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Case Report

A case of angio lymphoid hyperplasia with eosinophilia treated by 980nm vascular diode laser

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Abstract Angiolymphoid hyperplasia with eosinophilia (ALHE) are benign, uncommon, reactive tumors manifesting mostly in Asian adults as isolated or grouped papules or nodules in the skin of the head and neck. Histologically these have proliferation of blood vessels with large endothelial cells and accompanying eosinophilic infiltrate presenting as intrinsic component of the lesion. These lesions are usually persistent causing cosmetic nuisance. Cryotherapy, surgical excision, pulsed-dye laser, carbon dioxide laser are different treatment modalities but all have their own failure rates. Here we report a case of ALHE in a 45 years old female presenting as a group of large painful nodules on left ear (pinna) for the past 20 years and progressively increasing in size and number. After histological confirmation of diagnosis, she was treated successfully by 908 vascular diode laser. Four treatment sessions were carried out at fortnightly interval with no side effects. 908nm vascular diode laser is a good treatment option for many vascular lesions.

Key words
Acantholytic, ATPC2,'dilapidated brick wall appearance'.

Introduction

Angiolymphoid hyperplasia with eosinophilia also known as epithelioid hemangioma, was first described in 1969 by Wells and Whimster. It is an inflamed vascular tumefaction, characterized by proliferation of histiocytoid endothelial cells with prominent lymphocytic and eosinophilic infiltration.[1] Immuno-histochemical study reveals a strong reactivity for CD31.[2]

Regarding pathogenesis, it is not clear whether it is a vascular neoplasm or a lympho proliferative process.

It is an uncommon condition, mostly presenting in Asians followed by white population. Mean age at presentation is 37 years in both males and females.[3]

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It usually presents present with red, brown or violaceous painful, pruritic, pulsatile, bleeding or asymptomatic single or multiple nodules on head and neck region, sometimes with associated regional lymphadenopathy. Rarely, the lesions can appear in other sites or extra cutaneous tissues as well. There are few case reports showing associated peripheral eosinophilia or nephrotic syndrome.[4]

Dermoscopy reveals a polymorphous vascular pattern of dotted and linear vessels, on a pink to a red background.

Differential diagnosis includes Kimura's disease, pyogenic granuloma, nodular Kaposi's sarcoma, angiosarcoma, cylindroma, epithelioid hemangioendothelioma and granuloma faciale.

Lesions are persistent and require treatment if they don't regress spontaneously within 3 to 6 months, cause cosmetic issues and systemic effects.

Day 1 Day 1 Day 14

Day 28 Day 42

Figure

Recurrence rates are high after topical or intra lesional corticosteroids, cryotherapy, electro-cauterization. Surgical excision and especially Moh's micrographic surgery is considered the treatment of choice in ALHE with the lowest failure rate of 44.2%. Followed by laser therapies i.e. Nd: YAG, pulsed dye and carbon-dioxide lasers as promising alternatives. The recurrence rate remains high over 50% requiring maintenance treatment.[5]

Case report

A 45 years old married lady from Sargodha reported to our dermatology outpatient department in CMH Rawalpindi with 20 years history of painful and recurrently bleeding nodules on the of pinna of left ear. The lesions were increasing in number and size for the past 5 years. She gave history of waking up in the morning with excruciating pain and often profuse bleeding from the lesions which used to stop after pressing the bleeding points with clean cotton cloth for few minutes. She was having a devastating effect of the disease on her quality of life. She did not have her old biopsy report but her previous medical documents revealed various treatment sessions done from different dermatology settings ranging from weekly cryotherapy, electrocautery, topical and intra lesional steroid injections for ALHE. She was referred to our hospital for plastic surgery which was refused by the department keeping in view the difficulty in surgical approach. She was referred to us for second opinion. Her physical examination revealed multiple red to violaceous, tender nodules covering antihelix, fossa of antihelix, concha, and fossa of helix; extending

