lesions filled with straw colored fluid. CHs are further categorized in micro or macro cystic varieties, depending upon their sizes. It was first described in 1828 by Redenbacker[2]. There are many modalities described for treatment of CHs. Resection of abnormal tissues was thought to be the main and most effective treatment modality in CHs but complications of surgery like inadvertent injury to the surrounding tissues, incomplete excision, scar and recurrence make it less favorite[3]. The complications of extensive surgery compelled surgeons to switch on to the less invasive and more effective treatment. Intralesional bleomycin injection (IBI) has been used as alternative treatment to achieve almost same rather cosmetically better results[2,3]. In Military Hospital, surgeons used to operate upon patients with CHs but due to convincing results of IBI reported in national and international literature, we have started this mode of treatment. Military Hospital is not only a tertiary care hospital but a referral hospital for all Armed Forces set ups; we have an influx of non entitled patients from the city but referred entitled patients from all over the country as well. We share our initial experience of managing 30 patients of CHs with IBI at Pediatric Surgery Department, Military Hospital.

Correspondence: Dr Naima Rasool, Department of Paediatric Surgery, MH Rawalpindi
Email: dr_naima_r@yahoo.com
Received: 05 April 2013; Accepted: 16 Sep 2013

METHODOLOGY

Patient's data was collected prospectively from Jan 2011 to Dec 2012. A total of 30 patients with peripheral CH were enrolled in the study.



Figue-1: Various responses to intralesional bleomycin injection (IBI) in cystic hygroma (CH).

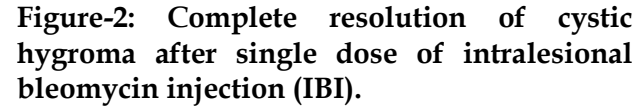


Figure-2: Complete resolution of cystic hygroma after single dose of intralesional bleomycin injection (IBI).

Figure-3: Good response of cystic hygroma after 4 doses of intralesional bleomycin injection (IBI).

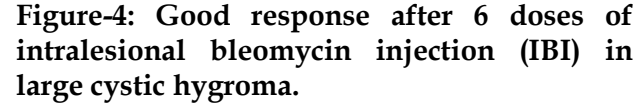


Figure-4: Good response after 6 doses of intralesional bleomycin injection (IBI) in large cystic hygroma.

All patients with peripheral cystic hygroma, presented in outpatient included in study. Patients having lesions with arterio venous malformations, thoracic or abdominal lymphangiomas and cysts less than 5 cm were excluded from the study. This data was collected after informed consent of the parents. Age of patients ranged from 15 days to 8 years. Diagnosis was made on clinical examination in most of the patients; doppler ultrasound was advised to exclude arteriovenous malformations. After preoperative counselling of parents about method and potential side effects of the IBI, procedure was done in the operation theater. One hour prior to the procedure the child was sedated by oral chloral hydrate in a dose of 25 mg/kg. An 18 gauge needle was passed through the lesion and fluid was aspirated from the cyst. Injection bleomycin in a dose of 0.5 mg/kg diluted in 10-15 cc of distilled water was injected into the lesion by rotating the same needle in 3-4 directions. Patients were kept under observation for 8-24 hrs and immediate side effects were noted. Oral analgesics were given routinely for at least 24 hrs.

Patients were called after 3 weeks and response was noted by clinical examination and measurement of size of the lesion. Dose of IBI was repeated after 4 weeks for the residual cysts. Response was noted in terms of excellent (complete disappearance), good (more than 50% reduction in size of cyst) and poor (less than 50% reduction in size of cyst).

Data analysis

Data was analyzed using SPSS version 15. Continuous variables like age and number of injections were derived as mean while categorical variable like gender, site of lesion, outcome of treatments and complications were described in percentages/frequencies.

RESULTS

Out of 30 patients, 12 (40%) were males and 18 (60%) were females. Cervico-facial region was the commonest site found in 19 patients (63.33%), followed by axilla in 6 patients (20%). Rest were in the lower abdominal wall, inguinal region and lower leg, the youngest patient was of 15 days while the oldest was 8 yrs of age (median age 4 years). Only three patients had cysts of size more than 10 cm, all other patients had cysts of size 7-10 cm. Eighteen patients (60%) showed complete disappearance of the lesion after single injection, 6 patients (20%) required second dose, in 3 patients (10%) injections were given 3 times, 1 (3.33%) vanished after 4 injections and 2 (6.66%) patients required 7 injections. In 27 (90%) patients the lesion completely disappeared and showed excellent results. Two patients (6.66%) showed good response and parents did not opt for further injections and only 1 patient (3.33%) showed poor response after 3 doses and parents opted for surgical excision (fig-1).

No serious side effects like pulmonary fibrosis were noted. Three patients had vomiting (3-4 episodes in first 24 hrs only). Six patients had complaints of pain and early increase in size (possibly due to inflammation), which were managed with the oral analgesics. Other minor complications like discoloration of skin, laxed over-lying skin and small residual fibrotic nodules were also noted. No recurrence noted in 2 months to 2 years period of follow up.

DISCUSSION

Cystic Hygroma (CH) is the cavernous type of peripheral lymphangioma, involving skin and superficial tissues. It is a multi locular cystic mass; cysts may be of variable sizes, involving head and neck in more than 70%, followed by axilla, abdomen and extremities[3]. A large lesion in the neck can cause significant cosmetic deformity, compression of vital structures, respiratory obstruction, dysphagia and symptoms of nerve compression[4]. Surgery has been the main stay of treatment but even in very skilled hands and with meticulous surgical technique, it carries significantly unfavorable results, including damage to adjacent structures, haemorrhage, scar, lymphatic discharge from wound and recurrence[3]. Many alternative non surgical treatments are described in literature including radiotherapy, cryotherapy, diathermy, laser, chemotherapy and intralesional sclerotherapy. Sclerosants that have been known are sodium morrhuate, dextrose, hypertonic saline, tetracycline, doxycyline, acetic acid, ethanol, boiling water, alcoholic solution of zein (ethibloc), fibrin sealant, triamcinolone, OK-432 and bleomycin[5]. These sclerosing agents are thought to work by ablating the endothelial cells of the disrupted lymphatic feeding into the lymphocele, decrease in lymph fluid production and eventually leading to collapse of the cyst[6].

