The Art of Immunosuppressive / Immune Modulation Therapy in Dermatology

reported by Dr. S. Y. Cheng

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Venue:	Sai Ying Pun JCC, Social Hygiene Headquarters
Speaker:	Dr. Libby Edwards
Organizer:	Social Hygiene Service, DH

The use of imiquimod in the treatment of genital warts had already been discussed in previous lecture on 15 April 1999. In this lecture, Dr. Libby Edwards further elaborated its use in common warts, plantar warts, molluscum contagiosum, herpes simplex infection and basal cell carcinoma by quoting various studies. The use of interferon in treatment of genital warts, basal cell carcinoma and squamous cell carcinoma was also discussed. Finally, the use of systemic retinoids, cyclosporin A and tacrolimus were briefly mentioned.

Use of imiquimod in dermatological conditions other than genital warts

In children and adults with common warts refractory to salicylic acid, the application of 5% imiquimod cream three times per week after paring, up to 12 weeks, had resulted in 67% response rate. Ninety percent of patients remained wart free after 3 months. This was in contrast with only 10% response rate of the vehicle group. Similar response rates were found when 5% imiquimod cream was applied under occlusion daily for 12 weeks on plantar wart. The application of imiquimod on either common wart or plantar wart had induced mild to moderate erythema, oedema and local pain.

The use of imiquimod cream had also been investigated on molluscum contagiosum. In one open trial, 13/16 adults and 6/12 children had complete resolution, mostly after one month of imiquimod application. However, the duration of treatment and dosing frequency were not known to the speaker. Irritation was commonly noted and more severe in children.

Experiment on mice had shown that imiquimod resulted in decreased length of recurrent outbreak and increased time to recurrence in herpes simplex infection. It might also suppress recurrences after discontinuation of medication.

A single centre, double blind, randomized and vehicle-controlled pilot study was done to evaluate the safety and efficacy of 5% imiquimod cream in treatment of nodular or superficial basal cell carcinoma. 5% imiquimod cream or vehicle was applied once/day, twice/day, once/week, twice/week or three times/week. The duration of treatment was at most 16 weeks or 2 weeks after clinical resolution. Histology was obtained at the end of study. The histological cure rate after 5% imiquimod application was 50%(once/week), 60%(twice/week) up to 100% (three times/week, once or twice/day). The corresponding cure rate for vehicle group was only 9.1%. Local irritation was the most common side effect. Severe erythema, erosion or ulceration occurred more frequently in the more frequent dosing group (once or twice/day).

Use of interferons

Interferon is a naturally occuring biological response modifier with anitviral, antitumor and antiproliferative properties through enhancement of immune system. Its use has been documented in hairy cell leukaemia, genital wart, AIDS related Kaposi's sarcoma and melanoma.

It had been shown that intralesional interferon injection (10^6 *iu*/injection) had resulted in clearance of genital wart in 36% of patients after 13 weeks, in comparison to only 17% in placebo. Most patients experienced flu-like symptoms and transient but insignificant leukopenia. Many patients had transient liver function impairment and chronic fatigue. However, interferon was not effective in prevention of recurrence of genital wart after primary therapy with cryotherapy or laser.

In one study, intralesional injection of interferon-a2, three times per week for three weeks was given to histologically proven basal cell carcinoma. Punch biopsies were performed at 12 weeks to look for remaining tumor and at one year to look for recurrence. In interferon group, the cure rate was 84%; whereas in the placebo group, the cure rate was 20%. The

advantages of interferon therapy in basal cell carcinoma are lack of scar and surgical risks at reasonable cost. The disadvantages would be multiple clinic visits and a lower cure rate than surgery or radiotherapy.

Intralesional injection of interferon-a2b, 1.5 megaunits three times per week for three weeks was also shown to produce 97% cure rate in squamous cell carcinoma. The advantages and disadvantages were similar to its use in basal cell carcinoma.

Systemic retinoids

Systemic retinoid was a vitamin A analogue compound which acts as biological modifier that enhances cell differentiation by controlling oncogene and growth factor expression. It was found to be able to shrink, prevent, or somtimes eliminate squamous cell carcinoma but less so in basal cell carcinoma.

Immunomodulator/Immunosuppressive drugs

Both cyclosporin A and tacrolimus selectively inhibit T cell response by inhibiting calcium dependant signal transmission mechanisms. Topical tacrolimus is not available commercially and is expensive. However, it has good response in atopic eczema and has been claimed to be as effective as topical corticosteroid.

In discussion after the lecture, Dr. Edwards mentioned that the response of systemic interferon in treatment of genital wart was not satisfactory. For 5% imiquimod, there was no clinical predictor for treatment failure in genital wart but the clinical response usually occurred at 2 to 4 weeks after treatment. It was suggested that late response might occur and the treatment might be continued for a longer duration even if the initial response was not satisfactory. In future, combination therapy with imiquimod plus either podophyllin or cryotherapy is possible.

Learning points:

5% imiquimod may turn out to be one of the new promising drugs in the treatment of common wart, plantar wart, molluscum contagiosum and basal cell carcinoma.