Fibrofolliculomas in Birt-Hogg-Dubé syndrome treated with a CO_2 and dye laser combination: a case report and literature review

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Abstract

Birt-Hogg-Dubé syndrome (BHD) can cause benign skin lesions such as fibrofolliculomas, as well as systemic manifestations including pulmonary cysts, kidney tumors, and recurrent pneumothoraces. We report the successful treatment of fibrofolliculomas in a patient with BHDs using a combination of fractionated ablative CO_2 laser and a flash lamp pulsed dye laser (FPDL). This combined method improves the CO_2 healing process's functional and cosmetic results; the first wavelength (ablative) has a greater capacity for excision and tissue regeneration, while the second (non-ablative) provides more control over the tissue healing process. The lesions were ablated up to the papillary dermis without enhancing the overall textural appearance. Therefore, deeper laser ablations may be able to stop dermal residual lesion relapses. In conclusion, fractionated CO_2 laser and FPDL can be used safely and effectively to reduce the appearance of facial hamartomas related to BHDs.

Introduction

The Birt-Hogg-Dubè syndrome (BHDs) is an uncommon hereditary autosomal dominant disorder that results from germline mutations on chromosome 17p11.2 of the folliculin (FLCN) tumor suppressor gene, which codes for the folliculin protein.[1] It usually manifests clinically as cutaneous fibrofolliculomas, multiple pulmonary cysts, recurrent spontaneous pneumothoraces, and renal tumors of different histological categories.

Clinically, there is great phenotypic variability, even within the same family,[2] but it is generally characterized by a combination of skin, kidney, and lung lesions and increased cancer susceptibility. At the age of 20 to 30 years old, pathological BHD manifestations start to show up, and patients are monitored primarily at the lung and kidney levels. Folliculin is expressed in the majority of tissues, including the skin, kidney, and lung; however, its exact function is still unknown. In the lung parenchyma, particularly in type I pneumocytes, folliculin appears to have a tumor-suppressor effect.[1] The spectrum of skin manifestations of BHDs is represented by non-cancerous skin lesions (fibrofolliculoma and trichodiscomas), which may not be clinically dangerous but may have an aesthetic impact and psychological effects.[3] The skin lesions usually appear in the second or third decade of life and are present in over 80% of individuals over 40 with the syndrome. Over time, the tumors grow bigger and more numerous. Fibrofolliculoma, a multiple noncancerous, dome-shaped tumor of the hair follicles, is most commonly seen on the face, neck, and, less frequently, on the upper part of the thorax, and it is typically described as having a smooth, waxy texture and an opaque white color or yellowish tone. Tumors vary in appearance, including epidermoid cysts or comedo-like plaques with keratin plugs. A large number of fibro-

folliculomas may be associated with hyperseborrhea (unusually high sebum production).[4]

Angiofibromas, perifollicular fibromas, and trichodiscomas – tumors of the hair disc that may look like fibrofolliculomas – are examples of additional tumors. Fibrofolliculomas, while rare and difficult to distinguish outside of BHDs, necessitate histological examination for diagnostic confirmation due to their clinical resemblance to other lesions.[5] The presence of fibrofolliculomas on the face can induce significant psychosocial stress and profound psychological distress.[3]

Therapy is not necessary for BHD skin lesions, as there is no chance of a malignant transformation.[6] However, aesthetic reasons are often the motivation behind treatments. Due to the scarcity of effective therapeutic drugs, the demand for different therapeutic approaches is essential.[7] Indeed, according to a recent analysis, there was no benefit observed in the treatment of fibrofolliculomas with topical rapamycin.[8] Destructive methods like electrocoagulation, excision, and/or ablative laser therapy with an erbium-YAG or carbon dioxide laser are currently used to treat fibrofolliculomas, although there is a high rate of recurrence and the possibility of side effects like inflammation, scarring, and hypo- and hyperpigmentation.[8] The dermatologist's experience in selecting the best course of treatment and a carefully chosen patient group minimizes these risks.

CO_2 laser vaporization capabilities showed a good compromise between aesthetic outcomes and a low rate of complications.[9,10]

Case Report

In this case report, utilizing the complementary effects of two distinct laser types, a CO_2 laser (TetraPro – DEKA, Calenzano, Italy) and a flash lamp pulsed dye laser (FPDL) (Synchro VasQ – DEKA, Italy), we have created a combined technique that enhances both the functional and aesthetic outcomes of the CO_2 healing process. The first wavelength (ablative) has a greater capacity for excision and tissue regeneration, while the second (non-ablative) offers more control over the tissue healing process.

