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Treatment Intervention of Chronic Plantar Wart Using Gardasil 9 Vaccine - A Case Report

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ABSTRACT

A case report on the regression of a hyperkeratotic chronic plantar wart, upon administration of the Gardasil 9 vaccine, is presented herein. A 42-year-old patient visited the clinic from September 2020 to May 2021, with symptoms and presentation typical of plantar wart, which contributed to severe disability while walking. The treatment prescribed was liquid nitrogen cryotherapy, curettage and topical salicylic acid. Over 7 months, the wart regressed along with severe treatment-associated inflammation, only to reappear. Gardasil 9 is administered free to secondary school children in Australia as part of the National Immunisation Program Schedule. The patient was a recent migrant and was not immunized, hence requested to be immunized. After a single dose, the patient experienced fever, shedding of wart tissue and surrounding skin. Complete healing took place within 2-3 weeks. It is thus proposed that Gardasil 9 be administered to migrants, and that it may also be considered for use as a therapeutic agent in chronic plantar warts. This may reduce the morbidity period, prevent autoinoculation, viral shedding and community spread.

Keywords: *Plantar Wart, HPV, Gardasil 9, Treatment*

Introduction

Plantar warts (PWs) or verrucae plantaris are cutaneous lesions on the plantar aspect of the foot, caused by some genotypes of the double-stranded DNA virus, Human Papillomavirus (HPV), namely 1, 2, 3, 4, 27, 29, 57, 60, 63, 65, 66 and 69. These genotypes are different from those associated with sexually transmitted infection (STI) and cancer, namely HPV 16, 18, 31, 33, 35, which are preventable by prophylactic vaccines (Witchey *et al*., 2018; Al-Awadhi *et al*., 2020; Boda et al., 2018). PW is most often diagnosed clinically from the presence of hyperkeratosis, with small dots or lines representative of thrombosed capillaries and tenderness. Bruggink, *et al*. (2013) and Garcia-Oreja, *et al*. (2022) demonstrated the presence of HPV in >93% of PW cases. Differential diagnosis with corns, calluses and

melanoma are ruled out by using dermatoscopy (Witchey *et al*., 2018).

Viral particles are shed from warts and are easily transmitted through common floors, shared footwear, swimming pools and bathrooms. The virus enters through minor abrasions and infects basal keratinocytes to form isolated or clusters of warts. Histologically, they cause wide-spread vacuolization and disturbance of epidermal cell differentiation resulting in tenderness (Grussendorf, 1980). The virus can remain dormant for up to 8 months and, when active, stays hidden from host immunity by restricting antigen presentation and raising T suppressor cell populations. Treatments, therefore, are intended to trigger viral exposure to the host immune system but are often not uniformly successful (Longhurst and Bristow 2013). Failure of natural killer and cytotoxic T cells to destroy viral tissue results in recalcitrant PWs (Witchey *et al*., 2018). The standard treatment at bulk-billed Medicare clinics is ablative therapy with liquid nitrogen (MBS online n.d.) and scraping which may cause intense side effects. Removal by carbon dioxide laser or erbium laser is recommended for ≥5 warts and requires hospital admission (MBS online n.d.). Over-the-counter medications such as salicylic acid, surgical cautery, needling and cryotherapy often result in inflammation, intense pain, secondary infection, additional expense and patient non-compliance for further sittings (Lipke, 2006).

Notably, a few case studies have shown the efficacy of HPV nonavalent vaccine (Gardasil) Merck Sharp & Dohme (Australia) on PW treatment (Daniel and Murrell, 2013, Landis *et al*., 2012, Abeck *et al*., 2015, Landini *et al*., 2015). Gardasil 9 is traditionally administered for the prevention of HPV associated STI and cancer. In Australia, the vaccine is provided free of cost to all secondary school children prior to their sexually active age.

The use of Gardasil 9 in a patient with long term recurring PW is described below. Ethics approval to publish the data of this study has been received from Swinburne University of Technology (Ethics code: 6402, 20226402-9765).

Methods

A 42-year-old female presented with a verruca on the mid-plantar aspect of the right foot in September 2020 (Fig. 1). She claimed to have recurrent pain spasms at the site and difficulty in walking. Upon clinical examination, it was diagnosed as a plantar wart. Upon enquiry, the patient described herself as a migrant to Australia and a regular swimmer at the local public swimming pools, where she would walk bare-foot. Her medical history revealed megaloblastic anaemia and PAP smear negative status. She had not received the Gardasil 9 vaccine after migration, as it was considered unnecessary for middle aged adults.