to helix as well. There were 16 different sized firm, pulsatile, warm nodules on the anterior of pinna with the largest in fossa of helix, measuring 1.8x 1.4 cm. Similarly five nodules were present on the back of ear. There was no regional lymphadenopathy. Her vital signs were in normal range. Systemic examination was unremarkable. Her incision biopsy was done to re-confirm the diagnosis. The histopathology report from AFIP number 8749 showed prominent proliferation of blood vessels with swollen endothelial cells. Eosinophil were present in abundance along with lymphocytes. No evidence of malignancy was seen. Hence diagnosis of Angiolymphoid hyperplasia with eosinophilia was confirmed. Her complete blood picture, peripheral blood film, coagulation profile, renal function tests, Hepatitis B and C screening, urine analysis and ultrasound abdomen did not reveal any abnormality and possibility of Kimura's disease was ruled out. Since she had tried different treatment modalities with no or minimal improvement in the past, we decided to use 980nm diode vascular laser for her. After informed consent we started her fortnightly treatment sessions with laser. Her wound was cleaned with pyodine solution before the start of procedure. In each session she was given local anesthesia with intra lesional plain 1% lignocaine, 5 minutes before procedure which was repeated when required. Pulse duration of 0.01 to 0.02 seconds in continuous mode with power of 35 W was used during procedure and spot size was adjusted depending on the size of nodule. There was minimal bleeding and no pain during the procedure. Cooling was done during the procedure with Eskimo air skin cooler device. All the lesions were touched till there was blanching and flattening of each nodule. She was given topical antibiotic and steroid combination cream to be used post treatment for 1 week and was given oral analgesics as well. After 4 fortnightly sessions she showed remarkable improvement with almost complete regression of nodules without any scarring. She was satisfied with the treatment. She was then called for monthly follow up for 6 months with no recurrence of disease.

Discussion

The pathogenesis of ALHE is debated between reactive vascular neoplastic and lympho-proliferative processes.[3] Studies showing association with arterio-venous shunts in 43 of cases on histopathology and history of preceding trauma very much like in pyogenic granuloma which is another vascular tumor, support the reactive vascular pathogenesis.[6] Renin production induced by these AV shunts stimulates angiogenesis and eosinophil activation and migration through angiotensin II production.[6] Further supporting evidence comes from occurrence in hyper estrogen states like pregnancy causing many vascular tumors.[7] Intra cytoplasmic staining of endothelial cells by Wilms tumor-1 antigen was also noted in 19 of 20 ALHE specimens further supporting the vascular hypothesis.[8] T-cell receptor gene rearrangement and monoclonality, association of few cases with peripheral T-cell lymphoma and correlation of few cases with human herpes virus 8 and human T-cell lymphotropic virus; supports its pathogenesis as a low grade T-cell lymphoma.[3,9-11]

In past AHLE and Kimura's disease were considered different spectrums of the same disease but now they are considered clinically and pathologically different diseases. They both are close differential diagnosis of each other and rarely can co-exist in same patient.[12] Kimura's disease occurs mainly in young Asian males with one or multiple asymptomatic nodules involving the subcutaneous tissue and salivary glands. There is usually associated regional lymph node involvement, peripheral blood

eosinophilia, and elevated IgE levels. In contrast, ALHE occurs predominantly in middle-aged women, as multiple small erythematous to violaceous nodules usually asymptomatic or associated with pruritus, bleeding, pulsations but rarely with symptomatic manifestations. Among these only 20% of cases are associated with peripheral eosinophilia.[13] Nephrotic syndrome, such as membranous glomerulonephritis or mesangioproliferative, is more common in Kimura's disease but has also been reported with ALHE.[4] We carefully excluded Kimura's disease in our case.

Central to the histology of ALHE is the proliferation of blood vessels of varying sizes lined by plump endothelial cells intra-dermally or rarely extending into subcutaneous tissue. These histiocytoid endothelial cells are enlarged, with abundant eosinophilic or clear cytoplasm and large vesicular nuclei. The cells are mostly cuboidal with occasional "hobnailing", which is related to the presence of cytoplasmic vacuoles in these cells, causing cytoplasmic protrusion into lumina. Mitoses are rare. Inflammation is the second defining characteristic feature. Lymphocytes and varying amounts of eosinophils diffusely surround and may infiltrate the blood vessels and may form distinct follicles with germinal centers. Histologically, florid lymphoid follicles with germinal center formation, eosinophilic infiltrates, eosinophilic microabscesses, and eosinophilic folliculolysis are salient features of Kimura's disease. In addition, there is lack of the histiocytoid/ epithelioid cells that are characteristic of ALHE.[1]

ALHE usually persist for years without regressing spontaneously except for occasional cases, which having significant impact on quality of life of patients due to cosmetic disfigurement and symptoms making surgical or medical intervention necessary. Evidence of variable success with different treatment options comes from literature.[5] Commonly used treatment options include topical and intralesional corticosteroids, topical timolol, topical tacrolimus 0.1%, topical 5% imiquimod.[14-16] Cryotherapy and electrodessication are also commonly used in selected cases with variable efficacy and their use is limited by chances of recurrence and scarring.[1,17] Tambe *et al.* in 2017 and Yadav D *et al.* in 2018 have reported successful use of radiofrequency ablation in different cases of ALHE.[18,19] Sotiriou *et al.* in 2009 showed that photodynamic therapy could be an alternative therapeutic approach for ALHE or could be used as a neoadjuvant treatment to reduce lesion size especially where size or site of lesions limits the efficacy or acceptability of other treatments. Carlesimo *et al.* has reported efficacy of oral isotretinoin in ALHE in 2007.[20] Horst in 2014 has reported successful treatment of ALHE with 40mg daily propranolol given for few months.[21] Low dose oral methotrexate has also been reported to improve a case not responding to corticosteroids with peripheral eosinophilia.[22] Mepolizumab or anti-interleukin-5 antibody was administered in a patient with ALHE associated with blood eosinophilia causing decreased local pruritus and disappearance of hypereosinophilia.[23] Oral dapsone, and oral pentoxifylline, intralesional interferon alpha-2a and indomethacin, were previously used but with high failure rates.[5]

