SUCCESSFUL TREATMENT OF FLORID CUTANEOUS WARTS WITH INTRAVENOUS CIDOFOVIR IN AN 11 YEAR OLD GIRL

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Abstract

Cutaneous warts, commonly seen in children and the immunosuppressed are socially distressing and are often resistant to traditional treatments. Here, we report an eleven year old girl with bilateral florid verrucous lesions on her hands, feet and chin which were refractory to a number of standard treatments including cryotherapy, cantharidin preparations, topical salicylic acid, surgical debulking techniques, oral Cimetidine and topical and intralesional Cidofovir. As the disfiguring lesions had a marked adverse effect on her quality of life, a trial of IV Cidofovir was instituted. We administered five cycles of IV Cidofovir with a one week interval between the first and second treatments, followed by two week intervals thereafter. This regime was well tolerated and we report dramatic resolution of the lesions with persistent clearance six months after completion of the fifth infusion. Resolution of recalcitrant warts with IV Cidofovir has been reported in a limited number of cases. Our experience supports its efficacy in this setting, and to our knowledge this is the first report of successful treatment of cutaneous warts with IV Cidofovir in a Pediatric case.

CASE REPORT

An eleven year old girl with a background of Milroy syndrome and mild asthma presented with a three year history of florid cutaneous warts. Examination revealed bilateral verrucous papules on the thumb, index and middle fingers, extensive bilateral plantar warts and several planar and exophytic warts on the lower lip and chin. (Fig. 1). The foot lesions caused discomfort on walking and, while the hand warts did not affect manual function, they were disfiguring and socially disabling. She became increasingly self conscious following teasing from her peers and covered the lesions in social settings. She became withdrawn and introverted and no longer enjoyed her favourite hobbies. The patient was born with global lymphoedema, which had been managed satisfactorily with compression garments and intermittent manual lymphatic drainage. Her development was appropriate for her age and she was systemically well.

TREATMENT

It was decided to treat the warts aggressively in view of the profound effect on the patient's quality of life. These lesions were resistant to several treatments including repetitive cryotherapy, multiple applications of Cantharone Plus® (Cantharidin 1%, salicylic acid 31%, Podophyllin 2%, Dormer Laboratories INC. Ontario, Canada) under occlusion; a preparation of 60% salicylic acid in emulsifying ointment was discontinued due to discomfort. Several bulky lesions on the hands were treated with curettage and diathermy under general anaesthetic on two occasions. This was well tolerated and yielded a good initial response. However, multiple lesions recurred within two months of treatment and only a single lesion on the index finger resolved completely. Surgical debulking was not repeated due to the lack of efficacy and risk of scarring. Other interventions included zinc supplementation, twice daily application of 3% topical Cidofovir for one month, a three month trial of 30mgs/kg/day of oral Cimetidine and intralesional Cidofovir injections, all of which were ineffective.

As the lesions had an adverse effect on her everyday life, it was decided to initiate IV Cidofovir at a dose of 5mgs/kg, which was administered with oral Probenecid pre and post infusion and intravenous hydration with normal saline as is standard with IV Cidofovir. The infusion was well tolerated apart from mild nausea and was repeated one week later followed by three further infusions at two week intervals. Her renal function was monitored closely and remained normal throughout the treatment period. Normal appearing skin surrounding the warts became mildly inflamed before becoming intensely itchy and resolving gradually within four months of the last infusion. A dramatic response with resolution of >90% of the lesions was observed, six months after completion of the fifth cycle of IV Cidofovir (Fig. 2). Her progress has been followed at two month

intervals and she has had no recurrence of lesions ten months after completion of this therapy.

DISCUSSION

Cutaneous warts caused by Human Papilloma Virus (HPV), a double-stranded DNA virus, may affect up to 10% of children and young adults.¹ There is no known association between HPV and Milroy Syndrome. Warty lesions are socially disabling and may impair hand function or discomfort on walking depending on their location. They are potentially distressing and can have a profound effect on quality of life. Warts are often resistant to therapy as in our patient whose lesions were unresponsive to multiple treatment modalities. Established treatments are often reliant on destruction of involved tissue with no specific antiviral effect. As viral DNA can survive in clinically normal skin, destruction of visible lesions alone does not ensure elimination of the virus.²

Cidofovir is a nucleoside analogue antiviral drug with broad-spectrum activity against DNA viruses. It inactivates viral DNA polymerase, halts DNA synthesis and induces apoptosis in HPV infected keratinocytes while the turnover of normal cells remains unchanged.³ A number of authors report successful treatment of common warts with topical Cidofovir in a pediatric population. Complete remission was obtained using Cidofovir 3% topically twice daily with treatment durations ranging from ten days to 10 weeks.⁴ Previously we successfully treated a refractory verruca in a child with acute lymphoblastic leukaemia with a six week course of topical Cidofovir⁵. Other authors report that an extensive verruca in an adult with AIDS reduced significantly within five days of commencement of a similar preparation.⁶

Systemic administration of Cidofovir is limited by potential adverse effects and is only approved by the US Food and Drug Administration for treating resistant CMV retinitis in patients with HIV. However, it has been used successfully in the management of other DNA viruses including recalcitrant molluscum contagiosum⁷ and orf. It is administered

intravenously due to poor oral bioavailability and has a short half life in serum but prolonged activity inside the target cell.⁸ A limited number of cases of effective treatment of recalcitrant warts with repeated cycles of systemic Cidofovir have recently been reported. Hivnor et al describe an HIV patient with extensive hand warts, resistant to several treatment modalities including topical Cidofovir, whose lesions cleared after a total of seven cycles of intravenous Cidofovir.⁹ Interestingly, resolution occurred in this case despite severe immunosuppression. Grone et al outline the successful treatment of extensive verrucous lesions with systemic Cidofovir over a five month period in a patient with myelodysplastic syndrome.¹⁰ Kottke et al report a man with disfiguring facial warts and HIV infection whose verrucous lesions cleared completely following five cycles of IV cidofovir.¹¹ His CD4 count remained low and the viral load was persistently high during the treatment course.

Potential side effects of IV Cidofovir include nephrotoxicity, with transient elevation of serum creatinine in up to 12% of cases and rarely progression to chronic renal failure.¹² Renal impairment secondary to proximal tubular cell injury is well recognized and is reduced by premedication with Probenecid and normal saline which decrease exposure of proximal tubular cells to Cidofovir, thereby reducing the potential for cellular damage.¹³ Less common side effects include uveitis / iritis and rarely neutropenia. Its accessibility is further limited due to its expense, with an average wholesale cost of €985 for a 375mg vial. Although IV Cidofovir has been used successfully in young children in the management of CMV retinitis and in renal transplant recipients,¹⁵ its use in dermatology has been limited to adults. To our knowledge, this is the first report of successful treatment with IV Cidofovir of cutaneous warts in a pediatric patient. Clinical trials and further experience are required to clarify the role of cidofovir in the management of

cutaneous warts in a pediatric population, but the dramatic response seen in our case suggests a possible role for recalcitrant disfiguring lesions.

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LEGENDS TO FIGURES

Figure 1. Extensive hyperkeratotic warts on hands prior to IV Cidofovir therapy.

Figure 2. 90% resolution of verrucous hand warts, after the fifth infusion of IV Cidofovir