

# **Intralesional immunotherapy with Measles-Mumps-Rubella Vaccine for recalcitrant facial warts; a report of two cases**

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Received: 16 July 2020

Accepted: 29 August 2020

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**DOI 10.5001/omj.2022.01**

## **Abstract**

Warts are common benign skin tumours that are caused by Human Papilloma Viruses (HPVs). Although asymptomatic, recalcitrant warts represent a frustration to both doctors and patients as they are cosmetically unacceptable in most cases. Recently, Intralesional immunotherapy by different antigens like Bacille Calmette–Guerin vaccine, candida antigen, and measles, mumps, and rubella (MMR) vaccine has shown promising efficacy in the treatment of warts. Here we report two cases in Omani males who presented in 2019 to the dermatology clinic at Nizwa Polyclinic, Nizwa, Oman with recalcitrant facial warts that resolved completely with single intralesional injection of MMR vaccine.

## **Introduction**

Warts are very common benign epithelial tumors caused by human papillomaviruses (HPVs); which are a large family of small, non-enveloped, double-stranded DNA viruses <sup>1</sup>. More than 180 different types of HPVs have been sequenced <sup>2</sup>. Clinical Manifestations of warts depend on the HPV type involved, the anatomic location, and the immune status of the host; which include: common warts, plane, plantar, filiform or digitate, myrmecia, mosaic, genital, and periungual warts <sup>3,4</sup>. To date, there is no consensus for the definition of recalcitrant warts, but it is generally described for warts that persist for more than 6 months after failure of at least 5 treatment sessions<sup>5</sup>.

Although they are asymptomatic and usually resolve spontaneously, most patients seek treatment for facial warts as they are cosmetically disfiguring <sup>6</sup>. Many topical, destructive and immunotherapeutic modalities are available for treatment but no modality is 100 % effective<sup>7</sup>. Facial warts, in particular, require cosmetically acceptable treatment. Recently, intralesional antigen immunotherapy has shown

promising efficacy and tolerance in the treatment of warts including facial ones <sup>7</sup>. Here we report two cases of recalcitrant facial warts, who had complete resolution with a single intralesional injection of the Measles-Mumps-Rubella (MMR) vaccine.

#### Case 1

A healthy 38 years old Omani male presented to the dermatology clinic at Nizwa Polyclinic, Oman with 8 months history of asymptomatic skin lesions over the beard area that increased after recurrent visits to the barbershop and use of razor for shaving. Examination showed numerous (about 60 in number) flat-topped and verrucous papules over the submandibular area of the neck (Figure 1a). Before presentation, he visited a private dermatology center for treatment, and 6 sessions of cryotherapy resulted in clearance but lesions recur again. A clinical diagnosis of a common and filiform warts was made based on clinical presentation. Treatment with intralesional MMR was discussed and he agreed verbally. We injected 0.2 ml of the MMR vaccine into the biggest wart. No complications were reported apart from mild temporary pain during injection. No adjunctive treatment was used. On follow up after 2 weeks, he showed complete clearance (Figure 1b), and further, follow up after 2 and 6 months showed no recurrence.





**Figure 1:** A 38 years old male with numerous (about 60 in number) warts over the beard area of the face and neck (a). After treatment with single intralesional injection of the MMR vaccine showing complete clearance (b)

## Case 2

A 42 years old male presented to the dermatology clinic at Nizwa polyclinic Oman with a one-year history of a papular eruption of over the face. He reported no associated symptoms and attributed eruption to a recent visit to a barbershop. He has no co-morbid and didn't use any oral medications recently. Examination showed multiple (about 40 in number), tiny, and grouped monomorphic papules over the mental area of the face that are distributed bilaterally (Figure 2a). A clinical diagnosis of recalcitrant cutaneous warts was made based on clinical presentation. Treatment with imiquimod cream, three sessions of cryotherapy, and one session of electrocautery was unsuccessful before presentation. As he had recalcitrant warts, treatment with intralesional MMR vaccine was offered and he agreed. We injected 0.1 ml of the MMR vaccine into biggest papule bilaterally. No other treatment was given. Follow up after 1 month showed complete resolution (Figure 2b), and further follow up after 3 months showed no recurrence. No complications were reported apart from mild tolerable temporary pain.



**Figure 2:** A 42 years old male with common warts over chin and neck (a). After treatment with a single intralesional injection of the MMR vaccine bilaterally (b).

