The treatment of cervicofacial lymphangiomas has been changing in recent years. OK-432 appears to be a relatively safe and effective treatment option for patients of all ages. An intracystic injection of OK-432 produces a local inflammatory reaction, leading to resolution of the lesion. Cosmetically, the outcome is excellent, leaving no lesions on the skin at the injection site, unlike other sclerosing agents. It may thus be considered as the treatment of choice, especially in cases where surgical treatment is associated with the possibility of serious functional or cosmetic side effects.

Key words: Lymphangioma. Sclerosing therapy. OK-432. Picibanil.

INTRODUCTION

Lymphangioma is a congenital malformation of the lymphatic system. It is histologically benign, although it may spread to neighbouring tissues and/or infiltrate nearby structures, acting as a malignant tumour, even causing life-threatening complications on occasion.1 Lymphangioma most commonly appears in childhood, particularly in children under the age of 2, and is rare in adults; it is most often located in the head and neck, hence, a differential diagnosis with lipoma, branchial cyst, haemangioma, dermoid cyst, cyst of the thyroglossal duct, plunging ranula, and lymphoma must be established.2

The tendency it has to infiltrate and surround adjacent tissues and major structures such as nerves and vessels makes it difficult to resect fully at surgery. To avoid complications derived from surgical treatment, various treatment options have been tried such as drainage, aspiration, laser, interferon alpha, and various sclerosing agents. Intralesional injection of sclerosing agents has the risk of provoking a scab at the injection site, with unacceptable cosmesis and hindering any subsequent surgical treatment.3

In 1987, intralesional injection of the sclerosing agent OK-432 was reported as a treatment alternative for lymphangiomas4 OK-432 (Picibanil; Chugai Pharmaceuticals Co., Tokyo, Japan) is a preparation of dead bacteria obtained by incubating a culture of type III \textit{Streptococcus pyogenes} A of human origin with penicillin G benzathine. Lyophilization is then performed to eliminate the streptolysin S and to avoid the possibility of infection with systemic repercussions. Therefore, OK-432 should not be applied to patients who are allergic to penicillins, given the potential risk of anaphylactic shock.

CASE REPORT

Twenty-seven year old female with no history of interest who attended our clinic because of painless, progressively growing tumoration in her left neck in the previous 2 weeks.
Upon physical examination, a soft non-pulsating mass measuring 5x4 cm in diameter was observed in the left supraclavicular region (Figure 1A) with no thrill, no reddening or other signs of inflammation.

Magnetic resonance imaging (MRI) revealed a well-defined macrocystic mass in the supraclavicular fossa, with no enhancement following administration of intravenous gadolinium (Figure 2). The fine needle aspiration (FNA) biopsy obtained a yellowish, serous fluid in which abundant lymphocytes were observed.

With these results, a diagnosis of cystic hygroma was made and it was decided to perform an ultrasound-guided puncture of the lymphangioma, aspirate its content and inject the OK-432 solution into the lesion. The solution was prepared by dissolving 0.1 mg of OK-432 in 10 mL saline solution. No local anaesthesia was required. Twenty millilitres of aspirate were obtained and replaced by the same volume of solution.

A moderate fever (38.5ºC) appeared following the injection and there was tender swelling at the site of injection over the following days, with some hardening over the course of the next 2 weeks. However, full regression of the lesion was observed one month after the intervention, without evidence of recurrence after 1 year of follow-up (Figure 1B).

**DISCUSSION**

Most lymphangiomas are diagnosed during childhood and are rare in adults. More than half are present at the time of birth and 90% are detected prior to the age of 2.5

A wide variety of non-surgical treatments have been proposed in an attempt to decrease surgical morbidity. Many authors, largely from Japan, have recommended the use of OK-432 as the treatment of choice for lymphangiomas.14 OK-432 induces sclerosis owing to its diffusion to the stroma, provoking irritation and inflammation that causes the retraction and contraction of the lesion associated with scarring. Prior to injection, as much lymph as possible must be aspirated, leaving the malformation as empty as possible. The exact mechanism of OK-432’s sclerosing effect is not yet well known. In addition to its sclerosing action, its immunomodulating effect is essential as it increases several cytokines, such as interleukin (IL) 1, IL-2, interferon gamma, IL-6, and tumour necrosis factor, in addition to the fact that it activates neutrophils, macrophages, killer cells and T cells, thus increasing endothelial permeability, accelerating lymphatic drainage and fostering retraction of the cystic cavity.5,7 Different studies conclude that macrocystic lesions, as in our case, respond better than cavernous or microcystic lesion thanks to the high degree of communication between
intralesional spaces, which allows greater diffusion of the sclerosing agent throughout the lesion.\textsuperscript{3}

Adverse reactions to OK-432 include low-grade fever for a few days that responds to antipyretics and a local inflammatory reaction with heat and a feeling of hardening, as occurred in our patient; however it does not harm the skin or form a scab. However, on occasions, patient monitoring is recommended to keep the airway from being compromised, especially in patients with lymphangiomas of the parapharyngeal space or the floor of the mouth.\textsuperscript{8}

In conclusion, intralesional OK-432 injection is a safe and effective alternative for the treatment of cervicofacial lymphangiomas; hence, it can be considered the treatment of choice for macrocystic lymphangiomas where surgical treatment is difficult. In addition, OK-432 can be re-injected after 3-4 weeks if the response is not satisfactory, thereby reserving surgical treatment for cases in which the action of the sclerosing agent is insufficient.

REFERENCES