

Use of imiquimod in the treatment of chronic periungual warts

Uso do imiquimode no tratamento de verrugas periungueais crônicas

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ABSTRACT

Warts are the most frequent periungual tumors presented in dermatological consultations. They are caused by several types of human papillomavirus (HPV), and some of these lesions evolve to a spontaneous cure. However, there are lesions that do not regress without a therapeutic approach, and some of them are resistant to several therapies. I present a case of a 14-year-old patient with disseminated periungual warts in both hands, resistant to several previous therapies, and who evolved with cure after the use of occlusive imiquimod.

Keywords: Warts; Nails; Drug therapy; Drug therapy, combination; Immunotherapy; Immunotherapy, active; Neoadjuvant therapy

RESUMO

Verrugas são os tumores periungueais mais frequentes nas consultas dermatológicas. São causadas por diversos tipos de papilomavírus humano (HPV), e parte destas lesões evolui com cura espontânea. Porém, existem lesões que não regredem sem uma abordagem terapêutica, e algumas que se mostram inclusive resistentes a diversas abordagens. Apresento caso de paciente de 14 anos, com verrugas ungueais disseminadas em ambas as mãos, resistentes a diversos tratamentos prévios, e que evoluiu com cura após uso de imiquimode oclusivo.

Palavras-chave: Verrugas; Terapêutica; Terapia combinada; Adjuvantes imunológicos; Fatores imunológicos; Unhas; Imunoterapia ativa; Imunoterapia

INTRODUCTION

Viral warts are highly prevalent dermatoses in the population, usually affecting the extremities of the limbs. They arise from infection by human papillomavirus (HPV) types 1, 2, 4, 27 and 57.^{1,2} Its diagnosis is generally clinical, and an analysis can be performed using dermoscopy to reveal the digitiform projections and capillary dilations^{1,3} or even histopathological examination for diagnostic confirmation and exclusion of differential diagnoses such as squamous cell carcinoma (SCC).^{4,5} Considered as the most common nail tumor, they can occur around the nail plate, being called periungual warts, while those occurring below the nail are referred to as subungual warts.¹

Warts can persist for years with little or no sign of inflammation. The spontaneous elimination of the infection can occur at any time, starting with a reduction in the size of the lesion and then progressing to its disappearance, a process that can last from a few months to years. Spontaneous healing in children can occur after just a few months, while in adults, the process can be much slower, with persistence for five to 10 years.^{5,6}

How I do?

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The approach to treating warts encompasses three main forms: destructive treatments, use of antiproliferative agents, and immunological therapies.^{1,2,5,7,8,9} Destructive treatments are the most performed and those with the highest level of recommendation, and include the use of chemicals such as acid solutions, interventions such as cryotherapy, as well as the use of laser, electrofulguration, and surgical excision.^{1,6} Use of podophyllin,⁷ 5-fluorouracil, and intradermotherapy with bleomycin² exemplify treatments with antiproliferative agents. Treatments using immunological therapies can be performed systemically, such as oral administration of cimetidine, levamisole or zinc sulfate;¹⁰ intralesional application of several immunostimulatory antigens, such as *Propionibacterium acnes*;¹¹ and using topical products applied on the sensitizing lesions, such as diphenycprone, or immunomodulators such as imiquimod (IQM).⁹

Topical imiquimod stimulates the immune response of the epithelium, both innate and adaptive, inducing the production of cytokines and migration of Langerhans cells.^{12,13} This allows its use for the treatment of a wide variety of benign and malignant skin conditions due to its potential antiviral, anti-tumor, and immunoregulatory effects.¹² Currently, the regulatory agencies of the United States (Food and Drug Administration - FDA) and Brazil (Brazilian Health Regulatory Agency - ANVISA) approved topical imiquimod for the treatment of anogenital warts, actinic keratosis, and superficial basal cell carcinomas. However, several studies demonstrate its beneficial

effect on the treatment of many other skin diseases, among them periungual warts.^{5,12,14,15,16}

I present the case of a 14-year-old immunocompetent patient with disseminated periungual warts on the fingers of both hands, resistant to several standard treatments, which evolved with an excellent response after the introduction of topical imiquimod.

METHODS

We report a case of an atopic, immunocompetent, 14-year-old patient with lesions for two years. He refers to onychotillomania, which is why the lesions spread to all the fingers, and he has already undergone treatments during this period with cryotherapy, chemocautery, and electrocauterizations, without success.

