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Original Article

Intralesional measles, mumps, and rubella vaccine for the treatment of recalcitrant warts: A case series and review of literature

Bini Chandran

Department of Dermatology, Ahalia Hospital, Musaffah, Abudhabi, United Arab Emirates.

***Corresponding author:**
Dr. Bini Chandran, Department of Dermatology, Ahalia Hospital, Musaffah, Abudhabi, United Arab Emirates.

drbinichandran@gmail.com

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ABSTRACT

Objectives: To document the response of recalcitrant warts to intralesional measles, mumps, and rubella (MMR) vaccine.

Materials and Methods: This case series reports the treatment response to intralesional MMR vaccine observed in 11 patients who attended the dermatology outpatient department with recalcitrant warts of more than 1 year duration. Only the largest wart was treated in each case. The intralesional treatment was repeated at an interval of 2 weeks.

Results: Nine patients (81.9%) showed complete response to treatment. One patient did not return for treatment after two sessions (9.1%). One showed incomplete treatment response (9.1%). The adverse reactions noted among the 11 patients were pain (3/11, 27.3%) and secondary bacterial infection (1/11, 9.1%).

Limitations: Results are based on a case series of 11 patients.

Conclusion: Intralesional MMR vaccine was found effective and safe in the management of recalcitrant warts.

Keywords: Measles, mumps, rubella vaccine, Recalcitrant warts, Immunotherapy

INTRODUCTION

A patient returning to the clinic, because you have not been able to solve his problem, is a challenge. Many dermatology conditions are chronic and comfort rather than a cure is the norm. For seemingly innocuous conditions like warts, first-line treatments usually involve keratolytics or destructive therapy. What happens when the patient keeps returning back, with frequent recurrences, looking for a cure? We are forced to critically evaluate how we tackle the disease and what other treatment options we can offer. Immunotherapy aims to stimulate the body's defense mechanism to get rid of the infection. This paper is a pointer toward measles, mumps, and rubella (MMR) vaccine immunotherapy and its efficacy in managing extensive recalcitrant warts. Patient selection is important to ensure a successful treatment outcome.

MATERIALS AND METHODS

This case series describes eleven patients who received MMR vaccine immunotherapy for recalcitrant warts. All patients were informed about the non-approved status of intralesional MMR vaccine

immunotherapy for warts. Patients (or guardian for children below 18 years) gave written informed consent for treatment. Eleven patients who attended the dermatology outpatient department with recalcitrant warts, defined as of more than 1 year duration and those which had been treated with at least one other modality (salicylic acid, imiquimod, destructive therapy-electrocautery, radiocautery, laser therapy, or cryosurgery) received MMR immunotherapy. 0.3 ml of reconstituted MMR vaccine (Priorix vaccine) was given intralesionally into the largest wart. Only the largest wart was treated. During the subsequent sessions, the treatment site remained the same. If the initially treated wart had reduced significantly in size and another larger wart was present, then the treatment site was changed. Treatment was repeated at an interval of 2 weeks for three sessions. Further sessions were given for patients with incomplete response.

RESULTS

The duration of warts, previous treatment received, comorbidities in the patients, the sites affected, number of treatment sessions, response to treatment, and adverse events are shown in Table 1. Complete resolution was noted in 9 out of 11 patients (81.9%) [Figures 1-3]. Patient No.9 [Table 1] discontinued treatment after 2 sessions. Patient No.11 [Table 1] had plane warts and showed incomplete response with only slight shrinking in size of warts.

The first sign of treatment response observed was necrosis of the treated wart. This sign was reassuring because, patient could be informed that the treatment was working. For patients in whom necrosis was difficult to observe with the naked eye, a close up photograph of lesion was taken with a mobile camera and enlarged. This helped to detect the signs of necrosis [Figure 4].