Bleomycin is an anti-neoplastic agent, which was first used in 1966, in a variety of malignant lesions where it works by inhibition of DNA synthesis. Intralesional Bleomycin as a sclerosing agent was used for the first time by Yura et al in Japan in 1977 for CHs and produced promising results[7]. It causes irritation of endothelial lining of CHs, which leads to non specific inflammation, fibrosis and involution. This reaction depends upon the dose of drug in relation to the per unit surface area of the lesion[8]. The recommended dose of IBI is 0.3-3 mg/kg/session. The frequency of session may be different from 1 week to 6

weeks as suggested in many studies[8-10]. Similar to these studies, our patients also responded after 2-3 weeks of the injection. It is used either in aqueous solution or oil emulsion, but it is more effective in oil preparation, because it stays in contact with tissues for longer period of time. The maximum cumulative dose of IBI is 5 mg/kg or 30 mg/(m^2) [2,9].

In our study, the male to female ratio was 1: 1.5, which is unlike other studies where male patients were more[9-11]. The commonest site was head, face and neck, almost 63% of lesion found in these sites, which is similar to other reported series[6,8,10]. Out of 30 lesions, 18 resolved after single dose (fig-2), rest of the 11 responded after 2-7 doses (fig-3,4). Only one patient did not give desired results after 3 injections, and it was surgically excised afterwards. Many studies have reported favorable results of IBI. Rozman et al in 2011 reported a series with 63%, 20%, and 17% best, good and poor response respectively[9]. Our study showed almost identical results with these previous national and international reports[9-12].

The reasons of failure or poor response of IBI are variable; this may be either mixed type of lesion, very small sized cyst or drug properly not injected in cyst[9]. Pulmonary toxicity is a known serious side effect of bleomycin, mostly noted when dose exceeds the maximum cumulative dose. In literature, studies suggested that, this is seldom noted with such low dose[9,10]. In our cases, minor side effects like pain due to early inflammation, vomiting, fever, laxed skin, regional pigmentation and residual fibrous nodule were noted. These are at par with other studies as well[3,9,13]. Although recurrence of CHs is documented in some studies, but none of our patients turned up with recurrence in maximum follow up of 2 years[7,9,10].

CONCLUSION

Intralesional bleomycin injection sclerotherapy is a safe and effective therapy for cystic hygroma with minimal complications.

REFERENCES

1. Donnelly LF, Adams DM, Bisset GS. Vascular malformations and hemangiomas: a practical approach in a multidisciplinary clinic. Am J Roentgenol 2000; 174:597-608.
2. Shankar VN. Lymphvasculogenesis and Lymphangioma – an Update. J Cancer Sci Ther 2011; 3: 5.
3. Mirza B, Ijaz L, Saleem M, Sharif M, Sheikh A. Cystic hygroma: An overview. J Cutan Aesthet Surg 2010; 3: 139-44.
4. Camitta BM. Abnormalities of lymphatic vessels. In: Kliegman RM, Behrman RE, Jenson HB, Stanton BF, eds. Nelson Textbook of Pediatrics. 18th ed. Philadelphia, Pa: Saunders Elsevier 2007: chap 489
5. Acevedo JL, Shah RK, Brietzke SE. Nonsurgical therapies for lymphangiomas: a systematic review. Otolaryngol Head Neck Surg 2008; 138: 418–424.
6. Hassan H, Aly KA. Management of cystic lymphangioma: experience of two referral centers. Annals of Pediatric Surgery 2012; (8) 123-128.
7. Sham ME, Sultana N. Vascular anomalies in maxillofacial region-Review. J Oral Maxillofac Surg Med Pathol 2012; 24: 137-146
8. Kumar V, Kumar P, Pandey A, Gupta DK, Shukla RC, Sharma SP et al. Intralesional bleomycin in lymphangioma: An effective and safe non-operative modality of treatment. J Cutan Aesthet Surg 2012; 5: 133-136.
9. Rozman Z, Thambidorai RR, Zaleha AM, Zakaria Z, Zulfiqar MA. Lymphangioma: is intralesional bleomycin sclerotherapy effective? Biomed Imaging Interv J 2011; 7:e182011.
10. Niramis R, Watanatittan S, Rattanasuwan T. Treatment of cystic hygroma by intralesional bleomycin injection: experience in 70 patients. Eur J Pediatr Surg 2010; 20:178–182.
11. Saddal NS, Sharif A, Ahmad S, Mirza F, Akhtar N, Anwarul-Haq, et al. Intralesional bleomycin injection a primary therapy for peripheral lymphangiomas. Pak J Med Sci 2007; 23: 220-2.
12. Kella N, Rathi PK, Sheikh U, Qureshi MA. Our experience of bleomycin sclerotherapy for peripheral lymphangioma in children and review of the literature. Pak J Med Sci 2011; 27: 60-3.
13. Rawat JD, Sinha SK, Kanojia RP, Wakhlu A, Kureel SN, Tandon RK et al. Nonsurgical management of cystic lymphangioma. Indian J Otolaryngol Head Neck Surg 2006; 58:355-57