

The Painful Purple Digit: An Alarming Complication of *Candida albicans* Antigen Treatment of Recalcitrant Warts

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Candida albicans (CA) antigen immunotherapy for recalcitrant warts is a novel treatment that has had much success in the recent past. Although several side effects are well documented in the literature, we report a new adverse reaction to CA antigen immunotherapy for verruca vulgaris of the distal fingertip. Our patient received an intradermal injection of CA antigen solution into periungual warts located on the distal left thumb and distal subungual area of the left index finger. Within 24 hours, the patient reported pain, edema, and a purple hue to only the index finger. Incision of the finger demonstrated no hematoma or compartment syndrome. Although the etiology is unknown, we believe the condition was most likely due to edema and vascular compromise secondary to a vigorous delayed-type hypersensitivity reaction, possibly leading to cyanosis of the distal index finger. We report this case to make physicians who use intralesional CA antigen aware of a new possible complication at this anatomic location.

THE USE OF IMMUNOTHERAPY to treat human papillomavirus (HPV) infection is currently on the rise. We describe a complication of *Candida albicans* (CA) antigen treatment of verruca vulgaris in the subungual area of the distal fingertip.

Case Report

A 20-year-old female presented for follow-up of recalcitrant periungual warts. After unsuccessful traditional wart treatments, including salicylic acid in flexible collodion (Duofilm, Stiefel Laboratories, Coral Gables, FL), liquid nitrogen, imiquimod (Aldara, 3M, St. Paul, MN), trichloroacetic acid, bichloroacetic acid, and bleomycin, the patient was offered a trial of CA antigen (Bayer, Spokane, WA). The patient appropriately responded to an initial trial of 0.2 cc of CA antigen solution for delayed-type hypersensitivity testing with 25 mm of induration. One month later, 0.1 cc (1:10 dilution) of CA antigen solution was injected intradermally to each periungual wart on the patient's left thumb and index finger. At her 1-month follow-up appointment, the patient reported ongoing inflammation and tenderness in both digits. At that time, there was no evidence of residual warts. However, the patient returned 3 months later, complaining of the recurrence of warts, and a verrucous lesion on each fingertip was

noted. The patient was then treated with another intradermal injection of *Candida* antigen solution (at the same dose as before) into the left thumb and index finger. Within 24 hours, the patient reported distal pain, swelling, and a purple hue to only the index finger (Fig 1). We became concerned with the possible complication of hematoma or compartment syndrome of the digit. The patient was sent for Doppler studies, which showed positive pulses in the digit. The patient was then referred to plastic surgery, and the distal digit was incised to rule out a hematoma. However, no hematoma was found at the time of surgery. The swelling resolved during the next few days, and the patient healed without further complication.

Discussion

Immunotherapy is currently recognized as a novel way to treat verruca vulgaris. Immunotherapy most likely increases the immune system's ability to recognize HPV.¹ In numerous studies, *Candida* antigen has been used for anergy testing in patients with head and neck cancer,² latent tuberculosis,³ inflammatory bowel disease,⁴ atopy,⁵ and other immunosuppressive disorders. It is also an experimental treatment of infections such as recurrent vaginal candidiasis⁶ and vulvovaginitis.⁷ Doses were based on the response size of the initial sensitization reaction. For example, previous studies reported in the literature used the following doses in children and adults: 0.3 cc with test site induration of 5 to 20 mm, 0.2 cc with test site induration of 20 to 40 mm, and 0.1 cc with test site

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Figure 1. Left distal index finger showing erythema, edema, and purple hue 24 hours after a second injection of CA antigen.

induration of greater than 40 mm.^{1,8} Other reported intradermal injection doses include 0.1 mL up to a total of 1.0 mL in a 1:1 mixture of CA antigen solution and 1% lidocaine.⁹

Previously reported common complications include pruritus and pain immediately and up to 24 hours following intradermal injections of CA antigen⁸; local reactions, including burning, blistering, and peeling⁹; and local erythema and edema.¹ Less common reported complications include rash, numbness, oozing, scarring, and transient constitutional symptoms such as fever and aches.⁹ However, Johnson and colleagues reported that in a study of 115 patients, there were no reports of prolonged pain after the initial injection period.⁸

We believe our patient had a vigorous response to the CA antigen, causing edema in the digit and compression of vessels, preventing venous return. The differential diagnosis included hematoma formation, a cyanosis-like reaction, trauma from the intralesional injection, or a compartment syndrome-type reaction to the CA antigen. The purple hue of the finger was suggestive of hematoma formation. However, when the finger was incised, no blood was found at the site of injury. This made the diagnosis of hematoma or direct vascular injury unlikely. We also considered the possibility that the patient experienced cyanosis of the left index finger secondary to edema and decreased perfusion following the injection, which might have explained the color of the distal finger. However, Doppler studies done 1 day after the injection demonstrated adequate perfusion. Therefore, cyanosis also appeared less likely to be the cause of the purple digit.

Compartment syndrome (increased pressure in an enclosed space most commonly formed by fascia) is often a clinical diagnosis made after trauma, ischemic injury,

or other causes of vascular compromise.¹⁰ Diagnosis is made by several signs and symptoms, including (but not limited to) severe pain, paresthesias, pallor, muscle edema and ischemia, and decreased pulses in the compartment affected.¹⁰⁻¹² Diagnosis calls for a high level of clinical suspicion and the measurement of compartmental pressures. Compartmental pressures greater than 20 to 30 mm Hg require a fasciotomy. Although diagnosis does not require pallor, paralysis, paresthesias, or the absence of distal pulses, patients are typically said to have "pain out of proportion to that expected for the injury," caused by muscle ischemia.¹⁰ Our patient indeed showed several features suggestive of compartment syndrome (particularly, pain out of proportion to the injury) (Table 1),¹³ and the patient was referred to plastic surgery for incision. Compartmental pressures, however, were not measured to make a formal diagnosis of compartment syndrome.

