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Efficiency of Photodynamic Therapy in the Treatment of Diffuse Facial Viral Warts in an Immunosuppressed Patient: Towards a Gold Standard?

M. Caucanas P. Gillard O. Vanhooteghem

Department of Dermatology, Sainte Elisabeth Hospital, Namur, Belgium

Key Words

Photodynamic therapy · Facial viral warts · Immunosuppressed 5-aminolevulinic acid · Papilloma virus · Organ transplant

Abstract

A 64-year-old man with a pulmonary transplant developed diffuse verrucae vulgares of the neck. After the failure of multiple cryotherapy treatments, 3 sessions of photodynamic therapy resulted in rapid therapeutic clinical success. This moderately painful and well-tolerated treatment is reproducible and can be very useful in treating papillomavirus infections in the immunosuppressed patient.

Case Report

We report the case of a 64-year-old man, who had been under immunosuppressive treatment for many years after a pulmonary transplant, who presented with diffuse viral warts on the neck and chin that had been present for 11 months (fig. 1). Cryotherapy sessions were conducted over the course of 9 months without success but with increasing intolerance to the related pain. Imiquimod had not been suggested due to its theoretical contraindications relating to the risk of a graft rejection and a graft-versus-host disease.

A photodynamic therapy (PDT) test session was carried out on the most prominent warts in the submental region, with a very clear improvement after 1 week (fig. 2). Two more sessions were conducted within a 10-day interval, using 2 fields of light each time, thus covering the entire surface of the neck (right and left sides). Three hours after an application of 5-aminolevulinic acid (Metvix®) under an occlusive and opaque dressing, a red light of 634 nm was delivered, with a 37 J/cm^2 light intensity for the duration of 9 min. A spray bottle filled with spring water, in combination with an integrated cooling fan, was used to decrease pain during illumination. Treatment was relatively well tolerated. The painful sensation lasted 1–2 h after illumination, whereas erythema and swelling decreased after 2–3 days. Side effects were well tolerated and were considered minor by the patient. Complete healing was archieved after 8 days.

Dr. Olivier Vanhooteghem

Department of Dermatology, Sainte Elisabeth Hospital , Place Louise Godin
BE–5000 Namur (Belgium)
Tel. +32 8172 0585, Fax +32 8173 0766, E-Mail ovanhooteghem@hotmail.com

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A fast and marked improvement was noted after only 2 sessions of PDT. A third session resulted in complete clearance (fig. 3). No recurrence was noted 1 year after the last session of treatment.

Discussion

Viral wart treatments include local keratolytic application, topical retinoids, cryotherapy, intralesional injection of bleomycin, imiquimod, laser CO_2, pulsed dye laser and intralesional immunotherapy [1]. The benefit-risk ratio in organ-transplanted patients is currently being evaluated [2]. PDT has proven to be successful in the treatment of actinic keratosis and basocellular carcinoma. At present, new indications are emerging, including verrucae vulgares.

Several studies show that protoporphyrin IX accumulation after 5-aminolevulinic acid application is not specific to tumour cells [3]. HPV-infected cells also accumulate protoporphyrin IX in a specific manner, as compared to the surrounding healthy cells [4, 5], as demonstrated by in vivo fluorescence spectroscopy [6]. PDT therapeutic effects are due to anti-inflammatory and anti-proliferative properties activated through the release of cytotoxic radicals that destroy keratinocytes via selective apoptosis [7].

Numerous clinical studies have demonstrated the efficiency of PDT in the treatment of viral warts of the hands [8] and feet, (recalcitrant [9–13] or not), including periungual warts. Several studies have shown that PDT is efficient in treating plane warts [14, 15], including those on the face [16]. Ohtsuki et al. [17] treated verrucae vulgares on the hands and feet with a clear clinical improvement in 68.3% of the patients. This improvement was confirmed by a placebo-controlled study led by Bastuji-Garin et al. [18]. In addition, Wang et al. [19] successfully treated 42% of recalcitrant viral warts, and Chong and Kang [20] reported complete healing of recalcitrant foot verrucae vulgares after only 3 PDT sessions. Schroeter et al. [21] treated periungual warts with full clinical success in 90% of patients after a mean of 4.7 sessions. Some authors suggested the use of a keratolytic pre-treatment (urea 10%, salicylic acid 10%, for 1 week) to enhance the treatment's efficiency, with complete healing in 75% of viral warts [6]. In the immunosuppressed subject, Granel-Brocard et al. [22] reported the therapeutic effect of PDT on recalcitrant warts.

