The 8th Annual Meeting
The Korean Society for Psoriasis

May 8, 2004
Grand Intercontinental Hotel Seoul, Seoul, Korea
Organized by The Korean Society for Psoriasis
Co-sponsored by
The Korean Dermatological Association
The Korean Society for Investigative Dermatology

인사말씀

대한건선학회 제8차 학술대회를 맞이하여 그 동안 성원하고 지원해 주신 회원 여러분들에게 감사의 인사를 드립니다. 우리 학회는 그 동안 매년 알차게 학술대회를 개최하면서 건선 및 관련 질환에 대한 회원들의 다양한 증례발표를 통하여 임상경험을 공유하게 되고, 기초과학분야에서 새로운 치료방법에 이르기까지 폭 넓은 지식을 깊은 연구발표를 통하여 나누어 왔습니다. 특히 근년에 이르러서는 건선의 면학학적, 분자생물학적 접근이 치료방법에 도입되어 새로운 도약이 될 수 있을 것으로 생각합니다.

금년도 건선학회는 회원 여러분의 기대에 보다 충실히 부응하기 위하여 처음으로 대상 질환의 범위를 구진인설성 질환 전체로 확대하였으며 이에 대한 연제는 오전 [자유연제 2]에서 발표될 것입니다. 또한 우리는 해외에서 저명한 두 분의 연자를 모시게 된 것을 기쁘게 생각합니다. Tokyo-Jikeikai Medical School의 Hidemi Nakagawa 교수는 최근 사용빈도가 높아지고 있는 사이클로스포린에 대한 일본 내 사용 지침을 일목요연하게 보여줄 것입니다. 또한 Baylor University Medical Center의 Alan Menter 박사는 최근 가장 주목을 받고 있는 biologics에 대한 여러분의 궁금증을 풀어줄 것입니다.

대한건선학회는 회원 상호간에 화기애애한 가족적인 분위기 속에서 의견교환을 하며 매사에 일치단결하여 피부과학 발전을 위한 견인차의 역할을 수행해 왔습니다. 이번 8차 학술대회도 회원 여러분이 그 동안 연구 경험한 것을 발표하고, 새로운 지식을 함께 나눌 수 있는 유익한 만남의 장이 되었으면 합니다. 또한 앞으로도 여러 회원들의 지속적인 후원과 지도편달을 바랍니다.

회원여러분 가정에 만복이 함께 하시고 건강하시기를 기원합니다.

2004. 5. 8

대한건선학회 회장

김 광 중

PRESIDENT'S MESSAGE

I would like to express my warmest gratitude to the members of the Korean Society for Psoriasis (KSP) and colleagues of the Korean Dermatological Association for their sincere support for the KSP and our annual meeting in May 8, 2004. Annual meetings of the KSP have provided us with great opportunities to share clinical experiences and to obtain comprehensive knowledge in the basic science and treatment of psoriasis. The remarkable progress we have seen recently from the integration of immunological and molecular biological achievement into the development of biologics will sure to make another turning point in the treatment of psoriasis in the years to come.

Our scientific programs have been prepared to meet your educational expectations. This year, for the first time, we have expanded our horizon to the realm of whole papulosquamous disorders. Your experiences and new insights in this field are welcome to the [free communications 2] during morning sessions. We are delighted to announce that we have two great international scholars for our meeting. Dr. Hidemi Nakagawa, Tokyo-Jikeikai Medical School, Japan, will provide us with the opportunity of reviewing recently-released Japanese consensus for the use of cyclosporine. Dr. Alan Menter, Baylor University Medical Center, USA, will fulfill our need for the knowledge on biologics, the hottest issue in psoriasis.

The leading role taken by the KSP in the academic achievement of dermatological society is from unanimous commitment and great friendship of our members that are hard to find in any other academic communities. I really hope the 8th annual meeting of the KSP would become a great opportunity for us to share our updated knowledge in the field of psoriasis. For this I cordially ask all of you to provide us with warm support for our society as ever. I hope the best for every single member of the KSP.

Looking forward to seeing you all in Seoul soon.

Thank you very much.

Sincerely,

Kwang-Joong Kim, M.D.
President of the KSP

INFORMATION

▶ Advance registration: not available

▶ On-site registration

Physicians: 20,000 W (including annual membership and registration)

Residents: free

▶ Official language

Except for special lectures and presentations by Japanese participants where English will be used, oral presentations for other sessions should be made in Korean language. However, presentation material should be prepared in English.

▶ Grand Inter Continental Seoul

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▶ Presentation

Choice of presentation method between beam projection and slide projection should be notified to us at the time of abstract submissions. Those who would like to use beam projection are advised to use Microsoft Power Point (version 97 or compatible). Double slide projection or overhead projection is not available for the presentation.

- Suggested duration of presentation

Free communications:	7 minute presentation + 3 minute discussion
Case reports:	5 minute presentation + 2 minute discussion
Educational lectures:	13 minute presentation + 2 minute discussion
Special lectures:	45 minute presentation + 10 minute discussion

진 행 순 서

09:30 - 09:55	Registration
09:55 - 10:00	Opening remark
10:00 - 11:00	자유연제 1 (Free communications 1)
11:00 - 12:00	자유연제 2 (Free communications 2)
12:00 - 13:30	Lunch / KSP council
13:30 - 14:30	특별강연 1 (Special lecture 1)
14:30 - 15:15	증례발표 (Case presentations)
15:15 - 15:30	Coffee break
15:30 - 16:30	특별강연 2 (Special lecture 2)
16:30 - 17:30	교육강연 (Educational lectures)
17:30	Concluding remark
18:00	Cocktail party

학 술 대 회

자유연제 1 (10:00～11:00) 좌장 : **김광중, 황규왕**

1. Insulin Like Growth Factor-II-Induced Interleukin-8 Production in Human Keratinocytes through Extracellular Signal-Regulated Kinase 1/2 Pathway and NF-κB Pathway

KIM Hye Jung,
BYUN Sung June, KIM Tae-Yoon
Department of Dermatology, The Catholic University of Korea, Seoul, Korea

2. Potentiation of UVB-Induced Apoptosis by Novel Phytosphingosine Derivative, Tetraacetyl Phytosphingosine in HaCaT Cell and Mouse Skin via Caspase Activation

KIM Hye Jung, KIM Su Jin, KIM Tae-Yoon
Department of Dermato-Immunology, The Catholic University of Korea, Seoul, Korea

