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Reports on Scientific Meetings

Shaping the management of psoriasis

Reported by PT Chan 陳寶德

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Speaker:	Dr. Kenneth Gordon Associate Professor, Division of Dermatology, Loyola University of Chicago, Illinois, USA
Organiser:	The Hong Kong Society of Dermatology and Venereology

Psoriasis affects not only the external appearance of patients but also has a significant impact on patients' psychological and social well-being. Previous studies have reported the presence of depression, frustration with treatment and interference with work in a significant percentage of psoriatic patients. Traditional treatment paradigm emphasised on the sequential use of less toxic treatment modalities, such as topical medications, to ultraviolet B and systemic treatment with retinoids, methotrexate or cyclosporin in patients with more severe diseases. However, therapy for psoriatic patients, especially those with severe diseases, is still far from optimal. Several obstacles may be present in the delivery of optimal treatment to psoriatic patients. They include embarrassment of patients that may prevent them from sharing their problems with others, indifference of doctors to patients' psychosocial problem, and fear in doctors to treat patients with full dose and long-term systemic treatment because of potential toxicities.

Psoriasis is an inflammatory skin disease. Cytokines from the inflammatory cells induce proliferation and alter the differentiation of keratinocytes, resulting in the typical psoriatic clinical phenotype. Biologic therapies are medications developed through molecular biologic techniques and are designed to target at specific points of the immune system. They have few end organ toxicities when compared with traditional systemic treatment for psoriasis and hence may be safe for long-term use. They may act through four different mechanisms, namely, elimination of pathogenic T-cells, blockage of T-cell migration or activation, immune deviation and binding to inflammatory cytokines. Alefacept, etanercept and efalizumab are approved by the FDA in the United States for treatment of psoriasis. Etanercept, in addition, is approved for the treatment of psoriatic arthropathy. Alefacept is a human fusion protein consisting of extracellular domain of lymphocyte function-associated antigen (LFA)-3 fused to the hinge sequences of IgG. It eliminates the pathogenic T-cells and blocks the costimulatory signal of LFA-3/CD2. It can result in long-term improvement, but this is only limited to those patients who respond initially to the drug. Etanercept is a recombinant human tumour necrosis factor (TNF) receptor fusion protein that reduces the effect of endogenous TNF by inhibiting its interaction with cell surface receptors. It is also an effective treatment for psoriasis but it has created concern for having the potential side

effects of tuberculosis reactivation, worsening of multiple sclerosis or congestive heart failure.

Efalizumab is a humanised monoclonal antibody that binds to CD11a which is one of the subunit of LFA-1. LFA-1, present on T-cells, binds with intercellular adhesion molecule 1 (ICAM-1) on other T-cells or endothelial cells. This interaction is important in mediating migration of T cells from the circulation and it acts as one of the co-stimulatory signal for activated T-cells. Efalizumab is administered subcutaneously on a weekly basis. Its efficacy in treating psoriasis has been demonstrated in several randomised, placebo-controlled, double-blind studies. Improvement in the efalizumab-treated patient occurs as early as week four. There is no difference in response in various subgroups defined according to site, age, sex and baseline psoriasis area and severity index. The improvement in clinical status is accompanied by a similar improvement in quality of life measures. This drug has been used in more than 1500 patients and long-term safety has been demonstrated in a subgroup of patients receiving more than 24 months of treatment. Flu-like symptoms, such as headache, myalgia, chills and fever, commonly occur in the first few doses of injection. There is no significant increase in rate of infection and development of solid tumour or lymphoma observed in clinical studies. The final proof of drug safety, however, relies on post-marketing long-term surveillance of efalizumab-treated patients. About 0.7% of efalizumab-treated patients have inflammatory flare during treatment or after discontinuation of drug. Depending on the severity of worsening, additional local or even systemic agents are used to control disease. Generalised inflammatory flare should be treated with an alternative systemic agent and may require efalizumab discontinuation.

Learning points:

The development of biologic therapies creates new alternatives in the management of psoriasis. Physicians should assess disease severity based not only on clinical status but also on its effect on patients' psychosocial well-being.