



EFFECT OF INTRALESIONAL BLEOMYCIN INJECTION IN LYMPHANGIOMA: A RETROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT

Lymphangiomas are benign hamartomatous lymphatic tumours occurring at all ages and nearly all regions of the body, most frequently seen in the neck (75%), axilla (20%) and inguinal area (2%). Surgical resection for complete removal in many cases is impossible. Tumour recurrences and nerve injuries are common complications following surgery therefore alternate to surgery as the treatment choice is not only desired by surgeons but also by the patients. Bleomycin has been very effective in the treatment of Lymphangiomas. In fact, it would be advisable to the upcoming surgeons to not even attempt to excise this benign tumour. We present a series of five cases encompassing various age groups visiting out department during last seven years who were diagnosed to have Lymphangiomas and who successfully got treated with Bleomycin injections and the best part, patients were very much satisfied as the cosmesis was maintained.

KEYWORDS

Intralesional Bleomycin Lymphangioma

INTRODUCTION

Lymphangiomas are benign Hamartomatous tumour of the lymphatics. Commonly found in the neck 75%, axilla 25%. Most of them are evident at birth (65%) while the remainder becomes evident by the age of 2 years. The reported incidence is quite variable, ranging between 1 in 1000 and 16000 live births.

The main stay of the therapy is surgical excision but due to its infiltrations along nerve and muscles total excision is not always possible without them getting damage, also there are chances of recurrence due to the remnants post-surgery. Moreover, the chief complains in most of the patients are the deformity it produces, and multiple incision scars is again the main concern that goes against the surgery. Quest for the alternative to surgery have been there since ages. Many sclerosing agents have been tried but due to the safety profile, availability and cost effectiveness Bleomycin stands out to gain its foothold among the treating surgeons.

The sclerosing agents causes irritation of the endothelial lining of the Lymphangioma which leads to inflammation, fibrosis and involution. In the present study, we have evaluated the clinical profile of all the lymphangioma cases coming to our unit and evaluated the efficacy of intralesional bleomycin as a sclerosing agent in its management.

Surgical excision is only possible when after multiple Bleomycin injections the cyst has involuted and has fibrosed because by this time the dissection becomes easier.

MATERIAL AND METHOD

All patients with a diagnosed case of Lymphangioma were included in the study. The bleomycin comes in a vial of 15 IU, which has to be diluted with 10 ml of sterile water to make it a concentration of 1.5 mg/ml. It was stored in a refrigerator in the normal temperature. All patients with soft cystic swellings over the head and neck region underwent CECT face and neck for final diagnosis. FNAC was done only in doubtful patient.

All patients were taken under general anaesthesia. Post operative monitoring of the vitals were done amongst all the patients. The ultrasound was used to localize the cyst. Wide bore needle 18 GZ with 10 ml syringe was take for aspirating the content, when filled the syringe was removed keeping the needle in the same place. The aspirate was kept in a separate container and diluted bleomycin was loaded.

The aspirate was measured, and Bleomycin was taken in one fifth of the amount of the aspirate. The Bleomycin was infused slowly once

under the ultrasound guidance. Postoperative the patient was monitored for body temperature and any change in the respiratory signs and symptoms. The aggregate dose was limited to less than 5 unit/kg. The response to the treatment was monitored clinically/Ultrasonographically minimum twelve weeks. The response was graded as excellent when complete disappearance, Good (>50% reduction), and Poor (<50%) reduction. Mean follow up period ranged from 6 months to one year.

Case 1

This patient was a seven-year-old girl presented with a soft swelling over the left cheek. The swelling was noted more since last two years. On examination of the swelling, it was soft, compressible, and non-tender. Xray PNS showed a normal sinus thereby ruling out any sinus pathology. The fluid was aspirated, and cytological examination showed mature lymphocytes suggestive of benign lesion probably a lymphangioma. Ultrasound showed a thin-walled cystic lesion below the skin. CECT of the face showed a thin-walled cystic lesion with multiple septations therefore confirming it to be a lymphangioma. The patient was posted for aspiration of the content and simultaneous infusion of the Bleomycin in the same conventional dose. Post operative review after two weeks showed a marked reduction of the cheek swelling with almost no remnant left and both cheeks were looking similar.