3. Differential Roles of Mitogen-Activated Protein Kinases in Insulin Like Growth Factor-II-Mediated Cyclooxygenase-2 Gene Expression in Human Keratinocytes

KIM Hye Jung, KIM Tae-Yoon
Department of Dermato-Immunology, The Catholic University of Korea, Seoul, Korea

4. A Study on the Relationship of the Severity of Psoriasis, Serum Soluble E-Selectin, MCP-1 and RANTES

KANG Ik-Joon, PARK Jung-Hun, KIM Nack-In
Department of Dermatology, College of Medicine, Kyung Hee University, Seoul, Korea

5. In Situ Expression of CD40 and CD40 Ligand in Psoriasis

OHTA Yukinori[1], MABUCHI Tomotaka[1], UMEZAWA Yoshinori[1], MATSUYAMA Takashi[1], OZAWA Akira[1], HAMADA Yuko[2]
[1]Department of Dermatology, Tokai University School of Medicine, [2]Department of Dermatology, Kitasato University School of Medicine, Japan

6. Evaluation for Cyclosporine Therapy Based on the Therapeutic Guidelines for the Treatment of 6 Patients with Generalized Pustular Psoriasis (GPP)

UMEZAWA Yoshinori[1], AKASAKA Emiko[1], MABUCHI Tomotaka[1], OHTA Yukinori[1], MATSUYAMA Takashi[1], OZAWA Akira[1], ASANUMA Hiroyuki[2]
[1]Department of Dermatology, Tokai University School of Medicine, [2]Asanuma Dermatologic Clinic, Chitose, Japan

자유연제 2 (11:00~12:00)

좌장 : 이규석, 최지호

1. A Study of Dermatological and Osteoarticular Features of SAPHO Syndrome

OH Jeong-Joon[1], LEE Joo-Heung[1], YANG Jun-Mo[1], LEE Eil-Soo[1], SUNG Duck-Hyun[2]
Departments of [1]Dermatology, [2]Rehabilitation, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

2. The Effect of Combination Therapy Using Narrow-band Ultraviolet B Phototherapy in Psoriatic Patients

JO Seong-Jin, YOUN Jai-Il
Department of Dermatology, Seoul National University College of Medicine, Seoul, Korea

3. The Effect of Alcohol and Smoking on Psoriasis

Lee Hae Woong, Kim Kyoung Jin, Choi Jee Ho
Department of Dermatology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

4. Role of Stess in the Pathogenesis of Psoriasis (Focus on Neuropeptides)

JANG Yong-Hyun, LEE Eun-So
Department of Dermatology, Ajou University School of Medicine, Suwon, Korea

5. A Case of Linear Lichen Striatus Combined with Linear Epidermal Nevus

KIM Won-Ho, KIM Sung-Sik, KIM Chul-Woo, KIM Kwang-Ho, KIM Kwang-Joong
Department of Dermatology, College of Medicine, Hallym University, Anyang, Korea

6. Generalized Lichen Nitidus: Treatment of Two Cases with Narrowband UVB

PARK Jae Hong, OH Jeong Joon, LEE Joo-Heung, LEE Eil Soo
Department of Dermatology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

특별강연 1 (13:30～14:30)

좌장 : 윤 재 일

Japanese Consensus Statement for Cyclosporin MEPC in Psoriasis Clinical Practice

NAKAGAWA Hidemi
Department of Dermatology, Tokyo-Jikeikai Medical School, Tokyo, Japan

증례보고 (14:30～15:15)

좌장 : 김태윤, 김기호

1. A Case of Psoriatic Arthritis Treated with Cyclosporin

KWON Oh-Eon, KIM Hong-Seok, SIM Seung-Joo, SONG Ki-Hoon, KIM Ki-Ho
Department of Dermatology, Dong-A University College of Medicine, Busan, Korea

2. Generalized Pustular and Erythrodermic Psoriasis Associated with Oral Terbinafine Therapy

KIM Byung-Soo, JANG Ho-Sun, JANG Bong-Suk, JO Ju-Hyun, KIM Moon-Bum, OH Chang-Keun, KWON Kyung-Sool
Department of Dermatology, Pusan National University College of Medicine, Busan, Korea

3. Koebner Phenomenon Caused by Allergic Contact Dermatitis to Zinc Pyrithione in Psoriasis

JO Ju-Hyun, KO Hyun-Chang, JANG Bong-Suk, KIM Moon-Bum, OH Chang-Keun, JANG Ho-Sun, KWON Kyung-Sool
Department of Dermatology, College of Medicine, Pusan National University, Busan, Korea

4. Psoriasis Associated with Crohn's Disease

JO Seong-Jin, YOUN Jai-Il
Department of Dermatology, Seoul National University College of Medicine, Seoul, Korea

5. A Case of Uremic Psoriasis Improved after Initiation of Hemodialysis

JO Seong-Jin, YOUN Jai-Il
Department of Dermatology, Seoul National University College of Medicine, Seoul, Korea

6. A Case of Generalized Pustular Psoriasis Associated with Systemic Lupus Erythematosus

KI Ho-Gyun, YUN Sook Jung, LEE Jee-Bum, KIM Seong-Jin, WON Young Ho, LEE Seung-Chul
Department of Dermatology, Chonnam National University Medical School, Kwangju, Korea

특별강연 2 (15:30~16:30)

좌장 : 김 낙 인

Targeted Management of Psoriasis: New Biologicals Provide Hope for the Patients

Alan Menter, M.D.
Division of Dermatology, Baylor University Medical Center, Dallas, U.S.A.

