

CASE AND RESEARCH LETTER

[Translated article] Refractory Anogenital Warts: Good Response to Photodynamic Therapy[☆]



Condilomas acuminados resistentes a los tratamientos convencionales con buena respuesta a tratamiento con terapia fotodinámica

To the Editor:

Anogenital warts are produced by specific genotypes of human papillomavirus (HPV). Although this condition is benign, its treatment can prove difficult owing to the lack of response, local adverse effects, and frequent recurrences¹. The mechanism of action of photodynamic therapy (PDT) involves destruction of specific previously sensitized cells and tissues with an exogenous photosensitizer that is activated by light of a given wavelength for an appropriate duration of exposure². The literature provides few data on its use in the treatment of genital warts, and, given that it is applied off-label^{3,4}, no clear guidelines have been prepared.

A 56-year-old man from Peru was evaluated for treatment of several anogenital warts on the penis. He had a long history of pustular psoriasis that had been treated with different drugs both in monotherapy and in combination with other agents (methotrexate, acitretin, ciclosporin, infliximab, etanercept, and ustekinumab), nonalcoholic fatty liver disease, and pulmonary tuberculosis during adolescence that had been treated appropriately.

He had had anogenital warts for 15 years. Biopsy and genotyping revealed HPV subtypes 6, 16, 40, 42, 53, and 61. After the initial diagnosis, the patient had received various local treatments, which, in order of prescription, included podophyllotoxin solution, imiquimod 5% cream, and treatments to which he did not respond: topical cidofovir 1%



Figure 1 Lesions before the first session of photodynamic therapy.

for 4 months, with partial but insufficient improvement of the lesions, as well as cryotherapy and sinecatechins, again with no response. The patient then received PDT based on methyl aminolevulinate³ (2 cycles of 2 sessions), with a minimal clinical response. From then on, treatment was with imiquimod 5% (3 times weekly for 12 weeks); the response was partial although insufficient and temporary. The patient's psoriasis improved during therapy with imiquimod, thus making it possible to reduce his immunosuppressive treatment (from methotrexate and ustekinumab to ustekinumab in monotherapy). Given the poor response to previous treatments (Fig. 1), a new cycle of PDT was started with 5-aminolevulinic acid⁴ at a concentration of 78 mg/g. The incubation time was 3 hours, and the irradiation

DOI of original article:

<https://doi.org/10.1016/j.ad.2020.08.021>

[☆] Please cite this article as: Pinilla Martín B, Rivera Díaz R, Monsálvez Honrubia V. Condilomas acuminados resistentes a los tratamientos convencionales con buena respuesta a tratamiento con terapia fotodinámica. *Actas Dermosifiliogr.* 2022;113:210–212.

<https://doi.org/10.1016/j.ad.2022.01.008>

0001-7310/© 2022 Published by Elsevier España, S.L.U. on behalf of AEDV. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).



Figure 2 Lesions before the last session of photodynamic therapy.



Figure 3 Four months after the end of treatment with photodynamic therapy.

tion time was 8.2 minutes with red light at 635 nm (Aktilite CL 128, Galderma). Local anesthetic with mepivacaine 2% was administered to minimize pain at the treatment site.

A clinical response was observed as early as the first cycle, with flattening of the lesions (Fig. 2), and a complete response was achieved after a further 3 cycles administered weekly. Four months after the end of treatment, the only finding was an atrophic plaque of scar tissue (Fig. 3). Tolerance was excellent, and no local or systemic adverse effects were recorded.

PDT receives little attention in the literature, and reports are mainly case studies and series. Use of PDT as monotherapy⁵ and in combination with other treatments (previous carbon dioxide laser^{6,7}, cryotherapy⁸, and curettage⁹) is promising, with response rates greater than 70%—in some series all patients achieve complete remission—and a low incidence of recurrence, possibly because this treatment modality also acts on subclinical lesions¹⁰. Nevertheless, these data should be interpreted with caution. In the present case, the fact that the response to treatment came some months after reducing immunosuppressive treatment leads us to believe that the absence of response to the previous treatments (including the first one with PDT) can be explained—at least in part—by the immunosuppression induced by the drugs the patient was taking. Patients with cellular immunosuppression of any cause are more susceptible to diseases induced by various types of viruses. The lesions induced by HPV in particular produce a more florid clinical picture (i.e., more numerous and larger lesions), a diminished response to treatment, and a greater incidence of relapse than in immunocompetent patients. Furthermore, the first application of PDT could have proven insufficient in the present case, since only 2 cycles were administered, compared with the 3 cycles subsequently administered. As this treatment is administered off-label, we do not know if there are differences in efficacy between the 2 photosensitizers currently sold for treatment of anogenital warts.