Fig 1. Pre and Post effect of Bleomycin injection in a seven-year-old female

Case 2

This 25 years old male had presented with swelling over the right side of the neck over a period of four years. The swelling was slow progressive, soft, and diffuse. CECT neck showed a non-enhancing lesion with multiple septations suggestive of lymphangioma. The patient was posted for intralesional infusion of Bleomycin into same syringe through which the cyst was aspirated. The patient was reviewed two weeks later which showed almost no remnant and there was no change in the colour of the skin.



Fig 2 Pre and Post effect of Bleomycin injection in a twenty-five-year-old male

Case 3

This patient was the youngest female in our series, was four years old. She presented with swelling over the left upper neck, noted by her mother two and a half months back. The swelling was diffuse, soft compressible with a positive transillumination test. The fluid was aspirated and sent for cytological test. Cytology revealed mature lymphoid cell and scattered cystic macrophages in a proteinaceous background suggestive of a benign cystic lesion lymphangioma. CECT neck revealed a well-defined cystic lesion, smooth walled with multiple septations suggestive of lymphangioma. Patient was posted for Intralesional Bleomycin infiltration under general anaesthesia in the ratio of 1:5. The vial containing 15IU of bleomycin powder was mixed with 10 ml sterile water to make a concentration of 1.5 mg/ml. 18 GZ needle in a 10 ml syringe was taken to aspirate the content and to infuse Bleomycin intralesionally in the same syringe. The post operative period was uneventful with no complications noted. The patient was reviewed after two weeks, and it showed marked improvement, but still small remnant was seen in the ultrasound. The mother was counselled for a second sitting to which she agreed, and the patient was posted for Intralesional infiltration with Bleomycin and again the patient was reviewed after two weeks. This time postoperatively no remnant was noted.



Fig 3 Pre and Post effect of Bleomycin injection in a four-year-old female

Case 4

This patient was a twenty-one-year-old male who had noted a soft diffuse swelling over the right side of the upper neck more since last two years. Ultrasound of the upper neck revealed a cystic swelling of the size 8x6cm extending from below the body of the mandible to the level of thyroid notch and from mid-line of the neck to the posterior border of the Sternomastoid. CECT neck revealed a well-defined multi septate cyst over the right side of the neck involving the anterior and posterior triangles of the neck. Patient was posted for Bleomycin infusion. Two weeks later the patient was reviewed, the patient was very much satisfied as the there was marked reduction in the size with no change in the colour of the skin.



Fig 4 Pre and Post effect of Bleomycin injection in a twenty-one-year-old male

Case 5

Patient was 19 years old male with complain of swelling over the right submandibular region noted since last 4 to 5 years, it was a diffuse

swelling soft in consistency, ultrasound of the neck revealed a cyst measuring 4.5 x 2cm over the submandibular region with few septa and no solid component. CECT neck revealed a well-defined multiseptated thin walled cystic swelling on the right submandibular region extending antero-superiorly along the inner aspect of the ramus of the mandible closely abutting the digastric muscle. Ultrasound guided aspiration of the cystic fluid was done, and the Bleomycin was injected via the same syringe the ration of 1:5 of the Bleomycin and the fluid was maintained. Patient was followed two weeks later and showed a clinical improvement of 50% the patient and parents were counselled to undergo a second sitting to which they have readily agreed



Fig 5 Pre and Post effect of Bleomycin injection in a nineteen-year-old male

RESULT

All patients with a diagnosis of Lymphangioma who required Intralesional injections of Bleomycin were included in the study. Two patients were female and three were males. The two young females were of four years and seven years. The two males were in their twenties and one were a teen. One female had a lymphangiomatous lesion over her cheek and the rest had swelling over their neck region. The patient with cheek swelling required two dose of Bleomycin injections in a span of 2 months, rest were done with single injection. Three patients had Excellent response to Bleomycin and two patients had a good response. None of the patients experienced any side effects to Bleomycin