교육강연 (16:30~17:30)

좌장 : 김상태, 원영호

1. Alefacept

CHOI Jee-Ho
Department of Dermatology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

2. Efalizumab

KIM Tae-Yoon
Kangnam St. Mary's Hospital, Department of Dermatology, Catholic University, Seoul, Korea

3. Infliximab

LEW Wook
Department of Dermatology, Yonsei University College of Medicine, Seoul, Korea

4. Etanercept

LEE Joo-Heung
Department of Dermatology, Sungkyunkwan University School of Medicine, Samsung Medical Center, Seoul, Korea

특별강연

연자 약력 및 초록

특별강연 1

특강연자 약력

Full Name : **Hidemi Nakagawa**, M.D., PhD

Affiliation : Department of Dermatology, Tokyo-Jikeikai Medical School, Tokyo, Japan

Birth Date & Place: May 26/1953, Miyazaki-city, Miyazaki-prefecture

Present Address: 5-32-13 Sendagi, Bunkyo-ku, Tokyo, Japan 113-0022

Education and Professional Appointments

1977: M.D.
Assistant (Junior Staff Member), Department of Dermatology, Faculty of Medicine, University of Tokyo

1980: Research Fellow, Department of Dermatology, Mass. General Hospital, Harvard Medical School

1982: Assistant (Senior Staff Member), Department of Dermatology, Faculty of Medicine, University of Tokyo

1983: Ph.D. Faculty of Medicine, University of Tokyo

1984: Instructor, Department of Dermatology, Faculty of Medicine, University of Tokyo

1988: Associate Professor, Department of Dermatology, Faculty of Medicine, University of Tokyo

1997: Professor and Chairman, Department of Dermatology, Jichi Medical School

2004: Professor and Chairman, Department of Dermatology, Tokyo-Jikeikai Medical School (from May/1)

Membership of Academic Societies

Society for Investigative Dermatology
International Federation of Pigment Cell Societies
The European Academy of Dermatology and Venereology
Japanese Dermatological Association
Japanese Society for Investigative Dermatology
Japanese Society for Clinical Dermatology
Japanese Society for Psoriasis Research
Japanese Society for Immunology
Japanese Society for Allergology
Japanese Society for Biochemistry
Japanese Society for Pigment Cell
Japanese Society for Skin Cancer
Japanese Society for Cutaneous Allergology
Japanese Cosmetic Science Society

Areas of Interests

Psoriasis: Genetics and Therapy
Atopic Dermatitis: Genetics, Pathogenesis and Therapy
Pigment Cell Biology and Pigmentary Disorders
Electron Microscopy

Award

Seiji Memorial Lecture Awardee (1983, Giessen, Germany: with Drs. Thomas B Fitzpatrick and Yoshiaki Hori)
Freddie Awards (2000, New York)

Bibliography

Original Papers in Japanese: 203
Review Articles and Textbooks in Japanese: 216
Original Papers in English: 113
Articles in English Books: 19

Japanese Consensus Statement for Cyclosporin MEPC in Psoriasis Clinical Practice

NAKAGAWA Hidemi

Department of Dermatology, Tokyo-Jikeikai Medical School, Tokyo, Japan

The efficacy of cyclosporin microemulsion preconcentarte (cyclosporin MEPC) in the treatment of severe psoriasis is well-established, as demonstrated by numerous clinical trials. However, many dermatologists still continue to have some concerns regarding its use mainly related to preconceptions about its side effects including renal impairment and hypertension, and the lack of guide-line for the appropriate and effective use of cyclosporin MEPC in the treatment of severe psoriasis. A Japanese consensus conference was convened last December following an international conference held in Paris last September in order to amend [the Japanese Guideline for Psoriasis Therapy with Cyclosporin MEPC]. Expert reviewers presented and deliberated Japanese as well as international evidence on cyclosporin MEPC related to clinical efficacy, patient selection and profiles of adverse drug reactions and reached a consensus as to the proposed recommendations of the use of cyclosporin MEPC. The main recommendations for the use of cyclosporin MEPC in the management of psoriasis are as follows: (1) patient selection should take into account clinical extent of disease (body surface area affected more than 30% and/or PASI score more than 12) and failure of previous treatments, as well as the degree of patient's QOL (quality of life) impairment; (2) cyclosporin MEPCshould be given in the dose range of 2.5-5.0mg/kg/day; (3) intermittent short course therapy of cyclosporin MEPC (average of 3 months duration) is preferable (even at the low dose of 2.5 mg/kg/day for 3 months, 70% improvement of PASI score has been achieved); (4) treatment regimens should be tailored according to the needs of each patient; (5) each patient's renal function as measured by serum creatinine level should be thoroughly assessed before and during treatment; (6) each patient's blood pressure should be carefully monitored before and during treatment and whenever necessary anti-hypertensive drugs should be initiated (ARB and ACE inhibitors are preferable); (7) extended periods of continuous cyclosporin MEPC use (more than 2 years) should be avoided whenever possible, as histological changes in kidney have been reported after 3 years of treatment; (8) when long-term continuous cyclosporin MEPC therapy is necessary in a subgroup of patients, yearly consultation by nephrologist is useful to accurately monitor renal

function; (9) adherence to treatment guide-line substantially reduces the risk of adverse events (current guide-line stipulates reduction of cyclosporin MEPC dose if serum creatinine increases by 30% above the baseline value even when this increase is within normal range); (10) the use of cyclosporin MEPC should be avoided immediately prior to and especially following PUVA therapy since all patients who developed squamous cell carcinoma had received PUVA before the initiation of cyclosporin. Cyclosporin MEPC therapy in the treatment of psoriasis has proven to provide rapid and sustained disease remission, and significantly improve patients' QOL. The side effect profile is well known and predictable, and adherence to treatment guide-line extensively reduces the risk of adverse events. The use of intermittent short course (around 3 months) cyclosporin MEPC therapy has been established as the optimum treatment regimen for most patients, although long-term continuous therapy remains necessary in a small subgroup of patients with refractory disease.

특별강연 2

특강연자 약력

Name : **Alan Menter**, M.D., P.A.

Dr. Alan Menter was born in England and received his dermatology residency training in South Africa. He subsequently undertook further postgraduate training and research at Guy's Hospital and St. John's Hospital for Diseases of the Skin in London, England. After moving to the United States, he completed a fellowship in Dermatology at Southwestern Medical School in Dallas. He was Board Certified in dermatology in 1977.

Dr. Menter has written over 118 articles and book chapters in medical publications and lectures extensively, nationally and internationally.

In addition to his medical practice, he is:

- Chairman of the Division of Dermatology at Baylor University Medical Center Dallas
- Clinical Professor of Dermatology at Southwestern Medical School Dallas
- Medical Director of the Baylor Psoriasis Center (1979-99)
- Board Member of the National Psoriasis Foundation
- Member of the Board of Directors American Academy of Dermatology (1995-97)
- President of the Texas Dermatology Society (1995-96)
- Chairman of the Task Force on guidelines for Standards of Care for Psoriasis (1990-93)
- Board Member and Texas State Chairman, Dermatology Foundation
- Included in "Best Doctors in America" (1993-2001)

Dr. Menter, his wife Pam, and their three children moved to Dallas in 1975 and became U.S. citizens. An international rugby player, Dr. Menter brought to Texas not only his dermatologic skills, but his love of all sports and politics.

