Switching between intralesional antigens: A promising therapeutic approach for recalcitrant warts

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INTRODUCTION

Multiple recalcitrant warts represent a continuing therapeutic challenge for both patients and physicians. Recently, intralesional immunotherapy by different antigens has been associated with promising efficacy and safety in the treatment of different types of warts, including recalcitrant ones.[1-3]

The therapeutic response to different types of intralesional antigens varies considerably between different studies. Many factors may explain this variability, including the differences in the type of the injected antigen, in the sensitivity and quantity of the injected antigen, in the studied population, and in the induction power of the T helper cell type 1 cytokine response.[2-4]

It has been assumed that the absent or partial response to intralesional antigen immunotherapy may represent a failure of specific antigen rather than a failure of modality.[2] Therefore, we propose that shifting from one intralesional antigen to another is a potential therapeutic option for individuals who have failed to respond. Herein, we present 2 cases of multiple recalcitrant warts that showed complete clearance with intralesional *Candida* antigen after failure of 5 sessions of mumps, measles, and rubella (MMR) vaccine and purified protein derivative (PPD).

Abbreviations used:

MMR: mumps, measles, and rubella
PPD: purified protein derivative

CASE REPORTS

Case 1

A 9-year-old boy presented with severe multiple recalcitrant common warts, defined as warts of more than 2 years' duration that did not respond to at least 2 different therapeutic modalities.[1] During 3 years, the patient received multiple treatments, without any improvement. These include salicylic acid ointment 10%, oral levamisole, 1 session of electrocautery, and finally 2 sessions of cryotherapy. Examination revealed numerous common warts on the dorsum aspect of the right foot and toes, besides many distant warts on the face and scalp. Postinflammatory depigmentation after an aggressive cryotherapy session was also observed (Fig 1, *A*). The mother of the patient refused any new destructive modality, and therefore we started a trial of MMR vaccine that was intralesionally injected, after a positive intradermal sensitization test result, into the largest warts at 0.3 mL every 2 weeks for 5 sessions. Unfortunately, this modality was not associated with any improvement. Given the refusal of any destructive approach, we decided to try another antigen. After a positive intradermal sensitization test result, *Candida* antigen (0.3 mL of 1/1000 solution) was then injected into the largest wart at 2-week intervals. The improvement was prominent after the first session and complete after the second one (Fig 1, *B* and *C*). Complete clearance of the distant warts was also observed. The adverse effects were few and in the form of pain during injection, erythema, edema, exfoliation, and influenza-like symptoms.

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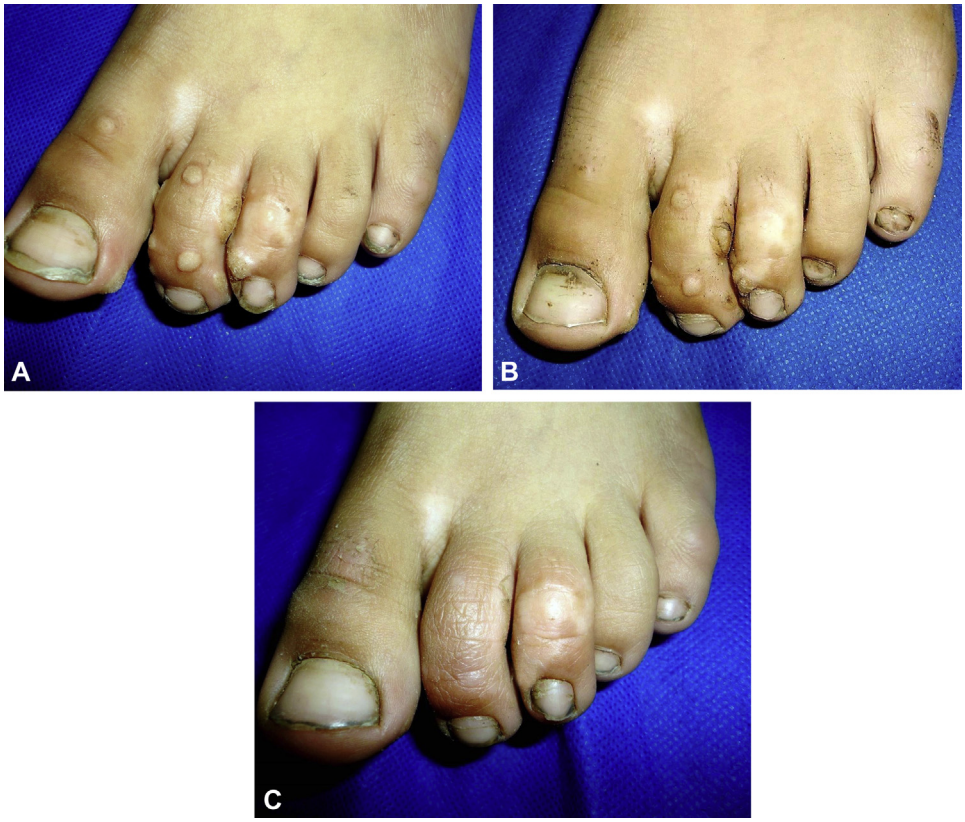

