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Intralesional Bacillus-Calmette-Guerin (BCG) vaccine for multiple non-genital viral warts

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Abstract

Background: The majority of treatment options available for warts are destructive with some limitations to their utility, especially in the setting of multiple lesions. Accordingly, there is a need for other treatment options. Immunotherapy is a promising method for such cases. Intralesional administration of Bacille Calmette-Guerin (BCG) vaccine is one of the immunotherapeutic methods. It was intended to display the results of BCG immunotherapy in the treatment of multiple non- genital warts in a group of patients at Al-Karak Government Hospital.

Objective: To evaluate the efficacy and safety of intralesional BCG vaccine in the treatment of non-genital multiple warts in a group of our patients at Al-Karak Government Hospital.

Methods: A total number of 15 immunocompetent patients with non-genital multiple warts, with an age range of (12-39) years were included. Intralesional BCG vaccine was injected into the largest wart at 0, 4 and 8 weeks. Patients were followed up every 4 weeks for a total of 6 months

Results: Complete response was noted in 12 patients after 4-16 weeks of the first injection, while 3 cases displayed a partial response. Few local and transient reaction were seen. No serious side effects were encountered.

Limitations: The results are based on a small sample size (15 cases) and there was no control group for comparison.

Conclusion: Immunotherapy with intralesional BCG vaccine is an effective and safe treatment option for immunocompetent patients with non-genital multiple warts.

Keywords: BCG vaccine, Viral warts, Immunotherapy, intralesional.

INTRODUCTION

Viral cutaneous warts are common and can sometimes pose a treatment challenge especially when multiple. Different treatment modalities have been used to treat viral warts including cryotherapy, chemical cautery, electrocautery, laser and surgery. All of the aforementioned modalities are destructive, require targeting each lesion, and recurrence may occur [1]. Immunotherapy is another treatment option for viral warts [2]. Immunotherapy induces a systemic T-cell mediated response that upregulates the immune system to destroy the targeted lesion and other distant lesions [3]. Different immunotherapeutic agents either systemic, intralesional or topical have been used and studied [3,4]. In this study we utilized intralesional BCG vaccine as an immunotherapeutic agent, to evaluate the efficacy and safety of using this method in the treatment of non-genital multiple viral warts.

MATERIALS AND METHODS

A total number of 15 patients were included in this study. 13 females and 2 males with an age range between 15-39 years (mean age 22 years ± SD). All patients were assessed at Al-Karak Governmental Hospital. Written consent was obtained from all patients. Inclusion criteria were clinically diagnosed non-genital multiple viral warts, patient's age between 12-55 years, healthy non-immunocompromised patient, and non-pregnant or lactating females. Baseline laboratory tests were done for each patient including a complete blood count, liver enzymes, creatinine and fasting blood sugar. These laboratory tests were repeated again during follow up.

Using an insulin syringe 0.1 ml of Bacille Calmette-Guerin (BCG) vaccine was injected into the lesion; a single wart only per patient (the largest lesion). The injection was repeated every 4 weeks at the same site until complete clearance was achieved with a maximum of three treatment session for each patient. The patients were followed up every 4 weeks for 6 months and adverse effects were recorded. Institutional Ethics Committee approval was obtained (Reference number: 592022). Clinical cure was defined as complete clearance of all viral warts both at the injected site as well as distant sites.

RESULTS

Clinical cure was achieved in 12 patients (80%), and 3 patients (20%) had a partial response (Figures 1+2; Figures 3+4, and Figures 5+6). There were no abnormalities in the requested laboratory tests on follow up.