He holds membership in:

- American Academy of Dermatology
- American Dermatological Association
- American Medical Association
- American Society for Laser Medicine & Surgery
- American Society of Dermatologic Surgery
- British Association of Dermatology
- Dallas County Medical Society
- Dallas Dermatological Society
- Society for Investigative Dermatology
- Texas Dermatological Society
- Texas Medical Association

Some of the recent publications written by Dr. Alan Menter:

1. Cather JC, Menter A. Hair loss and plaquelike skin lesions. BUMC Proceedings. 2001;14:101-103.
2. Cather J and Menter A. Novel Therapies for Psoriasis. Am J of Clin Dermatol 2002; 3(3): 159-173
3. Abdelmakek N, Gerber L. Terry, Menter A. CardiacCutaneous Syndromes. J Am Acad of Dermatol. J Am Acad dermatol 2002;46:161-83.
4. Cather JC, Menter A. Targretin for psoriasis. J Am Acad of Dermatol (in press)
5. Cather JC, Menter A. Methotrexate and Cyclosporine Combination Therapy forPsoriasis. J Am Acad of Dermatol (submitted)
6. Menter A. PUVA Phototherapy: Assessing and Optimizing the Risk/Benefit Ratio. Skin & Allergy News (supplement) 2001; 3-14
7. Menter A. The Impact of Psoriasis on Quality of Life. Arch Dermatol. March, 2001; 137:280-284
8. Cather JC, Menter A. Diffuse eruption of pigmented papules. BUMC Proceedings. 2001; 14:185-186.
9. Cather JC, Abramovits WA, Menter A. Cyclosporine and Tacrolimus in Dermatology. In Dermatology Clinics. Norman Levine (ed): W.B. Saunders Company, 2001,19:119-137.
10. Cather JC, Menter A. Pruritic eruption on the chest, arms, and buttocks. BUMC

Proceedings. 2001;14:301-302.
11. Menter A. Pharmacokinetics and Safety of Tazarotene. J Am Acad Dermatol 2000; 43:S31-4.
12. Bowcock A, Shannon,W, Du F, Duncan J, Cao k, Aftergut K, Cather JC, Fernades-Vina M, Menter A. Insights Into Psotiasis and other Inflammatory Diseases from Large-scale gene expression studies. Human Molecular Genetics, 2001, Vol.10, No 17 1793-1805, Oxford University Press
13. Cather, J.C., Menter A. Purplish, pruritic papules on the limbs. BUMC Proceedings. 2001;14:449-451
14. Lebwohl M, Drake L, Menter A. Koo J, Gottlieb A, Zanolli M., Young M., McClelland P. Consensus conference: Acitretin in combination with UVB or PUVA in the treatment of psoriasis. J Am Acad Dermatol 2001;45:544-53.
15. Cather JC, Menter A. Vesicular eruption including the mouth. BUMC 2002; 93-94.
16. Menter MA, Guest Editorial, Tazarotene in Women, Skin & Allergy News, January 2002.
17. Cather JC, Menter MA, Cather J Christian. Meandering linear pruritic lesion. BUMC Proceedings 2002;15:219-220

Targeted Management of Psoriasis: New Biologicals Provide Hope for the Patients

Alan Menter, M.D.

Division of Dermatology, Baylor University Medical Center, Dallas, U.S.A.

Psoriasis is a disfiguring, chronic, immune-mediated skin condition that requires lifelong treatment. The most common form of the disease is plaque-type psoriasis, which accounts for about 80% of all cases. Plaque psoriasis is a highly visible disease, characterized by well-demarcated, thick, red, pruritic, painful lesions covered with silvery scales. Approximately 25% to 30% of patients with psoriasis have moderate to severe disease.

Psoriasis has an impact on health-related quality of life comparable to other major medical diseases such as cancer, arthritis, hypertension, heart disease, diabetes, and depression. Some patients feel stigmatized because of their psoriasis, and many experience additional psychological or psychiatric problems such as social anxiety or depression.

While there are multiple agents approved for the treatment of psoriasis, none of them is curative and their long-term administration is limited by treatment-emergent toxicities.

Many patients report dissatisfaction with currently available therapies because they are ineffective for their psoriasis, are associated with side effects, or they impact negatively on quality of life. A new class of biological agents has been developed that targets the pathologies underlying psoriasis, and based on favorable efficacy and safety results in clinical trials some of these are now approved by the United States Food and Drug Administration for clinical use in the US and by Switzerland. Biological agents offer new hope for patients with psoriasis that their chronic condition can be effectively and safely controlled.

Systemic Therapies

emic therapies makes it difficult for physicians and patients to assess the ability of these therapies to improve quality of life.

Biologic Therapies: Achieving Patient Satisfaction

Biologic therapies specifically target key pathogenic events in the psoriatic cascade, in particular inhibiting the activation and/or trafficking of T cells and proinflammatory cytokines. To date, two biologic therapies that modulate T-cell function, efalizumab and alefacept, have

been approved. Several tumor necrosis factor-α (TNF-α) antagonists, including etanercept, infliximab, adalimumab, and onercept, are also in various stages of clinical development for treatment of psoriasis worldwide. The degree of satisfaction experienced by patients receiving the biologic therapies for psoriasis will be related, at least in part, to their efficacy, safety, and convenience. The progress of the agents farthest along in clinical development, efalizumab, alefacept, infliximab, and etanercept, has been thoroughly reviewed recently.

