Psoriasis Exacerbation after *Candida* Antigen Immunotherapy Injection

Sameh Magdy Sarsik Sarah Hamdy Soliman

Dermatology and Venereology department, Faculty of Medicine, Tanta University, Tanta, Egypt

Established Facts

- *Candida albicans* (CA) immunotherapy is effective for treatment of resistant warts, through stimulation of Th1 response and development of anti-Human Papilloma Virus T-lymphocyte response.
- Side effects of CA are usually mild and tolerable.

Novel Insights

- Emphasizes the effectiveness of *Candida albicans* (CA) in treatment of resistant filiform warts.
- CA immunotherapy may exacerbate psoriasis, through stimulation of Th1 response in the mean of TNF α and IL-17.
- CA may not be the best option for psoriatic nor psoriasis susceptible patients.

Keywords

Wart · Immunotherapy · *Candida* antigen · Nail psoriasis · Psoriasis

Abstract

Background: Immunotherapy as wart treatment has been proposed as a successful and well-tolerated treatment option. However, as their action is not confined to the site of injection, the activation of the immune system in a way may alter the immune state of the patient. **Case Presentation:** A case of 29-year-old patient who experienced psoriasis exacerbation and psoriatic arthritis within days following *Candida* antigen immunotherapy injection for resistant filiform wart management. **Conclusion:** *Candida* antigen injection may cause psoriasis exacerbation, as TNF α and subsequent

T-helper 1 induction is crossroad in both psoriasis and *Candida* antigen immunotherapy. Therefore, we report this case to state that besides the effectiveness of *Candida* antigen for wart therapy, caution should be considered if used in patients who are susceptible to psoriasis with meticulous follow-up or better to apply an alternative treatment option.

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Introduction

Immunotherapy with *Candida albicans* (CA) antigen has been a traditional option for wart treatment being safe, effective, and inexpensive [1]. It works through induction of T-cell mediated immune response, with the release of interleukin-2 (IL-2) and interferon-gamma

Fig. 1. a Psoriatic changes of fingernails, showing pitting and onycholysis. **b** Psoriatic changes of both thumbnails with pitting, salmon patch, and onycholysis.

(INF- γ) that act against human papilloma virus (HPV) [2]. Side effects of CA were known to be transient and well-tolerated, but serious side effects had been reported as well. Here, we report the exacerbation of psoriasis following CA injection, and to our knowledge, no similar case was reported.

Case Presentation

A 29-year-old male patient presented to our department between March and May 2019 with multiple resistant filiform warts on the beard area of 6 months duration. The patient was healthy otherwise. We tried several regional destructive methods in the form of multiple electrocautery sessions and 8 cryotherapy sessions but with no satisfactory outcomes and many recurrences. We also tried acitretin 25 mg/day for 3 months without much improvement. Based on failure of all previous lines of treatment, we decided to start immunotherapy treatment. On September, the patient received PPD and MMR test doses to which he did not respond, and then, we switched to CA, sensitivity test was done, and the patient developed erythematous wheal (15 mm) after 24 h. The patient received 2 injections of 0.1 mL of 1:100 of CA, 2 weeks apart, with complete clearance of warts subsequent to the second injection. Therefore, injections were discontinued.

On October 2019, the patient returned to our department for his follow-up, with no recurrence of the warts, but he was complaining of nail lesions of both hands (Fig. 1a, b), and the thumb nail of the right hand manifested the most pathognomonic findings in the form of pitting, salmon patch, and onycholysis with erythematous border (Fig. 2). By reconsidering patients' medical profile, he had been diagnosed with mild nail psoriasis since 2011 (NAPSI = 13), and always had mild relapses that were controlled using topical treatments, the last one was in November 2018. The patient's father had also been diagnosed with psoriasis in June

Fig. 2. Dermoscopy of the right thumb nail showing pitting, salmon patch, and onycholysis with erythematous border, NAPSI = 6.