The advantages of PDT are numerous. It is a safe, noninvasive technique, which yields effective therapeutic results in multiple series of patients [17, 23]. The risk of secondary infection after PDT is insignificant, and the cosmetic results are excellent [7]. The technique is particularly interesting in slow-healing subjects and acts selectively, allowing healthy surrounding skin to remain intact and functional [24]. The use of one or several fields of light enables treatment of many lesions at the same time, thus limiting the risk of wart spread and recurrence between sessions. The drawbacks are pain and local side effects such as erythema and swelling, which is generally mild and well tolerated (table 1, table 2, table 3).

Immunosuppressed patients often present with extensive viral warts. Controlling the spead of these warts is of great importance because they can potentially be a source of neoplasia [25]. Our case report shows that PDT can be very efficient in the treatment of verrucae vulgares in immunosuppressed organ-transplanted patients. The technique is easy to implement, resulting in minimal side effects and reproducible results.

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We think that PDT should be considered as a gold standard in the treatment of facial verrucae vulgares in immunodepressed patients.

Disclosure

All authors certify that they have no conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject of this manuscript.

Table 1. Efficiency of PDT: patient characteristics, treatment and localisation

Study[a]	Patients (n)	Age (years)	Sex		Treatments	Immunologic status	Level of evidence	Localisation
			F	M				
Lu [15]	18	18–41	13	5	RPW	NS	D	1
Ohtsuki [17]	6	22–45	2	4	RVV	NS	D	2, 3
Morton [24]	12	20–45	8	4	RVV	NS	D	4
Lin [16]	3	15–25	2	1	RPW	NS	D	1
Granel-Brocard [22]	1	54	1	0	RVV	ID	D	3
Wang [19]	12	18–70	2	10	RVV	IC	D	2, 3
Schroeter [21]	20	10–55	17	3	RVV, NPT	NS	D	4
Schroeter [12]	31	6–74	18	13	RVV	NS	D	3
Mizuki [14]	1	13	0	1	RPW	NS	D	1
Fabbrocini [6]	67	18–40	31	36	RVV	NS	C	3
Stender [9]	45	20–84	26	19	RVV	IC	C	2, 3
Stender [13]	30	22–74	16	14	RVV	3 ID	D	2, 3
Stender [10]	52	16–79	42	20	RVV, RPW	5 ID	D	1, 2, 3, 5
Smetana [5]	1	NS	NS	NS	NS	ID	D	2
Stender [11]	4	NS	NS	NS	RVV	NS	D	2, 3, 6, 7
Ammann [23]	6	21–31	2	4	RVV	NS	D	2

F = Female; M = male; NS = not specified; RVV = recalcitrant verrucae vulgares; RPW = recalcitrant plane warts; ID = immunodeficient; IC = immunocompetent; NPT = no previous treatment. 1 = Face; 2 = hand; 3 = foot; 4 = periungual; 5 = arm; 6 = knee; 7 = heel. [a] First author [reference].

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Table 2. Efficiency of PDT: session specifics

Study[a]	Photosensitizer	Occlusion (h)	Session (n)	Interval
Lu [15]	ALA 10%	4	2–3	2 w
Ohtsuki [17]	ALA 20%	5	10	2–3 w
Lin [16]	ALA 20%	3	4–5	1 w
Granel-Brocard [22]	MAL	3–4	2	2 m
Wang [19]	ALA 20%	4	4	2 w
Schroeter [21]	ALA 20%	3–6	1–13	2 w
Schroeter [12]	ALA 20%	4–8	1–7	NS
Mizuki [14]	ALA 20%	6	2	NS
Fabbrocini [6]	ALA 20% versus PLC	5	3	1 w
Stender [9]	ALA 20% versus PLC	4	6	1–2 w
Stender [13]	ALA 20%	5	1–3	10 d
Stender [10]	ALA 20%	4–5	3	1 w
Smetana [5]	ALA 20%	4	1	
Stender [11]	ALA 20%	12	2–3	NS
Ammann [23]	ALA 20%	5–6	1	

MAL = Methyl-aminolevulinic; ALA = aminolevulinic acid; PLC = placebo cream; w = week; m = month; d = day. [a] First author [reference].