All except two patients [numbers 6 and 11, Table 1] showed necrosis at the second session. Patient 6 showed an increase in the number of lesions after the first session. Patient was informed about the lack of treatment response, but the patient chose to continue treatment. During the third session, necrosis was noted and after a total of four sessions lesions completely subsided. Patient No.11 had plane warts and did not manifest necrosis even after four sessions [Figure 5]. Patient no.2 [Figure 6] and patient No.10 had used keratolytics just before the consultation and had inflamed warts at presentation. These patients responded faster to treatment and required less than 3 sessions for complete resolution.

Patient number 7 [Table 1] had diabetes mellitus, which was well controlled, but developed cellulitis on the treated toe. Cellulitis subsided with a course of antibiotics and warts subsided after three sessions [Figures 7a-c]. Patient number 8 [Table 1] had psoriasis and the warts were spreading in

Table 1: Clinical profile and treatment response in patients treated with intra-lesional measles-mumps-rubella vaccine.

Patient	Age in years	Gender	Duration of warts (years)	Site	Previous treatment	Sessions	Response	Comorbidity	Adverse effects
1	52	Male	3	Chin, neck	Cautery, imiquimod	5	CR	Hypertension	Nil
2	35	Male	1	Neck	Salicylic acid, cautery	1	CR	Nil	Nil
3	42	Male	1	Periungual	Salicylic acid	3	CR	Nil	Pain
4	30	Male	1	Hands, feet, periungual	Salicylic acid, cautery	3	CR	Nil	Pain
5	48	Male	1	Inguinal	Salicylic acid,	3	CR	Nil	Pain
6	36	Male	1	Forehead, forearms	Salicylic acid, cautery	4	CR	Nil	After 1 session–lesions increased
7	43	Male	2	Feet	Salicylic acid, cautery	3	CR	Diabetic neuropathy	Secondary infection
8	44	Male	2	Feet, legs	Salicylic acid, imiquimod	3	CR	Psoriasis	Nil
9	10	Male	1	Palm	Salicylic acid, cryotherapy	2	Necrosis noted. Discontinued treatment after 2 sessions	Nil	Pain
10	29	Male	1	Hands	Salicylic acid, cautery	2	CR	Nil	Nil
11	38	Male	1	Plane warts	Salicylic acid	4	IR	Nil	Nil

CR: Complete response, IR: Incomplete response

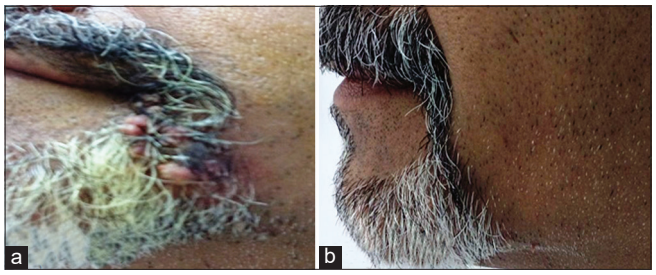

Figure 1: (a) Recalcitrant warts of 3 years – before intralesional treatment with measles-mumps-rubella vaccine; (b) the same patient after four sittings of intralesional treatment with measles-mumps-rubella vaccine.

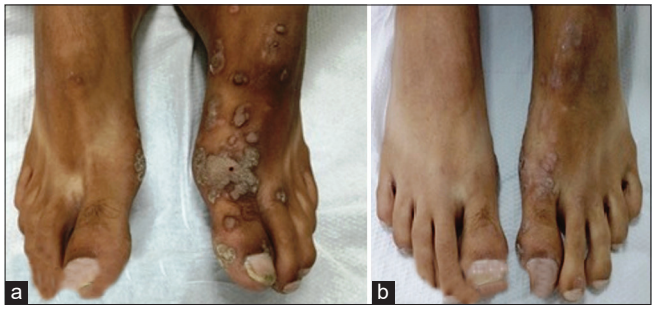

Figure 2: (a) Recalcitrant warts of 1 year involving the foot – before intralesional treatment with measles-mumps-rubella vaccine; (b) the same patient after four sittings of intralesional treatment with measles-mumps-rubella vaccine.

