TREATING PLANTAR WARTS: UTILISING NATURAL IMMUNITY TO INDUCE WART REGRESSION

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In a previous article in the ‘Podiatry Focus’ section, the treatment of plantar warts (or verrucae) has been described (Bristow, Greenwood, 2009). These skin lesions are notoriously difficult to treat, even in immune-competent individuals, and as a recent review has highlighted there are currently no definitive treatments (Kwok et al, 2011). Practitioners often resort to using a range of topical preparations which can prove costly to the patient and can be a source of frustration. This article reports on one specific treatment approach that was first reported in 1969 and is now, following recent work, enjoying a renaissance in wart treatment. A description of the possible mode of action and the current evidence is given. The treatment is called the Falknor’s needling method, named after the author who first wrote about this procedure in 1969 (Falknor, 1969).

**Pathophysiology and clinical appearance of verrucae**

Verrucae are caused by infection of the living cells of the plantar epidermis (primarily the stratum basale) by the human papilloma virus (HPV). There are over 100 strains of HPV, of which three antigenically heterogeneous HPV subtypes 1, 2 and 4 are known to cause verrucae and also warts on the hands (Sterling et al, 2001). The virus infects the basal epithelium after gaining access through microscopic lacerations in the surface of the skin. Once the viral cells invade the host cells, they can remain latent for up to 8 months (Moghaddas, 2004). When the virus is triggered within the host cell the mutated skin cells proliferate, in particular within the stratum spinosum resulting in abnormal keratinisation of the cells. The pathophysiology of this abnormal cell proliferation is observed clinically as an area of skin which appears ‘cloud-like’ or ‘warty’ in structure. Other clinical observations include the interruption of surface skin dermatoglyphics to make way for the hyperproliferating infected cells (Figure 1). As the stratum spinosum lies in close proximity to the dermal capillary vessels, often the capillary loops become enmeshed among the proliferating cells and are

![Figure 1. Plantar wart (verruca). Note the ‘cloudy’ or ‘cauliflower’ appearance of the wart and the skin straie diverging around the lesion.](www.bdng.org.uk)
dragged along with the cells towards the surface of the skin. This explains the appearance of the dark coloured spots within the wart. These are not always seen however, therefore other diagnostic observations must be made during clinical assessment.

Ordinarily, the cellular damage caused to the host cell by a virus triggers the generation of cytotoxic T cells targeted to eradicate the infected cells. This is not apparently so in the case of HPV-infected cells, where there is an absence of antigen-presenting proteins on the host cell wall inhibiting an immune response and therefore suppressing inflammation. However, spontaneous regression of the warts is often seen (Nakayama et al, 2011), which would suggest that an immune response can be induced by HPV, although this can be considerably delayed or absent in adults and the immunosuppressed.

**Traditional treatments and their mechanisms of action**

The aim of most treatments is to remove the affected epidermal cells using topical chemicals or physical debridement and/or to initiate an immune response targeted at the infected cells. One of the most popular treatments, salicylic acid, is supposed to have a twofold effect: firstly acting as a keratolytic agent, which disrupts intercellular cohesion, causing desquamation of the HPV-infected epidermal cells (Huber, Christophers, 1977), and then by causing the initiation of a beneficial immune response (Sterling et al, 2001).

Another common treatment approach is cryotherapy, where the tissue destruction takes place in two phases. Firstly, the fast freeze and slow thaw causes disruption to the cell wall and organelles due to the intercellular ice crystal formation. This is followed by ischaemic necrosis (the second phase) due to cryogenic damage to the microvasculature of the skin (Wilkes, Fraunfelder, 1979). Cryotherapy does not kill the HPV, but destroys the cells infected by the virus (Jones, Darville, 1989), however the process of cell death itself will induce a degree of inflammation, but this may not be enough to destroy the virus.

The main deficiency of such treatments is that they are not uniformly successful. This lack of efficacy could be due to the unique nature of the HPV not eliciting an immune response or down to individual treatment technique.

