



Vulvar Squamous Cell Carcinoma Following Fractionated Laser Therapy for Vulvar Lichen Sclerosus, a Case Report of a 24 Year Old Woman

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Abstract

Vulvar Lichen Sclerosus (LS) is a chronic inflammatory dermatosis, which can develop into Vulvar Squamous Cell Carcinoma (VSCC). Long-term and compliant treatment with ultra-potent topical corticosteroids can reduce or even prevent risk of malignant progression. We report a case of a 24 year old woman who received three cycles of non-ablative fractional laser therapy with the “Diva Tight Laser” (a combination of fractionated non-ablative CO₂ laser and Erbium:YAG laser) for yet untreated LS. Six months later she was diagnosed with VSCC. To our knowledge, this is the first case that is reported of the development of vulvar carcinoma after laser treatment for LS. We emphasize the importance of correct management in patients with LS, as there is a potential risk of developing VSCC in case of incorrect treatment.

Keywords: Lichen Sclerosus (LS); Vulvar Squamous Cell Carcinoma (VSCC); LS-VSCC; Ultra-Potent Topical Corticosteroids (UTCS); Fractionated CO₂ laser

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Received Date: 21 Oct 2020

Accepted Date: 04 Nov 2020

Published Date: 13 Nov 2020

Citation:

Groenewegen KL, Voss FO, van
Beurden M, Zijlmans HJMAA, Vermaat
H. Vulvar Squamous Cell Carcinoma
Following Fractionated Laser Therapy
for Vulvar Lichen Sclerosus, a Case
Report of a 24 Year Old Woman. *J
Gynecol Oncol.* 2020; 3(5): 1045

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Introduction

Lichen sclerosus is a chronic inflammatory dermatosis, mostly affecting postmenopausal women in the anogenital area, but also found in premenarchal girls [1]. The incidence rate of vulvar Lichen Sclerosus (LS) has nearly doubled in 20 years, with a peak incidence of 33.4 per 100.000 woman-years above 50, compared to only 3.5 in 20 years to 24 year old women [2]. The etiology of LS is presumably a combination of genetic, immune genetic and autoimmune factors [3]. Standard treatment for LS consists of Ultra-Potent Topical Corticosteroids (UTCS), aiming to reduce symptoms and prevent skin alterations [4,5]. LS can develop into Vulvar Squamous Cell Carcinoma (VSCC) through differentiated Vulvar Intra-Epithelial Neoplasia (dVIN), which occurs in approximately 6.7% (20 years cumulative incidence rate) [2]. Long-term compliant UTCS treatment in LS patients can prevent the development of VSCC [6]. We report on a 24 year old healthy woman with LS that developed VSCC after being treated primarily with laser therapy. To our best knowledge, no similar cases have been reported before.

Case Presentation

A 19 year old woman visited a gynecologist for vulvar pain and pruritus. She was healthy with no relevant family history and only used oral contraceptives. Although no abnormalities were seen, she was prescribed Daktacort cream (miconazole nitrate 20 mg and hydrocortisone acetate 10 mg), which had little to no effect. At the age of 24, she visited a laser clinic because she felt unheard and was suspicious of having LS. The skin therapist described fusion of the labia minora with atrophic plaques and fissures near the introitus, and confirmed the diagnosis LS. No biopsy was taken. The patient was advised to visit a gynecologist or dermatologist to start with clobetasol propionate 0.05% ointment. Despite this advice, she first received three cycles of non-ablative fractional CO₂ laser (10.600 nm) in combination with Erbium:YAG laser (Er:YAG, 1540 nm, spot size 12 × 12, density 150 cd, 3.4 joule/22.5 cm, pulse-duration 0.75/5, 4.5 Watt, 1 Hz), with an interval period of 5.5 weeks. The fissure on the left labium minus had progressed to an ulcer at the third visit. In all visits this anomaly was not lasered. After three laser treatments, the patient reported much improvement of the white atrophic areas, and mild improvement of the vulvar pain, pruritus,

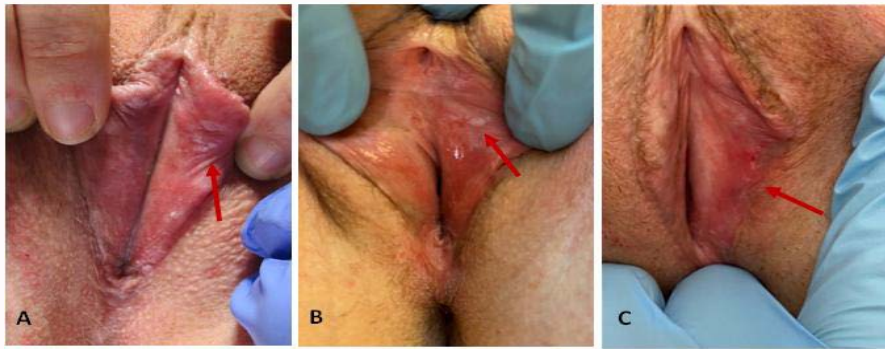


Figure 1: A: Situation after 3 cycles of CO₂/Er:YAG laser therapy and 2 months of UTCS treatment with Clobetasole propionate 0.05% ointment. The anomaly had progressed into an erosion of 1 cm in diameter B: Situation just before surgery, after 3 months of UTCS treatment. Clitoral phimosis and atrophic plaques are seen, with on the left labium minus a small ulcerative lesion. A biopsy showed a VSCC. C: Situation after the radical local excision.

dysuria and dyspareunia. Although the patient was suspicious of the ulcer, the skin therapist was less alarmed for a malignancy at the patient's age.

