



Case report

Treatment of multi-position condyloma acuminatum using topical CO₂ laser combined with photodynamic therapy – Report of 6 cases

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ABSTRACT

Background: Condyloma acuminatum(CA) is a venereal disease associated with a high rate of recurrence due to the rapid replication and subtle immune escape mechanism of Human Papillomavirus(HPV). Topical CO₂ laser can remove verruca accurately. Photodynamic therapy with 5-aminolevulinic acid(PDT-ALA) is also an effective therapy which targets on HPV infected sites. Some studies demonstrate that when combined with use of CO₂ lasers, photodynamic therapy can become more effective.

Methods: We attempted to clinically cure a series of CA grown on cervix, urethra, urinary meatus, vulva, crissum and anal canal with treatment of topical CO₂ laser combined with ALA photodynamic therapy and report herein 6 cases.

Results: Topical CO₂ laser combined photodynamic therapy for CA achieved a complete response after 3 courses of treatment. No recurrence was found after 6-month follow-up in 6 cases, and the HPV PCR detection for all was changed from positive to negative.

Conclusion: When it comes to CA treatment, the combination of photodynamic therapy and CO₂ laser usage can give full play to their own respective superiority, and the curative effect is more significant.

1. Introduction

Condyloma acuminatum is a common venereal disease caused by HPV infection. Due to the rapid replication and subtle immune escape mechanism of HPV, CA is difficult to cure and is associated with a high rate of recurrence. The common traditional treatments include cryotherapy, CO₂ lasers, electrocautery and so on, all of which can be painful, may not completely clear up latent HPV infection, and do not always prevent recurrence.

However, as an established therapy, photodynamic therapy results in “targeted phototoxicity” due to an interaction between light, a photosensitizer and oxygen that can cause diseased tissue destruction and HPV elimination. It has been proved that when combined with use of CO₂ lasers, photodynamic therapy can become more effective [1]

We attempted to clinically cure a series of CA with a CO₂ laser combined with PDT and report herein 6 cases.

2. Cases

The lesions grown on cervix, urethra, urinary meatus, vulva, crissum and anal canal. Cases 1–6 can be found in Table 1. All patients had histories of unsafe sexual contact. The acetowhite test for all lesions

was (+), and HPV PCR detections were all positive (Figs. 1, 3, 5, 7, 9, 11, 13, 14).

3. Treatment

First, the warts must be fully exposed, routinely cleaned and disinfected, then located using acetic acid. Treatment for the first time to use a CO₂ laser (ML-2030CI; Qizhi laser technology Co., Ltd., Wuhan, China) for wart removal. Excision was performed in continuous wave mode. The wavelength is 10.6 μm and the output power of laser is usually arranged from 3.0 to 6.0 W according to the size and thickness of warts. The laser beam was guided by a manipulator to focus it on the lesion. The wart was grasped with a surgical clamp in order to visualize its peduncle during the excision. Along the edge of wart, the epidermis was incised carefully down to the dermal epidermal junction (DEJ), until the wart totally removed. This procedure was finally completed by a CO₂ laser vaporization of the damaged mucosal surface to avoid external bleeding [2]. Second, a 20% ALA solution was prepared by dissolving 118 mg ALA (pH = 4; FudanZhangjiang Bio-Pharmaceutical Co., Ltd., Shanghai, China) in 0.5 ml sterile 0.9% NaCl immediately prior to its application. It's important to emphasize that the ALA solution must be fresh dissolved and the period of preservation

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Table 1
Cases introduction.

	Age	Gender	Position	Size(cm ³) (thelargest one)	Number	HPVTypes	HPV types (after treatment)	Adverse reaction
Case1	24	F	cervix	2.5*2.3*1.5	1	11/ 81	(-)	Swelling, erythema (Fig.13)
Case 2	32	M	urethra	0.5*0.5*0.3	1	11	(-)	(-)
Case 3	32	F	urinary meatus	0.2*0.2*0.1	8	11	(-)	Burning pain, Stinging
Case 4	23	F	vulva	0.7*0.5*0.3	5	6	(-)	burning,erosion, exudation (Fig.14)
Case 5	64	F	crissum	0.1*0.1*0.1	21	11/42/81	(-)	(-)
Case 6	26	M	anal canal	0.5*0.3*0.2	11	6/11	(-)	Erythema



Fig.1



Fig.2

Fig. 1. [{Figs. 1 and 2}] Pre- and post-treatment images of lesion on cervix. (Case1).



Fig.3

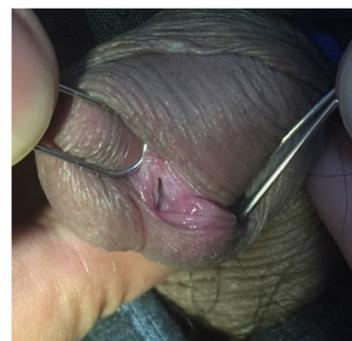


Fig.4

Fig. 2. [{Figs. 3 and 4}] Pre- and post-treatment images of lesion on urethra.(Case2).



