

Efficacy of intra-lesional bleomycin sclerotherapy for the treatment of hemangioma-Case report

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Abstract:

Vascular anomalies are one of the challenging diseases to manage, presenting in different age groups and with varied clinical course, of which hemangiomas are common which are vasoproliferative neoplasms and can occur in any organ. Depending on the age at presentation they are classified as congenital and infantile hemangiomas. Not much attention has been paid regarding the imaging and treatment modalities of vascular malformations particularly hemangiomas due to scarcity of literature related to this condition. Majority of

these vascular malformations are self-limiting, but in a few cases these lesions may grow with age which can be treated surgically or by sclerotherapy which has been the safe, less invasive, economical and easily available modality for treating hemangiomas. Bleomycin is the main sclerosing agent used which is a cytotoxic anti-tumor antibiotic which was later found to have anti-cancer properties. In our case, a 9 year old male child presented to our institution with a lump in the left side of abdomen since birth. Contrast enhanced CT abdomens was suggestive of a vascular malformation. Patient was treated with sclerotherapy with intralesional bleomycin for which good results were noted by decrease in the size and vascularity of the swelling.

Key words: hemangioma; vascular anomalies; bleomycin; sclerotherapy

Introduction:

Vascular malformations and hemangiomas are hamartomas that are grouped into a class of benign tumors and can be found anywhere in the body. Virchow was the first to categorize vascular anomalies based on histologic features¹. Later Mulliken and Glowacki proposed biologic classification based on clinical presentation, histopathologic features². The prevalence varies in different age groups being 2% in neonates (increased prevalence in preterm neonates), upto 10% till the age of 1 year. These lesions are more common in infancy and childhood. Simultaneously multiple organs may be involved including hepatic, pulmonary, mediastinal, gastrointestinal, cerebral hemangiomas. These lesions are benign comprising of irregularly arranged vascular tissues. Hemangiomas are characterised by rapid proliferation of endothelial cells. The etiology of hemangioma remains unknown. Three phases were noted in the evolution of hemangioma namely rapid proliferating phase, involuting phase and involuted phase³. The clinical course, severity and complications of the condition depends on the site of occurrence of the lesion like airway obstruction, visual disturbances. Although these lesions frequently resolve, in 5% of cases complications such as pain, ulceration, bleeding from local site, residual scarring is seen.

Case Report:

A 9 year old male child presented to our institution with a lump in the left side of abdomen since birth. As per the history given by parents, child had swelling over left side of abdomen since birth which was small in size comparable to the size of a lemon and was static till 6 years of age .The swelling had gradually increased in size since last 18 months and had attained the present size. Child also had history in difficulty in breathing since last 6 months.

On examination there is a single, oval shaped lump in the left side of abdomen occupying almost entire left half of abdomen measuring approximately 10*5 cm, soft in consistency with well demarcated margins, moving with respiration, skin over the swelling is erythematous, surrounding skin is normal (Figure.1). USG abdomen was done suggestive of ?lymphatic malformation and was advised for CT abdomen. Contrast enhanced CT abdomen was done suggestive of large extensive subcutaneous lesion on the anterior abdominal wall suggesting possibility of lymphatic malformation, second possibility of slow flow thrombosed vascular malformation.



Figure 1: showing huge lump occupying left half of abdomen with an erythematous surface

Interventional radiologist opinion was taken for further management and was advised intralesional bleomycin sclerotherapy. After obtaining informed consent from the parents, treatment using Bleomycin injection was decided as the first treatment option. Bleomycin injection was performed under local anesthesia. Procedure was uneventful. Patient was given analgesics after the procedure for control of pain and fever. Evaluation of treatment results were carried out in subsequent follow up sessions. Fortunately, patient had improved with a single session of bleomycin injection which was evidenced by decrease in the size of the swelling. It was also noticed that the swelling had faded after bleomycin injection. An apparent color change was noted from red to grey during the resolving phase of hemangioma (Figure 2). Further follow up sessions were conducted for next 3 consecutive months which showed that there is no increase in the size of the hemangioma. Parents were well satisfied with the results of the treatment.