## Discussion

Viral warts are highly contagious and can spread via direct skin contact, especially if there are predisposing factors like skin maceration<sup>8</sup>. In our cases, the cause attributed to contamination at a barbershop. There is a habit for men in Oman to visit barbershops for beard shaving weekly. Proper sanitation at these places can't be guaranteed, raising an issue that needs further public education from health care workers especially dermatologists. Local spread of pre-existing warts also called Pseudo-Koebnerization, is very common after hair removal methods especially with razors due to skin breach<sup>9</sup>. An electrical trimmer is a preferred alternative for men with existing facial warts as it is less likely to seed the virus<sup>9</sup>. In addition, they should be educated not to touch their warts to avoid spreading of warts to other parts of the body or to other people.

Many modalities for treatment have been reported for facial warts including topicals, systemic medications, destructive methods, and intralesional immunotherapy with different agents<sup>7</sup>. Imiquimod cream is FDA approved for genital warts, but have been used effectively for facial warts, especially plane ones<sup>10,11</sup>. Disadvantages include the risk of post-inflammatory hyperpigmentation (PIH) and high cost. Clouth *et al.* reported few side effects with another topical treatment; Sinecatechins ointment<sup>12</sup>, however, it is not widely available. Topical cantharidin, a vesicant produced by beetles in the order Coleoptera, is another reported topical treatment option<sup>13</sup>, however, it has a risk of PIH especially in skin types 3 to 5 and scarring.

Oral Isotretinoin, a retinoid that is used primarily for severe acne, have also been reported to be effective for recalcitrant facial plane warts with either a fixed dose of 30mg/day or a mean dose of 0.5 mg/kg/day for at least 12 weeks<sup>14,15</sup>. Drawbacks include prolonged treatment period and side effects like cheilitis, dry eyes, and the need for monitoring of lipid profile and liver function tests.

Laser and light therapies have also been reported as an alternative treatment for recalcitrant facial warts<sup>8</sup>. Pulsed Dye Laser (PDL) which uses a 585 nm wavelength has shown a high clearance rate<sup>16</sup>. This option is limited by cost, the requirement of multiple visits, and pain. Yttrium aluminum garnet laser (YAG laser) is another option with a single session treatment but again limited by cost and risk of scarring and PIH<sup>17</sup>. Intralesional 2% zinc sulfate solution is another uncommon modality of treatment, but again limited by the need for special preparation and can cause textural changes that are cosmetically unacceptable<sup>18</sup>.

Intralesional immunotherapy by different agents like the MMR vaccine, *Candida albicans* antigen, Purified protein derivative vaccine (PPD), and *Bacillus Calmette-Guérin* (BCG) vaccine have gained recent attention for treating warts, including recalcitrant ones. Among them; PPD and MMR were shown to be the most effective modalities for lesion clearance at primary and distant sites and also reduce recurrence<sup>19</sup>. The mode of action of intralesional immunotherapy is still unknown but

is has been reported that it is associated with the release of different immunoregulatory cytokines such as interleukins 2 and 12, interferon  $\alpha$ , and tumor necrosis factor- $\alpha$  that stimulate a strong immune response against HPV<sup>20,21</sup>.

In an open-label study, Nofal et al. (2015) studied intralesional injection with 0.3 ml of the MMR vaccine for 65 patients with recalcitrant warts<sup>7</sup>, 41 patients (63%) had a complete response, and 2 had a recurrence. In another single-blinded randomized clinical trial by Awal *et al.* (2018) for common warts, the complete response was 68%<sup>22</sup>. In both studies, most patients required more than one session. However, It is not stated how many patients had facial warts in these studies and the response rate among them. Temporary Pain is the commonest side effect reported as in our cases, other less frequently reported side effects include flu-like symptoms, itching, erythema, and edema<sup>7,22</sup>. From our observation in the above cases, both patients had complete responses by a single intralesional injection of the MMR vaccine without any adjunctive treatment. However, further randomized clinical trials is needed to study the efficacy of intralesional MMR for patients with numerous recalcitrant facial warts.

## **Conclusion**

Intralesional immunotherapy with the MMR vaccine seems to be safe and effective for recalcitrant facial warts and can save the patient's time and stress. Further studies are needed to assess the efficacy of this modality of treatment for patient with numerous facial warts.

## **Declaration of patient consent**

The authors certify that both patient have given consent for their images and clinical information to be reported in the journal. The authors explained that names will not be published but anonymity can't be guaranteed.

## **Acknowledgements**

We thank both patients for giving consent to publish the case.

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