Fig.5



Fig.6

Fig. 3. [{Figs. 5 and 6}] Pre- and post-treatment images of lesion on urinary meatus.(Case3).

shouldn't exceed 4 h, for it has poor stability [3]. A thin sterile absorbent cotton fiber was soaked in the solution and was gently sealed to the lesions and the adjacent skin (1 cm border). Then the lesions and dressings were occluded with food-grade cling film, outside of which was covered with thick gauze for protection. When it comes to cervical or anal canal verruca, a condom stuffed with sterile gauze is used to fix the dressing. Finally, after 3 h in light free conditions, the sites were

irradiated with a helium–neon laser (Yage Laser Apparatus Co., Ltd, Wuhan, China) with a peak emission at 630 nm to a total dose of 150 J/cm² for 30 min. The course of treatment of PDT is usually 3 times. During the treatment, if any verruca recurs, additional CO₂ laser treatment sessions are necessary. Besides, patients were advised to pay attention to local hygiene, abstain from sex, and avoid spicy food and fatigue. Follow-up visits were performed after 7,15 days and 1, 3,



Fig.7



Fig.8

Fig. 4. [Figs. 7 and 8] Pre- and post-treatment images of lesion on vulva.(Case 4).



Fig.9



Fig.10

Fig. 5. [Figs. 9 and 10] Pre- and post-treatment images of lesion on crissum.(Case 5).



Fig.11



Fig.12

Fig. 6. [Figs. 11 and 12] Pre- and post-treatment images of lesion on anal canal.(Case 6).



Fig. 7. [Fig. 13] One week after the first PDT treatment, the patient of case 1 experienced an adverse reaction of swelling, erythema of the cervix. We didn't deal with it.



Fig. 8. [Fig. 14] Three hours after the second PDT treatment, the patient of case 4 experienced an adverse reaction of burning, erosion, exudation of the vulva. After 2 times of treatment suspension, the symptoms disappeared and the treatment continued.

6,12months.

4. Results

Topical CO₂ laser combined photodynamic therapy for CA achieved a complete response after 3 courses of treatment. No recurrence was found after 6-month follow-up, and the HPV PCR detection for all was negative (Figs. 2, 4, 6, 8, 10, 12). As for adverse reactions, patients occasionally had mild epithelium edema, erythema and topical burning pain (Table 1).

5. Discussion

Condyloma acuminatum is a common venereal disease that usually occurs in the genital area, in which there is a moist and hidden environment conducive to HPV growth and reproduction. Traditional treatments such as cryotherapy, CO₂ laser and electrocautery had the advantage of rapid wart removal, but they could not completely clear up latent HPV infection, leading to a high rate of recurrence.

When using PDT-ALA as a noninvasive therapy, the exogenous ALA enters the infected tissue and is absorbed by target cells. Then ALA is metabolized to protoporphyrin IX (PpIX), whose absorption band is usually 360 ~ 400 nm for blue light and 500 ~ 635 nm for red light [4]. After irradiation with the aforesaid certain wavelengths of light (we used 630nm's red light to a total dose of 150 J/cm² for 30 min in this study), the PpIX is in an excited state, releasing harmful factors such as free radicals and singlet oxygen which lead to cellular damage and death selectively. However, the surrounding healthy tissues were not damaged. Furthermore, PDT can trigger various immune reactions. Recent studies demonstrate that PDT-ALA could induce a favorable infiltration of immune cells, such as CD4 + T cells and dendritic cells in infected sites, which could be responsible for healing and long-term efficacy [5]. Studies indicated that application of PDT-ALA can not only significantly reduce CA recurrence rates [6], but also HPV viral loads can decreased significantly after PDT treatment as well [7].

As for CO₂ laser treatment, the choice of which is based on the ability of its wavelength to both effectively ablate tissue down to a depth that is needed and simultaneously coagulate tissue. It is significant to choose the proper amount of thermal destruction to effectively treat. Increasing the fluence and density would increase the depth of ablation and coverage, respectively, and may be appropriate for more nodular or infiltrative tumours. However, for warts grown on mucosal surface in these cases, we used the low output power laser (3.0–6.0 W) to wipe away much of the warts gently as the lesions separate at the DEJ, leading to almost no smoke to evacuate. Also, studies found that higher power laser causes less thermal injury, because of the increased speed of cutting and reduced contact time with surrounding cells [8]. The thermal injury has been proved could expose antigens to the immune system. Researchers found that CD68 markers were identified only in the dermis and completely absent in the epidermis during HPV infection, however, after thermal injury, they were found in the epidermis during physiological and reparative regeneration [9]. Furthermore, several studies have previously shown that thermal injury of the skin induce cellular immune responses, such as recruitment of

neutrophils and macrophages, as well as induce expression of various immune mediators, which could contribute to clearance of HPV [10,11].

In these cases, the use of CO₂ lasers combined with photodynamic therapy was adopted. On the one hand, a CO₂ laser can remove verruca quickly and accurately. As epidermal integrity is disrupted by CO₂ laser vaporation, using ALA immediately after laser vaporation can improve the absorption of ALA and effectiveness of PDT. At the same time, hemostasis can be achieved by carbonizing the damaged epidermis. On the other hand, photodynamic therapy utilizing enzymatic reaction and photodynamic effects, cannot only significantly reduce the recurrence rate by eliminating surrounding recessive HPV-infected areas [12], but also avoid epithelial adverse stimulation caused by repeated physical therapy. We conclude that the combination of photodynamic therapy and CO₂ laser usage can give full play to their own respective superiority, and the curative effect is more significant.

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