Fig 1. Multiple common warts on the dorsum of the right foot and toes. **A**, Before treatment with intralesional *Candida* antigen after failure of 5 sessions of mumps, measles, and rubella vaccine. Note the depigmentation after an aggressive cryotherapy session. **B**, Partial response after 1 session. **C**, Complete clearance after 2 sessions.

No recurrence of the warts was observed during a follow-up period of 2 years.

Case 2

The second patient was a 20-year-old woman with plantar warts of more than 3 years' duration. She had received many therapeutic modalities, including topical retinoic acid, salicylic acid 20%, oral zinc sulfate, and 3 sessions of cryotherapy that resulted in the development of a doughnut wart (Fig 2, *A*). Examination revealed a large doughnut wart on the undersurface of the big toe and 5 small nearby warts on the inner surface of the second and third toes.

We stopped cryotherapy sessions and decided to use intralesional immunotherapy by PPD antigen that was injected, after a positive presensitization intradermal test result, into the doughnut wart at 0.3 mL every 2 weeks for 5 sessions, without any improvement. Given the experience of the previous case, we switched to *Candida* antigen after a positive presensitization test result. It was injected into the doughnut wart at 0.3 mL of 1/1000 solution at 2-week intervals. This switching was associated with a significant response after the first session and complete clearance after the second one (Fig 2, *B* and *C*), without recurrence for 6 months.

DISCUSSION

We present 2 challenging and frustrating cases of recalcitrant warts. This was particularly true, given the multiple therapies the patients received (>2 modalities) and the long duration of warts (>3 years). We started with MMR vaccine and PPD in accordance with the assumption of expected high sensitivity to these antigens because they are a part of the routine vaccination schedule in Egypt (both patients were immune after a preinjection sensitization test). Furthermore, many studies have shown the success of MMR and PPD in treating recalcitrant warts.[1-5] However, this was not the case in the present study and the patients did not show any improvement after 5 sessions. Consequently, we decided to change to another antigen, *C albicans*, which was successful in both patients.

There is no definite explanation for the absence of response to MMR and PPD and the good response