Surgical excision is the treatment of choice but is limited by local recurrences, due to inability to define the exact margins in this complex vascular proliferation, may be seen. There were higher rates of recurrence post excision with earlier age of onset, longer duration of disease, multiple lesions, bilateral lesions, pruritus, pain, and bleeding.[12] Treatment failure was found in 40.8% of 908 reviewed cases treated by excision.[5] In addition, surgery can be disfiguring

and difficult, especially in the periauricular region. Mohs micrographic surgery with complete margin examination has been proved effective therapeutic option so far.[24,25]

Laser therapy can be a useful modality in ALHE especially in cases with difficult surgical approach. Lasers with oxy-hemoglobin as chromophore i.e. vascular lasers have shown promising results in this aspect so far. First of all Argon laser was used in 1988.[26] PDL laser both 585nm and long pulsed 595 nm with deeper penetration of around 2.5mm has been effectively used. Copper vapor laser (CVL) with pulsed yellow light of 578nm has also been used tried showing that the thickness of the lesion plays a role in the treatment response and overall effectiveness of treatment with the CVL.[27] Carbon dioxide laser is an ablative laser with water as its chromophore and hence has less target selectivity in ALHE as compared to vascular lasers. But because it excises and thermo coagulates simultaneously, it can be used as a good de-bulking agent in ALHE cases either alone or in combination with other lasers.[28] Treatment failure was observed in 50.0% ALHE cases treated with pulsed dye laser, 54.6% with carbon dioxide laser, and 66.7% with argon laser.[5] In a study three patients with ALHE were treated with PDL at 595-nm wavelength or with a combined sequential application of 595-nm PDL and 1,064-nm Nd: YAG wavelengths. Complete resolution of the lesions was achieved in two patients with ALHE; a partial response was seen in one patient.[29] The combination of pulsed dye laser and CO2 laser (for debulking) in the treatment of ALHE in 14 patients who exhibited clinical response after a mean of 2.4 ± 0.4 treatment sessions was reported.[30] A novel dual-therapeutic approach consisting of surgical excision followed by treatment with the pulsed dye laser has also been reported.[31]

Diode laser has versatile medical uses based on various tissue reactions it induces, such as coagulation, vaporization, or welding leading to its usage in skin closure of surgical excisions.[32] The 980 nm diode laser has found a wide usage range in dentistry, urology, gynecology, and vascular surgery but data regarding use in dermatology is relatively lacking. It has commonly been used subcutaneously or intra vascular to induce lipolysis or to coagulate varicose leg veins.[33] Modern Ultra pulsed 980 nm diode lasers have short exposure times avoiding local overheating and resulting in vaporization at temperatures >300 °C and ablating tissue into fragments along with deep tissue penetration. By changing laser parameters, different tissue effects can be generated and hence can have multiple indications. These lasers offer coagulation for vascular lesions with a low risk of scarring. They can vaporize cysts, warts, and cutaneous metastases. The 810 nm diode laser with powers varying between 2.5 and 3.5 watts has successfully treated labial vascular lesions.[34] The diode laser 980-nm has been used by defocused irradiation mode with an output of 3 watt in continuous wave for treatment of venous lake on lips.[35] Similarly its effective use in 300 different cases including cutaneous vascular lesions, cysts, pseudo cysts, warts and melanoma cutaneous metastasis is also documented. The vascular lesions treated included Cherry angioma, venous lake of the lip, angiokeratoma, spider nevus, granuloma telangiectaticum, port wine stains, facial telangiectasias and couperose. For vascular lesions, pulse duration was ≤0.01 s and pulse pause was 0.3–0.5 s. The power varied between 25 and 40 W.[33] We are the first to report its successful usage in case of ALHE. We used almost comparable parameters of pulse duration and power during our treatment protocol.

Conclusion

Thus 980 nm vascular diode is a promising treatment option for cases of ALHE resulting in complete cure with no recurrence of lesions. It is cost effective, feasible for both doctor and patient, causes minimal adverse effects and can even be used in cases presenting with multiple lesions with difficult surgical approach.

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