Table 3. Efficiency of PDT: response to treatment

Study[a]	Light source	Cure rate	Follow-up
Lu [15]	Laser 635 nm	CR: 17 persons	6 m
Ohtsuki [17]	RL 633 nm	PR: 68.3%	4 w
Lin [16]	RL 633 nm	CR: 100%	1–3 m
Granel-Brocard [22]	RL 570–670 nm	CR: 100%	5 m
Wang [19]	RL 590–700 nm	CR: 5 persons	8–16 m
Schroeter [21]	RL 580–720 nm	CR: 90%	5.9 m
Schroeter [12]	RL 580–720 nm	CR: 88%	3 m
Mizuki [14]	Metal Halide Lamp 630–700 nm	CR: 100%	5 m
Fabbrocini [6]	Tungsten lamp, 630 nm	CR: 75% under ALA-PDT; 22.8% under PLC-PDT	22 m
Stender [9]	RL 590–700 nm	CR: 100% under ALA-PDT; 71% under PLC-PDT	18 w
Stender [13]	Halogen lamp	CR: 73%	12 m
Stender [10]	White light from slide projector	CR: 58%; ID: 1 person	3–17 m
Smetana [5]	Xenon lamp, RL 590–700 nm	Dramatic clearance	2 y
Stender [11]	Unfiltered lamp	CR: 100%	6 w to 1 y
Ammann [23]	Visible light from slide projector	CR: 1 person	2 m

PDL = Pulsed dye laser; CR = complete response; PR = partial response; RL = red light; IPL = intense pulsed light; NS = not specified; MoW = mosaic warts; MyW = myrmecia warts; VIS = visible light; wIRA = waterfiltered infrared A; ALA = aminolevulinic acid; PLC = placebo cream; ID = immunodeficient; m = months; w = weeks; y = years. [a] First author [reference].

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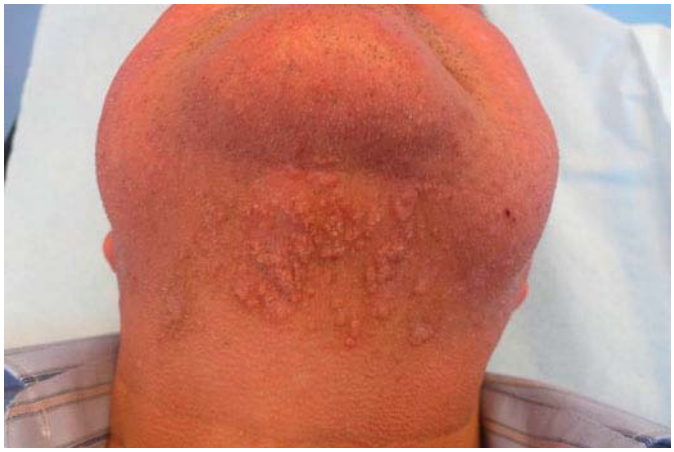

Fig. 1. Viral warts of the neck in a pulmonary transplanted patient under immunosuppressive treatment.

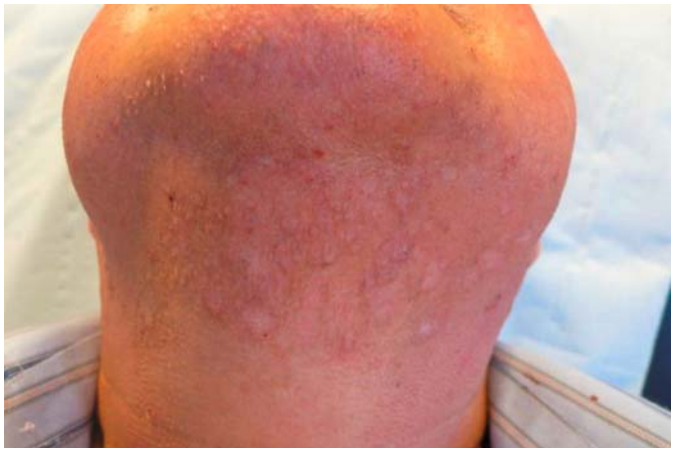

Fig. 2. Clinical image after healing of the test area.

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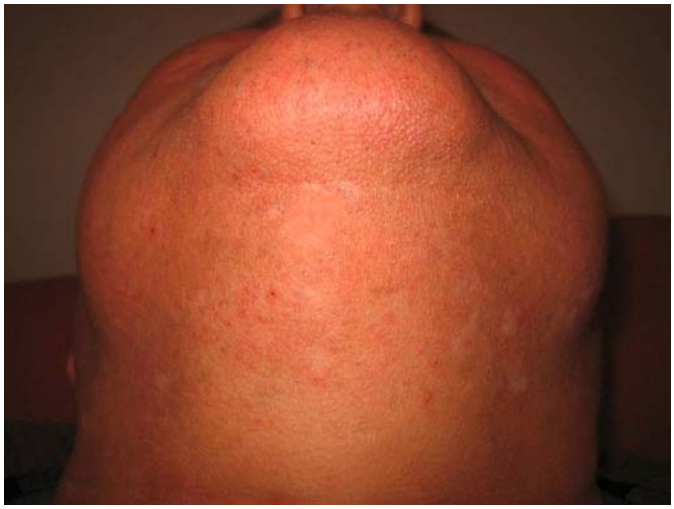

Fig. 3. Complete healing of the warts after three sessions of PDT.

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