자유연제1

Insulin Like Growth Factor-II-Induced Interleukin-8 Production in Human Keratinocytes through Extracellular Signal-Regulated Kinase 1/2 Pathway and NF-κB Pathway

KIM Hye Jung, BYUN Sung June, KIM Tae-Yoon

Department of Dermatology, The Catholic University of Korea, Seoul, Korea

Psoriasis is primarily a lymphocyte driven disease and angiogenesis-dependent disease. Interleukin-8 (IL-8) is known to proangiogenic factor and detected in psoriatic lesion. It has been reported that insulin like frowth factor-II (IGF-II) is overexpressed in psoriasis and is believed to plays a role in the pathogenesis of psoriasis by regulating the expression of angiogenic factor such as IL-8. However, the specific molecular function of IGF-II in promoting angiogenesis remains to be investigated. In order to study the relationship between IGF-II and IL-8 that are upregulated in psoriasis, we monitored IL-8 expression in IGF-II-treated human keratinocytes and explored the signaling pathways of IL-8 expression by IGF-II. IGF-II increased the IL-8 mRNA and protein levels in human keratinocytes. The up-regulation of IL-8 expression by IGF-II was reduced by pretreatment with inhibitors of tyrosine kinase, Src, PI3-kinase and ERK, but not by p38. Furthermore, IGF-II remarkably increased the DNA binding activities of NF-κB and AP-1, and the IL-8 promoter activity. However, cotransfection with IκB mutant blocked the IGF-II-induced IL-8 promoter activity. In addition, cotransfection with dominant negative MEK1 mutant, but not with dominant negative p38 mutant, blocked the IGF-II-induced IL-8 promoter activity. These results suggest that IGF-II is involved in the pathogenesis of psoriasis by inducing IL-8 gene expression through the tyrosine kinase-Src-ERK1/2-AP-1 pathway, and the PI3-kinase and NF-κB pathway.

Keywords: IGF-II; IL-8; ERK; p38; NF-κB; AP-1; psoriasis

Potentiation of UVB-Induced Apoptosis by Novel Phytosphingosine Derivative, Tetraacetyl Phytosphingosine in HaCaT Cell and Mouse Skin via Caspase Activation

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Inappropriate apoptosis is a possible cause of epidermal hyperproliferation in skin disease such as psoriasis. UVB irradiation has been successfully used to treat this kind of skin disorders. We previously demonstrated that the novel phytosphingosine derivatives, tetraacetyl phytosphingosine (TAPS) induced apoptosis in HaCaT. In the present study, we investigated the effect of UVB irradiation and/or TAPS, on the induction of apoptosis in HaCaT cells. 10 mJ/cm^2 of UVB irradiation or 10 μM of TAPS alone exhibited weak cytotoxicity but co-treatment of 10 mJ/cm^2 of UVB and 10 μM of TAPS synergistically enhanced the cytotoxicity and apoptosis in HaCaT measured by MTT assay, TUNEL assay and FACS analysis. The cells co-treated with UVB and TAPS showed much higher levels of cleaved caspase-3, -8, -9 and Bax than with UVB or TAPS alone, whereas Bcl-2 level was decreased by co-administration of UVB and TAPS. In hairless mice, co-treatment of UVB and TAPS synergistically increased apoptosis, as shown in the HaCaT co-treated with UVB and TAPS. Furthermore, UVB irradiation caused an increase of apoptotic cells in the epidermis and the TAPS-treated mice showed an increase of apoptotic cells in the dermis as well as in the epidermis. These results suggest that the TAPS co-treatment synergistically increases the level of UVB-induced apoptosis via caspase activation by regulating the level of pro-apoptotic Bax and anti-apoptotic Bcl-2.

Key words: UVB / TAPS / apoptosis / mice / caspase / Bax / Bcl-2

Differential Roles of Mitogen-Activated Protein Kinases in Insulin Like Growth Factor-II-Mediated Cyclooxygenase-2 Gene Expression in Human Keratinocytes

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Psoriasis is a chronic disease characterized by abnormal epidermal proliferation and inflammation. IGF-II is increased in psoriatic lesions, especially in the serum or blister fluid of psoriasis patients. In order to investigate the relationship between IGF-II and the inflammatory response, we monitored inflammatory factor COX-2 expression in the IGF-II-treated human keratinocytes and explored the IGF-II signaling pathways with respect to the expression of COX-2. IGF-II induced COX-2 mRNA and COX-2 protein levels in the normal keratinocytes and HaCaT. The up-regulation of COX-2 expression by IGF-II was reduced by pretreatment with inhibitors of tyrosine kinase, Src and PI3-kinase. The inhibition of ERK and JNK1 also reduced the increased expression of COX-2 genes by IGF-II, but the inhibition of p38 did not. To further examine the roles of these MAPKs in IGF-II-induced COX-2 expression, we performed COX-2 promoter analysis using dominant negative plasmids of MEK1, p38 and JNK1. Although IGF-II increased COX-2 promoter activity approximately 2.5-fold, this increase was blocked by cotransfection with dominant negative plasmids of MEK1 or JNK1 mutant. However, dominant negative p38 mutant did not block the IGF-II-induced COX-2 promoter activity. In addition, inhibition of ERK or JNK1 reduced the increases of IGF-II-induced PGE2 synthesis or cell proliferation. These results suggest that IGF-II induces COX-2 expression through the tyrosine kinase-Src-ERK and tyrosine kinase-PI3-kinase pathways, but not via the p38 MAPK pathway, and that the basal JNK activity is required for the upregulation of COX-2 by IGF-II in HaCaT, as well.

Keywords: IGF-II/COX-2/ERK/p38/JNK

A Study on the Relationship of the Severity of Psoriasis, Serum Soluble E-Selectin, MCP-1 and RANTES

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Psoriasis is a chronic relapsing disease characterized by epidermal hyperproliferation, and epidermal and dermal inflammatory cell infiltrations. The etiology of this disease is still unclear. Recently, there has been growing interest in the probable role of a T cell mediated immune response in the pathogenesis of psoriasis. These T cell infiltrations in connection with various cytokines, growth factors, adhesion molecules and chemokines are well known in the early stages of psoriasis. Increment of E-selectin, as a adhesion molecule, and chemokines(eg. MCP-1, RANTES) are already being investigated in psoriasis. But there are few reports about increment of these molecules in concern with the severity of psoriasis.

In this study, We investigated a possible correlation between disease activity in psoriasis and serum soluble E-selectin, MCP-1 and RANTES, respectively for the evaluation of serum soluble E-selectin, MCP-1 and RANTES as severity indices or disease markers.

Fifteen patients with psoriasis and fifteen normal controls were included in this study. The patients were evaluated by the symptoms and signs according to PASI scores. We measured soluble E-selectin, MCP-1 and RANTES levels in the blood samples drawn from the patients and normal controls.

Serum soluble E-selectin levels, serum MCP-1 levels and serum RANTES levels were significantly increased in psoriatic patients compared with normal controls. And although, a positive correlation was observed between serum soluble E-selectin levels, serum RANTES levels and PASI scores, there was no significant correlation between serum MCP-1 levels and PASI scores.

