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# **Fibrofolliculomas in Birt-Hogg-Dubé Syndrome treated with a CO<sub>2</sub> and dye laser combination: a case report and literature review**

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**Availability of data and materials:** the data supporting the findings of this study are available from the corresponding author upon reasonable request.

## **Abstract**

The Birt-Hogg-Dubé Syndrome (BHDs) can cause benign skin lesions like fibrofolliculomas as well as additional systemic symptoms like 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<sub>2</sub> laser and a Flash Lamp Pulsed Dye Laser (FPDL). This combined method improves the CO<sub>2</sub> healing process's functional and cosmetic results; while the first wavelength (ablative) has a greater capacity for excision and tissue regeneration, the second wavelength (non-ablative) provides more control over the tissue healing process. The lesions were successfully ablated up to the papillary dermis without leading to an enhancement in the overall textural appearance. Therefore, deeper laser ablations may be able to stop dermal residual lesion relapses.

In conclusion, fractionated CO<sub>2</sub> 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.<sup>1</sup> 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,<sup>2</sup> 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 level.

Folliculin is expressed in the majority of tissues, including the skin, kidney, and lung, however, its exact function is still unknown; folliculin in the lung parenchyma, particularly in type I pneumocytes, seems to have a tumor-suppressor effect.<sup>1</sup>

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.<sup>3</sup>

The skin lesions usually appear in the second or third decade of life and are present in over 80% of individuals over 40 who have 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.

Individuals' tumors vary in appearance; they can include epidermoid cysts or comedo-like plaques with keratin plugs. A large number of fibrofolliculomas may be associated with hyperseborrhea (unusually high sebum production).<sup>4</sup>

Angiofibromas, perifollicular fibromas, and trichodiscomas—tumors of the hair disc that may look like fibrofolliculomas—are examples of additional tumors. Although fibrofolliculomas are uncommon

and challenging to identify outside of BHDs, a histological examination is required to confirm the diagnosis because of the lesion's clinical similarities to other lesions.<sup>5</sup> When fibrofolliculomas are present on the face, it can cause a great deal of psychosocial strain and extreme psychological distress.<sup>3</sup>

Therapy is not necessary for BHD skin lesions as there is no chance of a malignant transformation.<sup>6</sup> 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.<sup>7</sup> Indeed, according to a recent analysis, there was no benefit observed in the treatment of fibrofolliculomas with topical rapamycin.<sup>8</sup> 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 a high rate of recurrence and the possibility of side effects like inflammation, scarring, hypo- and hyperpigmentation.<sup>8</sup> The dermatologist's experience in selecting the best course of treatment and a carefully chosen patient group, however, minimizes these risks.

CO<sub>2</sub> laser vaporization capabilities showed a good compromise between very aesthetic outcomes and a low rate of complications.<sup>9,10</sup>

## **Case Report**

In this case report, utilizing the complementary effects of two distinct laser types, a CO<sub>2</sub> 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<sub>2</sub> healing process; the first wavelength (ablative) has a greater capacity for excision and tissue regeneration, while the second wavelength (non-ablative) offers more control over the tissue healing process.

The CO<sub>2</sub> 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<sub>2</sub> laser system.

This study reported the clinical case of a 44-year-old Caucasian woman having a BHDs family history. The patient was enrolled for treatment of multiple hard, flesh-colored papules on her face, that were identified as fibrofolliculomas. The diagnosis of BHDs was performed by skin biopsy and genetic counseling and testing. The onset of symptoms occurred at the age of 18 years old. 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<sub>2</sub> 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. When capillary hemorrhage obstructed deeper ablation, the procedure was interrupted. After CO<sub>2</sub> laser therapy, the FPDL (handpiece spot size 10 mm; fluence 8 J/cm<sup>2</sup>; 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 swelling in the face were observed immediately after the procedure, but these conditions considerably disappeared after a week. Until full reepithelization, the recommended course of home care included applying antibiotic cream twice a day following thorough wound cleansing with gauze and saline.

In the six weeks following the procedure, a full reepithelization 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 factor of protection. 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 is administered and certain treatment options that have been documented in the literature may not produce the best cosmetic results.<sup>8,11,12</sup>

Patients' papules decreased when treated with topical medications (metronidazole, tretinoin, or rapamycin); nevertheless, oral therapy was frequently ineffective in treating numerous cutaneous hamartomas.<sup>8,11</sup> 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, hypo-, and hyperpigmentation.<sup>8</sup>

Laser surgery provides less thermal adverse effects than electrocoagulation and allows for more accurate ablation, even in difficult-to-reach anatomical locations.<sup>11</sup>

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<sub>2</sub> therapy, resulting in a 92% reduction in lesion count.<sup>13</sup>

Following a CO<sub>2</sub> laser treatment, it is critical to track the healing process in order to achieve the desired aesthetic outcome. When used in conjunction with the CO<sub>2</sub> laser, the FPDL has two distinct effects: it reduces the inflammatory and vascular component<sup>14,15</sup> and also regulates the inflammatory and regenerative process to encourage non-hypertrophic healing.<sup>15</sup> Both lasers must be used in the same session because FPDL works best when the inflammatory process is still ongoing, regulating the healing process and reducing fibrotic deposition.<sup>16-20</sup>

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.

Due to the rarity of BHDs, more studies with further patients and longer follow-up periods will be required to validate this therapeutic approach as a recognized treatment for BHDs.

## **Conclusions**

In conclusion, fractionated CO<sub>2</sub> laser and FPDL can be used safely and effectively to reduce the appearance of facial hamartomas related to BHDs.



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