

SHORT COMMUNICATION

Quadrivalent Human Papillomavirus Vaccination: A Promising Treatment for Recalcitrant Cutaneous Warts in Children

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Cutaneous human papillomavirus (HPV)-induced warts are common in the general population, especially among children. Prevalence rates among primary schoolchildren are between 22% and 33% (1). In childhood, in particular, the spontaneous resolution rate of HPV-induced warts is high. Half of primary schoolchildren will be free of warts within one year (2) and approximately two-thirds of warts clear without treatment within 2 years (3). However, dermatologists still see a high number of children with extragenital warts that do not resolve spontaneously for years and cause psychological (particularly if located on the hands and fingers) and physical (pain and irritation if located sub- or peri-ungually) problems. At present a large number of different approaches to treat these problematic warts are used in clinical practice, but there is no universally effective treatment (4). During the last few years a number of publications have reported high clearance rates after repeated intralesional injections of immune-stimulating mumps or Candida antisera (5), or commercially available mumps, measles and rubella vaccine (6–8). A report of successful treatment of recalcitrant plantar warts in a 59-year-old healthy woman by administering quadrivalent HPV vaccine in the patient's arm in 3 doses at 0, 2 and 6 months (9), formed the basis for our current case study, using the vaccine in children aged 9–11 years who had had therapy-resistant extragenital warts for years.

MATERIAL AND METHODS

All 6 children had had painful and/or embarrassing recalcitrant extragenital warts for more than 2 years (Table I) and a number of therapeutic approaches had failed. In all children topical salicylic acid, duct tape occlusion therapy and cryotherapy, alone or in combination, had been performed. In addition, imiquimod ($n=3$), laser treatment ($n=2$), cimetidine ($n=1$), topical 5-fluorouracil (5-FU) ($n=5$) and glutaraldehyde ($n=5$) had failed.

Table I. Data for children responding to quadrivalent human papillomavirus (HPV) vaccination

Patient	Age, years/sex	Duration, months	Clinical presentation
1	10/F	48	Multiple plantar
2	9/F	32	Multiple palmar
3	9/F	60	Multiple palmoplantar
4	11/M	36	Multiple palmoplantar
5	10/M	34	Multiple palmoplantar
6	10/F	48	Multiple plantar

Administration of the vaccine was therefore started. The vaccine was administered in 3 separate intramuscular injections in the deltoid region of the upper arm. Permission was obtained from parents and referring paediatricians. The vaccine is licensed for use at 9 years of age and over in Germany. No other vaccination regime was performed 4 weeks prior to this treatment, during the active vaccination process and 4 weeks afterwards.

RESULTS

The vaccine was well-tolerated, with local swelling, lasting only for a short time, in some children. In 4 children healing of warts was documented between the 2nd and 3rd vaccination, 1 girl was disease-free after the first vaccination and only 1 child had flat warts still present at the time of the third vaccination, with complete healing shortly afterwards (Fig. 1).

DISCUSSION

There is a therapeutic need for an effective treatment for long-standing clinical warts in children. A new treatment modality is immunotherapy by repeated intralesional injections of known antigens (5–8). Landis et al. (9) successfully treated recalcitrant plantar warts

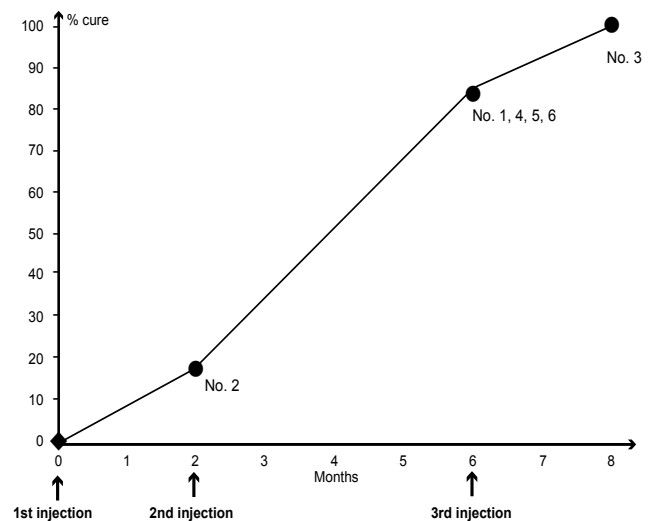


Fig. 1. Time-point of complete healing of warts in vaccinated children.

with the HPV vaccine used in this series in a 59-year-old healthy woman.

In our case study, enrolling children up to the age of 11 years, a complete healing of recalcitrant warts was documented. However, the effects seem to be age-related. The treatment protocol failed in 3 of 4 adults and in 3 out of 6 adolescents aged 14–17 years who had long-standing therapy-resistant warts on the hands or feet (data not shown).

At present we can only speculate about the mode of action of this therapy. Since extragenital cutaneous warts are mainly caused by infection with HPV-types 1–4 or 26–29, and the successfully used quadrivalent HPV vaccine comprises HPV-6, 11, 16 and 18, a cross-protective effect is thought to be likely (9, 10). It is well-established that papillomavirus-like particles, based on L1 capsid protein, are able to induce a specific CD8⁺ activation signal (11). Hormones, on the other hand, are known to influence the expression of HPV proteins (12). With the beginning of puberty the major histocompatibility complex (MHC) class I molecule of the HPV-infected cells disappears, resulting in a decrease in the vaccine-induced HPV-specific cytotoxic T-cell immune response. This may be a factor explaining the age-dependent therapeutic response to the vaccine.

The present study has some limitations; it includes only a small number of patients and lacks a placebo arm. However, all patients were refractory to multiple previous treatments and had a long history of the disease. The rapid response observed shows that vaccination with the quadrivalent HPV vaccine has the ability to become an elegant, well-tolerated therapy for recalcitrant warts in children. Further research is necessary, using placebo-controlled randomized studies to look at patients of different age groups. Especially girls in whom HPV-vaccination is strongly recommended and in whom costs are usually covered by the health insurance are the preferred study group.

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