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Case report

Photodynamic therapy in vulvar lymphangioma: Case report

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ABSTRACT

- The aim of this case report was to evaluate the treatment of vulvar lymphangioma applying photodynamic therapy (PDT). Patient aged 61 years, complained of vulvar region burning, local pain, which caused intense discomfort for over 5 years. She had developed vulvar edema, papules and vesicles that drained clear exudate, in which histological finding confirmed the vulvar lymphangioma. A red diode laser (Photon Lase III, DMC, Brazil) was applied locally after a 2% methylene blue aqueous solution (MB) in the vulvar target area. It was used a 660 nm wavelength light source, irradiance- 100 mW/cm^2, radiant energy-20 J/cm^2, exposer time-40 s, applied weekly at 10 points onto vulvar area in a total of 5 sessions. A clinical improvement post PDT was observed as well as a better quality of life. Post 3 years follow up no recurrence was observed. The clinical response followed MB- mediated PDT suggested a non-invasive, secure and low-cost treatment.

1. Introduction

Cutaneous vulvar lymphangioma (CVL) is considered a rare and benign proliferation of lymphatic vessels in the deep dermis and subcutaneous area, which corresponding to 4% of all vascular malformations [1].

Clinically, the CVL is classified either on the superficial (circumscribed lymphangioma) or on the deepest (cystic hygroma, cavernous lymphangioma), as well as a congenital or acquired. The major difference between these types is related to the deformities extent, the size and location of blood vessels [1,2].

The acquired CVL etiology may be associated with the surface disruption of the skins lymph channels, hindering them from reaching the peripheral drainage channels in the deep layers. Either by the obstruction of these channels may occur due to surgery, radiation therapy, genital tuberculosis, chronic lymphedema, Crohn's disease, local infectious and obesity [3,4].

Treatment also depends on the symptoms which may correspond to pain, pruritus, burn sensation, edema, suppuration or lymphorrhagia, excoriation, erosions, ulcerations of the skin and recurrent infections, which may result in intense discomfort and psychosexual disorders.

The definition proposed by Whimster, in 1976, described unless the deep cisterns are entirely removed in the treatment excision, recurrence may occur [5,6]. The literature reveals that surgery is the preferential treatment, followed by criocauterization or electrocauterization and, recently, vaporization by carbon dioxide, argon or Nd: YAG laser [6,7,8].

2. Case report

A 61-year-old patient, with symptoms as burning and local pain for 5 years, showed papules and pooled vesicles as well as bulky edema that drained a clear exudate from the vulvar region was enrolled at Lasertherapy outpatient clinic in Pérola Byington Hospital (Fig. 1).

The pelvic and genital ultrasonography did not demonstrate deep lymph cisterns. The histological diagnosis showed cystic dilation in the lymphatic channels, with protein content in the papillary dermis, few erythrocytes and thin-walled endothelial cells, confirming the CVL. No alterations on biochemical exams were identified.

The photosensitizing agent (2% methylene blue aqueous solution) was applied under the epidermis. Right after the diode laser, 660 nm wavelengths, power density- 100 mW/cm^2, radiant energy-20 J/cm^2,

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Fig. 1. Vulvar aspect pre-treatment.

Fig. 2. Vulvar aspect post treatment.

exposer time- 40 s at 10 points on vulvar area, totaling 5 sessions, was applied weekly (Fig. 2).

3. Results

The patient was followed clinically for 3 years. No pruritus, edema, discomfort or burning sensation in the treated area was observed with a significant improvement of patient's quality of life.

4. Discussion

The CVL is a benign and infrequent condition that occurs in any location on the skin. The vulvar manifestation is even rarer reported [9,10].

Surgery is the gold standard treatment for vascular malformations and the incomplete resection can lead to 12% recurrence rate [11]. In addition, the radical removal can lead to undesirable side effects, such as local chronic pain by a neurological or vascular damage, as same as bleeding and further infections. The possibility of study on conservative and effective laser treatment with less adverse-effect had been stimulated the further analysis.

The PDT has a photochemical effect, which leads to photo-induced cell death, consequently local and systemic immune modulation in the target tissue, such combination results in a photo-physical-chemical reaction. The PDT's photosensitizers are attach to blood vessels and cell components, as lysosomes, mitochondria, plasmatic membrane, nucleus, endoplasmic reticulum and Golgi complex [12–14].

The methylene blue (MB) is known as a phenothiazine dye applied in pharmacology, microbiology and medical use for around 100 years [15].

In the cell, the methylene blue accumulates, preferentially, in the mitochondria. MB in aqueous solution is present in monomers form (dilute solutions), dimers and larger aggregates (well concentrated solutions), which the absorption bands are, respectively, between 600 and 664 nm and 590 nm. Then, this non-toxic and photostable photosensitizer, is absorbed by a red light and has high singlet oxygen quantum yield, as same as has the capacity to generate several radical species. MB has melanin affinity, it is more lipophilic than porphyrin derivate, binds actively to cell organelles, triggering the inflammatory mechanism decline and leading the cell homeostasis. In addition, it demonstrates, in vivo, inactivation to skin diseases, bacteria, virus, fungi and several types of tumors [16,17,18,19].

There are studies evaluating PDT-MB in wound healing, resulting in edema, inflammation changes, granulation tissue, number of fibroblasts, re-epithelialization and necrosis [20,21].

In recent decades, PDT in blood vessels has been described and its application on the lymphatic system or lymphangiogenesis, is beginning to be explored for the inflammatory processes, infectious, post vaccination or post transplants as well as tumor metastases containment. According to Kirslak et al study, the PDT anti-lymphatic action occurs through deep lymphatic vessels regeneration and recanalization [22–24].

Moreover, bloodborne pathogen eradication has been related to PDT for some years and MB is one of the photosensitizing agents approved for this purpose. The PDT-MB approach should be considered for superficial vascular destruction and cutaneous vascular lesions treatment modality [13,15].

The literature recommends 25 J/cm^2 fluence for vascular PDT treatment that lead to lymphatic occlusion and augment vascular permeability, thereby improves the inflammatory response and edema [22,25].

In the present study, the option of methylene blue usage was given by its photochemical effect described, previously. Our applied dose was based on a vulvar dermatosis pilot study, in which the 20 J/cm^2 fluence demonstrated an anti-inflammatory and lymphangiogenesis effect, resulting in effective clinical response. In public health, as developing countries, MB is considered a low-cost photosensitizer, compared to porphyrin derivatives.

PDT has acquired prominence since it can be used to selectively attach to lymph vessels and to block the lymphatic drainage in a particular area, allowing the control of metastasis, post-transplant rejection and infectious spread. It is important to emphasize that the recovery of lymphatic vessels post PDT depend on the energy density delivered to the tissue.

5. Conclusion

The vulvar lymphangioma can cause intense local discomfort besides lymphorrhea, limiting patients' quality of social and sexual life. Surgery, laservaporization, electrocauterization, criocauterization,

however the destructive procedures can result in anatomical changes, due to scars or keloids formation. The PDT application in vulvar lymphangioma can be considered as an alternative therapy, comfortable and with cost effectiveness. Furthermore, PDT prevents scaring or deformities, while maintaining a functional vulva. As the study is unpublished, the post PDT recurrence rates are not yet established and a long-term follow up should be required.

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