

Fractional erbium-doped yttrium aluminum garnet laser 2940 nm-assisted delivery of topical timolol solution for the treatment of histiocytoid hemangioma



Mohammed Albeshri, MD,^a Hadeel Alseleem, MD,^b and Ahmed Alhumidi, MD^c
Unaizah and Riyadh, Saudi Arabia

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INTRODUCTION

Angiolymphoid hyperplasia with eosinophilia (ALHE) or histiocytoid hemangioma is an unusual benign vascular tumor predominantly affecting middle-aged adults.¹ Most patients have pink papulonodular lesions on the scalp, neck, and peri- and postauricular regions.² Although the cause remains undetermined, recent studies suggest that it is a vasoproliferative process in response to trauma, external otitis media, oral contraceptives, or pregnancy, associated with an inflammatory infiltrate predominantly composed of eosinophils. Therefore, patients usually have elevated serum immunoglobulin E and peripheral blood eosinophilia. ALHE may be chronic and usually recurs after treatment. We demonstrated the successful use of a topical beta-blocker, 0.05% timolol maleate solution, and fractional erbium-doped yttrium aluminum garnet (Er-YAG) 2940 nm laser in the treatment of ALHE.

CASE REPORT

A previously healthy 35-year-old pregnant woman presented to our clinic with multiple mildly pruritic, reddish-brown papulonodules of approximately 3 × 3 cm on the right postauricular region, which had developed over the last few weeks. During the third trimester of pregnancy, gradual enlargement of multiple lesions was observed on the right posterior helix of the ear and the lateral aspect of the postauricular skin surface of the right ear. Moreover, she experienced bleeding when

Abbreviations used:

ALHE:	angiolymphoid hyperplasia with eosinophilia
Er-YAG:	erbium-doped yttrium aluminum garnet laser 2940 nm
LADD:	laser-assisted drug delivery

scratching and combing her hair, especially in the hot climate. She denied any history of trauma, atopy, fever, and otitis media. On examination, multiple reddish-brown papulonodules of varying sizes were observed on the right posterior helix of the ear and the lateral aspect of the postauricular skin surface of the right ear. The lymph node examination was unremarkable. Her laboratory investigation results (including complete blood count with differential leukocyte count, renal, thyroid, and hepatic profiles) were within normal limits. Treatment was deferred until post-delivery, and an appointment was scheduled. Two months post-delivery, the patient returned to the clinic. There was no change in the size and number of lesions. A deep skin punch biopsy was performed under local anesthesia and revealed dermal infiltration of inflammatory cells admixed with blood vessels (Fig 1, A). Observation under a high-power microscope revealed lymphocytes, eosinophils, and plumped endothelial cells (Fig 1, B). Therefore, she was diagnosed with ALHE. Topical timolol maleate solution drops (0.05%) were administered twice daily by instructing the patient to apply

From the Division of Dermatology, Department of Medicine, College of Medicine and Medical Sciences, Qassim University^a; College of Medicine and Medical Sciences, Qassim University^b; and King Saud University.^c

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Correspondence to: Mohammed Albeshri, MD, PO Box 992, Unaizah, Alqassim, 51911, Kingdom of Saudi Arabia. E-mail: Mohammed.Albeshri@ucm.edu.sa.

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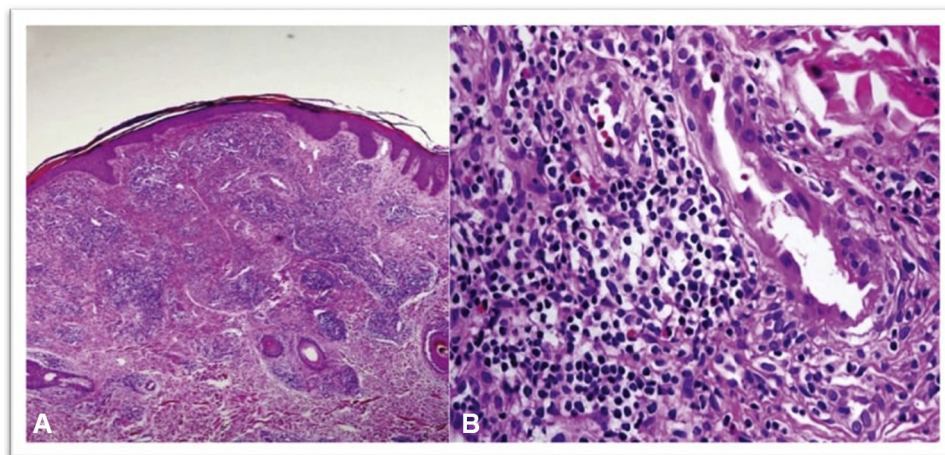


Fig 1. **A**, Photomicrograph of the skin biopsy exhibited dermal inflammatory cells with vascular proliferation. **B**, Higher power view revealed lymphocytes, scattered eosinophils, and swollen endothelial cells. (**A** and **B**, Hematoxylin-eosin stain; original magnifications: **A** and **B**, $\times 40$.)

2-3 drops of the solution each time on the affected area and then massaging it for a few seconds to enhance absorption. Two weeks later, the dosage was gradually increased to thrice daily.