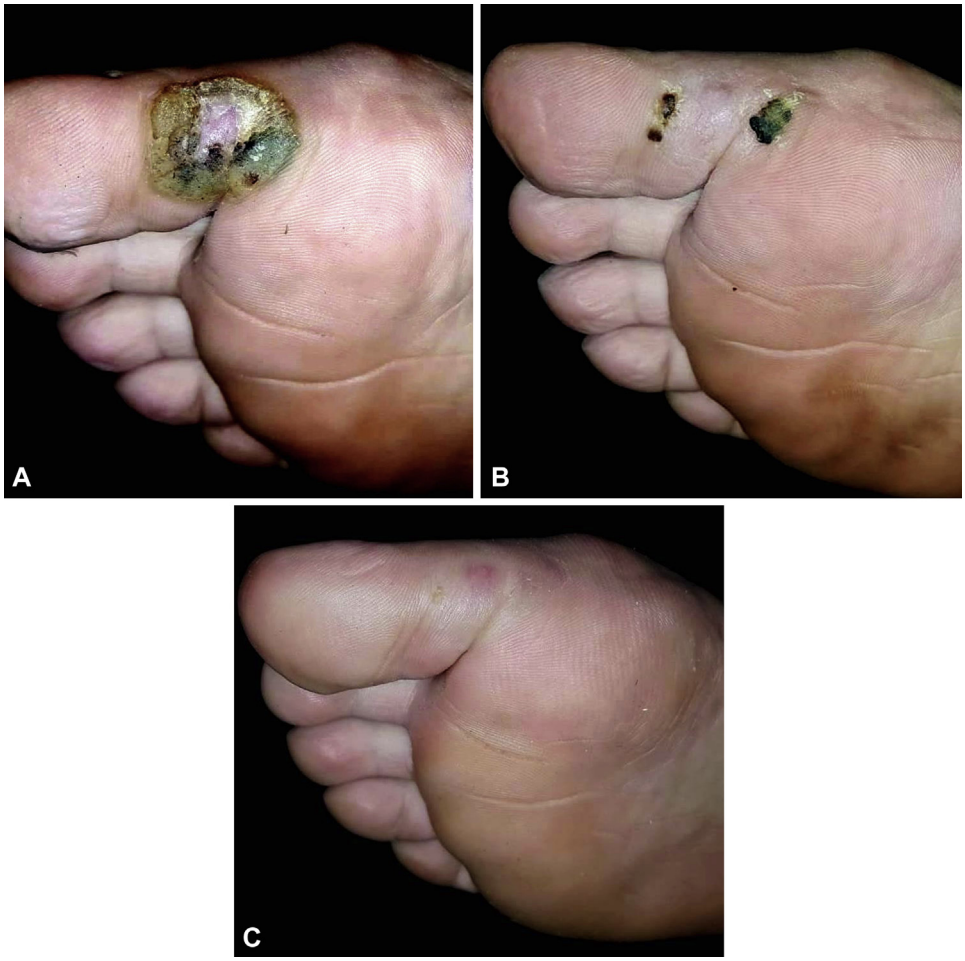

Fig 2. Large doughnut wart on the sole of the right foot. **A**, Before treatment with intralesional *Candida* antigen after failure of 5 sessions of purified protein derivative. **B**, Partial response after 1 session. **C**, Complete clearance after 2 sessions.

to *Candida* antigen in our patients, especially considering the similar proposed mechanisms of action of intralesional immunotherapy by different antigens and the similar reactivity (erythema and induration 5-10 mm) to the 3 antigens in the sensitization tests.[6,7]

The brisk inflammatory response associated with *Candida* antigen injection in some cases[8] may partly explain the significant response in the presented cases. These inflammatory responses were obvious in our patients, particularly the influenza-like symptoms, the severe exfoliations and necrosis, and the marked erythema and edema. Another explanation may be the high sensitivity to *Candida* antigen resulting from the common, extensive exposure to candidal infections in the first 2 years of life in our community, as well as worldwide. Furthermore, differences in the processing, presentation, and cytokine production by the injected antigens may also contribute to the difference in response.

In line with our concept, Majid and Imran[9] suggested that "patients showing a negative response to one antigen can be tested with other antigens such as *Trichophyton* or mumps." We switched to *Candida* antigen for both patients 2 months after the last session of MMR and PPD to avoid any extended effect, although that was not expected after failure of 5 sessions, as was previously reported.[2]

CONCLUSION

In conclusion, we present a novel approach in the field of intralesional antigen immunotherapy that showed clearance of recalcitrant warts on switching from one antigen (MMR vaccine and PPD) to another (*Candida*). Therefore, switching between intralesional antigens might represent a therapeutic alternative for the treatment of recalcitrant warts and might help clinicians improve the outcome of intralesional antigen immunotherapy. Future studies

involving a large number of patients are warranted to precisely evaluate the effect of switching between different intralesional antigens in the treatment of different types of warts.

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