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CASE SERIES AND REPORTS

Bleomycin sclerotherapy for lymphatic malformation after unsuccessful surgical excision: case report

Scleroterapia con bleomicina per malformazioni linfatiche dopo fallimento dell'escissione chirurgica: caso clinico

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SUMMARY

Lymphatic malformations (LMs) are benign cystic masses resulting from the abnormal development of lymphatic channels. Lymphatic malformations occur primarily in the head and neck region. Surgical excision of lymphatic malformation is followed by high rate of recurrence and a high risk of complications. Bleomycin is an established antineoplastic drug. It can be used as a sclerosing agent in vascular anomalies. We present a child who was unsuccessfully treated with four surgical resections, with peripheral palsy of facial nerve as complication. The lymphatic malformation was successfully treated in our institution with intralesional administration of bleomycin.

KEY WORDS: Lymphatic malformation • Bleomycin • Sclerotherapy

RIASSUNTO

Le malformazioni linfatiche (LMS) sono masse cistiche benigne derivanti dallo sviluppo anormale dei canali linfatici. Le malformazioni linfatiche interessano principalmente il distretto testa-collo. L'asportazione chirurgica di malformazioni linfatiche è seguita da un alto tasso di recidiva e vi è un elevato rischio di complicanze. La bleomicina è un farmaco antineoplastico approvato. Tale farmaco può essere usato come agente sclerosante nelle anomalie vascolari. Presentiamo il caso di un bambino sottoposto a quattro interventi chirurgici senza successo, complicati da una paralisi periferica del nervo faciale. La malformazione linfatica è stata da noi trattata con successo con la somministrazione intralesionale di bleomicina.

PAROLE CHIAVE: *Malformazione linfatica • Bleomicina • Scleroterapia*

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Introduction

Lymphatic malformations (LMs) are developmental anomalies of lymphatic system consisting of abnormally-formed lymphatic channels and cystic spaces [1 2]. Lymphatic malformations occur primarily in the head and neck, accounting for 75% of all cases. They are typically detected at birth, and 90% is clinically apparent by the age of 2 years [1 3]. There are three morphologic types of LMs: microcystic, macrocystic and combined (combination of microcystic and macrocystic components) [3]. LMs in head and neck region cause pain, bleeding, infection, muscular atrophy, malocclusion, speech difficulties, feeding problems, airway obstruction and cosmetic deformities [1-3].

Several methods have been used to treat LMs including surgical excision, sclerotherapy, laser therapy and radiofrequency ablation [1 4]. Historically, first-line therapy for LM has been surgical excision. However, complete excision is usually not possible, and there is a high rate of recurrence [2]. There are also postoperative complications such as nerve injury (up to 45%), airway obstruction caused by swelling, haematoma formation and wound infection [2 4]. Sclerotherapy has emerged as a promising alternative to surgical management for LMs in children [1 2]. Several different sclerosing agents and injection protocols have been documented in the literature, with varying amounts of success (OK-432, bleomycin, doxycycline, sodium tetradecyl sulfate 3%, alcoholic solution of zein, ethanol) [1 4 5].

Bleomycin was first developed as an antineoplastic antibiotic, and its sclerosing effect was discovered later [3 6-8]. The mechanism involves damage to endothelial cells with a nonspecific inflammatory reaction and occlusion of vessels [3 9-11]. Intralesional bleomycin injections have been shown to be an effective treatment for haemangiomas and vascular malformation lesions [5]. Pulmonary fibrosis as a complication after intralesional treatment with bleomycin has never been reported [1 5].

Case report

A 6-year-old boy with left-sided swelling of the face and neck was brought to our department. He was previously treated at different institution when he was 4.5 years old. The child had had four partial resections during a 1.5 year period by different surgical teams. There were no exact data on previous diagnostic and treatment procedures. One month before he was admitted to our institution, after the last surgical resection and drainage, and the swelling had increased followed by intense pain. The child had breathing and feeding difficulties. Local status revealed peripheral palsy of facial nerve (mandible branch of facial nerve) (Fig. 1). Several scars at left side of the neck and submandibular region from previous surgical interventions were also noticed. At our department, laboratory findings were within normal range. MRI was as follows: expansive, multilocular cystic lesion at left parotid region expanding to pterygoplatinal fosa, parapharyngeal space, submandibular and carotid space on left side, surrounding large vessels. Craniocaudal diameter of single unilocular lesion was 45 mm. Distal border of lesion was at level 12 mm below mandibular margin. Cysts fluid was T2W/T1W hyperintense, with proteinic or haemorrhagic characteristics (T1W not shown). Conclusion: LM of parotid region and pterygopalatinal fossa (Fig. 2).