Treatment of the wart began with regular sittings of liquid nitrogen freezing and wart-scraping. In Dec 2021, she requested alternate treatment due to intense pain post-cryotherapy. She was prescribed 20% salicylic acid treatment. When the pain subsided, she was advised to resume liquid nitrogen freezing and curettage. The patient was also a health professional and was familiar with literature by Daniel and Murrell, (2013), Landis, *et al*. (2012), Abeck, *et al*. (2015) and Landini, *et al*. (2015). After 7.5 months, she requested for Gardasil 9 vaccine to be administered, due to the pain associated with treatment-associated inflammation and regrowth of wart tissue. According to the prior studies shared, the clinician agreed to prescribe the vaccine, which she procured on payment. Therapeutic Goods of Australia or TGA (2011) recommends the vaccine until 45 years of age, hence she was eligible. The patient received a single dose of Gardasil 9 in April 2021.

Results

Figure 1 describes the evolution of the wart over time (Sep 2020 to April 2021) followed by complete shedding of wart material and surrounding skin after the immunization. Vaccine side-effects included 1 day of fever up to 39°C. Treatment response was within 2 weeks, with complete resolution of pain and wart tissue within 1 month.

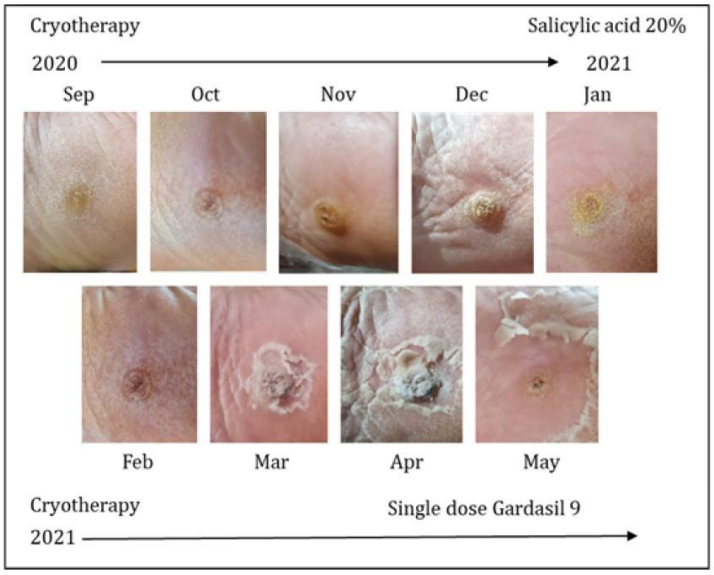

Figure 1: Phases of plantar wart growth and response to treatments in the case studied.

Discussion

Gardasil 9 is a nonavalent vaccine provided to secondary school students in Australia to prevent transmission of sexually acquired HPV and contains HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58 genotypes (TGA, 2011). The patient with the PW did not receive the vaccine earlier, as she had only

entered Australia in the last two years. The treatment-resistant PW and side-effects of topical treatments made it hard for her to perform her daily duties. Upon immunization with Gardasil 9, healing took place within a month. It can be speculated that T lymphocytes and neutralizing antibodies raised against Gardasil genotypes (Munk-Madsen *et al*., 2018; Pattyn *et al*., 2019) were capable of cross-reacting with epitopes on the PW HPV genotype, leading to destruction of viral infected keratinocytes and prevention of spread of virions to healthy skin cells. Diagnosis of the infecting virus and its genotype could not be carried out due to constraints, and this limitation is acknowledged.

Lessons from this case suggest that (a) it might be useful to consider providing Gardasil 9 to the new migrant population in Australia (b) Gardasil 9 could be considered as a rapid and painless treatment strategy as it did not cause soft tissue inflammation as did the previous treatments. The only downside was the presence of fever for a day.

Conclusion

This case study adds to the support of the use of Gardasil 9 in populations that have not being previously vaccinated as a therapeutic intervention for treating plantar warts. Where possible and affordable, this may be a non-ablative treatment option for plantar warts and should be included in the treatment regimen of Medicare bulk-billed clinics to prevent long term morbidity of the condition and recurrent clinic visits. Where feasible, this may be accompanied by a laboratory diagnosis for HPV DNA. Future studies on genotypes of the virus in the wart will enhance justification of this proposition. Faster treatment and recovery from PW lesions will minimize viral shedding, reduce autoinoculation and community transmission.

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