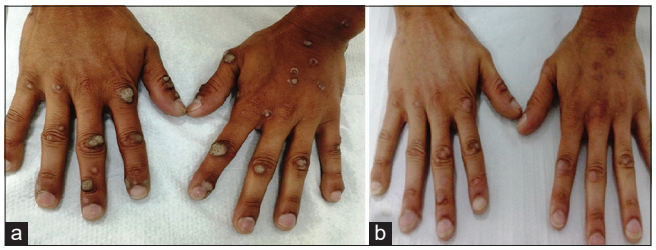

Figure 3: (a) Recalcitrant warts of 1 year involving the hands – before intralesional treatment with measles-mumps-rubella vaccine; (b) the same patient after four sittings of intralesional treatment with measles-mumps-rubella vaccine.

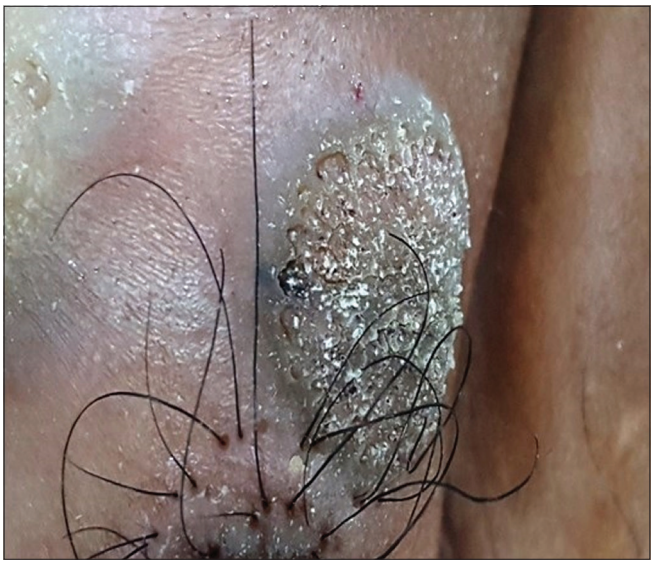

Figure 4: First sign of response to intralesional treatment with measles-mumps-rubella vaccine – necrosis (see the black discoloration) at the tip of the treated wart (at the end of 2 weeks).

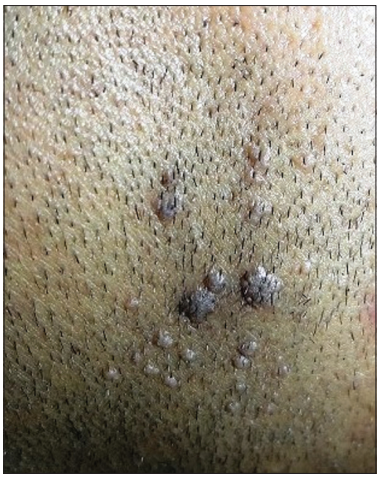

Figure 5: No signs of necrosis in plane warts after three sessions of intralesional treatment with measles-mumps-rubella vaccine – indicator of poor response to treatment.

the vicinity of psoriatic lesions that were treated with topical steroids. He had received methotrexate, which was stopped 1 year before MMR therapy. Patient number 9 [Table 1], who was a 10 year old child, did not return for treatment after the second session. After two sessions, the child had no adverse effects and there was evidence of necrosis, suggesting a positive response to treatment. The child returned back to home country where warts resolved after one session of trichloroacetic acid application by another dermatologist.

The advantages noted for this treatment modality were – relatively less pain, no scarring, less expense, and less number of treatment sessions compared to other modalities. This therapy was found to be useful for warts covering large anatomical areas and for periungual warts where conventional cryotherapy and cautery may cause pigmentary disturbances and permanent scarring.

DISCUSSION

The drawbacks of intralesional MMR in the management of recalcitrant warts include dependence on a modality not approved for the management of warts, secondary infection, flu-like symptoms, pruritus, burning, erythema, and edema.[1-10] However, the only adverse reactions noted in this series were

pain and secondary infection. The recurrence rates following the MMR immunotherapy could not be commented upon since long-term follow-up is not available for these patients.