In his first consultation, he presented multiple periungual lesions in all fingers of both hands, with more exuberant involvement of the right thumb (Figure 1). A destructive treatment was proposed, with the application of phenol 88% in the clinic followed by application of fuming nitric acid in weekly sessions, associated with daily home use of a commercial solution of 16.5% salicylic acid and 14.5% lactic acid (SA+ LA). The patient did not attend the sessions regularly as planned, but maintained the home use of the solution, completing four sessions of application of the acids in eight weeks. Despite noticing a partial improvement in his condition, he reported a high impact on his quality of life due to the dark yellowish aspect that chemocautery left on his fingers, and requested changes in therapy (Figure 2).



FIGURE 1: Clinical aspect at the first consultation. **A** - Overview of the involvement of periungual warts on the fingers of both hands. **B** - Aspect of the right thumb, most affected finger

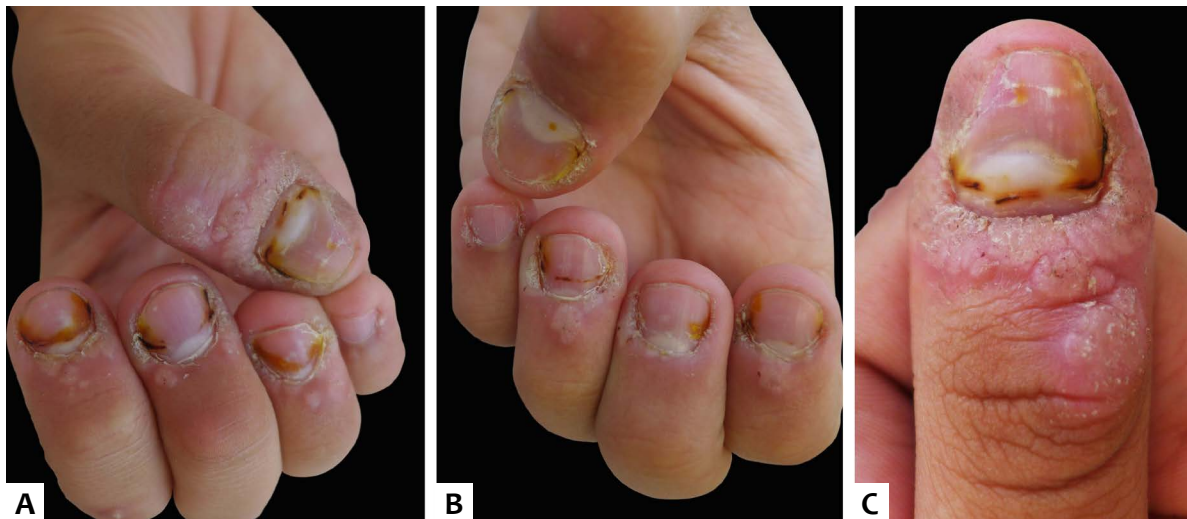


FIGURE 2: Clinical aspect after four chemocautery sessions with phenolic acid 88% and fuming nitric acid associated with daily applications of 16.5% salicylic acid and 14.5% lactic acid, eight weeks after the first consultation. **A and B** - Overview of the involvement of periungual warts on the fingers of both hands. **C** - Aspect of the right thumb, most affected finger