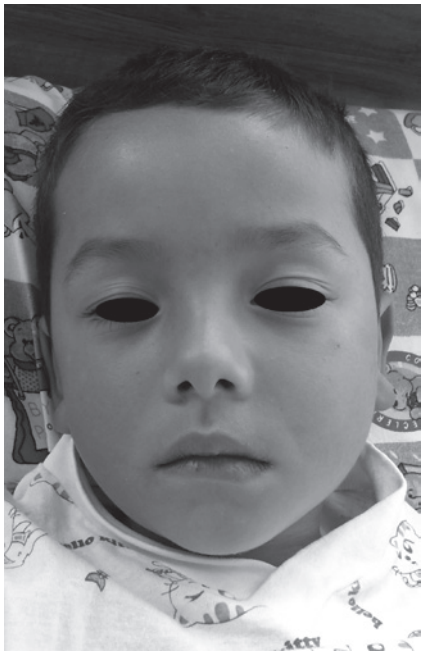

Fig. 1. Patient at admission with left-side swelling of face and neck and facial nerve peripheral palsy.

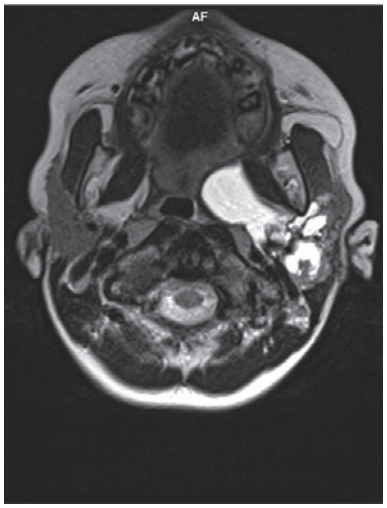

Fig. 2. NMR revealing macrocystyc lymphatic malformation of left parotid region expanding to pterygopalatinal fosa, parapharyngeal, submandibular and the carotid space.

Under general anaesthesia, excision of scar at the left parotid region was performed. Intralesional injection of two cysts with 20 G needle was performed, followed by aspiration of 7.5 ml and 1 ml of haemorrhagic fluid (infection and intralesional haemorrhage). The dose of bleomycin administered was 1 mg/kg body weight, 8.5 ml in total (15 mg bleomycin dissolved in 15 ml normal saline). After injection, the patient was given a course of antibiotics and analgetics. Postoperatively, side effects were minimal (transient local swelling). Eight months after bleomycin sclerosation, MRI revealed that there was nearly complete regression of LM with single cyst at parotid region 10 mm in size (Fig. 3). The child had no functional symptoms, with good aesthetic appearance (Fig. 4).

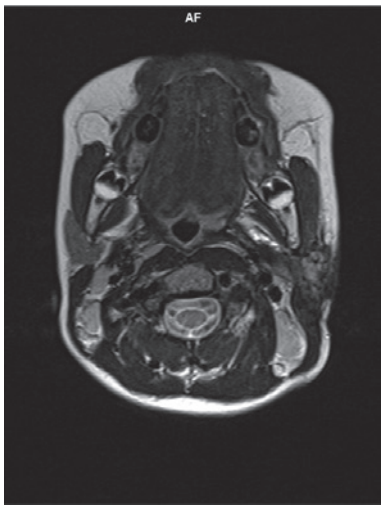

Fig. 3. Postoperative NMR showing nearly complete regression.