Figure 1: Before treatment

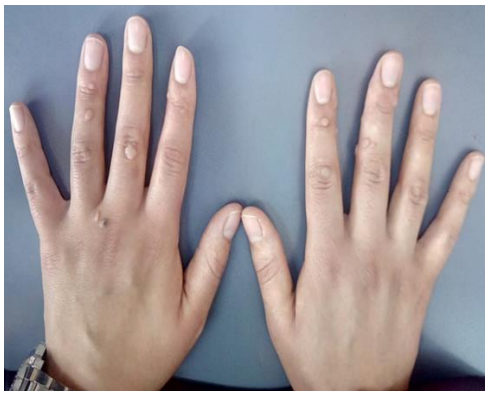

Figure 2: After 12 weeks of first injection

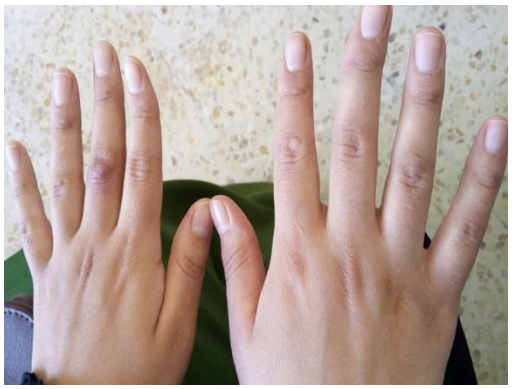

Figure 3: Before treatment

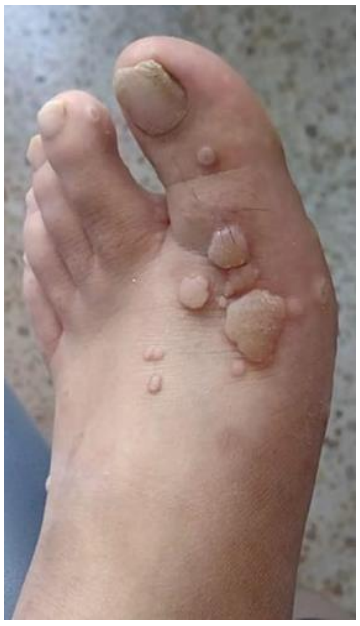

Figure 4: After 12 weeks of first injection

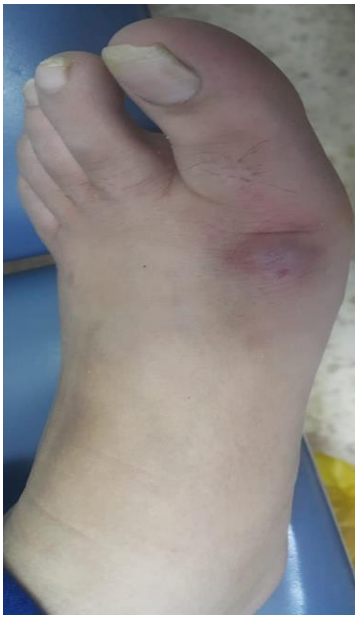

Figure 5: Before treatment

Figure 6: After 8 weeks of first injection

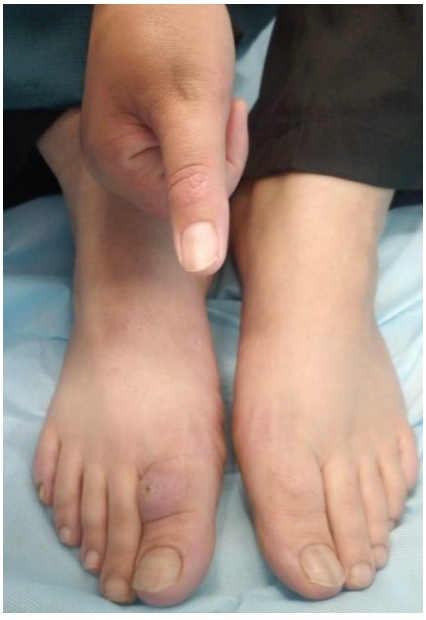

Table1: clinical response of patients in this study.

Patient`s number	Age	Sex	Response to treatment
1	18 years	Female	Cured after 4 Weeks
2	28 years	Female	Cured after 4 Weeks
3	16 years	Female	Cured after 16 Weeks
4	12 years	Male	Cured after12 Weeks
5	21 years	Female	Cured after 8 Weeks
6	16 years	Female	Cured after 8 Weeks
7	23 years	Female	Cured after 4 weeks
8	29 years	Female	Cured after 12 Weeks
9	30 years	Female	Cured after 12 Weeks
10	38 years	Female	Cured after 12 Weeks
11	18 years	Female	Cured after 16 Weeks
12	28 years	Male	Partial response
13	39 years	Female	Partial response
14	15 years	Female	Partial response
15	34 years	Female	Complete response after 8 weeks

Table:2 Treatment related side effects in patients of this study

Side effect	Number of patients	Percentage
Local pain	11	73%
Fever	8	53%
Local redness	5	33%
Local swelling	5	33%
General weakness	5	33%
Scar at injection site	2	13%
Ulcer at injection site	1	7%

