Case Series
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Intralesional Bleomycin Sclerotherapy of Lymphangiomas in Children: Our Initial Experience

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Abstract

Objective – We report our initial experience with intralesional bleomycin sclerotherapy of macrocystic lymphangiomas in three pediatric patients. **Case Reports** – Case 1. A 3.5-month-old male child presented to our institution with a radiologically verified macrocystic lymphangioma of the left thoracoabdominal region. After 2 cycles of sclerotherapy complete regression of the tumefact was achieved. Case 2. A 23-month-old male child presented with a radiologically confirmed lymphangioma in the sternal region. In total, he underwent 6 cycles of sclerotherapy in about 7 months. At first there was no response to therapy, but after the last cycle, the end result was excellent. Case 3. A 2-month-old male child presented with a radiologically confirmed lymphangioma of the left axillary region. He underwent 4 cycles of sclerotherapy in 4 months. The end result was excellent - complete regression of the tumefact. **Conclusion** – In all our cases, intralesional bleomycin sclerotherapy was successful alone and showed very good end results. There were no serious side effects in any of our cases. Therefore, bleomycin is a safe alternative to surgical treatment of lymphangiomas in the pediatric population.

Key Words: Bleomycin ▪ Lymphatic Malformations ▪ Sclerotherapy.

Introduction

In the most recent ISSVA classification, vascular anomalies are classified in two types: "vascular tumors" and "vascular malformations". The latter are subclassified as capillary, lymphatic, venous and arteriovenus malformations (1). Cystic lymphatic malformations (LMs), or lymphangiomas, are the most common congenital lymphatic anomalies. They occur as solitary lesions of variable size, and their appearance defines their classification into macrocystic, microcystic, or mixed cystic LMs. They commonly infiltrate soft tissues, and they can be found anywhere on the body, from the extremities to the abdominal or thoracic cavities (2). The incidence rate of cystic LMs is ~ 1:2000–4000, with no variation between genders. Most patients (80–90 %) are diagnosed before the age of two (3). The congenital form typically occurs before the age of 5 years, and is due to the improper connection of the lymphatic channels. In most cases, a clinical diagnosis can be made on the basis of the history and examination findings. As needed, dermoscopy and biopsy can be used to confirm the diagnosis, and imaging may be warranted to assess the depth and extent of the lesion (4). As most congenital lymphangiomas can now be diagnosed during intrapartum with advanced radiological techniques, EXIT (ex utero intrapartum treatment) is one of the treatment options with improved maternal and fetal outcomes (5). On clinical examination, these lesions appear soft, compressible, nontender, transluminant and without any bruit (6). Ultrasound usually shows a multicystic lesion with internal septations, and no blood flow is detected on Color - Flow Doppler. CT and magnetic

resonance imaging (MRI) delineate their extent, and show their relationship with other anatomical structures better than ultrasound (7). Definitive diagnosis can only be achieved by histopathological examination, after surgical excision. Sclerotherapy has emerged as a promising alternative to surgical management for LMs in children (8). There are several different sclerosants, but the most commonly used are bleomycin, picibanil (OK-432), absolute alcohol, betadine, sodium tetradecyl sulfate and doxycycline (9). Bleomycin was first developed as an antineoplastic antibiotic, and its sclerosing effect was discovered later. The purpose of this study is to present our initial results using an intralesional injection of bleomycin in treating lymphangiomas in the pediatric age group.

Case Reports

Case 1. A 3.5–month old male child presented to our institution with a radiologically verified (MRI) macrocystic lymphangioma of the left thoracoabdominal region. It was first noticed at 34 weeks' gestation by antenatal sonography screening. The dimensions were 81 × 62 × 22mm. Family history was negative for vascular malformations. There were no other comorbidities. Ultrasound was performed to calculate the volume of the lymphangioma (approx. 38 ml). The child was taken to the OR, where 0.5 IU/kg per dose of aqueous bleomycin was given intralesionally. Firstly we aspirated the cyst fluid using US guidance with a 22G needle. Then diluted aqueous bleomycin (concentration 0.2–0.5 IU/mL) was instilled into the cyst in a volume equal to that of the aspirated fluid but not exceeding 20 mL. Postprocedural observation was uneventful, and the child was discharged home on the same day. He was admitted to our department after 1 month to receive a second dose of sclerotherapy. The parents reported minor swelling and erythema immediately after the injection, which lasted two days. After two doses of bleomycin, complete regression was achieved, and the end result was excellent. Follow up was after 7 months, when the child had no issues. Photographs were taken before and after completion of therapy (Fig. 1 and Fig. 2).

Fig. 1. *Photograph taken on admission to our department shows a large tumefact of the left thoracoabdominal region.*