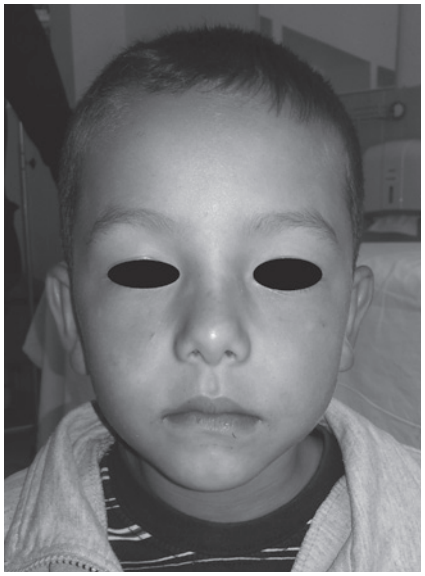

Fig. 4. Patient at five months postoperatively with good functional and aesthetic results.

Discussion

Lymphatic malformations are developmental anomalies of the lymphatic system that occur most commonly in the head and neck region followed by axilla and mediastinum [2 3 12]. The precise aetiology of LMs is still unknown [1]. In 50% of cases they are present at birth with 80% to 90% diagnosed within the first two years of life [1 13]. Initially they usually present as a painless, soft mass with wide variations in the growth rate [1 2]. Rapid growth can occur as a result of trauma, intralesional haemorrhage and thrombosis [1]. Spontaneous regression is very rare [1 3].

The management of LM is challenging because of the infiltrative nature of this lesion especially in the head and neck region [1]. The treatment success of LM depends on the type of the lesion, ana-

tomical location, demarcation and involvement of vital structures. Different treatment modalities for LM have been reported in the literature including surgery, sclerotherapy, laser therapy radiotherapy and radiofrequency ablation [1 3]. Historically, the primary treatment option for LM was surgical intervention [1 4 10]. Complete excision of LM is usually not possible [3 4 12]. Injuries of vital structures, such as facial palsy (up to 33%), recurrence" of a LM, dilatation of persistent anomalous channels secondary to scarring and obstruction, bleeding and other complications can occur after surgical treatment [12]. Our patient had four previous unsuccessful surgical excisions of LM under general anaesthesia at other institutiona. There was no documentation explaining these attempts. The child had scars on the left side of the neck and left sumbandibular region, with facial nerve damage on the left side as a complication. Laser therapy is effective for superficial microcystic malformation, so it was not a treatment option for our patient [1]. Since the anatomical location of LM was extremely unfavourable, and there were several previous unsuccessful attempts at surgical excision, we decided to use a sclerotherapy as a treatment option.

In the past few decades, sclerosing therapy has emerged as a promising alternative to surgical management [2]. Sclerotherapy is the mainstay for treatment of macrocystic LM. Surgery is usually used as complementary therapy [1]. Various sclerosing agents have been tried including ethibloc, corticosteroids, hypertonic glucose solution, sodium morrhurate, doxycycline, quinine, bleomycin and OK-432 [1 2]. Bleomycin is anti-tumour agent, discovered by Umezawa in 1966. Treatment response of lymphomas and testicular tumours established its chemotherapeutic use [5]. Bleomycin has a specific sclerosing effect on vascular endothelium [11]. This effect was successfully therapeutically used by Jura et al. in 1977 for treatment of LM by intralesional bleomycin injection [5 11]. There are several reports of successful treatment of haemangioma and vascular malformations with bleomycin [3 5 6 9 11]. The known adverse effects are pulmonary fibrosis, anaphylaxis and hyperpigmentation [9]. The pulmonary manifestation of bleomycin toxicity is dose dependent, and pathogenesis of this effect is not known [7]. Pulmonary fibrosis after intralesional injection of bleomycin has never been reported [1 2 11]. Our choice for treatment of this patient was bleomycin because it is easy available, inexpensive and has well known effectiveness. A single treatment with bleomycin was sufficient for successful treatment of our patient with neglible side effects. This intervention caused less stress to parents compared to previous treatments, with minimal scaring, and only two days hospitalisation. Eight and a half months of follow-up was unremarkable.

Conclusions

A number of treatment methods are available for LMs of the head and neck region. Surgical treatment of LMs can be associated with significant morbidity. Intralesional injection of bleomycin has minimal and controllable local and systemic adverse effects. Sclerosation of LMs with bleomycin in our case was highly effective compared to several surgical resections.

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