CO\textsubscript{2} Laser Treatment of Multiple Oral Hamartomas in Cowden’s Syndrome: A Review and Case Study

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Background: Cowden’s syndrome is a genetic disorder characterized by multiple oral hamartomas and an increased risk of internal malignancy. These mucocutaneous lesions can be physically disfiguring and psychologically distressing. As a result, patients frequently seek treatment for their destruction. Removal of oral hamartomas is often a challenge due to their sensitive location and high risk of recurrence.

Objective: To review the clinical use, effectiveness, and safety of a fractional ablative laser to treat multiple oral hamartomas in a patient with Cowden’s syndrome.

Materials and Methods: A thorough literature review pertaining to treatment of oral hamartomas and a discussion of an illustrative case showcasing successful lesional destruction with a fractional ablative carbon dioxide (CO\textsubscript{2}) laser in a 33-year-old man with Cowden’s syndrome.

Results: Multiple oral hamartomas were effectively removed with fractional CO\textsubscript{2} laser vaporization. No infection, scarring, dermatitis, nor lesional recurrence were observed 6 months post-treatment.

Conclusion: Fractional CO\textsubscript{2} laser vaporization can be used effectively to treat multiple oral hamartomas associated with Cowden’s syndrome.

Keywords: laser surgery, Cowden’s, carbon dioxide, fractional ablative, treatment, hamartomas

Introduction
Cowden’s syndrome (CS) is a rare genodermatosis of autosomal dominant inheritance and variable expression.\textsuperscript{1–3} Its prevalence is unknown but is estimated at 1 in 200,000.\textsuperscript{4}

Clinical manifestations of the disease include mucocutaneous lesions, thyroid abnormalities, fibrocystic breast disease, uterine leiomyomas, gastrointestinal hamartomas, macrocephaly, and developmental delay. Malignancies of the breast, thyroid, kidney, and endometrium appear later in life.

The syndrome was named after Rachel Cowden in 1963 who presented with multiple oral papules and cystic breast cancer.\textsuperscript{3} The primary indicator of CS is the presence of multiple asymptomatic cutaneous hamartomas, which typically develop prior to internal disease. The International Cowden Consortium dictates a diagnosis of CS when the pathognomonic skin lesions (trichilemmomas, papillomas, fibromas, acral keratoses) and a combination of major (malignancies) and minor (gastrointestinal polyps) criteria are in evidence. The disease is caused by a mutation in the \textit{PTEN} tumor suppressor gene located on chromosome 10 which encodes for a protein with phosphatase activity.\textsuperscript{4} Individuals with a germline \textit{PTEN} mutation are at increased risk for internal malignancy, especially in the breast, thyroid, and endometrium.\textsuperscript{3,5}

Laser technology has been used to successfully treat a wide variety of cutaneous lesions including trichilemmomas, syringomas, xanthelasma, and angiofibromas.\textsuperscript{6,7} Since the last systematic review of CO\textsubscript{2} laser vaporization of multiple cutaneous hamartomas was published by Wheeland et al in 1989\textsuperscript{8} and the technology has undergone substantial evolution,\textsuperscript{9} the purpose of our publication is to provide an updated evaluation of the safety and efficacy of fractional ablative laser skin resurfacing for the treatment of multiple oral hamartomas in a patient with CS.
Literature Review
Three databases (PubMed, MEDLINE, Wiley Online Library) were mined from inception until September 1, 2021, utilizing search strings based on fractional ablative laser resurfacing and mucocutaneous lesions in Cowden’s syndrome. Additional studies were identified through Google Scholar web search and bibliographies from the aforementioned database search results.

Case Report
A 33-year-old man with Cowden’s syndrome and a 10-year history of numerous (>50) small (1-to-5 mm diameter), firm, flesh-colored papules on his lower lip mucosa presented for evaluation and treatment considerations (Figure 1). The papules were previously biopsied with histopathologic confirmation of benign hamartomas. Medical history included a diagnosis of testicular cancer, which had been eradicated by orchidectomy 12 years prior to presentation. Previous treatment of the hamartomas with topical sirolimus provided no significant cosmetic improvement and the patient refused further topical treatment due to its associated inconvenience and skin irritation. Because the papillomatous papules on the lower lip and adjacent mucosa continued to increase in size and number with worsening friability and easy bleeding, the patient was inclined to seek in-office treatment.