Figure 2 : showing decrease in the size and vascularity of the swelling after intralesional bleomycin sclerotherapy with minimal hyperpigmentation(a minor complication)

Discussion:

Vascular anomalies are classified into vascular tumors and malformations based on cellular kinetics and clinical presentation. Vascular tumors are known for endothelial hyperplasia whereas vascular malformations occur due to venous dysmorphogenesis with normal endothelial turnover⁴. Vascular malformations are classified in 5 different varieties based on the type of affected tissue namely capillary, lymphatic, venous, arteriovenous malformations and a combination of these varieties⁵. Among these, venous malformations are reported to be the most common type which arise due to venous dysmorphogenesis. They exhibit a stagnant blood flow leading to thrombosis, due to which patient presents with complaints of excessive tissue growth, pain, discoloration of skin⁶. The clinical presentation depends on the location involved.

Hemangiomas are the most common benign tumors of soft tissues in infancy and childhood. The most commonly affected sites include head and neck, followed by trunk and extremities. Conrad Pienaar et al treated hemangiomas with intralesional bleomycin injection which act on S0 stage of cell cycle and inhibit cellular proliferation⁷. The angiogenesis of hemangiomas are well modulated with bleomycin injection evidenced by change in colour of the lesion from red to purple or grey after treatment.

Different modalities of treatment were proposed depending on the site affected, size of lesion. Mulliken et al. proposed surgical intervention by circular excision with purse-string suturing⁸. But this method was proved to be ideal modality of treatment in small lesions on the face, or large lesions in any other site on the body. However large and especially facial lesions cause considerable anxiety and worry among the parents during which surgical excision could be a demanding modality with questionable aesthetic results. On the other hand, sometimes hemangiomas may affect vital structures like lips, eyelids, nose. Zide et al reported the need for the surgery in case of disfiguring lip hemangiomas highlighting the difficulty in using surgery as the primary modality of treatment⁹. Although surgical results are impressive, there is a considerable risk of scar burden.

Intralesional bleomycin can be given at any age and stage of hemangioma with a good response rate. Bleomycin should be injected during the proliferative phase of hemangioma affecting the natural phenomenon of increase in the size of the lesion during the first year of life¹⁰. Size of the lesion had not seemed to affect the treatment result with intralesional bleomycin injection.

Various sclerotherapy agents are used for the treatment of venous malformations like bleomycin, acetic acid, OK-432, doxycycline¹¹. Bleomycin is a cytotoxic, glycoprotein antibiotic isolated from *Streptomyces verticillus* by Dr. Umezawa in Tokyo¹². It has been used in the treatment of vascular malformations and hemangiomas due to its sclerosing effect on endothelial cells (similar to alcohol or sodium tetradecyl sulphate) and anti-neoplastic

effect(apoptotic effect on rapidly growing cells) by inhibiting DNA synthesis¹³. It has also been shown to be more effective in the treatment cystic type of hygromas. The lesions should be evacuated as much as possible before injecting a sclerosant to ensure an effective contact between the sclerosant and the endothelial lining of the lesion¹⁴. The advantage of this sclerotherapy is that it doesn't leave a scar tissue and is easily available at a cheaper cost and high success rate besides the risk of minimal toxicity due to the drug. The dosage of the drug is decided based on weight of the child and size of the lesion. The disadvantages of the sclerotherapy is that in case of very large lesions child needs multiple general anesthetics and hospital admission. Other less common complications include hypopigmentation and superficial scarring. Pulmonary fibrosis is a major complication reported with high doses of bleomycin injection¹⁵. It is reported that total dose must not exceed 5mg/kg especially in infants. Hence intralesional bleomycin injection is a simple modality of treating hemangiomas and other vascular malformation although completion of treatment may take a few months in case of huge hemangiomas.

Conclusion:

Our study concludes that intralesional bleomycin appears to be a safe, economical and effective modality of treating vascular malformations like hemangiomas alternative to surgical treatment. However follow up is required to identify recurrences. Hence this modality of treatment is used in case of large lesions and lesions at sites where surgical resection is difficult with better cosmetic care.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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