Lymphangioma Circumscriptum Post Radiotherapy for Penile Cancer Treated with CO_2 Laser

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ABSTRACT Lymphangioma circumscriptum (LC) is a rare, benign condition, predominantly characterized by the malformation of lymphatic skin vessels. Its onset may be congenital or due to secondary causes such as radiotherapy, infections, or surgical procedures. We present the case of a 55-year-old patient with a pathologic history of squamous cell carcinoma of the penis followed by radical penectomy. Due to metastasis to the locoregional lymph nodes, the entire affected area was subsequently treated with radiation therapy, receiving a total dose of 55.8 Gray. Eight years after this treatment, translucent vesicles filled with a clear liquid appeared on the scrotum. Histopathology confirmed the diagnosis of LC and therapy with CO_2 laser was applied, resulting in a favorable outcome. LC of the scrotum may present a long-term radiotherapy-induced complication of this site. Our clinical experience showed that the CO_2 laser was the therapy of choice as the vesicles entirely disappeared and healed as white scar-like lesions.

KEY WORDS: lymphangioma circumscriptum, CO_2 laser, penile squamous cell carcinoma, lymphadenectomy, radiotherapy

INTRODUCTION

Lymphangiomas are defined as hamartoma of the lymphatic vessels of the skin. They can appear on the tegument site of the entire body, in particular on the legs and torso, but also in the oral cavity including the mouth floor, lips, and tongue or in the genital area including the penis, scrotum, and vulva. Lymphangioma circumscriptum (LC), the most frequent type of lymphangiomas, manifests in children as well as in adults (1,2). LC can occur as a primary abnormality or secondary to damaged lymphatic channels.

Subcutaneous lymphatic cisterns are linked to the pathogenesis of LC. They appear during embryogenesis and are not connected to the lymphatic system. The lymph is thus not able to drain from the adjacent tissue. The cisterns are coated with muscular fibers, which are able to contract. Via this pressure, the protrusion of the overlying skin is initiated (3).

Acquired LC erupts in adulthood, possibly due to injuries of the deeper lymphatic system induced by radiation therapy, surgery, in association with Crohn's

disease, or caused by infectious processes such as filariasis, lymphogranuloma venereum or tuberculosis (4,5). Damage of the deep lymphatic vessels causes lymphatic stasis with backflow; this process leads to the abnormal enlargement of the superficial lymphatic vessels which clinically translates to the appearance of the characteristic vesicles (6).

Frequently, the lesions are more extended than expected considering the visible number of vesicles. Complications include erysipelas-like reactions after minor injuries or infections and inflammatory processes.

PATIENTS AND METHODS

We present the case of a 55-year-old-patient with a history of ulceration on his penis 10 years ago. A biopsy confirmed the diagnosis of keratinizing, undifferentiated squamous-cell carcinoma (SCC). MRI findings indicated infiltration of the corpus cavernosum and a short penis, and the patient underwent radical surgery with penectomy and urethral opening in the perineum.

On physical examination and CT, there was evidence of enlarged inguinal nodes on both sides. First, a complete bilateral groin dissection was performed, with preservation of the crossa saphena and of the adipose tissue superficial to Scarpa's fascia, without transposition of Sartorius muscle. Of the 29 inguinal lymph nodes taken, two superficial nodes showed tumor metastases (inguinal node 1/13 right and inguinal node 1/16 left) and thus pathologically classified the patient into stage III (pT2 pN2(2/29) Mo Ro G3).

A delayed pelvic node dissection was done without pathological evidence of further metastases.

Due to this finding, a radiotherapy of the affected inguinal area with 5×1.8 Gray/week for eight weeks and a total dose of 55.6 Gray was recommended. Overall, the radiation therapy was well-tolerated by the patient; during the sessions, inguinal erythema with humid epitheliolysis appeared, with good response to local disinfectant, anti-inflammatory, anti-itching, and epithelizing treatment. As a follow-up, CT was performed on a regular basis without any indications of other distant metastases.

One year ago, the patient re-presented himself at our hospital with vesicular lesions on the scrotum. They appeared pink, translucent, and filled with a clear liquid on an erythematous background. The surface of these pustules was smooth and some appeared centrally umbilicated, resembling molluscum contagiosum or genital warts (Figure 1). These vesicles moistened the inguinoscrotal area, forcing the patient to use diapers. He also stated that he still observed scrotal swelling 3 years after penectomy.