After written informed consent was obtained, treatment sites were anesthetized with topical and intralesional lidocaine. The lower lip papules were vaporized using multiple consecutive passes of a fractionated CO₂ laser (Fraxel: repair; Solta Medical, Pleasanton, CA) with a 2-mm spot size at 225 mJ energy and 10 W of power. Intraoperative side effects consisted of lesional friability, difficulty with hemostasis, edema, and erythema. Dilute acetic acid and ice water compresses were applied to the ablated skin immediately post-treatment for 15 minutes and repeated 4 times daily. The wounds were kept well lubricated with a compounded mix of mupirocin and Aquaphor ointments which was applied after each application of the dilute acetic acid compresses until re-epithelization was complete (7 days). Topical sirolimus was not provided after treatment due to its previous untoward side effects and the patient’s vehement refusal to resume its use. Marked lesional reduction and improved lip contour with the absence of tissue friability was evident and maintained at 6 weeks post-treatment (Figure 2). No lesional recurrence was reported 6 months hence.

![Figure 1](https://doi.org/10.2147/CCID.S357282) Numerous small, firm, flesh-colored papules (biopsy-proven benign hamartomas) on the lower lip mucosa prior to treatment.
Discussion

Cowden’s syndrome is a rare condition and its associated multiple hamartomas pose a therapeutic challenge. While the increased risk for internal malignancy in CS is the primary concern, the psychological, social, and physical implications associated with multiple facial papules can also be debilitating.

Prior treatments including 5-fluorouracil injections, oral retinoids, sirolimus, surgical excision, laser ablation, cryosurgery, dermabrasion, and electrodesiccation and curettage have limited clinical utility. Advances in laser technology over the past 3 decades have led clinicians to examine their effectiveness in treating this aesthetically challenging condition.

Successful removal of hamartomas in patients with CS was initially achieved utilizing ablative carbon dioxide (CO$_2$) or erbium: yttrium-aluminum-garnet (Er:YAG) laser systems. Their use dwindled with the subsequent development of fractional lasers and other specialized laser techniques that reduced postoperative recovery time and risk of complications.

The advent of fractional lasers launched a new approach to treatment in patients with CS suffering from multiple hamartomas. In contrast to traditional ablative lasers wherein the entire epidermis and variable portions of the dermis are vaporized, fractional photothermolysis creates microscopic wounds in the treated skin thereby inducing coagulation without confluent epidermal damage. As a result, this method of laser delivery stimulates collagen remodeling and re-epithelization while reducing post-treatment recovery time and risk of untoward side effects and complications such as scarring and dyspigmentation typically associated with ablative (non-fractional) laser skin resurfacing.

In addition, a specialized technique utilizing a “pinhole method” of CO$_2$ laser vaporization has proven effective for a broad range of dermal lesions, including multiple trichilemmomas in a CS patient. Similar to fractional laser treatment, this laser technique induces collagen regeneration by creating microscopic holes which penetrate from the epidermis to the deep dermis and is associated with fewer side effects and quicker healing.
Laser ablation is not always sufficient in removing unwanted papules when performed alone. Therefore, combination laser treatment with topical or oral sirolimus has been advocated. Sirolimus is an mTOR inhibitor and analog of rapamycin that is commonly used as an immunosuppressive agent after organ transplantation. The PTEN mutation linked to Cowden’s syndrome results in inhibition of the PDK1/Akt/mTOR pathway. Administration of sirolimus plays an important role in regulating the cell cycle thereby preventing abnormal cell proliferation and reducing the recurrence of multiple hamartomas. Serious side effects and complications may result from taking sirolimus and patients must be monitored for unusual symptoms.

**Conclusion**

There are now several different treatments that can be used singly or in combination to reduce multiple hamartomas. The development of fractional CO\(_2\) laser technology has enabled practitioners to apply yet another tool to provide long-standing clinical improvement with reduced untoward side effects. Critical to the success of this technology is the expertise of the practitioner as well as appropriate postoperative management and wound care to ensure optimal healing and cosmetic outcomes. Despite the excellent safety record and clinical effectiveness of these specialized lasers, their improper intraoperative use and/or inadequate post-treatment patient care could potentially result in incomplete lesional eradication and/or adverse side effects.