During the 3-week follow-up, the lesions were of the same size, with only a modest change in color from purple to dark brown. This color change suggested that timolol was a potential treatment option but likely required more efficient delivery into deeper tissues. Laser-assisted drug delivery (LADD) is an efficient technique, which generates a penetrating ablative zone that destructs the epidermis and portion of the dermis, allowing further penetration and absorption of topically applied drugs to enhance skin uptake.³ Therefore, we added fractional 2,940 nm Er-YAG Laser (ACTION II, Lutronic) to the management plan. The laser sessions were conducted in the outpatient clinic once a week, using a topical eutectic mixture of local analgesic lidocaine 2.5% and prilocaine 2.5% (EMLA cream 5%) 15 minutes before each laser session. The patient was instructed to apply topical timolol maleate solution drops (0.05%) thrice daily between sessions. Images were taken before the beginning of treatment and weekly thereafter to monitor the lesions' response. Five laser sessions were provided over five weeks, and the laser parameters were as follows: 1st session: fluence 12 j/cm² single pass, interval of 0.5 seconds Density = 5%, spacing = 585 microns, and pulse duration (dwell time) = 250 microseconds; 2nd session: fluence 14 j/cm² double pass, interval of 0.5 seconds Density = 5%, spacing = 585 microns, and pulse duration (dwell time) = 250 microseconds;

3rd session: fluence 16 j/cm² double pass, interval of 0.5 seconds Density = 5%, spacing = 585 microns, and pulse duration (dwell time) = 250 microseconds; 4th session: fluence 18 j/cm² triple pass, interval of 0.5 seconds; 5th session: fluence 18 j/cm² double pass, interval of 0.5 seconds. After the 5th session, there was a significant clinical improvement and complete clearance of the lesions (Fig 2). Follow-up was scheduled weekly while undergoing laser treatment and monthly after clinical improvement.

DISCUSSION

ALHE is an uncommon, benign vascular proliferation. Differential diagnoses include Kimura's disease, a chronic disorder characterized by subcutaneous nodules in the head and neck.² Clinical diagnosis is confirmed by the proliferation of blood vessels and eosinophilic inflammatory infiltrates on skin biopsy. It can have spontaneous regression; however, the associated symptoms and disfiguring courses may need treatment. Until recently, treatment options have included surgical excision, pulsed dye laser, and topical and intralesional corticosteroids. Other reported modalities included intralesional interferon alpha-2a, indomethacin, pentoxifylline, and chemotherapeutic agents such as vinblastine, mepolizumab (anti-interleukin-5), oral isotretinoin, propranolol, and topical imiquimod.⁴ The symptoms typically persist for years, with recurrence in > 40% of cases. Early age at onset, long disease duration, multiple lesions, and symptomatic disease are associated with a high recurrence rate.⁵ However, disease recurrence and possible poor cosmetic outcomes are challenges.

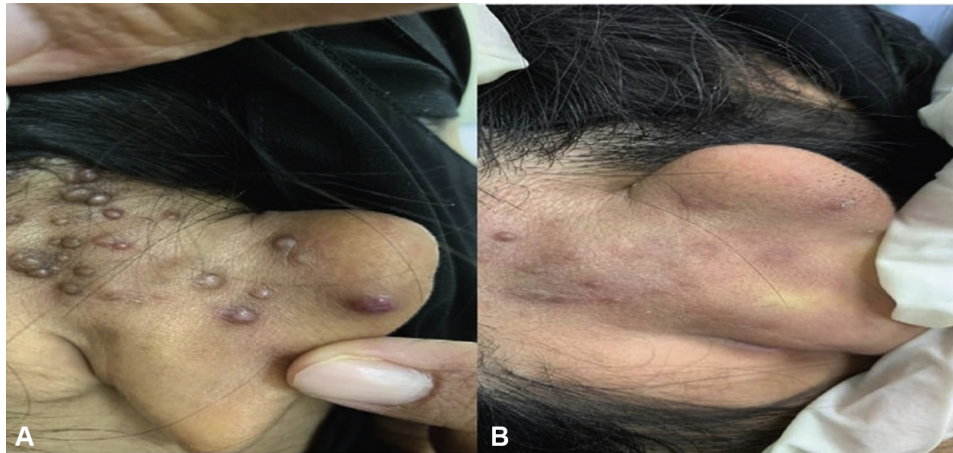


Fig. 2. **A**, Multiple-grouped hyperpigmented, soft-to-firm papulonodules present in the right retro-auricular area. **B**, After the fifth session of LADD of timolol, complete resolution of the lesions with only post-inflammatory erythema and dyspigmentation in the postauricular region of the right ear.

Based on the notion that ALHE is of vascular origin, and recent advances and expenditures on the use of beta-blockers on vascular lesions other than infantile hemangiomas, such as pyogenic granuloma and angiokeratoma of Fordyce, we considered topical timolol drops as a treatment option. We successfully used fractional Er-YAG to improve the penetration and absorption of 0.05% topical timolol into the tissues. LADD led to a marked improvement in size and color resolution with complete clearance of the lesions over a period of five weeks, and the patient remained disease-free at the nine-month follow-up.

Since its launch in 2009, LADD utilizes ablative fractional lasers to increase the dermal uptake of locally applied drugs.⁶

Via the creation of microscopic ablation zones, the epidermis and a portion of the dermis being destructed enables deeper penetration and absorption of topically applied medications.³ In dermatology, LADD is becoming an increasingly popular therapeutic technique used to improve a wide range of dermatology conditions, particularly vitiligo, scars, warts, and androgenetic alopecia among many other indications.³

In conclusion, ALHE may lead to poor cosmetic outcomes with impact on patients' psycho-social wellbeing, resulting in further aesthetic procedures. Our patient experienced only mild post-laser dyspigmentation, which was improved by 90% without

any intervention. Considering that this simple, in-office, non-invasive treatment strategy was successful, combination treatments are promising, and further studies are recommended.

Conflicts of interest

None disclosed.

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