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# Clearance of recalcitrant warts in idiopathic immune deficiency following administration of the quadrivalent Human Papillomavirus vaccine.

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## Summary

Human papillomavirus induced cutaneous warts are potentially serious and debilitating. In immuno-suppressed patients these warts may be resistant to standard therapies. We report a case of a young patient with a primary immune deficiency whose recalcitrant cutaneous warts regressed completely following administration of the quadrivalent human papillomavirus vaccine.

## Introduction

Cutaneous human papillomavirus infection is a common consequence of immune compromise in a variety of contexts, including inherited immune-deficiency, HIV infection and post-transplantation[1]. Cutaneous warts arise in up to 25% of immunosuppressed patients and often prove recalcitrant or refractory to numerous and prolonged treatments [1]. Though usually benign, cutaneous warts cause symptoms related to the psychosocial effects of the disease, mechanical interference, pain and deterioration in functional abilities of patients. These symptoms and effects are exacerbated in cases where warts are widespread, thick or located on the hands, feet or face.

## Report

We present a case in which persistent cutaneous HPV warts in an immune compromised patient completely resolved following vaccination with the quadrivalent HPV vaccine.

A 17 year old male patient was referred to the immunology department of our hospital after an incidental finding of neutropaenia and lymphopaenia. This was uncovered during routine screening prior to consideration of isotretinoin treatment for facial acne vulgaris. Further investigation showed a persistent neutropaenia (0.6 x $10^9$/L) and a CD3 lymphopaenia (total: 1x$10^9$/L, CD4: 129x$10^6$, CD8: 92x$10^6$/L) which was diagnosed as idiopathic. He had normal T and B cell maturation, normal neutrophil respiratory burst, normal immunoglobulin levels and immunoglobulin sub-classes. His HIV serology was negative, he had normal autoimmune serology testing and maintained responses to previous vaccinations. He was given prophylaxis with co-trimoxazole 480mg daily.

Other than more severe recurrent childhood infections than his peers, the patient had been systemically generally well. However he had a seven-year history of persistent hand (Fig. 1) and similar foot warts which had not resolved despite treatment with repeated cryotherapy, imiquimod and numerous over-the-counter topical treatments. He was referred to the dermatology department in the same hospital for further review of his hands and feet. Though not extensive, the warts were persistent and caused significant impact on quality of life. The patient did not exhibit signs of atopy.

The patient received the standard three dose course of Gardasil® quadrivalent papillomavirus vaccine. After the second dose of the vaccine, the warts began to regress and complete resolution of all warts was reported within weeks after the third vaccine dose (Fig. 2). There was no recurrence of the warts up to two years post vaccine. The patient experienced no adverse effects from the vaccination.

Although there is evidence against the bivalent or quadrivalent vaccine having an effect on HPV disease in the cervix or on genital warts[9-10], there is limited anecdotal evidence for the role of the vaccination as a therapy for cutaneous warts. Four individual case reports in immune competent individuals[4-7] suffering from extensive cutaneous warts exist, in all cases the warts resolved following treatment with the HPV vaccine.

In a more recent report[8] an elderly patient with chronic lymphatic leukaemia in remission and lymphopaenia and neutropaenia following chemotherapy for breast cancer also experienced resolution

of cutaneous warts following vaccination, though in that case the warts had been present prior to the immune suppression. To our knowledge, no reports exist of patients with innate or inherited immune suppression whose cutaneous warts have been treated with the HPV vaccine.

A previously reported case also supports a potential role for HPV vaccination in cutaneous warts in the context of WHIM syndrome[2].

Though the resolution of warts in this patient following vaccination may be coincidence, the clinical course, timing and lack of effect of conventional treatments over many years argue against this.

The mechanism by which vaccination against HPV types which are not the causative agent in cutaneous warts might have a therapeutic effect is unclear. There is similarity between the genomes of HPV 2 subtypes (27 and 57) and HPV 6 which may lead to cross-reactive immune responses. An alternative, or additional hypothesis might be that the quadrivalent vaccine or its adjuvant stimulates immune responses non-specifically leading to clearance via a generalised up-regulation of immunity. Furthermore there is evidence that prophylactic vaccination against HPV can stimulate responsive lymphocyte activation[3] against virally infected cells, which may lead to targeted immune clearance.

This patient exhibited a similar immune phenotype to that which might be expected in iatrogenic immunosuppression due to calcineurin inhibitors (i.e. for organ transplant recipients). No published evidence exists to date of the efficacy of HPV vaccination for treatment of cutaneous warts in such patients, but given the importance and size of that population future interventional studies would seem warranted.

Human papillomavirus infection can lead to cutaneous warts which, in the immunosuppressed, can persist with significant impacts on quality of life. We present the first reported case of full resolution of HPV warts in a patient with idiopathic immune suppression following administration of the quadrivalent HPV vaccine.

## Learning Points

- Cutaneous warts are potentially serious and debilitating

- Cutaneous warts may be resistant to standard therapy in immune suppressed patients.

- The quadrivalent HPV vaccine may be of potential benefit in these patients.

**Figure 1: Cutaneous hand warts at initial presentation of the patient.**

**Figure 2: Cutaneous hand warts 6 months after the third dose of quadrivalent human papillomavirus vaccine.**

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