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Reports on Scientific Meetings

Immunotherapy for viral skin conditions and other dermatoses

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Date:	13 November, 2003
Venue:	Holiday Inn Golden Mile, Hong Kong
Speaker:	Professor Brian Berman School of Medicine, University of Miami, USA
Organiser:	The Hong Kong Society of Dermatology and Venereology

The therapeutic indications of 5% topical imiquimod (Aldara) cream include keloid, anogenital wart (AGW), common wart, molluscum contagiosum and basal cell carcinoma (BCC).

Keloid

Topical imiquimod induces local interferon. In an experiment of mice treated with topical imiquimod, interferon was elevated within 2 cm around the site of application. Interferon does not only upregulate the expression of tumour suppressor p53, but also enhances the natural apoptosis that is commonly lost in keloid, tumour or virus infected cell. Cellular apoptosis is regulated by 14 different genes. The mutant p53 gene in keloid is dysfunctional and, in part, explains the perpetual deposition of collagen.

In one study on 11 keloids that were excised and followed by daily imiquimod on the suture line for two months, none of them recurred six months after treatment. There was no evidence of systemic toxicity. The major side effects were reversible erythema and mild hyperpigmentation. Instead of excision, keloid could be shaved by surgery or flattened by carbon dioxide laser. The clinical result of topical imiquimod after these alternative techniques was also promising.

The imiquimod-induced gene modification could be demonstrated by gene array analysis. However the clinical benefit of imiquimod on keloid, as a monotherapy, had been challenged. To evaluate the clinical efficacy, the speaker and his colleagues conducted a randomised vehicle-controlled trial. At the end of the second month, clinical benefit of imiquimod was only similar to that of the vehicle. The speaker argued that the conclusion was premature because abnormal collagen had half-life of 6 to12 months.

Anogenital wart

FDA has approved topical imiquimod for treatment of anogenital wart (AGW). Due to the presence of virus envelope, human papilloma virus (HPV) is resistant to desiccation. In fact, the traditional destructive therapy works by damaging the infected epidermal cell (host) rather than killing the virus. HPV can be found at 1 cm from the visible wart. When the infected genital area is large, destructive therapy is not feasible. Immunotherapy becomes a logical treatment option.

Topical imiquimod cleared AGW with successful rate of 81%. A higher rate of success was observed among female and uncircumcised male patients.

Apart from clearing visible AGW, imiquimod facilitates the long-term memory in virus clearance. While surgery cleared the AGW for an average of five months, imiquimod prolonged the clearance time to 17 months in clinical trials. The clearance time was prolonged further to 19 months by combining imiquimod with surgery. The maximum treatment period of topical imiquimod was 16 weeks.

Common wart

Although imiquimod is not FDA-approved for treatment of common wart, a number of case reports demonstrated its efficacy and safety. The speaker showed a successfully treated case of common wart that had been recalcitrant to standard therapies including carbon dioxide laser, cryotherapy, surgery and 5-fluorouracil. Moreover, an open labelled non-controlled study proved the efficacy of imiquimod in treatment of common wart. Although some patients did have immunosuppression such as HIV infection and renal transplant, half of the subjects responded satisfactorily to imiquimod. One-third of the subjects had complete clearance. Interferon caused organ transplant rejection in previous studies. Nevertheless the safety of imiquimod in renal transplant patients was established in United States and European studies.

To optimize the benefit of imiquimod in hyperkeratotic plantar wart, either salicylic acid or retinoid can be added. Salicylic acid is used because of its keratolytic effect. The antiproliferative effect of retinoid makes the epidermal cell less hospitable to the virus. One suggested regimen was to apply salicylic acid in the morning and imiquimod at night.

Molluscum contagiosum

Molluscum contagiosum is a DNA virus that antagonises chemokine activities, decreases antigen recognition and inhibits cellular apoptosis. All these mechanisms can be reversed by imiquimod.

According to FDA, imiquimod can be used in perianal or anogenital wart down to six-year-old. Children are predisposed to molluscum contagiosum, therefore paediatric safety profile of imiquimod becomes an important issue. The safety was reassured by one study in which 12 infected children were treated with daily imiquimod for one month. The children were four to ten years of age. There had been no leucopenia, chills, myalgia or headache. One patient suffered from fever that could be accounted by concurrent upper respiratory tract infection. Although mild erythema was noted in some patients, none of them dropped out the study because of adverse effects.

Basal cell carcinoma

Basal cell carcinoma fails to express Fas receptor. Therefore it escapes from the immunologic surveillance and continues to grow. This process is reversed by imiquimod. The efficacy was demonstrated in one multi-centre double blind trial in which superficial BCC was treated by daily imiquimod for six weeks. Clinical cure rate was 98% and histologic cure rate was 82% at one year. However the result of long-term tumour clearance is pending.

Learning points:

Topical imiquimod is FDA-approved for treatment of anogenital wart. Other potential uses are for common wart, molluscum contagiosum, keloid and superficial basal cell carcinoma.