Poor response of plane warts to MMR vaccine (as observed in one patient) has been previously noted in literature.[1]

Various treatment modalities to stimulate the immunity are tried in patients manifesting recalcitrant warts and these include BCG vaccine, MMR vaccine, purified protein derivative, *Mycobacterium* w vaccine, Vitamin D, *Candida* antigen, and autoimplantation.[1-15]

Cell-mediated immunity against human papilloma virus helps in spontaneous resolution of warts. Immunotherapy modulates the immune system and helps in clearance of warts. Relative ease of procurement makes MMR vaccine an attractive option. Further, most people have been exposed to this vaccine in childhood as part of the national immunization program, hence, the possibility of adverse reactions is rare.

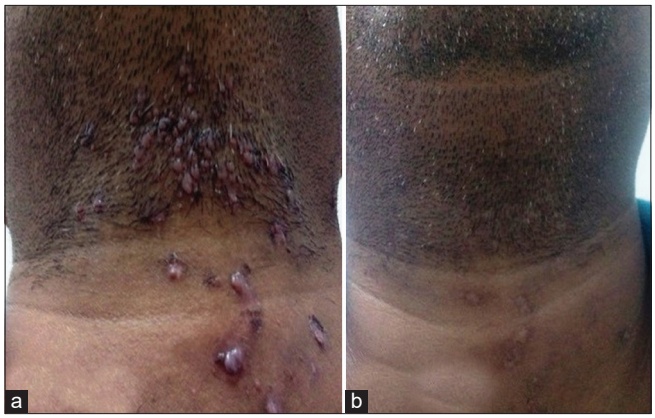

Figure 6: (a) Recalcitrant warts of 1 year – before intralesional treatment with measles-mumps-rubella vaccine; (b) the same patient after one sitting of intralesional treatment with measles-mumps-rubella vaccine.

The previous studies have employed two methods of MMR administration. In both methods, MMR vaccine is injected only into the largest wart. In both methods, injections were repeated after 2–3 weeks and 3–6 sessions were given.

In one method, 0.1 ml vaccine is given intradermally.[1] Reaction is read after 48 h. The dose of MMR vaccine given for treatment depended on the size of the induration with the test dose. If the size of reaction was 5–20 mm, 0.3 ml vaccine is given. If the induration was 21–40 mm in size, 0.2 ml vaccine is given, and for an induration of >40 mm, 0.1 ml of vaccine is given. In the alternate method, 0.3–0.5 ml of vaccine is injected into the wart.[2-10]

Na *et al*., in a 2-year retrospective study of using MMR vaccine as intralesional immunotherapy for warts, noted that among 136 patients, 26.5% showed complete response.[1] Adverse effects noted were pain, pruritus, and burning. They concluded that a complete response following MMR immunotherapy was higher when warts were of <6 months duration, a better response was seen in common warts when compared to plane warts and efficacy increased with the number of treatment sessions.[1]

Shaheen *et al*. in a randomized controlled trial of intralesional tuberculin versus MMR vaccine included four children aged <10 years and patients with genital warts.[2] With MMR vaccine, complete clearance was attained in target wart in 80% and in distant wart in 40% of cases. Adverse effects noted were pain, swelling, redness, and vasovagal attack. They also assessed IL-12 levels after treatment and found that levels were higher in MMR-treated group.[2]

Zamanian *et al*. studied the efficacy of intralesional MMR vaccine in a double-blind randomized controlled clinical