These results suggested that serum soluble E-selectin and serum RANTES levels could be used as a marker of the disease activity in psoriatic patients.

In Situ Expression of CD40 and CD40 Ligand in Psoriasis

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CD40-CD40 ligand (CD40L) interaction provides a signal that contributes to the initiation of cellular immune responses. However, little information on the *in vivo* expression of CD40 and CD40L in cutaneous inflammation has been reported. Objective: To investigate the potential role of CD40-mediated signals in the pathogenesis of psoriasis.

In situ CD40 and CD40L expression was examined immunohistochemically in different stages of psoriatic lesions; fully developed and initial pinpoint.

In normal skin, faintly positive immunoreactivity for CD40 was seen in the basal keratinocytes and dermal endothelial cells. These showed almost the same intensity to that seen in the psoriatic lesional skin. In the dermal infiltrates of psoriatic lesions, CD40 was intensely expressed and some of these positive cells appeared to be dendritic in shape. Whereas CD40 expression was observed almost in all specimens of psoriatic lesion, the expression of CD40L was predominantly detected in the initial pinpoint lesions of psoriasis. These seemed to be distributed closely with CD40 positive cells.

These results suggested that CD40L-triggered signals could be involved in the early stage of psoriatic lesion formation.

Evaluation for Cyclosporine Therapy Based on the Therapeutic Guidelines for the Treatment of 6 Patients with Generalized Pustular Psoriasis (GPP)

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Because generalized pustular psoriasis (GPP) is a rare disease, it is difficult to conduct a comparative study among the therapeutic modalities at a single medical institution. The chief of The Ministry of Health, Labor and Welfare asked us to make a guidelines regarding GPP treatment in 2000. Therapeutic Guidelines for the Treatment of GPP were published at 2003 (Umezawa Y. et al. Arch Dermatol Res 295: S43-S54, 2003). The unique feature of these guidelines is, at first the severity of the patients condition is classified by the skin symptoms and laboratory data, and then medication dosage is determined by the classification. At this time, we are treating 6 patients with GPP based on these guidelines. Six patients with GPP (3 male and 3 female) are being treated. The average age of them is 40.3 years old. According to this method of classification in severity, one case was classified as a mild case, while 5 cases were classified as moderate cases. We administered cyclosporine 3.0 mg/kg/day for the mild case, and 3.0-4.0 mg/kg/day for the moderate cases. Using this treatment, five out of the six patients have shown improvement.

자유연제 2

A Study of Dermatological and Osteoarticular Features of SAPHO Syndrome

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The term SAPHO syndrome has been coined to describe symptom complex that present with sterile inflammatory bone lesions together with various skin lesions. Although we have increasing report of SAPHO syndrome, we still do not know the exact pathogenesis. Bony abnormalities in SAPHO syndrome might be arguably related with psoriatic arthropathy but the confusion might come from the heterogeneity of this syndrome. Therefore, elaboration of the diagnostic criteria and nosologic status of SAPHO syndrome based on clinical studies is very important. We performed this study to investigate clinical features of SAPHO syndrome in Korean patients.

Among those who visited Samsung Medical Center between January 2000 and December 2001, nine patients were diagnosed as SAPHO syndrome. All of nine patients were analyzed for clinical, laboratory and radiologic features.

Male to female ratio of patients was 1:8. Median age at onset of SAPHO syndrome, when the skin or osteoarticular symptoms first manifested, was 48.2 years. All nine patients complained about the anterior chest wall pain that again substantiated importance of this manifestation in SAPHO syndrome. Of six patients who revealed skin lesions, palmoplantar pustulosis was observed in four patients, generalized pustular psoriasis in one patient, and psoriasis vulgaris in one patient. None was associated with severe acnes nor culture study of bony lesions revealed any association with P. acnes. Of five patients who could remember the onsets of skin and bone symptoms, four had skin lesions that had preceded bone lesions. This suggests that we should follow up our patients with PPP with high index of suspicion of developing SAPHO syndrome. Radiologic and radioisotope studies showed abnormal findings such as increased uptake of axial skeletons including chest wall, with less involvement of extremities. Considering milder clinical course of SAPHO syndrome than more destructive psoriatic arthropathy, it is important to make a proper differential diagnosis to avoid unnecessary investigations and treatments.

The Effect of Combination Therapy Using Narrow-band Ultraviolet B Phototherapy in Psoriatic Patients

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The successful use of narrow-band ultraviolet B (NBUVB) phototherapy for the management of psoriasis has prompted the examination of various combination treatments with NBUVB.

Of the 87 psoriasis patients, 69 patients (Group I) were treated with the calcipotriol-NBUVB and other 9 patients (Group II) with the acitretin-NBUVB. The other 9 patients (Group III) were treated with combination of calcipotriol ointment, acitretin and NBUVB phototherapy. Phototherapy was done once daily three times a week and the dose was gradually increased. Calcipotriol ointment was applied twice a day and 10~30mg/day of acitretin was medicated according to the severity of psoriasis.

The PASI score was used to evaluate the effects of each treatment method and the patients were classified to clearing, improvement, and failure. On assessing the therapeutic results, Group I showed 53.6% of clearing, 31.9% of improvement and 14.5% of failure and group II showed 22.2% of clearing, 66.7% of improvement and 11.1% of failure. As regards group III, 77.8% of clearing and 22.2% of improvement was shown.

Our results demonstrated that using either calcipotriol ointment or acitretin with NBUVB phototherapy is effective therapeutic method for psoriatic patients.

The Effect of Alcohol and Smoking on Psoriasis

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The interaction between genetic and environmental factors seems to play a role in the causes and exacerbation of psoriasis. Recently, several evidences have been reported that smoking and alcohol drinking have a detrimental effect on psoriasis. This study aimed to explore smoking and alcohol drinking as risk factors or exacerbation factors on psoriasis in Korean psoriatic patients. Data collected from 131 psoriatic patients and 130 control subjects were analyzed to determine whether there was any association between smoking/alcohol drinking and psoriasis. The proportion of psoriasis patients using tobacco and alcohol was much higher than that of the control group ($p<0.05$). Smoking was more strongly associated with psoriasis among women and alcohol consumption among men. Drinkers tended to have more severe psoriatic lesions in PASI score analysis ($p<0.05$). Smokers also tended to have high PASI score than nonsmoker, but there was no statistical difference. The linear correlation was observed between PASI score and each parameters, such as frequency and amount of alcohol consumption. Furthermore, there was dose-dependent correlation between quantity of smoking and severity of psoriasis.