The exact etiology of our patient's findings remains unknown. Given that the symptoms resolved in a few days, our patient could have experienced purpura related to trauma from the intralesional injection and healed without functional impairment (Fig 2). Furthermore, a compartment syndrome-like reaction to the CA antigen in the distal digit remains a possible explanation. To the best of our knowledge, the literature contains no other reports of compartment syndrome-type reactions following a CA antigen injection. More important, physicians should be aware of this possible complication when CA antigen is used to treat verruca vulgaris located on the fingertips. On the basis of our experience, we recommend following up

Table 1. Clinical Features of Compartment Syndrome in Case Report Patient

Signs/Symptoms	Patient with Compartment Syndrome	Our Patient
Pain out of proportion to injury	Yes	Yes
Paresthesias in distribution of nerve passing through compartment in question	Yes	Not formally assessed
Pain on passive stretch of muscle within compartment	Yes	Yes
Tenseness of compartment on palpation	Yes	Yes
Weakness of muscles within compartment	Yes	Unable to assess because of severe pain

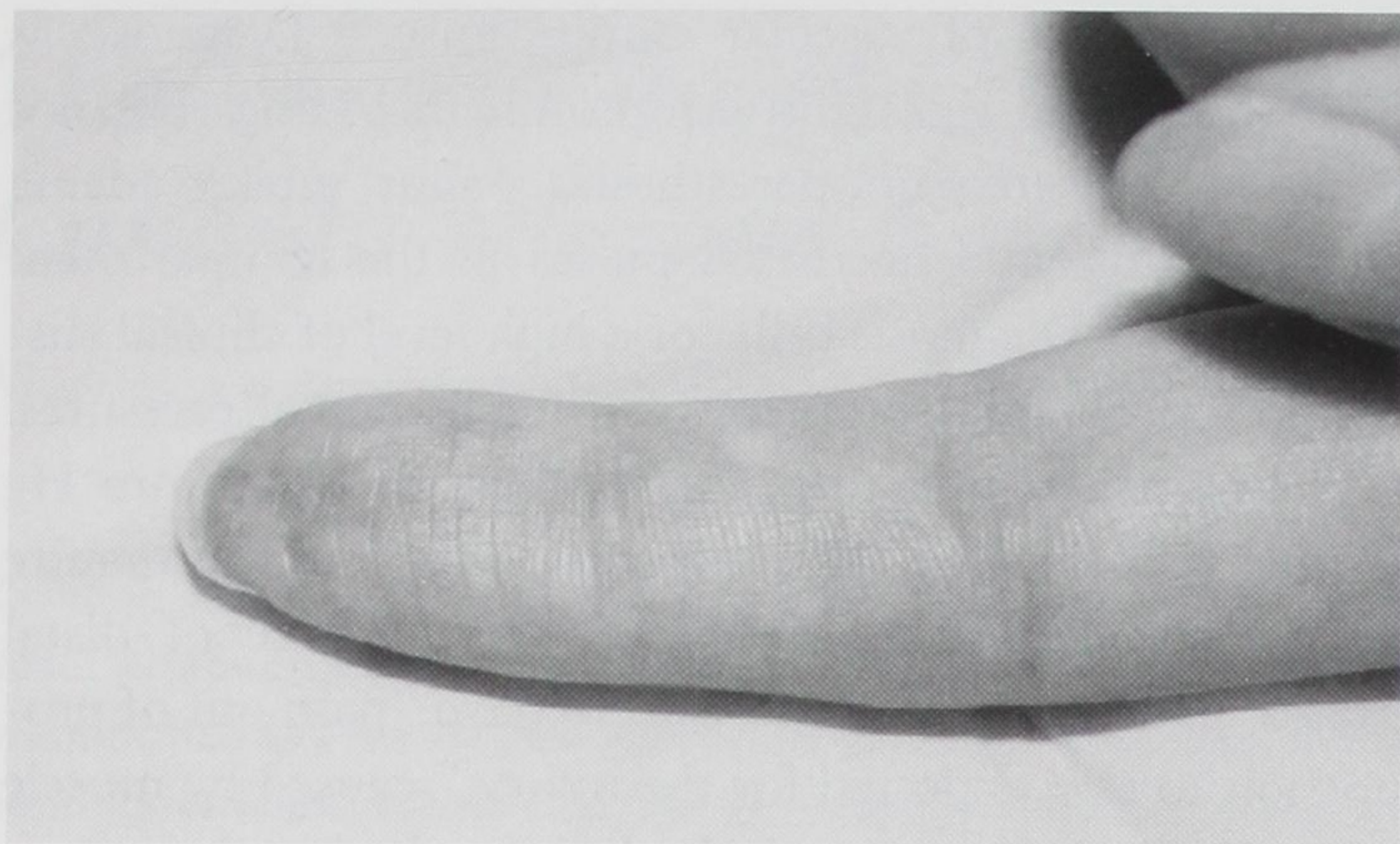


Figure 2. Left distal index finger 4 months after a CA antigen injection, showing significant scarring from the incision but no evidence of a periungual wart.

the patient conservatively with serial Doppler examinations, measuring compartmental pressures if signs and symptoms are suggestive of compartment syndrome, and avoiding unnecessary surgical exploration.

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