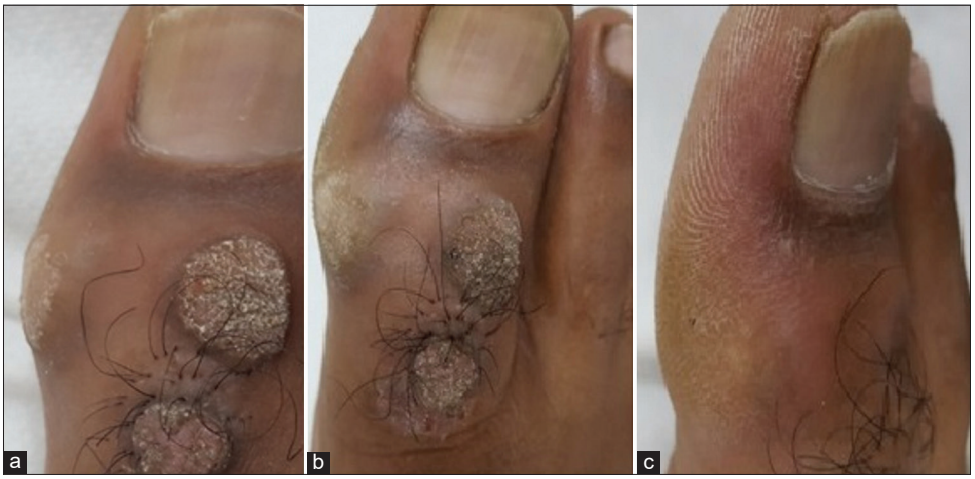

Figure 7: (a) Recalcitrant warts big toe – before intralesional treatment with measles-mumps-rubella vaccine; (b) the same patient after intralesional treatment with measles-mumps-rubella vaccine; (c) the same patient after further sessions of intralesional treatment with measles-mumps-rubella vaccine.

trial. Comparing the efficacy of MMR vaccine against normal saline, they noted complete cure in 75% of those who received MMR vaccine as against the 25% in the control group.[5]

Shah *et al*. in 2016 in a prospective study, which included genital warts, noted that MMR vaccine gave complete clearance in 72% and partial clearance in 16%. None of their patients developed a recurrence in 6 months.[4]

Nofal *et al*. in 2015, in a prospective study found complete response in 63% of treated warts and in 74.5% of distant warts. They found a recurrence rate of 4.8% after 6 months and concluded that the treatment was promising, safe, and effective.[3]

Saini *et al*. in 2016, in a prospective study of 86 patients in 10–45 years age group noted complete clearance in 46.5% and partial response in 20.9%. About 82% had clearance of distant warts. Recurrence rate was 5% in 6 months. They opined that a better response was noted with more sessions, increased dose, and by using test dose method.[6]

Awal and Kaur in 2018 did a single-blind, randomized, placebo-controlled study. They reported that 68% of patients in the MMR group showed complete response compared to the 10% in the control group who received normal saline. Recurrence rate in the MMR and control groups were 2.7% and 6% respectively.[7]

Chauhan *et al*. in 2019, in a prospective study of 52 patients noted that 82.4% had complete clearance. In 7.8% of patients, the warts subsided completely after one dose itself.[8]

El-Magiud *et al*. in 2020 did a randomized controlled trial on the efficacy of intralesional MMR vaccine versus cryotherapy in the treatment of common and plantar warts. About 70% of the patients in the MMR group showed complete response, while in the cryotherapy group, 45% of the patients showed complete response.[9]

Mohta *et al*. in 2020, compared the efficacy and safety of intralesional MMR vaccine to intralesional Vitamin D3 in children aged 8–16 years. They noted complete clearance of the injected wart in 86.7% of the MMR group and in 76.7% of the Vitamin D3 group. Further, no recurrences were noted at 6 months follow-up in the MMR group as against 6.6% recurrence in the Vitamin D3 treated group.[10]

Limitations

This is a case series with small number of patients and there is no long term follow up available for the treated patients.

CONCLUSION

The literatures as well as the current series show that intralesional MMR vaccine is an effective and safe treatment option for the treatment of common warts. Patients should be offered this treatment option if the warts are recalcitrant or if conventional modalities have a high risk of causing permanent adverse effects such as pigmentary disturbances and scarring. Patient selection is important since patients with plane warts or any underlying immune defect may not be good candidates for immunotherapy with MMR vaccine.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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