CASE REPORT

Successful Treatment of Recalcitrant Ungual Wart with Tuberculin Purified Protein Derivative Immunotherapy

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Summary
Despite a variety of therapeutic options that is available, treatment of warts remains challenging and rate of recurrence is high. Intralesional immunotherapy is an emerging therapy for warts. Tuberculin purified protein derivative (PPD) is one of the immunotherapeutic antigens used for the treatment of warts. Here we report a case of recalcitrant periungual wart successfully treated with tuberculin immunotherapy.

Key Words: *Immunotherapy; Tuberculin; Purified protein derivative; Periungual wart*

Introduction
Wart is a benign skin tumour caused by Human Papillomavirus.[1] It typically presents as well-circumscribed single or multiple papules with a hyperkeratotic surface.[1] Ungual wart is common and can be painful as it burrows deep and erode the underlying tuft of the distal phalanx. It can also cause fissures, which predisposes the nail to paronychia.[1]

Ungual warts can be difficult to treat. Previous literature has reported various therapies, including topical keratolytic, cryotherapy, electrocautery, or laser therapy.[1-2] However, the expected cure rate ranges from 60 – 70% only.[1] Furthermore, none of the treatments is free from side effects such as blisters, pigmentary changes, ulcers and onychodystrophy.[1-2]

Recurrences are common as warts may be partially visible around the nail. The remaining wart may extend underneath the nail plate, which makes it challenging to deliver effective treatment.[1] Prevalence of recurrence rate of ungual warts range from 6% to 100% in adults.[3] Total or partial nail avulsion may be employed

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to counter this problem. However, it is not the first-line treatment as there is a risk of destroying the nail bed, nail matrix or underlying bone.[1]

Immunotherapy is an emerging modality for the treatmentof ungual warts. It stimulates cell-mediated immunity, which results in wart clearance.[1-4] Here, we report a case of recalcitrant periungual wart, successfully treated with intralesional immunotherapy of tuberculin purified protein derivative (PPD).

Case Report

An 18-year-old immunocompetent male patient presented with a painful periungual growth of the left thumb for 2-years duration. He failed previous therapies, which were a partial nail avulsion and 10 sessions of cryotherapies. The cryotherapy involved liquid nitrogen spray, delivered at 10 -15 seconds with 2 freeze-thaw cycles. On examination, there was a 15 x 10 mm hyperkeratotic, dark brown plaque on the left thumbnail bed. Removal of the surface with a surgical blade revealed thrombosed capillaries. The surrounding nail was dystrophic. A diagnosis of ungual wart was made.