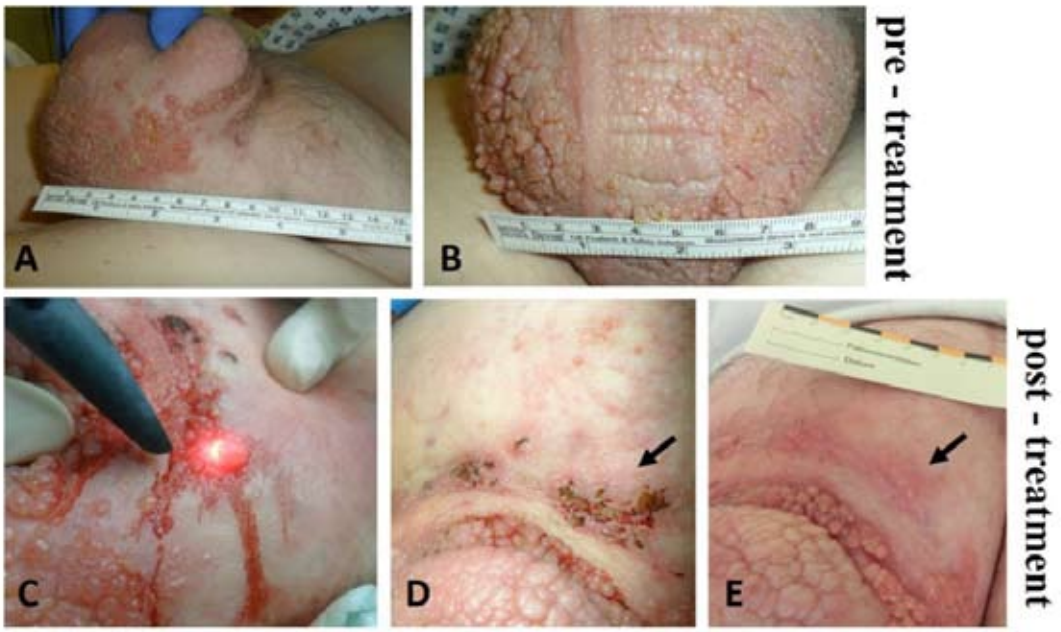

Figure 1. An overview of the pre- and post-treatment situation of the lymphangioma circumscriptum lesions with a CO_2 laser. (A) The scrotum with typical pink, translucent vesicles filled with a clear liquid on an erythematous background; (B) Magnification of the scrotal surface with distinct lesions; the genital area is swollen. (C) Lymphangioma circumscriptum lesions are being treated with a CO_2 laser. (D) Healing has started; the wound heals with crusts. (E) The long term outcome with remaining white scar-like lesions. Arrows indicate the same treated areas.

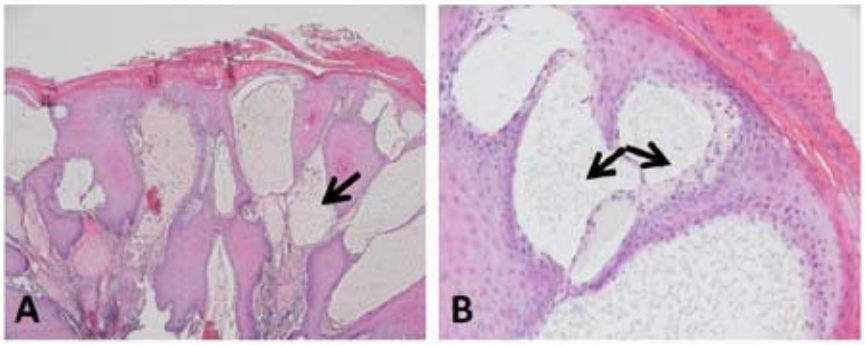

Figure 2. Histopathology images obtained from the biopsy of the patient`s LC lesions. (A) Hematoxylin and eosin (HE) stain, ×2.5. Squamous hyperplastic epidermis with underlying dilated lymphatic vessels and low/moderate inflammatory infiltrate in the surrounding tissue. (B) HE stain, ×20. Squamous epidermis with hyper- and parakeratosis, with underlying and ectatic lymphatic vessels. Arrows indicate the dilated vesicles containing lymphatic fluid.

RESULTS

Biopsy and histopathology revealed characteristic modifications of LC: irregular, broad, tortuous lymphatic channels dissecting the connective tissue with vesicles containing lymphatic fluid, lymphocytes, neutrophils, and macrophages; some dermic lymphatic bundles covered by hyperkeratotic epithelium, reactive pseudoepitheliomatous hyperplasia, and minimal chronic inflammation (Figure 2).

A subsequent pelvic CT scan did not provide any indications of the presence of lymph nodes or metastases. LC vesicles were treated by CO_2 laser in four treatment sessions. The therapy sessions where performed in local anesthesia with lidocaine 1 % (Xylocitin) 10 mL using a CO2 pulsed laser beam (wavelength 10600 nm, power 7 Watt) in a noncontact manner. The energy was delivered through an articulating arm with a straight hand piece (Sharplan), the diameter of the beam at the focal point was 5 mm.