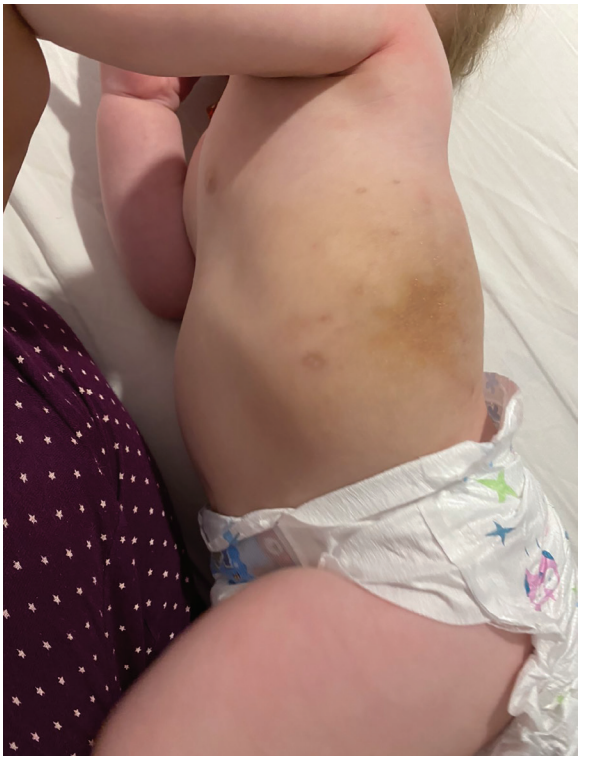

Fig. 2. *Photograph taken after 2 cycles of sclerotherapy shows complete regression.*

Case 2. A 23–month old male child presented with a tumor in the sternal region, which was noticed at birth, and the parents stated that it was growing gradually. Family history was negative for vascular malformations. There were no other comorbidities. An MRI was performed and the

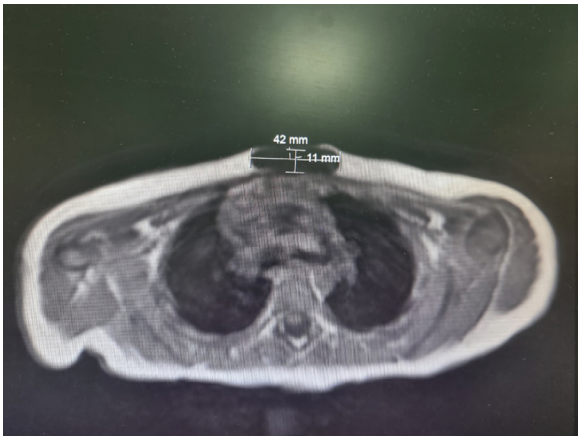

Fig. 3. *MRI image of lymphangioma in Case 2.*

diagnosis of macrocystic lymphangioma was confirmed. Its dimensions were 42 × 42 × 11 mm (Fig. 3). On admission to hospital, the same protocol was applied as in case 1, with the same dose regimen of bleomycin solution (0.5 IU/kg). The parents reported hyperemia and induration after the second and third injections, which lasted 1 day. In total, he underwent 6 cycles of sclerotherapy in about 7 months (one dose monthly). After the last cycle, the end result was excellent - complete regression was achieved. Follow up was after 10 months, when the child had no problems.

Case 3. A 2–month old male child presented with a radiologically confirmed macrocystic lymphangioma in the left axillary region. The dimensions of the tumefact were 63 × 22 × 35 mm. Family history was negative for vascular malformations. There were no other comorbidities. The same protocol was applied as in the previous patients. The parents reported mild hyperemia at the site of the injection which lasted 2 days. He underwent 4 cycles of sclerotherapy in about 4 months. The end result was excellent - complete regression of the tumefact without induration. Follow up was after 7 months, when the child had no issues.

Discussion

The first three patients treated with intralesional bleomycin sclerotherapy for lymphangiomas at our department, showed excellent results. In line with other published data, we found that macrocystic and mixed types of lymphangiomas responded well to treatment. The patients all had different localizations of the lymphangiomas. Two of the three patients had mild hyperemia at the injection site (66,6%), one had induration (33,3%). None of them had recurrences. The mean follow up was 7 months. The dosage we used in all of our patients was 0.5 IU/kg. Immediate complications included skin erythema at the injection site, local swelling, mild tenderness and fever, which were controlled by oral antipyretics, also reported in the study by Rozman et al. (10). However, no life-threatening complications, such as respiratory obstruction and severe hypersensitivity reaction to bleomycin, were observed. The bleomycin doses used in sclerotherapy are small, in comparison to cytotherapeutic doses, which may be associated with pulmonary fibrosis (11). Although surgical excision has been considered to be the treatment of choice by most surgeons, it is associated with tedious dissection, along with a large amount of morbidity, in the form of disfigurement and damage to vital structures, and ugly scars. The choice of treatment should be individualized in relation to several factors, such as bilaterality, age of onset, growth rate, depth, extent, anatomical location, and potential deformity and/or dysfunction (12). Also the treatment modality for lymphangiomas depends on the relevant center's experience and personal preference. Generally, surgical treatment is indicated in large, deep, bilateral lymphangiomas which are causing either symptoms or disfigurement, and are potentially life threatening. Several studies using bleomycin as an intralesional sclerosant have shown favorable results compared to surgery. Tanigawa et al. described the effective use of bleomycin fat emulsion for the treatment of lymphangiomas (13). In a study by Orford et al., intralesional bleomycin showed an excellent response in 44% and a good response in another 44% patients, with minor transient side effects (14). A recent study by Arun et al., with intralesional application of bleomycin, showed that 68% of participants had a good response (15). In our short study, we found the response was good in all our patients.

Conclusion

The cases we describe showed lymphangioma regression similar to that observed in other studies. Bleomycin has a tolerable side-effect profile. All the patients had mild hyperemia at the site of the injection, one had a swelling, and one had induration. In the light of all the above, the use of bleomycin as an intralesional agent for lymphangioma appears to be safe and rewarding.

Conflict of Interest: The authors declare that they have no conflict of interest.

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