



CASE REPORT

Effect of Sublingual Isolated Transfer Factors in a Case of Therapy Resistant Periungual Warts

Marcella Nascimento e Silva, MSc, MD^{1*} and Karla Gonçalves, Pharm.B²

¹*Clínica Optimize, Centro Médico Monte Sinai, Avenida Presidente Itamar Franco, Brazil*

²*Faculdade de Farmácia, Universidade Federal de Juiz de Fora (UFJF), Brazil*

*Corresponding author: Marcella Nascimento e Silva, Clínica Optimize, Centro Médico Monte Sinai, Avenida Presidente Itamar Franco, 4001. Sala: 713 - Leste - CEP 36033-318, Cascatinha - Juiz de Fora -MG, Brazil, Tel: +55-32-3025-4344



Abstract

Background: Periungual warts (PW), also known as verruca vulgaris, are caused by the human papilloma virus and appear as skin lesions located around the nailfold but can also affect the nail plate. Unfortunately, some of the therapies mentioned are destructive by nature and can also damage the nail matrix, hyponychium or underlying bone.

Case description: Here we describe a patient resistant to a range of standard treatments. His clinical condition dramatically improved after use of isolated transfer factors (TF).

Conclusion: As shown in this case, TF could be a possible effective alternative to treat therapy resistant PW and we hope this report will lead to further investigation, including controlled trials with TF in this patient group.

Keywords

Periungual warts, Therapy resistant, Transfer factor, Imuno TF®, Case report

keratolytics, immunotherapy etc) [4,5]. Unfortunately, some of the therapies mentioned are destructive by nature and can also damage the nail matrix, hyponychium or underlying bone, in addition to the possibility to not solve the clinical condition [2].

Here we describe a patient resistant to a range of standard treatments. His clinical condition dramatically improved after use of isolated transfer factors (TF, which consist of oligo- or polypeptides isolated from porcine spleen). TF are formed by short chains of amino acids with small pieces of ribonucleic acid (RNA) attached [6]. They are produced by T helper cells [7] and contain two subunits within its molecule: tufstin (peptide fraction, believed to be the subunit that stimulates the production of macrophages) and splentopentin, providing immune system-enhancing activity [8]. The release of TF is an indication that T helper cells (Th1 immunity) are active in the mechanistic elimination of pathogens (reason why there were chosen for the treatment of the patient here described), stimulating the production of new T helper cells, natural killer (NK) cells, macrophages and cytotoxic T cells. The general strengthening of the Th1 response is also the result of the suppression in the production of Th2 cells and their related cytokines such as IL-4, IL-5, IL-6 and IL-13, while there is an increase in Th1 cytokine levels (essentially IFN- γ) [9,10].

Although transfer factors are known since 1950s, recent technological improvements including ultrafiltration and peptides characterization, have made the technology a safe therapeutic option [11], available as oral nutritional supplement (under the commercial

Introduction

Periungual warts (PW), also known as verruca vulgaris, are caused by the human papilloma virus and appear generally as skin lesions located around the nailfold, but can also affect the nail plate [1,2]. The challenge in treating the latter is the difficulty to target the virus effectively. To date, no single therapy has been 'the gold standard' for PW, and it usually shows recurrence after treatment [2,3]. Common treatment options include both physical approaches (chemical- and electro-cautery, radiotherapy, hyperthermia, cryotherapy, radiotherapy, laser ablation and others) and local or systemic pharmacological options (inhibitors of mitosis,



Citation: Silva MN, Gonçalves K (2020) Effect of Sublingual Isolated Transfer Factors in a Case of Therapy Resistant Periungual Warts. J Dermatol Res Ther 6:089. doi.org/10.23937/2469-5750/1510089

Accepted: August 06, 2020; **Published:** August 08, 2020

Copyright: © 2020 Silva MN, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Table 1: Timeline of unsuccessful interventions before treatment with transfer factors.

Date	Previous interventions to the treatment
August 2017	One treatment of electrocoagulation.
September - October 2017	Two treatments of cryotherapy, including home use of urea 40% + salicylic acid 2% topical cream (once daily for the whole period).
Late October 2017 - early January 2018	Imiquimod 5% topical cream (3-times a week) and oral zinc (20 mg/day, once daily).
January 2018	One treatment of cryotherapy.
January 2018 - April 2018	One treatment of cryotherapy and home use of salicylic acid 16.5% + lactic acid 14.5% solution (3-times per week), alternated with retinoic acid 0.1% cream (3-times per week).
May 2018	One treatment of cryotherapy.
May - July 2018	Homeopathy with <i>Thuya occidentalis</i> 30CH, 5 globuli (3-times daily) and fluorouracil 0.5% + salicylic acid 10% + lactic acid 5% cream (3-times per week).
August 2018	One treatment of cryotherapy.
August - October 2018	L-lysine 500 mg (3-times daily, with the meal).
September 2018	Intralesional bleomycin (3 IU).

name of Imuno TF®) in countries such as Brazil, Spain and South Africa, to cite a few.