2019. Throughout the current relapse, the patient's NAPSI score was 41, and the target NAPSI of the mostly affected nail (Rt. Thumb) was 6.

The patient also complained of joint pain, stiffness of the right thumb, subsequently was referred to the rheumatology department for evaluation. Rheumatoid factor was negative; C-reactive protein was 48 mg/L, and joint ultrasonography showed effusion of the interphalangeal joint. CASPAR score = 6, which was suggestive for psoriatic arthropathy simultaneously with the clinical findings and family history. Consequently, the patient received subcutaneous methotrexate 25 mg/week with folic acid supplements.

Fig. 3. a Fingernails after 3 months of methotrexate treatment, showing marked improvement. **b** Thumbnails after 3 months of methotrexate treatment, showing marked improvement.

Table 1. Uncommon side effects of intralesional immunotherapy for wart treatment

Study	Type of wart	Site of wart	Recalcitrant wart	Immunotherapy/dose	Combination	Uncommon side effects
Perman et al. [8]	Verruca vulgaris	Periungual/left index digit	Yes	CA/1:10 concentration	No	The painful purple digit
Crowley et al. [9]	Verruca plantaris	Both feet	Not mentioned	CA/not mentioned	No	Uveitis
La'Pelusa et al. [10]	Not mentioned	Right fifth digit	Yes	CA/0.1-mL of 50 m/mL CA	No	The painful purple digit
This case (2020)	Filiform wart	Face-beard area	Yes	CA/0.1 mL of 1:100 CA	No	Nail psoriasis and arthropathy

CA, *Candida albicans*.

Following 3 months of treatment, the patient presented with marked improvement of both nail lesions (NAPSI = 15) and arthritis (Fig. 3a, b).

Discussion

Immunotherapy is considered a promising, reliable method for wart treatment; however, their effect extends beyond the site of injection [3]. The therapeutic outcomes of intralesional immunotherapeutic antigens could be attributed to stimulation of T-helper (Th1) responses as evidenced by the predominance of Th1 cytokines as IFN- γ , IL-2, IL-12, and TNF α , the latter two cytokines are capable of activating cytotoxic T-lymphocytes and natural killer cells to eliminate HPV-infected cells [3, 4]. A study conducted by Kim et al. [5] revealed that con-

secutive injections of *Candida* antigen intensify anti-HPV T-lymphocyte response which results in wart regression. Moreover, yeast immunotherapy induces IL-23 by dendritic cells and IL-17 by T-cells as proposed by Bellgrau and Tamburini [6]. Although side effects of CA are usually temporary and well-tolerated such as pain, erythema, swelling at the injection site, and fever [7], more severe and/or uncommon side effects had been also reported (Table 1).

Psoriasis is a systemic inflammatory disease that affects 3% of the population, dysregulation of the immune system in psoriasis induces overexpression of inflammatory cytokines [11], which principally belong to Th1 response profile, for instance, TNF- α , IFN- α , IL-2, IL-6, IL-8, IL-12, and leukemic inhibitory factor-1, lowered levels of IL-1, IL-4, IL-5, and IL-10 along with increased levels of the critical IL-23, IL-23 receptors, and Th17 cytokines

which direct a hyper-proliferation of the epidermis on the histological level and correspondingly development of erythematous plaques with lamellate silvery-white scales clinically [12]. Nail psoriasis affects 15–79% of psoriatic patients in the form of nail pitting, leukonychia, red spots of the lunular, and crumbling of the nail plates when the nail matrix is affected, while oil-drop discoloration (salm-on patch), splinter hemorrhages, subungual hyperkeratosis, and onycholysis indicate the involvement of nail bed [13].

Based on the above-mentioned mechanisms, we suggest that CA potentially caused psoriasis exacerbation of the current case, as both overlap at Th1 response in the mean of TNF α and IL-17, and we also recommend using an alternative treatment option for psoriatic patients as well as for psoriasis susceptible individuals.

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Statement of Ethics

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Conflict of Interest Statement

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