The patient visited a dermatologist two weeks later, who described clitoral phimosis, architectural change and pelvic floor hypertonia. On both labia majora mild white streaks were seen, and on the left inside an erosion. No biopsy was taken. Induction therapy was started, comprising topical clobetasol propionate 0.5 mg/kg ointment once daily for 4 weeks, with additional paraffine/Vaseline 500/500 mg/g as an emollient. After one month, the erosion on the left labium minus had partly healed, but showed progression of hyperkeratosis. After the second month, the area had changed into an elevated erosive anomaly of 1 cm in diameter (Figure 1A). A 3 mm punch biopsy revealed a lateral VSCC, not associated with HPV. Depth of invasion could not be determined.

The patient was subsequently referred to the Antoni van Leeuwenhoek hospital, Amsterdam, where she underwent a radical local excision (Figure 1B). Histology showed a well differentiated invasive VSCC, with a diameter of 5 mm and a maximum thickness of 1 mm to 2 mm. Lymphovascular invasion and perineural growth were both absent. All margins of at least 2 mm were radically excised. One margin showed dVIN. A subsequent re-excision of the scar and a left groin sentinel biopsy revealed no abnormalities (Figure 1C). The VSCC was classified as FIGO stage Ib carcinoma.

Discussion

We report on a 24 year old woman with a 5 year history of presumably undiagnosed and untreated LS, who received primarily three cycles of fractionated non-ablative CO₂/Er:YAG laser therapy, before starting treatment with clobetasol propionate 0.05% ointment. Two months after UTCS treatment, she was diagnosed with a VSCC on the left labium minus. To the best of our knowledge, no patients have been reported who received fractionated non-ablative laser for primary LS and subsequently developed a VSCC.

Several points of attention in this case should be discussed, both concerning the course of disease and choice of treatment.

Firstly, the primary diagnosis of LS could have been incomplete, as the distinction between LS and dVIN is difficult to make both clinically and histologically [7]. In a study where 60 LS biopsies were revised, 42% turned out to be dVIN [7]. In this case, the fissure that was present at the first visit of the laser clinic could already have been

dVIN or even have contained micro-invasion. As the first biopsy was taken five months hereafter, it remains unclear whether the VSCC was already present.

Secondly, the delay in treatment with UTCS could have played a role in the progression of LS into dVIN and subsequently VSCC, since we know that UTCS can reduce the risk of LS progressing to VSCC [6]. Even more, it took several years before the patient visited the laser clinic to confirm her self-suspected diagnosis of LS. The clinic advised her to visit a gynecologist or dermatologist first for proper treatment with clobetasol propionate 0.05% ointment, but left the responsibility with the patient and started laser therapy anyhow. The cumulative incidence rate of a VSCC in women with LS after 5 years is 2.1% [2]. However, this particular cohort did not report any women below the age of 30 and it is unclear whether those patients received UTCS treatment. Since our patient was not treated appropriately for several years, her risk of developing a VSCC could be higher.

Thirdly, the CO₂/Er:YAG laser could potentially be a cause of VSCC development, since the precise histological or carcinogenic effect of fractionated laser on vulvar epithelium in LS is unknown [5,8]. Mechanical or chemical trauma and injuries can locally aggravate LS, which is known as the Koebner phenomenon or isomorphic response [4]. The laser may have aggravated surrounding LS tissue *via* Koebnerization, by which new lesions appear at the site of injury. Currently, none of the guidelines recommend fractionated laser therapy (CO₂ or Er:YAG) as superior treatment to UTCS, since there is no supporting grade 1 level evidence. Treatment with topical clobetasol propionate 0.05% is the golden standard [4,5], as it achieves a significant decrease in patient-reported symptoms [9]. The European Academy of Dermatology and Venereology guideline proposes to only use laser therapy if UTCS treatment has failed, based on evidence levels 2+ and 3 (case-control studies and case-reports) [4]. Currently two well-designed studies are being performed. One is the CURLS trial, a phase 3 randomized trial in which fractionated CO₂ laser therapy is compared to topical clobetasol propionate in vulvar LS [10]. A second randomized double-blind trial examines the efficacy of fractionated CO₂ laser therapy in women with histologically proven LS (NCT03665584). Depending on the outcome of these studies, laser therapy might become a reasonable treatment option for LS in the future.

Finally, it is important for physicians to refer a patient when necessary. The characteristics, risks and current treatment standards of a condition should be known. In LS, a biopsy is recommended if

the diagnosis is uncertain, when areas do not improve with treatment and especially when neoplastic change is suspected, e.g. persistent cases of hyperkeratosis, erosions or ulcerations [5]. In this case, the patient should have been properly diagnosed and treated, before starting with non-ablative laser therapy. Moreover, referral to an experienced gynecologist or dermatologist was indicated for the erosion, preferably within at short notice [5].

Conclusion

In conclusion, we would like to address the following: First of all, practitioners should be aware of the clinical features of LS and take a biopsy when uncertain or in suspicion of malignancy. Secondly, practitioners should be aware of the risks of developing VSCC in LS when not properly treated. And finally, as presented in this case, LS is a disease in need of an expert opinion. Therefore, we would advise practitioners to refer patients with suspected LS to a dermatologist or gynecologist for proper induction therapy following current guidelines.

Acknowledgement

The patient approved of using personal information and photo's for this case report and is aware that this data will be published in a medical journal.

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