Alcohol drinking and smoking seem to be the risk factors and exacerbating factors on psoriasis in dose-dependent manner. The possibility that simple modification lifestyle may reduce both the prevalence and severity of psoriasis.

Role of Stess in the Pathogenesis of Psoriasis (Focus on Neuropeptides)

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Psoriasis is a common, chronic, recurrent, inflammatory disease of the skin characterized by round, circumscribed, erythematous plaques, covered by silvery scale. Although its etiology is not entirely clear, much clinical evidence suggests components of the nervous system including psychological and neurogenic factors can influence the course of psoriasis. The disease has been reported to be initiated and/or exacerbated by emotional or psychological stress. However, the nature of the association between stress and psoriasis remains unclear, in part due to the lack of substantial evidence regarding the participation of cutaneous neurogenic factors in the pathogenesis of psoriasis. To examine the possible participation of neurogenic factors in the pathogenesis of psoriasis, we used immunohistochemistry to compare the expression of substance P (SP), nerve growth factor (NGF) and neuropeptide degrading enzyme, neutral endopeptidase (NEP) in the lesional skin of psoriasis patients (n=10) and compared them to skin of normal control (n=10). When compared with normal skin, skin of psoriasis patients showed the following characteristic features: (i) an increase in SP-containing nerve fibers in the entire epidermis and perivascular areas of papillary dermis; (ii) a strong immunoreactivity for nerve growth factor (NGF) throughout the epidermis and papillary dermis; (iii) increased expression of neutral endopeptidase in the papillary dermis. The concentrations of SP and calcitonin gene related peptide (CGRP) in psoriasis patients (n=8) were measured by enzyme-linked immuno-sorbent assay and compared to normal controls (n=8). The difference in the concentration of SP in the psoriasis group compared to control group was not significant (P=0.13). However, the control group contained significantly more CGRP than the psoriasis group (P=0.001). Taken together, the hyperactivity of SP, NGF and NEP accompanied with hyposecretion of CGRP may play important roles in the pathogenesis of keratinocyte proliferation in psoriasis patients.

A Case of Linear Lichen Striatus Combined with Linear Epidermal Nevus

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Lichen striatus presents as a sudden eruption of discrete pink, red, or skin colored 1 to 3 mm flat-topped papules in a configuration commonly following Blaschko's line. The etiology is unknown but reports of its occurrence in siblings, atopic individuals, and in the spring, and summer support genetic, infectious, and environmental factors. Epidermal nevus are characterized by closely set, skin colored, brown or gray brown verrucous papules, which may coalesce to form well-demarcated papillomatous plaques. A linear configuration of epidermal nevus is common, especially for lesions on a limb. Such lesions may appear to follow Blaschko's line. In our case, 8 year-old man had linear lichen striatus and linear epidermal nevus, respectively on the right leg & ankle along the same Blaschko's line. Because Blaschko's line is interpreted as the migratory pathway of the clone of skin cell in embryology, His skin lesions might be developed at the same time by any common cause during embryogenesis. It is a very rare and interesting case and so we report a case of linear lichen planus combined with linear epidermal nevus.

Generalized Lichen Nitidus: Treatment of Two Cases with Narrowband UVB

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Liche nitidus is an uncommon, chronic, papulosquamous condition that is characterized by multiple, 1-2 mm, flesh-colored, shiny, dome-shaped papules. Usually, the condition is asymptomatic, although it may sometime be associated with pruritus. The eruption classically involves the genitalia, upper extremities, trunk, but in rare instances, it may become generalized. The clinical course of generalized lichen nitidus is unpredictable, with most patients experiencing spontaneous resolution, but the condition can become persistent and refractory to treatment. We describe two patients with generalized lichen nitidus that responded favorably to phototherapy with narrow band UVB(NBUVB).

A 10-year-old male presented with generalized tiny glistening discrete papules on trunk and lower extremities. Skin lesions developed 2 years before the visit, and no subjective symptom was associated. NBUVB was initiated with starting dose of 250 mJ/cm^2, with an increment dose of 100 mJ/cm^2. After 41 treatments with maximal dose of 1900 mJ/cm^2 and total dose of 45.5 J/cm^2, his skin lesion cleared. Another patient was 33-year-old male who presented with generalized tiny glistening discrete papules on whole body. Skin lesions developed 3 years before the visit and he complained about severe itching. After topical diphenylcyclopropenone (DPCP) for 10 months, his lesion improved, but 8 months after the discontinuation of therapy, the lesion recurred. Biweekly NBUVB initiated with starting dose of 400 mJ/cm^2, with an increment dose of 100 mJ/cm^2 per session. After 36 treatments with maximal dose of 1300 mJ/cm^2 and total dose of 37.9 J/cm^2, skin lesion has nearly subsided.

Various treatment methods including DPCP, astemisol, cetrizine, and antituberculous drugs have been tried for generalized lichen nitidus. Due to small number of subjects and occasional spontaneous resolution, the efficacy of the treatment modalities is very hard to evaluate. Interestingly, natural sunlight exposure as well as PUVA has been occasionally reported to be helpful in this condition. We think the two patients in our report treated with NBUVB are substantiating possibility of phototherapy as a safe and effective treatment modality.

증 례 보 고

A Case of Psoriatic Arthritis Treated with Cyclosporin

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physical therapy, avoidance of joint stress and patient education for prevention of repetitive injury. As for more severe involvement, various medications like NSAID, sulfasalazine, retinoids, methotrexate, cyclosporin, or TNF-neutralizing agent (etanercept) are required.

A 26-year-old man had 2-months history of abrupt pain and swelling on T-M joints, left shoulder and both hip joints, left knee, finger and toe joints in asymmetrical pattern. Simultaneously he presented with erythematous scaly plaques on the left shin and macerated patch on the penis. The laboratory tests showed negativity for serum RA factor and ANA and positivity for HLA-B27 and elevated titers of ASO, CRP, ESR. Plain X-ray showed the mild degenerative change on finger, knee, toe joint. 99mTc-bone scan showed the marked uptake in the left sternoclavicular junction, MCP joint of R1 finger, MCP joints of L2-5 fingers, left knee, MTP joints of R2-4 toes. Initially sulfasalazine 1000mg/day was placed but not so effective. We treated with cyclosporin 250mg/day for 8 weeks with tapering after marked improvement, along with sulfasalazine and NSAID, and topical calcipotriol and glucocorticoid for skin lesions. Now, he is free of arthritis symptoms after about 6 months medications.