The CO_2 laser system with the special PSD® (Pulse Shape Design) emission technology, which permits complete control of the laser effect on the tissue, was used; both fractional scanning and freehand handpieces are included in this CO_2 laser system.

This study reported the clinical case of a 44-year-old Caucasian woman with a family history of BHDs. The patient was enrolled for treatment of multiple hard, flesh-colored papules on her face, which were identified as fibrofolliculomas. The diagnosis of BHDs was performed by skin biopsy, genetic counseling, and testing. The onset of symptoms occurred at the age of 18. Treatments were preceded by a five-day preventive period during which an antiviral (acyclovir 400 mg three times/day) was prescribed. A local anesthetic with a 5% lidocaine cream was applied 40 minutes before treatment with a CO_2 laser. The 10,600 nm wavelength laser with a range of output of 0.2-1 W and a frequency of 5-10 Hz was used. The carbonized tissue that resulted from the layer-by-layer vaporization of the epidermis was removed using saline-soaked gauze and quickly dried with fresh gauze.

Figure 1. Female patient affected by Birt-Hogg-Dubé Syndrome. Right lateral view (**A**), frontal view (**B**), and left lateral view (**C**) of the patient before the laser therapy. Right lateral view (**D**), frontal view (**E**), and left lateral view (**F**) of the patient at 2 months follow-up after the last treatment session.

When capillary hemorrhage obstructed deeper ablation, the procedure was interrupted. After CO_2 laser therapy, the FPDL (handpiece spot size 10 mm; fluence 8 J/cm^2; pulse duration 0.5 ms) was used. The lesions were successfully ablated up to the papillary dermis, leading to an improvement in their number and size and an enhancement in the overall textural appearance.

Following these procedures, the patient experienced minimal pain and no complications. Significant redness and facial swelling were observed immediately after the procedure, but these conditions disappeared after a week. Until full reepithelialization, the recommended home care course included applying antibiotic cream twice daily after thorough wound cleansing with gauze and saline. In the six weeks following the procedure, a full reepithelialization without scarring was noted, and the patient expressed great satisfaction with the aesthetic outcome. The patient was also instructed to apply sunscreens with a high protection factor. The excellent outcome of the combined laser treatment is reported in the high-definition photos acquired before and after laser therapy (Figure 1). The follow-up at 2 months after the last treatment session showed no recurrences. Therefore, deeper laser ablations may be able to stop dermal residual lesion relapses.

Discussion

Fibrofolliculomas can be resistant to treatment or recur after it has been administered, and certain treatment options documented in the literature may not yield the best cosmetic results.[8,11,12]

Patients' papules decreased when treated with topical medications (metronidazole, tretinoin, or rapamycin); nevertheless, oral therapy was frequently ineffective in treating numerous cutaneous hamartomas.[8,11] Fibrofolliculomas are currently also treated with destructive techniques such as electrocoagulation and dermabrasion, despite a high recurrence rate and potential adverse effects including inflammation, scarring, and hypo- and hyperpigmentation.[8]

Laser surgery provides fewer adverse thermal effects than electrocoagulation and allows for more accurate ablation, even in difficult-to-reach anatomical locations.[11]

Laser treatment is widely used and well accepted as well; in a recent article, Patel and colleagues report that a patient with BHDs was successfully treated for fibrofolliculomas with a combination of fractionated and non-fractionated ablative CO_2 therapy, resulting in a 92% reduction in lesion count.[13]

Following a CO_2 laser treatment, tracking the healing process is critical to achieve the desired aesthetic outcome. When used in conjunction with the CO_2 laser, the FPDL has two distinct effects: it reduces the inflammatory and vascular component[14,15] and also regulates the inflammatory and regenerative process to encourage non-hypertrophic healing.[15] Both lasers must be used in the same session because FPDL works best when the inflammatory process is still ongoing, helping to regulate the healing process and reduce fibrosis deposition.[16-20]

According to our experience, due to its functionality, combined laser therapy is a viable treatment option for BHD skin lesions and should be the first choice for treating fibrofolliculomas.

Given the infrequency of BHDs, additional studies involving a larger patient cohort and extended follow-up durations will be necessary to validate this therapeutic strategy as an established treatment for BHDs.

Conclusions

In conclusion, fractionated CO_2 laser and FPDL can be used safely and effectively to reduce the appearance of facial hamartomas related to BHDs.

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