In the case described herein, fractional ablative CO\(_2\) laser vaporization was effectively used as the sole treatment to reduce multiple oral hamartomas associated with Cowden’s syndrome with minimal recovery and post-treatment side effects. Further investigation regarding CS, hamartoma morphology, and advances in laser technology may elucidate critical information to optimize the treatment approach for this clinically and aesthetically complex condition.

**Ethics and Consent Statements**

Institutional approval was not required to publish these case details. Written informed consent was obtained by the patient for publication of the case details.

**Disclosure**

The authors report no conflicts of interest in this work.

**References**

1. Aslam A, Coulson IH. Cowden syndrome (multiple hamartoma syndrome). *Clin Exp Dermatol*. 2013;38(8):957–959. doi:10.1111/ced.12140
2. Chippagiri P, Banavar Ravi S, Patwa N. Multiple hamartoma syndrome with characteristic oral and cutaneous manifestations. *Case Rep Dent*. 2013;5:109–114.
3. Mester J, Eng C. Cowden syndrome: recognizing and managing a not-so-rare hereditary cancer syndrome: Cowden Syndrome. *J Surg Oncol*. 2015;111(1):125–130. doi:10.1002/jso.23735
4. Lopes S, Vide J, Moreira E, Azvedo F. Cowden syndrome: clinical case and a brief review. *Dermatol Online J*. 2017;23(8):52–55.
5. Pilarski R, Burt R, Kohlman W, et al. Cowden syndrome and the PTEN hamartoma tumor syndrome: systematic review and revised diagnostic criteria. *J Natl Cancer Inst*. 2013;105(21):1607–1616. doi:10.1093/jnci/djt277
6. Klein A, Bäumler W, Landthaler M, Babillas P. Laser thermal therapy of benign skin tumors: review and update. *Int J Hyperthermia*. 2011;27:762–770. doi:10.3109/02656736.2011.599049
7. Pecaro BC, Garchime WJ. The CO\(_2\) laser in oral and maxillofacial surgery. *J Oral Maxillofac Surg*. 1983;41(11):725–728. doi:10.1016/0278-2391(83)90189-1
8. Wheeland RG, McGillis ST. Cowden’s disease—treatment of cutaneous lesions using carbon dioxide laser vaporization: a comparison of conventional and superpulsed techniques. *J Dermatol Surg Oncol*. 1989;15(10):1055–1059. doi:10.1111/j.1524-4725.1989.tb03122.x
9. Aslam A, Alster TS. Evolution of laser skin resurfacing: from scanning to fractional technology. *Dermatol Surg*. 2014;40:1163–1172. doi:10.1097/01.DSS.0000452648.22012.a0
10. Alster TS. Cutaneous resurfacing with CO\(_2\) and erbium: YAG lasers: preoperative, intraoperative, and postoperative considerations. *Plast Reconstr Surg*. 1999;103(2):619–632. doi:10.1097/00006534-199902000-00040
11. Brightman LA, Brauer JA, Anolik R, et al. Ablative and fractional ablative lasers. *Dermatol Clin*. 2009;27(4):479–489. doi:10.1016/j.detc.2009.08.009
12. Metelitsa AI, Alster TS. Fractionated laser skin resurfacing treatment complications: a review. *Dermatol Surg*. 2010;36(3):299–306. doi:10.1111/j.1524-4725.2009.01434.x
13. Chang I, Lee Y, Seo Y, Kim C, Lee J, Im M. Treatment of multiple trichilemmomas with the pinhole method using a carbon dioxide laser in a patient with Cowden syndrome: multiple trichilemmomas treated by CO\(_2\) laser. *Dermatologic Ther*. 2015;28(2):71–73. doi:10.1111/dth.12212
14. Botsali A, Caliskan E, Eşme P, Dündar Ö. Oral hamartomatous lesion of Cowden’s disease treated with the combination of erbium: YAG laser and topical sirolimus. *Dermatol Ther*. 2019;32(5). doi:10.1111/dth.13002

15. Iacobas I, Burrows PE, Adams DM, et al. Oral rapamycin in the treatment of patients with hamartoma syndromes and PTEN mutation. *Pediatr Blood Cancer*. 2011;41(2):321–323. doi:10.1002/pbc.23098

16. Alster TS, Li MK. Dermatologic laser side effects and complications: prevention and management. *Am J Clin Dermatol*. 2020;21:711–723. doi:10.1007/s40257-020-00530-2