Treatment of Warts with Candida Antigen Injection

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ABSTRACT

Background: A safe, simple, effective method of treating warts is needed.

Objectives: To evaluate 1) safety of candida antigen injections for the treatment of common warts, 2) patient satisfaction with the treatment.

Methods: Chart review and telephone follow-up of 149 patients treated for common warts by intradermal and intralesional candida antigen injections.

Results: 104 were reached by telephone for follow up
Side effects: 54 patients (52%) mild, local reactions, no severe reactions.
Satisfaction: 79 patients (76%) "very happy", 10 (10%) "happy", 13 (12%) "unhappy" and 2 (2%) "very unhappy". 85 patients (82%) would repeat the treatment if needed.
Resolution of warts: 73 patients (70%) had complete cure within 8 weeks of the last injection.

Conclusion: Candida antigen injection for the treatment of common warts is safe and well accepted by patients. A randomized controlled trial will be required to conclusively prove efficacy for this treatment.

INTRODUCTION

Common warts (verruca vulgaris and plantaris), while not life threatening, are a source of embarrassment to patients and frustration to physicians. No easy, inexpensive treatments have been shown to work consistently. While warts are usually self-limited, patients often seek treatment due to discomfort or unacceptable cosmetic appearance. Dermatologists saw 8.5 million visits for warts in 1994, while family physicians and others saw another 9.2 million.

Caustic treatments (various acids) destructive techniques (electrical cautery, curettage, laser, freezing), poisoning with chemotherapeutic agents, and excision are often unsuccessful, expensive and are rarely pleasant.

The efficacy of candida antigen as an immunotherapeutic agent for treatment of warts has been suggested. Some practitioners have enthusiastically incorporated it into their practices despite lack of any published data to support the procedure. In 1984, a study presented at the Annual Conference of the American Academy of Family Practice, demonstrated an eradication rate of 65% in 66 patients injected with 1:1000 candida antigen. This study has never been published.

If safe and effective, candida antigen injection would offer several advantages over current therapies for warts. There is extensive experience using candida antigen as a control in tuberculosis testing and allergy testing. Injection does not appear to cause scarring. Patient disability and pain are markedly reduced. The procedure is easy to learn and the materials are inexpensive and readily available.

This study was designed to evaluate the safety of candida antigen injection for the treatment of common warts, and patient satisfaction with the treatment.

METHODS

Patients

All patients were recruited from the referral, outpatient procedures practice of one of the authors (JLP). Most had failed home treatment or treatment by other physicians.

Treatment protocol

A wart treatment form was completed, including the history of the warts, duration, past treatments, description, and number and location of the warts injected. Candin®, a standardized, skin test strength solution of Candida albicans antigen was used. A mixture of equal parts candida antigen solution with 1% lidocaine was given intralesionally as well as intradermally at the base of the lesion using a 1 cc syringe with a 30 gauge needle. Approximately 0.1 cc of the mixture was used per wart. When multiple warts were present, as many warts as possible were injected using a maximum of 1.0 cc of the mixture per visit. Areas injected included the hands, plantar surfaces, and lesions on the upper or lower extremities. Facial lesions and genital warts were not included. Injections were repeated every 4 weeks for three injection visits or until there was no evidence of warts.

Study Design

The study was a chart review with a telephone follow-up survey. The charts of all patients who were treated with candida antigen between the months of January 1993 and April of 1995 were reviewed. One hundred forty-six charts were complete. The subject (or parent/guardian) was interviewed using a standardized telephone survey 13-40 months later. Of the one hundred forty-six patients, thirty had phone numbers disconnected or changed, eleven patients could not be reached despite multiple attempts and one patient did not recall having the treatment. One hundred and four patients were reached, and all agreed to participate in the study. Patients were assured of the confidentiality of their answers.

Subjects were asked about response, side effects of treatment, and satisfaction. Side effects were elicited with an open-ended question, then with specific questions about pain, swelling, scarring, oozing and itching. Subjects were asked to rate their satisfaction on a Likert scale (very happy/somewhat happy/unhappy/very unhappy). The script of the phone survey is available from the authors.

Warts were defined as cured if they were "totally gone" within eight weeks of completing the candida antigen injection and with no reoccurrence since.

Informed Consent

Consent for the procedure was obtained by the physician at the time of the treatment. The Institutional Review Board of MidMichigan Regional Medical Center approved the follow up portion of the study.

RESULTS

Table I reflects the distribution of patients by gender, age, and race. The age range was 3-62 years old. All but one subject was Caucasian.

Safety

A total of 56 patients (54%) reported the side effects recorded in Table II. Most side effects were minor and involved reaction at the injection site. Two patients reported reactions that they considered to be systemic side effects. One patient reported generalized body aches and nausea approximately twenty-four hours after the injection of the candida antigen. Symptoms resolved after two hours with no treatment. A parent reported their child had a brief, low grade fever which resolved without treatment.

Patient satisfaction

The patients were asked how satisfied they were with the treatment (Table III). Most (86%) were pleased with the treatment and most (82%) would repeat the treatment again if needed. Those who were dissatisfied cited either discomfort with the injection or lack of response to the treatment.