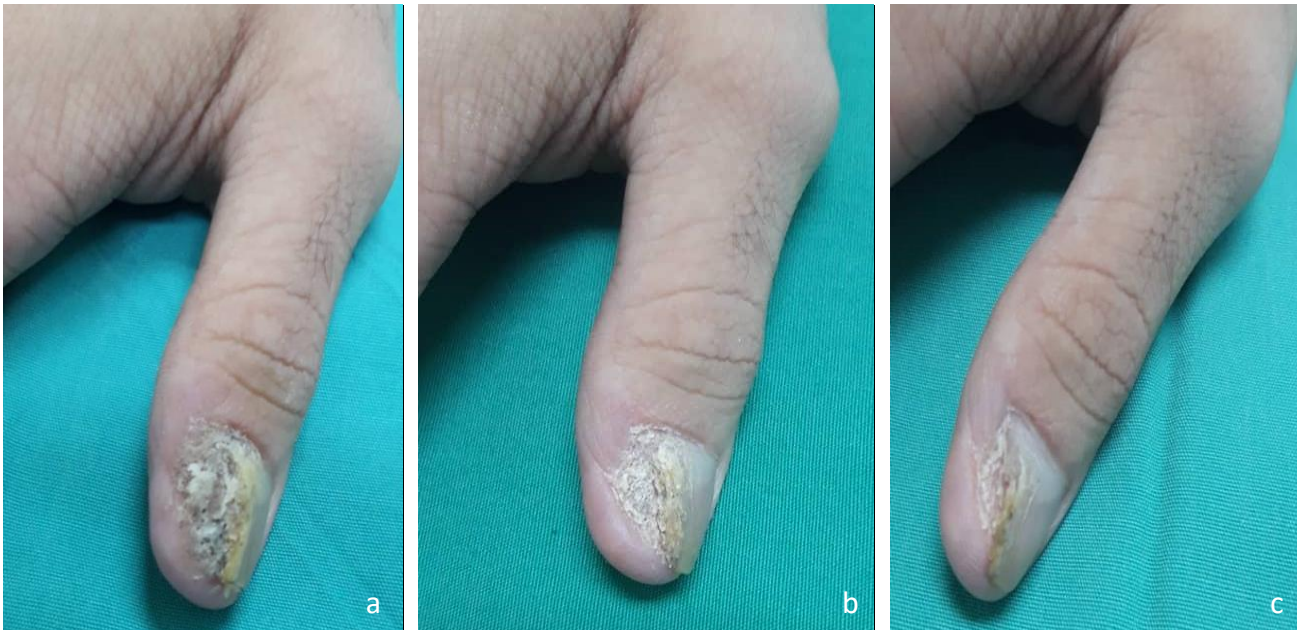
He received an intralesional injection of tuberculin PPD at a dose of 2.5 Tuberculin Unit (0.14ml). The injection was done using a 1 ml-syringe and 26-gauge needle.[5] Two weeks later, the wart's size reduced to almost 50% (8.57x5.22mm). Another tuberculin PPD of the same dose was administered. At 4-week follow up, the wart resolved entirely (***Figure 1***). He reported pain during injection, which resolved spontaneously three to four hours later. There was no erythema, blister or oedema observed at the injection site. There was also no fever, malaise, myalgia or arthralgia.

Discussion

Immunotherapy exerts its effects in treatment of wart by mounting a delayed-type of hypersensitivity reaction[4,6] which involved stimulation of Th1 cytokines.These cytokines then activates cytotoxic and natural killer cells to eradicate the HPV from the epidermis.[6]

Tuberculin is a purified protein derivative extracted from *Mycobacterium* tuberculosis cultures.[7] It is used widely for tuberculosis screening, especially in countries where the disease is endemic, such as in Malaysia. Tuberculin is used across all age groups, including infants, children and pregnant women.[7] As tuberculosis is endemic in our

Figure 1: (a) Pre-treatment; (b) Week 2 post-injection; (c) Week 4 post-injection



country, this therapy may be useful in our population as majority of patients are sensitized to it. We chose tuberculin because it is readily available in our centre.

Previous literature works have reported tuberculin's efficacy rate in treating warts, ranging from 29.4% to 93%.[8-13] A network meta-analysis reported that tuberculin and MMR were the most effective treatments for achieving complete primary and distant wart recovery compared to other immunotherapeutic agents, cryotherapy and imiquimod.[14] Abou-Taleb et al[15] compared intralesional (IL) vitamin D3 vs IL PPD in treatment of multiple warts, and significantly, higher clearance rates for all warts were observed with IL PPD compared to IL vitamin D. In the study by Wan Syazween et al[5], comparing efficacy and safety between Tuberculin PPD and cryotherapy, complete wart clearance rates were higher with immunotherapy than cryotherapy; also immunotherapy has a positive effect on distant, untreated warts.

The most common adverse events reported were local injection site reaction such as pain, erythema and oedema.[14] These side effects were often transient and resolved after a few days. Very rarely, immunotherapy may result in painful digit syndrome. La Pelusa et al and Perman et al reported distal pain, swelling, and purple hue of finger pos-immunotherapy. Both patients, however, recovered with complete resolution of the wart after the event with treatment with oral prednisolone.[17-18]

Conclusion

This case report highlights the efficacy of tuberculin immunotherapy on recalcitrant ungual wart. This treatment should be recommended for treatment of recalcitrant wart particularly in difficult to treat area such as subungal and periungal region. More studies are needed locally to treat recalcitrant warts using intralesional immunotherapy for patients who fail liquid nitrogen cryotherapy.

Conflict of Interest Declaration

The authors have no conflict of interest.

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