DISCUSSION

Management of multiple warts represents a challenge for both patients and doctors. The majority of cases of common warts may resolve spontaneously within two years. About one-third of cases, however, may not resolve and become recalcitrant [1,5]. Many destructive and immunotherapeutic treatment options have been used to manage recalcitrant warts. Studies have shown that there is an important role for cell-mediated immunity in the management and control of human papilloma virus infection [6]. Intralesional immunotherapy using different agents including bacillus-Calmette-Guerin (BCG) have been used recently to treat recalcitrant multiple warts and showed to be an effective treatment modality [3,7,8]. Intralesional immunotherapy induced a systemic response and affected warts at distant locations to the injection site [9]. The mechanism of action of this treatment modality is related to activation of CD4 lymphocytes and an increase in cytokines (interleukin-1, interleukin -2, and tumor necrosis factor –alfa). Both Interleukin -1 and tumor necrosis factor-alfa possess antiviral effects against human papilloma virus by downregulation of its gene transcription [3,10]. Complete response of resistant warts has been reported with the use of intralesional BCG immunotherapy [11]. A complete response was achieved within 9 weeks of first intralesional BCG injection in 75% of patients treated with intralesional BCG injected in one lesion only [8]. In another study the complete response rate was 70% within 12 weeks of first intralesional BCG injection [7]. In our study 80% of the cases showed complete response (cured) (Figure-1,2; Figure-3 and 4, and Figure5,6). Ten of our patients showed complete response within 12 weeks of first intralesional BCG injection and only two patients showed complete response after 16 weeks. Our results concur with other studies [7,8]. Our results displayed a higher cure rate (80%), when compared to other studies that yielded a complete response rate of 42.7% [13]. Local pain, fever, local tenderness, local swelling, general weakness, ulceration and scarring at the site of injection were the side effects encountered in our patients. All symptoms were transient and improved within 7 days. Similar side effects were seen in other studies [7,8]. Granulomatous hepatitis was reported as a complication of intralesional BCG injection for wart treatment in an immunocompetent patient [14]. None of our patients developed any serious side effects and all the laboratory tests done during the follow up period including liver function tests were within normal limits for all our patients. Serious side effects were not reported in other similar studied [7,8,11].

CONCLUSION

Intralesional BCG can be considered as a safe, effective, inexpensive treatment modality that can be used in cases of non-genital multiple and recalcitrant warts with promising results.

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الحقن الموضعي بلقاح بي سي جي (BCG) لمعالجة الثآليل المتعددة والغير تناسلية

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الملخص

الخلفية والأهداف : غالبية خيارات العلاج المتاحة للثآليل هي وسائل للتدمير الاتلافي للثاليل والتي قد يحد من استخدامها في الحالات الي تكون فيها الثآليل متعدده ويصعب تدمير واتلاف كل ثالول على حدا، وبالتالي، هناك حاجة لخيارات علاجية أخرى. العلاج المناعي هو طريقة واعدة لمثل هذه الحالات. يعتبر الحقن الموضعي بواسطة لقاح BCG (بي سي جي) لاحد الثآليل عند المصاب إحدى طرق العلاج المناعي. من خلال هذة الدراسة نعرض نتائج العلاج المناعي بواسطة لقاح BCG (بي سي جي) في علاج الثآليل المتعددة غير التناسلية عند مجموعة من المرضى في مستشفى الكرك الحكومي في الاردن **و**تقييم فعالية وسلامة الحقن الموضعي للقاح BCG (بي سي جي) لاحد الثآليل في علاج الثآليل المتعددة غير التناسلية عند مجموعة من المرضى في مستشفى الكرك الحكومي.

منهجية الدراسة : تتضمن الدراسة عدد إجمالي 15 مريضاً لديهم ثآليل متعددة غير تناسلية، تتراوح أعمارهم بين (12–39) سنة. تم حقن لقاح BCG (بي سي جي) موضعيا لاحد الثآليل وبالذات الثألول الأكبر في الفترات الزمنية 0 و 4 و 8 أسابيع. تمت متابعة المرضى كل 4 أسابيع لمدة 6 أشهر

النتائج: لوحظ استجابة كاملة في 12 مريضا بعد 4–16 أسبوعا من الحقن الأول. 3 حالات ابدت استجابة جزئية. شوهد القليل من الاثار الجانبية الموضعية والعابرة. لم تحدث أي آثار جانبية خطيرة.

المحددات: النتائج مبنية على حجم عينة صغير (15 حالة) ولم تكن هناك مجموعة تحكم اخرى للمقارنة.

الاستنتاجات: العلاج المناعي بوسطة الحقن الموضعي بلقاح BCG (بي سي جي) لاحد الثثاليل المتعددة هو خيار علاجي فعال وآمن للمرضى ذوي المناعة الطبيعية المصابين بالثآليل المتعددة غير التناسلية. كانت الاثار الجانبية الموضعية في موقع الحقن عديدة ولكنها عابرة ، ولكن التندب فقط كان ثابتا

الكلمات الدالة: لقاح بي سي جي (BCG) الثآليل الفيروسية، العلاج المناعي، الحقن الموضعي.