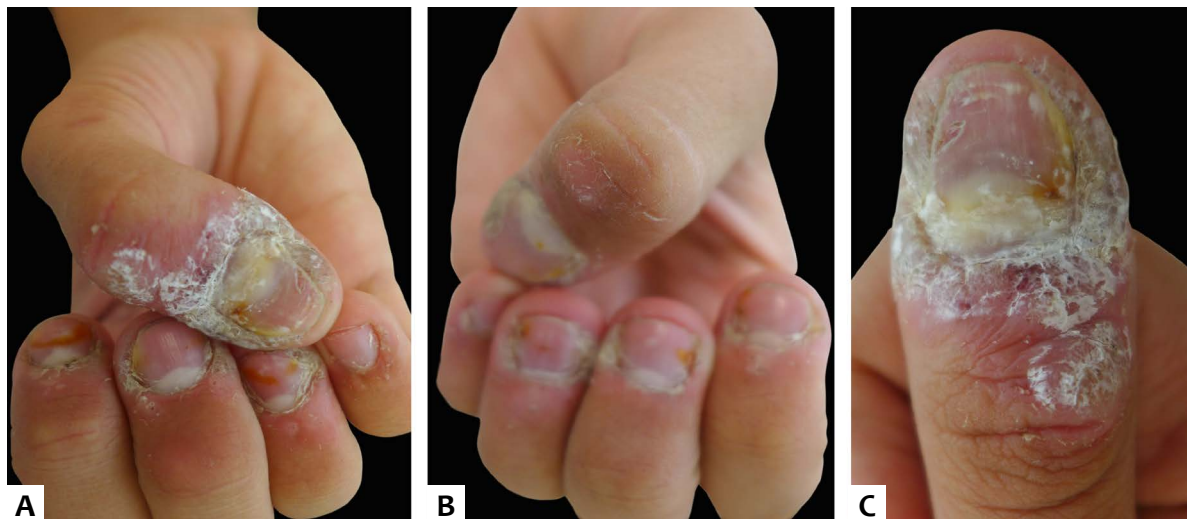


FIGURA 3: Aspecto clínico após duas sessões de quimiocauterização com ácido tricloroacético a 35% associado a aplicações diárias de solução de ácido salicílico 16,5% e ácido láctico 14,5%, dez semanas após a primeira consulta. **A e B** - Visão geral do acometimento das verrugas periungueais dos dedos de ambas as mãos. **C** - Aspecto do polegar direito, dedo mais acometido

We opted to maintain a destructive approach, this time with weekly applications in the clinic of trichloroacetic acid 35% associated with the use of SA + LA daily at home. After two weekly sessions, he again reported discomfort due to the whitish aspect that the warts keratin presented (Figure 3); thus, it was decided to change the therapy again. Due to the history of using various destructive treatments previously and before his first consultation, during the ten-week follow-up at the clinic, we decided to change the approach to an immunostimulatory. He was instructed to keep using SA + LA daily in the morning and imiquimod 5% cream in occlusion at

night for five consecutive days a week. The patient applied the cream and occluded it with a bandage from Monday to Friday; on Saturday and Sunday, he only used morning SA + LA.

RESULTS

After four weeks of using SA + LA every morning and occlusive IQM on five consecutive nights a week, the patient showed complete regression of the condition, with no impact on quality of life during treatment due to color changes as previously reported in other approaches, without complaints of pain, irritation or ulceration of the lesions (Figure 4).



FIGURE 4: Clinical aspect after daily applications of 16.5% salicylic acid solution and 14.5% lactic acid in the morning and imiquimod 5% cream in occlusion at night on five consecutive days of the week, 14 weeks after the first consultation. **A and B** - Overview of treatment response of the fingers of both hands. **C** - Aspect of the right thumb, finger initially most affected

DISCUSSION

The use of IQM to treat periungual warts has been described with different results. An open trial assessed the efficacy, safety, and tolerability of imiquimod 5% topical cream in 15 patients with resistant and recurrent periungual and subungual warts over 16 weeks. Twelve patients (80%) completed the therapy, presenting complete resolution after a mean of three weeks and with no recurrences after six months.¹⁶ On the other hand, an evidence-based review conducted by Cochrane on the effectiveness of IQM in the treatment of extragenital warts showed a rate ranging from 27% to 89% of patients who achieved a complete response.¹⁵

The frequency and application of the product varied considerably from study to study, with authors who used it only three times a week to others who prescribed it five times a week, occlusive, and associated with keratolytics.⁵ Another review on the use of IQM in extragenital warts concluded, based on small case series and case reports, that its combination with destructive or keratolytic treatments can improve the penetration of the topical IQM and lead to better clinical outcomes.⁵ We opted for this more aggressive dosage in the case presented, given the chronicity and exuberance of the lesions, seeking a more significant immune mobilization of the patient and a higher chance of obtaining a satisfactory response. It

is noteworthy that due to the mechanism of action of the drug is based on a stimulus of the skin immune response, cases of warts in patients with immunosuppression or using immunomodulatory drugs tend not to have a satisfactory response.^{5,12,13,15}

Another aspect that favors the use of IQM is its tolerability with few adverse events when compared to other commonly used modalities.¹⁶ In the case presented, one of the reasons for the patient's low adherence to the several treatments was precisely the adverse event caused by traditional therapies, which did not occur with the topical immunostimulator.

More randomized controlled studies are needed to determine the efficacy of the IQM, assessing the frequency of dose and application as well as its ideal combination with other therapeutic measures in the treatment of periungual warts. However, the knowledge of successful cases such as the one presented here becomes valid to have an alternative treatment option in cases resistant to standard treatments.

CONCLUSION

The present report demonstrates that the treatment of periungual warts with topical immunotherapy using imiquimod seems to be a valid therapeutic option, especially when associated with keratolytics such as the formulation of lactic acid and topical salicylic acid. ●

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Approval of the final version of the manuscript; study design and planning; preparation and writing of the manuscript; data collection, analysis, and interpretation; active participation in research orientation; intellectual participation in propaedeutic and/or therapeutic conduct of studied cases; critical literature review; critical revision of the manuscript.