Efficacy

Tables IV and V and Figure I reflect the overall results of the treatment protocol with 70% having total cure of warts within eight weeks of completing the protocol. It was observed that even uninjected warts on distant parts of the body often disappeared.

Six percent had resolution of warts after eight weeks and therefore did not fit the definition of "cure". Five percent continued to have warts despite finishing three treatments, and 19% did not complete the protocol series.

DISCUSSION

Immune mechanisms have been suggested to explain the spontaneous resolution of warts. If this immunity could be stimulated, lasting wart resolution could result. The stimulated immune system would destroy all warts on the body, relieving the necessity of local treatment of every wart. There are many possible explanations for the mechanism of action of immunotherapy. It is postulated here that a local immune reaction generalizes and somehow enhances resolution of distant lesions ("bystander effect"). Various agents and application methods have been investigated- 9 .

The primary goals of this study were to assess safety and patient satisfaction with candida antigen injection for the treatment of common warts. Candida antigen is approved as a control for skin testing and in allergy testing. The manufacturer1 0 lists possible local reactions (swelling, hives, pruritus, edema, induration and vesiculation) for standardized solutions and more severe reactions (bullae, dermal exfoliation and cellulitis) for unstandardized solutions. Systemic reactions have not been reported, though Type 1 anaphylactic reactions are theoretically possible.

The majority of reactions reported in our study were consistent with local reactions. The two patients who reported potential systemic side effects (body aches and fever) had mild, transient symptoms inconsistent with those previously associated with candida antigen use. They were unlikely to be due to the treatment. Most local "side effects" were tolerable and seemed to be associated with the natural course of wart disappearance. This study supports the safety of candida antigen in the treatment of warts, though with widespread use, more serious side effects might become apparent.

The typical course of an effective treatment usually involved erythema and itching at the wart site within a day or two of injection. The wart would either spontaneously regress or become discolored and peel. The warts usually resolved within two to eight weeks of the injection. Numerous patients, however, have reported resolution of the warts after the eight week cut off period in this study despite being present "for years". It is possible that the arbitrary cutoff of eight weeks was too short.

The second question addressed patient satisfaction. This is where injection with candida antigen may hold significant advantages over other treatments. Eighty-five percent of the patients treated indicated they were pleased with the treatment and most would repeat the treatment if needed. Even patients who did not have complete cure often had some improvement in the wart number or size.

The study gives some evidence for efficacy of this treatment modality. Of the one hundred four patients treated, 70% had a complete cure with three or fewer injections. This percentage of cure is consistent with the cure rates seen with other forms of wart treatments yet with less toxicity. Plantar warts appeared to be most resistant.

There are several concerns that must be addressed before the procedure is widely adopted. The population in the study was almost exclusively Caucasian; issues of keloid formation may have been missed. Patient recall bias may have been a factor since there was an extended period of time between treatment and the follow-up phone survey. However, results of the phone survey were consistent with patient records when office follow up was recorded. Without using a placebo, it cannot be assured that candida antigen is the active agent. As always, evaluation of the efficacy of wart treatment is complicated by the high rate of spontaneous remissions.

Reviewer recommended lit search and comment on the risk of candida hypersensitivity syndrome.

CONCLUSIONS

Injection with candida antigen is a promising option in the treatment of common warts. The majority of patients in the study tolerated the procedure well. Side effects, when reported, were minor and localized to the site of injection. Patients were happy with the treatment and would choose it again.

Enthusiasm for this method of wart treatment should be tempered with caution until the efficacy is supported by evidence from randomized controlled trials. Optimal treatment intervals, solution concentrations, maximum total dosages, and dosage per lesion are yet to be determined.

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Table I. Patient demographics (N=104)

Gender
Male 56 (54%)
Female 48 (46%)

Age
3-9 14 (14%)
10-19 58 (56%)
20-39 19 (18%)
40-62 13 (12%)

Race
Caucasian 103 (99%)
Hispanic 1 (1%)

Table II. Reported "side effects" of candida antigen injection (N=104)

No side effects	48 (46%)
Reported side effects	56 (54%)

Specific "side effects"

Warmth/redness	2 (2%)
Rash/blister	2 (2%)
Burning/pain with injection	18 (18%)
Pain after injection	
Mild	11 (11%)
Moderate	2 (2%)
Severe	1 (1%)
Pressure/numbness	2 (2%)
Wart turned color/peeled	9 (9%)
Body aches	1 (1%)
Fever	1 (1%)

Table III. Patient satisfaction with the candida antigen treatment (N=104)

Satisfaction with treatment

Very happy	79 (76%)
Happy	10 (10%)
Unhappy	13 (12%)
Very unhappy	2 (2%)

Would repeat treatment 85 (82%)

Table IV. Cure rates after each injection of candida antigen

1st injection (N=104)	36 (35%)
2nd injection (N=56)	26 (46%)
3rd injection (N=16)	11 (69%)
Overall (N=104)	73 (70%)

Table V. Overall results of candida antigen protocol (N=104)

Complete cure	73 (70%)
Late resolution (>8 weeks) of warts	6 (6%)
Did not complete 3 injections	20 (19%)
No cure despite 3 injections	5 (5%)

Figure I. Summary of study results