In the present case, we observed an optimal response to treatment, with no recurrences during the 4 months of follow-up after the end of treatment. We administered local anesthetic to prevent pain during exposure to the light source, and tolerance of treatment was excellent.

In conclusion, PDT could be a safe and effective approach for the treatment of anogenital warts. It is especially useful in immunosuppressed patients with lesions refractory to standard treatment.

Conflicts of interest

The authors declare that they have no conflicts of interest with respect to the drug used in the present report.

References

1. AEPCC-Guía: Condilomas acuminados, 2015 [Accessed 19 May 2020]. Available from: http://www.aepcc.org/wp-content/uploads/2019/04/AEPCC_guiaCONDILOMAS-ACUMINADOS-ISBN.pdf.
2. Gilaberte Y, Serra-Guillén C, de las Heras ME, Ruiz-Rodríguez R, Fernández-Lorente M, Benvenuto-Andrade C, et al. Terapia fotodinámica en dermatología. *Actas Dermosifiliogr.* 2006;97:83–102, [http://dx.doi.org/10.1016/S0001-7310\(06\)73359-2](http://dx.doi.org/10.1016/S0001-7310(06)73359-2).
3. Agencia Española de Medicamentos y Productos Sanitarios. Ficha técnica de Metvix 160 mg/g crema, 2019 [Accessed 19 May 2020]. Available from: <http://cima.aemps.es/cima/pdfs/es/ft/64968/64968.ft.pdf>.
4. Agencia Española de Medicamentos y Productos Sanitarios. Ficha técnica de Ameluz 78 mg/g gel, 2017, 2019 [Accessed 19 May 2020]. Available from: <https://cima.aemps.es/cima/dohtml/ft/11740001/FichaTecnica.11740001.html>.

5. Zhao W, Shan XF, Wang CL, Liu XZ, Li Z, Xiao HL, et al. Topical 5-aminolevulinic acid photodynamic therapy for intra anal-rectal warts. *J Dermatol Treat.* 2020;31:241–4, <http://dx.doi.org/10.1080/09546634.2019.1594670>.
6. Zhang L, Li X, Liu X, Gao Y, Tang Q. Treatment of multi-position condyloma acuminatum with topical CO2 laser combined photodynamic therapy – report of 6 cases. *Photodiagnosis Photodyn Ther.* 2019;25:436–9, <http://dx.doi.org/10.1016/j.pdpdt.2019.01.030>.
7. Hu S, Yang Y, Jiang B, Su D, Zhang L, Huang Z, et al. Treatment of condyloma acuminatum using the combination of laser ablation and ALA-PDT. *Photodiagnosis Photodyn Ther.* 2019;25:193–6, <http://dx.doi.org/10.1016/j.pdpdt.2018.12.006>.
8. Mi X, Chai W, Zheng H, Zuo YG, Li J. A randomized clinical comparative study of cryotherapy plus photodynamic therapy vs. cryotherapy in the treatment of multiple condylomata acuminata. *Photodermatol Photoimmunol Photomed.* 2011;27:176–80, <http://dx.doi.org/10.1111/j.1600-0781.2011.00592.x>.
9. Lu YG, Yang YD, Wu JJ, Lei X, Cheng QH, He Y, et al. Treatment of perianal condyloma acuminatum with topical ALA-PDT combined with curettage: outcome and Safety. *Photomed Laser Surg.* 2012;30:186–90, <http://dx.doi.org/10.1089/pho.2011.3040>.
10. Hu Z, Li J, Liu H, Liu L, Jiang L, Zeng K. Treatment of latent or subclinical genital HPV infection with 5-aminolevulinic acid-based photodynamic therapy. *Photodiagnosis Photodyn Ther.* 2018;23:362–4, <http://dx.doi.org/10.1016/j.pdpdt.2018.07.014>.

B. Pinilla Martín*, R. Rivera Díaz, V. Monsálvez Honrubia

Servicio de Dermatología, Hospital Universitario 12 de Octubre, Madrid, Spain

Corresponding author.

E-mail address: belenpinillamartin@gmail.com

(B. Pinilla Martín).