**The theory of autoinoculation in the context of the pathophysiology of warts**

The antigenic heterogeneity of HPV has important implications for the immunology of human warts, primarily that no demonstrable immune reactions are elicited. The process of wart regression remains poorly understood. Nevertheless, the immunological alterations which occur in patients with regressed or cured warts compared to patients with active warts, particularly increased cell-mediated response and antibodies specific to the virus, support a possible role for immunity in the resolution of warts (Briggaman, Wheeler, 1979). The generation of a host systemic immune response in order to eradicate the HPV virus in hand warts has been shown to be achieved through use of a vaccine in one case (Venugopal, Murrell, 2010). However, the main problem with plantar warts is that the infected...
cells sit among thickened, superficial epidermal cells which lie some way away from a viable blood supply, therefore reducing the chance of the exposure of the expressed viral proteins to the immune system. In addition, research into the viral life cycle supports the need to intervene at an early stage of infection (Frazer, 2009), when the viral gene expression is less productive than late-stage gene expression (Hubert, 2003). Therefore, two things to consider are early intervention and triggering the systemic immune response to respond to localised infection.

Work conducted by Horn et al (2005) showed that intralesional immunotherapy using injection of Candida, mumps or Trichophyton showed significantly higher response rates. This response was accompanied by proliferation of peripheral blood mononuclear cells to HPV antigens, supporting the theory that an HPV-directed, cell-mediated immune response plays a role in wart regression (Horn et al, 2005). While useful in any patient with warts, intracellular immunotherapy may be of particular use in individuals with a large number of lesions as opposed to singular lesions due to the cost implied.

Autoimplantation therapy in the treatment of multiple warts has been tested by several researchers (Shivakumar et al, 2009; Nischal et al, 2012; Srivastava, Bajaj, 2010). This is a simple technique, which encourages a cell-mediated immune response to combat warts (including verrucae). Shivakumar et al (2009) removed a section of a wart and implanted the tissue into a surgically made cavity in the forearm of the same patient. Of the 60 patients who underwent this procedure, 91% were totally cleared of warts two months post-implantation. Nischal et al (2012) conducted a similar study where the entire wart lesion was implanted into the forearm in 35 participants. Twenty (74%) of the patients showed complete clearance of the warts within three months of the procedure. Another method of autoinoculation, conducted by Srivastava and Bajaj (2010), involved the removal of a portion of the viral
wart tissue followed by the maceration of the cells in distilled water. The suspension was then injected into the gluteal region on the same patient. Sixty-two people underwent the procedure of which 35 (66%) had resolution of warts two months post-procedure. All of these studies were conducted on people who had recalcitrant warts, including palmo-plantar warts.

The evidence supporting autoinoculation techniques is strong, however although such invasive procedures may be justified for those individuals with multiple, widespread warts, they may not be considered to be effective for the treatment of single recalcitrant verrucae. An alternative treatment, the Falknor’s needling technique, may be a more suitable procedure for such cases. Although this method requires anaesthetising the tissues local to the verruca, it is relatively less invasive than the procedures already described and technically easier, and it may still initiate a similar immune response (Falknor, 1969).

Falknor’s needling method
Falknor (1969) described a procedure that involved anaesthetising the region of skin where the verruca presented followed by the insertion of a needle into the verruca until it exits the verruca tissue, entering the underlying dermis and subcutaneous fat layer. Once the boundary between the verruca capsule and the underlying fat is pierced the needle is then removed and the same process is repeated, in an area of tissue immediately adjacent to the previous puncture until the entire surface of the verruca has been punctured (Figure 2). Falknor reported only two failed cases out of 126 verrucae he treated using this technique.

Although published in 1969, Falknor’s method was not widely adopted or researched until some 32 years later when interest resurfaced among practitioners looking for a new, viable treatment option for stubborn verrucae. In 2011, a published research paper reported a 50% resolution 8 weeks post treatment (Skilton, Mehar, 2011), however the number of participants used in the study was relatively small (14 cases) compared to Falknor’s work, with a short follow-up period. In 2013 Longhurst and Bristow reported the retrospective analysis of 46 cases of verruca treated with this technique and found that 69% (31 out of 45) had resolved following the needling treatment. Considering the recalcitrance and average duration of the lesions included was 4.5 years, this technique may offer hope to those with stubborn, long-standing lesions. Figure 3 shows one participant from the Longhurst study, before and after needling treatment.

The encouraging results of the Falknor technique support the theory that an immune response may be taking place as a result of the procedure. As the process involves a needle passing through infected cells and entering a vascular region of non-infected cells, it might be plausible to propose that a degree of autoinoculation is taking place therefore initiating a cell-mediated immune response. This still remains a theory, which requires further substantiation preferably by in vitro cell analysis, but the clinical benefits are clear. As with all human intervention studies, an appropriately designed randomised controlled trial would provide information of the efficacy of this treatment.

References

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