The product has already been used in treatment of different infection diseases, as can be seen in detail in a review article from Viza, et al. [11]. One of the most important clinical studies showing the ability of TF to prevent viral infection has been published in the *New England Journal of Medicine*. In this controlled study, TF was used in children with acute leukaemia. Patients were randomized, receiving either TF or placebo. Sixteen patients in the TF group and 15 in the placebo were exposed to varicella zoster virus. Only one patient in the TF group became infected versus 13 in the placebo group [12]. This encouraged to test the product for the patient with the case of periungual warts described in this paper.

Case Description

A 52-year-old man businessman sought dermatological care at our center in June 2017. He complained of injuries in the back of the right and left hand fingers. On clinical examination, he had hyperkeratotic verrucose plaques on the back of the 1st, 4th and 5th left hand fingers and on the back of the 1st and 2nd right hand fingers (no photo was taken at this time). In dermoscopy, he presented thrombosed vessels, a suggestive picture of PW. He was being followed up with rheumatology due to the diagnosis of ankylosing spondylitis and had been using adalimumab regularly for the last 7 years. The patient underwent several different treatments for PW (Table 1).

After all treatments, the patient returned with either no clinical response (Figure 1A), or with an exacerbation of the disease (emergence of new keratotic papules in the palmar region). Because of the therapy resistant nature of the disease and the reported success of transfer factors in the treatment of viruses [11], treatment with isolated TF (Imuno TF®, InfinityPharma, Brasil) was star-

ted in February 2019: 2 sublingual drops of a 100 mg/mL solution, 3-times daily after the meal. No other concomitant treatment was prescribed. The patient returned after 2 months (April 2019), reporting (almost) complete disappearance of the PW (Figure 1B). In the follow-up visit, in May 2019, the patient remained in remission (Figure 1C) and the dose was reduced to twice-daily for one more month. The dermoscopy performed after the treatment also showed the improvement in the patient's condition. In his last visit (February 2020), he was still in remission. During all the period using TF, no adverse reaction was observed or reported by the patient.

Discussion

The importance of immunotherapy in the treatment of warts had already been shown in the 70s and 80s, with the use of dinitrochlorobenzene, which induces cell-mediated immunity [13]. However, to our knowledge, this is the first report on the use of isolated TF for PW - although there have been reports on the efficacy of TF in other warts: In combination with levamisole for flat wart patients [14], and in 2 pediatric patients (aged 2 and 12) with the Wiskott-Aldrich syndrome [15,16].

TFs are part of the immune system, and they are believed to act as a unique type of messenger used in cell-to-cell communication. They behave as hybrids between interleukins and antibodies, carrying messages from one cell to another (like interleukins), and binding to antigens in a similar manner to what antibodies do. They consist of small natural peptides which are non-species-specific: They are composed of oligoribonucleotides attached to a peptide molecule inherent and have shown efficacy in a wide range of different viruses [10,11]. Their possible role in this case is due to could be related to their immunoregulatory effects, strengthening the Th1 response. The remission observed after 9 months is a good indicative of the potential of this therapy for PW.