DISCUSSION

Lymphangioma is a common congenital lesion arising from malformed lymphatic system. About 60% of it appears at birth, 80% manifest within two years of life or may present at any time in life^[1]. The most common site of occurrence of these lesions is the Head and Neck (75%) with no sex predisposition. Lymphangioma was classified as Macrocytic (>1cm), Microcystic (<1cm) or Mixed containing both components as suggested by Ogita S et al^[2]. Lymphangioma are thought to arise from a combination of the following: failure of the lymphatics to connect to the venous system, abnormal budding of the lymphatic tissue and sequestered lymphatic rests that retain their embryonic growth potential. These lymphatic rest can penetrate adjacent structures or dissect along fascial planes and eventually becomes canalized. The nature of the surrounding tissue determines whether the lymphangioma is Capillary, Cavernous or Cystic^[3]. Lymphangioma has been categorized into three varieties a) Lymphangioma simplex, composed of capillary sized thin-walled lymphatic channel b) Cavernous lymphangioma c) Cystic lymphangioma, composed of cysts of few mm to several cm in diameter. Different varieties frequently coexist.

Surgery had been the mainstay in the treatment of Lymphangioma. However even in the most experienced hands it still carries a complication rate as high as 12-33% and a recurrence rate of 15-53%^[4]. Sclerotherapy provides a viable alternative to surgery in patient with macrocystic lymphatic malformation^[5]. Bleomycin and OK-432 are currently the most popular sclerosants. Desired effect of Bleomycin is achieved by its local action, which depends on availability of drugs per unit surface area of the lesion^[6,7].

Pradyumna Pan et al had a study on 36 patients, 27 were male and 9 females, 21 patients were seen before 1 year of age. 30 patients were cystic hygroma, intralesional Bleomycin injection showed complete resolution in 16 patients (44.4%), good in 17 patients (47.2%), poor in 3 patients (8.3%). The cavernous variety showed excellent response (100%)^[8].

Salim Bilici et al did study on 20 cases, where 11 were males and 9 females. Showed excellent response in 50% cases (10/20), good response in 40% (8/20) of cases and poor response in 1 patient^[9]. V Kumar et al in their study on 35 patients, 19 patients were seen before

first year of age. 28(80%) were cystic hygroma 1 cavernous and 6 were of mixed type, intralesional Bleomycin infiltration showed excellent response among 7(20%), good in 26(74.29%), and poor in 1(3.5%) case 10.

Literature published from time to time has also showed that it's not only Lymphangioma of the head and neck that is effective, even the Lymphangioma of other region such as Tongue 11, Chest wall and Axilla are also effective on Bleomycin injection^[10].

In our 5-case series, 2 were females and 3 were males. The youngest patient was female of 4 years old. All cases of lymphangioma were of head and neck region commonly involving the submandibular region. One female had a lymphangioma of the cheek region. Preliminary USG was done in all cases followed by CECT head and neck and it was found to be macrocystic, multilocular lesions in 4 cases and one case had a solitary cystic lesion involving the left cheek. Intralesional Bleomycin infiltration was done in all cases. 4 cases had excellent response with almost total regression of the swelling, one patient had good response, one of them underwent second intralesional Bleomycin infiltration and waiting for the post op follow up. None of the patients experienced any of the side effects of Bleomycin.

CONCLUSION

Bleomycin injection is very effective for treatment of macrocystic and mixed type lymphangioma of the head and neck or any other surface area of the body. In most cases it may obviate the need for surgery and the resultant scar mark or other complications of surgery such as neural paralysis or bleeding, in fact it is easier and more comfortable to handle the recurrence with intralesional Bleomycin than surgery without complication.

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