CO_2 laser works like a cutting tool. Because the depth of penetration is 0.1 mm, the result is a discreet scar (a limited area of tissue injury with little fibrosis and scarring). The post-treatment evolution was favorable, and only white scar-like lesions remained visible (Figure 1).

DISCUSSION

The appearance of LC is distinct, and the clinical diagnosis can easily be established, especially when the clinician is aware of the disease (7); the biopsy of such lesions is however required to confirm the diagnosis and establish suitable treatment. In the case of our patient, lesion biopsy was equally necessary to exclude further malignancy, considering its pathological history.

The clinical aspect of the scrotum in LC with the described translucent vesicles is similar to acquired lymphangiectasis (LA) post radiotherapy in breast cancer. LA vesicles may additionally appear pedunculated and hypertrophic, with a slightly purplish color. However, for patients who underwent surgery with subsequent radiotherapy and who complain years later about translucent blistering on the respective zone, the formation of angiosarcoma, LC, LA, or lymphangiomatous cutaneous metastases need to be considered (8).

Angiosarcomas present the histopathological appearance of well-differentiated areas that comprise an anastomotic network of sinusoidal vessels with no blood, separated by a single row of endothelial cells with nuclear atypia with a large nucleo-cytoplasmic ratio (9. In some cases, no clear histopathological diagnosis can be established, as LC and LA are indistinguishable both clinically and histopathologically. Both are histopathologically characterized by enlarged lymph spaces which are boarded by normal or flattened endothelial cells; the overlying epidermis is hyperkeratotic and acanthotic. Although there are no histopathological differentiating criteria between LC and LA, some authors note that LC subcutaneous lymphatic cisterns are coated with muscles, a finding which is reported to be absent in LA.

Another type of lesions to be differentiated from LC and which also appear after radiation therapy (40-60 Gray) are atypical vascular lesions. These are small papules or patches in irradiated skin. Histologically, they are composed of thin-walled lymphatic vessels, usually limited to the dermis (10).

By performing a PubMed search for "lymphangioma circumscriptum scrotum" we only found 13 listed cases, with none of them addressing LC of the scrotum post SCC or radiotherapy. In 1985, LaPolla et al. (11) described the case of a woman who developed LC after radiation therapy for SCC of the cervix,

while Short *et al.* reported patient who developed SCC 11 years after LC treatment (12). Sims et al. found three other cases with LC in the vulva; 2 of them being associated with SCC and the 3rd with hidradenitis suppurate (13). We believe that our case is the first of its kind in the medical literature. In addition, our patient had the feature of having undergone radical penis amputation, with subsequent radiotherapy after detection of metastatic infiltration at the locoregional lymph node level. Metastases, however, were only discovered after the pelvic lymphadenectomy and histopathological analysis of all the 29 removed lymph nodes.

Overall, LC treatment options include surgical excision, laser ablation, flash lamp pulsed dye laser, electrocoagulation therapy (14), cryotherapy (15), suction-assisted lipectomy, the wait and watch approach, and sclerotherapy (6). Whimster, however, demonstrated that surgical excision of the vesicles without concurrent removal of subcutaneous cisterns does not result in healing (16). After surgery, scrotal reconstruction can be done with free skin grafts or rotated skin flaps. Postoperative complications are mainly recurrent swelling, prolonged lymphatic drainage, and local infections.

We chose to treat the LC lesions with CO_2 laser and achieved satisfying results and healing with remaining white scar-like lesions.

Sasaki et al. compared the efficacy of the CO_2 with the Nd:YAG laser; at the end of the four treatment sessions, blisters had disappeared, the patient did not have to use diapers anymore, and quality of life improved considerably. The patient preferred the results obtained with the Nd:YAG laser, as the lymph release was stopped after ablation with this type of laser. The authors concluded that both long-pulsed Nd:YAG and CO_2 laser are effective in the treatment of LC (17), although some authors have reported therapeutic failures (18).

CONCLUSION

LC are malformations of the lymphatic vessels of the skin, typically with translucent blisters filled with clear liquid. As such, LC is a long-term complication of chronic lymphedema and radiotherapy, showing similarities with LA of the irradiated post-tumor breast. Patient tumor history and the presence of the distinct scrotal lesions enabled a quick diagnosis. The physician should be aware of the possibility of such radiotherapy-induced long-term "damage" in order to avoid misdiagnosis and subsequent inappropriate treatment, as the clinical appearance is similar to various infectious diseases or tumors. Surgery with concomitant removal of lymphatic cisterns remains the treatment of choice, but the laser treatments have also successfully proven their efficacy. Of these, the CO_2 laser offers a minimally invasive alternative with satisfactory functional and cosmetic results, especially for large lesions that cannot be addressed surgically.

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