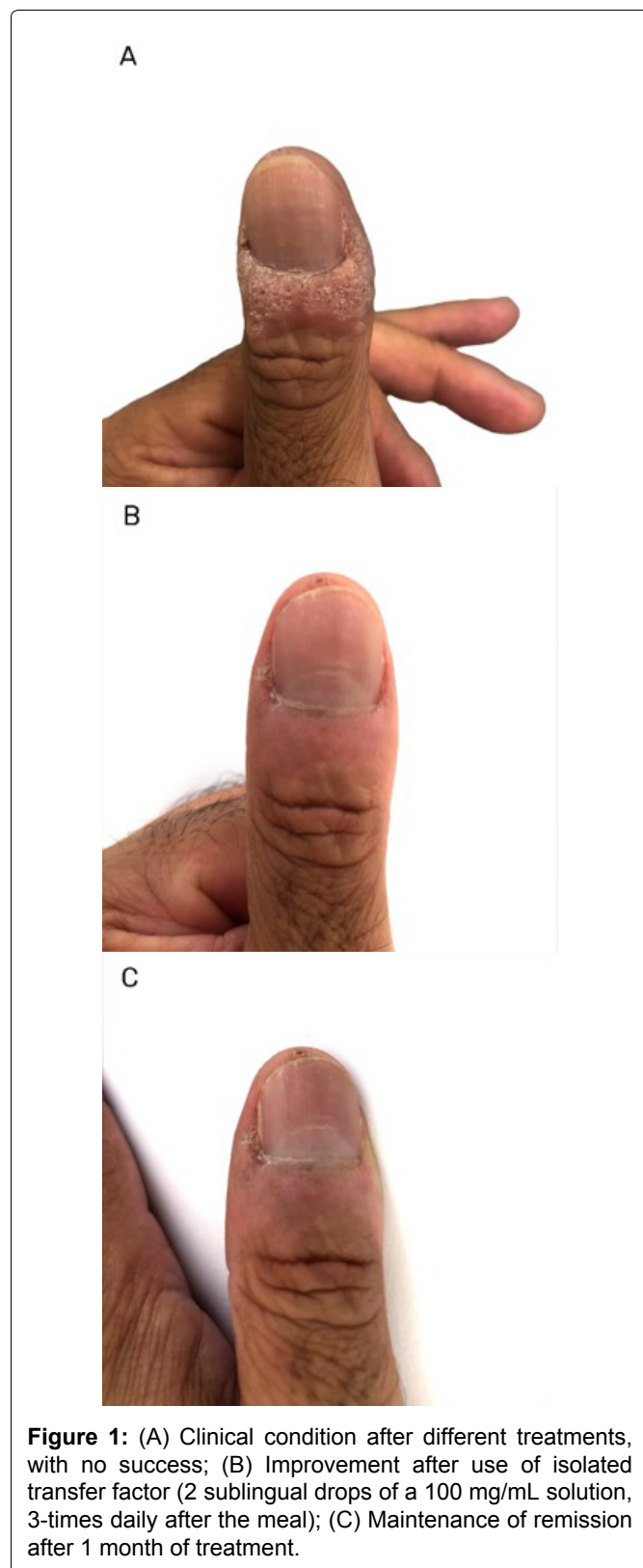


Figure 1: (A) Clinical condition after different treatments, with no success; (B) Improvement after use of isolated transfer factor (2 sublingual drops of a 100 mg/mL solution, 3-times daily after the meal); (C) Maintenance of remission after 1 month of treatment.

Conclusion

As shown in this case, TF could be a possible effective alternative to treat therapy resistant PW and maintain the patient in remission. We hope this report will lead to further investigation, including controlled trials with TF for this clinical condition.

Acknowledgements

Not applicable.

Funding Sources

None.

Conflict of Interest

The authors have no conflict of interest to declare.

References

1. Leung NL, Lee SK (2010) Viral infections of the hand. *Curr Orthop Pract* 21: 568-572.
2. JC S, JB K (1998) Viral infections. In: RH C, JL B, DA B, SM B, editors. *Rook Textbook of Dermatology*. Oxford: Blackwell 1015-1021.
3. Lim JTE, Goh CL (1992) Carbon dioxide laser treatment of periungual and subungual viral warts. *Australas J Dermatol* 33: 87-91.
4. Soni P, Khandelwal K, Aara N, Ghiya B, Mehta R, et al. (2011) Efficacy of intralesional bleomycin in palmo-plantar and periungual warts. *J Cutan Aesthet Surg* 4: 188-191.
5. Schroeter CA, Kaas L, Waterval JJ, Bos PM, Neumann HAM (2007) Successful treatment of periungual warts using photodynamic therapy: A pilot study. *J Eur Acad Dermatol Venereol* 21: 1170-1174.
6. Berrón-Pérez R, Chávez-Sánchez R, Estrada-García I, Espinosa-Padilla S, Cortez-Gómez R, et al. (2007) Indications, usage, and dosage of the transfer factor. *Rev Alerg Mex* 54: 134-139.
7. Fudenberg HH, Fudenberg HH (1989) Transfer factor: Past, present and future. *Annu Rev Pharmacol Toxicol* 29: 475-516.
8. Salazar-Ramiro A, Hernández P, Rangel-Lopez E, Pérez de la Cruz V, Estrada-Parra S, et al. (2018) Dialyzable leukocyte extract (transfer factor) as adjuvant immunotherapy in the treatment of cancer. *MOJ Autoimmune Dis* 1: 1-7.
9. Krishnaveni M (2013) A review on transfer factor an immune modulator. *Drug Invent Today* 5: 153-156.
10. White A (2009) *Transfer Factors & Immune System Health*. (2nd edn), North Charleston, USA. BookSurge.
11. Viza D, Fudenberg HH, Palareti A, Ablashi D, Vinci CD, et al. (2013) Transfer factor: An overlooked potential for the prevention and treatment of infectious diseases. *Folia Biol* 59: 53-67.
12. Steele RW, Myers MG, Vincent MM (1980) Transfer factor for the prevention of varicella-zoster infection in childhood leukemia. *N Engl J Med* 303: 355-359.
13. Lee S, Koo Cho C, Gie Kim J, Il Chun S (1984) Therapeutic effect of dinitrochlorobenzene (DNCB) on verruca plana and verruca vulgaris. *Int J Dermatol* 23: 624-626.
14. Zhengyi J, Xincheng Y, Shizheng X (1999) A clinical analysis of lavamisole and transfer factor in the treatment of flat wart. *J Hubei Med Univ* 3.
15. Ormerod AD, Finlay AY, Knight AG, Mathews N, Stark JM, et al. (1983) Immune deficiency and multiple viral warts: A possible variant of the Wiskott-Aldrich syndrome. *Br J Dermatol* 108: 211-215.
16. Stevens DA, Ferrington RA, Merigan TC, Marinkovich VA (1975) Randomized trial of transfer factor treatment of human warts. *Clin Exp Immunol* 21: 520-524.