Generalized Pustular and Erythrodermic Psoriasis Associated with Oral Terbinafine Therapy

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Terbinafine is a member of allylamine class of antifungal agents with an estimated 7.5 million individuals worldwide having used for the treatment of dermatomycosis. Adverse effects have been reported in 10.5% and with cutaneous side effects, 2.3% of patients receiving oral terbinafine. The most common adverse reactions involve the gastrointestinal, hepatic, cutaneous and central nervous systems. Cutaneous adverse reactions include erythema, pruritus, urticaria, fixed drug eruption and alopecia. However severe and life threatening cutaneous reactions such as Stevens-Johnson syndrome, toxic epidermal necrolysis, exacerbation or induction of psoriasis and erythroderma with severe desquamation have recently been reported with terbinafine. We describe 61-year-old man with a history of psoriasis who developed generalized pustular psoriasis after oral terbinafine therapy. After discontinuing terbinfine, the patient was treated with topical calcipotriols and corticosteroids, and the skin eruption gradually improved.

Koebner Phenomenon Caused by Allergic Contact Dermatitis to Zinc Pyrithione in Psoriasis

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Zinc pyrithione is a shampoo base that has been shown to be safe, effective for dandruff and scalp psoriasis. Presumably it decreases the cell turnover rate in hyperproliferative dermatoses such as psoriasis and has fungistatic and antimicrobial activity, but its exact mode of action is unknown. In psoriasis, external factors, such as trauma, infection, and drugs may provoke aggravated manifestation of psoriatic skin lesion. Rarely, primary irritant or allergic mechanisms are likely factors of psoriatic flare and koebnerization. The 45-year old female patient had had a stable psoriasis for 25 years, and no any other skin disease. Within 20 days, she had aggravated scaly erythematous patch on scalp, where the shampoo was applied and developed pustular psoriasis on both forearms at the same time. Patch testing revealed a relevant sensitization to zinc pyrithione and we observed symptomatic aggravation by provocation testing with zinc pyrithione shampoo again. We report a rare case aggravated psoriasis induced allergic contact dermatitis due to zinc pyrithione after using antidandruff shampoo.

Psoriasis Associated with Crohn's Disease

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Psoriasis is a skin disorder characterized by well-circumscribed, inflamed, scaling plaques and Crohn's disease is an inflammatory condition affecting any aspect of the gastrointestinal tract. An appreciation for the role of tumor necrosis factor-α in both diseases has proven very important and a close examination reveals epidemiologic, genetic and pathologic connections between these diseses.

A 52-year-man visited our clinic for 3-years history of psoriasis on elbows, buttock, and legs. He had been treated with topical corticosteroids, but his lesions waxed and waned. He also had Crohn's disease which was presented as abdominal mass and pain 5 years ago and had been treated with mesalazine. He was HLA-B27 negative and did not show other abnormality on physical examination and laboratory investigation. A week later, he developed abdominal pain and was diagnosed as bowel stenosis due to Crohn's disease. The ileocolectomy was done, thereafter he was treated with topical corticosteroid for psoriasis and with sulfasalazine and azathioprine for Crohn's disease.

A Case of Uremic Psoriasis Improved after Initiation of Hemodialysis

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Remissions of long-standing psoriasis have been reported in patients starting either hemodialysis or peritoneal dialysis for end-stage renal disease (ESRD).

A 52-year-man visited our clinic for 10-years psoriasis. He had been treated with topical corticosteroids, calcipotriol and phototherapy but showed poor response. He had diabetes mellitus, but did not show other abnormality on the physical examination. Two years later, he developed swelling, headache and chronic fatigue and was diagnosed as chronic renal failure due to diabetes mellitus. At that time, the PASI score was 45 and his skin lesion was evaluated as severe state. The arteriovenous-fistula operation for hemodialysis was done. Three weeks after start of hemodialysis, his skin lesions improved significantly (PASI score was 6) and remitted persistently over two-year follow-up period.

A Case of Generalized Pustular Psoriasis Associated with Systemic Lupus Erythematosus

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Generalized pustular psoriasis (GPP) is an acute, systemic form of psoriasis, characterized by fever, chills, rigors, and generalized pustule formation on the skin. The concomitant occurrence of lupus erythematosus and psoriasis has been reported sporadically. But the coexistence of GPP and systemic lupus erythematosus (SLE) has occurred rarely. We herein report a case of GPP in a 19-year-old female, who has had a history of SLE since the age of 14 years. 5 years ago, she was made a diagnosis of SLE and took a methylprednisolone pulse therapy for complicated lupus nephritis and hemolytic anemia at the department of pediatrics in our hospital, and then was controlled by oral glucocorticoids only, which was stopped 4 months before her visit. She was presented with generalized grouped tiny pustules surrounded by erythematous patches on the trunk. On the present illness, generalized pruritic erythematous scattered papuloplaques was developed 1 month before the development of above lesion. We used oral, topical glucocortioids and hydroxychloroquine for her cutaneous lesion and lupus nephritis, respectively. After then, her cutaneous lesion improved, so steroids were tapered. She went on a picnic in the summer 1week before her second visit, and her lesions were aggravated abruptly and formed generalized pustules. She also complained of fever and chills. On the labaratory exam, leukocytosis, proteinuria and elevated ESR, CRP were found. Histopathological exam revealed subcorneal, intraepidermal spongiform pustules, acanthosis, regular elongation of rete ridges, capillary proliferation and perivascular inflammatory cells infiltration in the upper dermis. Thus we diagnosed this case as GPP and treated with oral glucocorticoids and retinoids.

교 육 강 연

Alefacept

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Alefacept (AmeviveTM, Biogen) is a recombinant 115kD dimeric glycosylated fusion protein composed of the first extracellular domain of human LFA-3 protein (also termed "LFA-3TIP" because it contains only the external domain of LFA-3) fused to the hinge and CH2 and CH3 sequences of human IgG1. It binds to CD2 on the surface of memory T cells, blocks co-stimulatory signaling between CD2 and LFA-3 on antigen-presenting cells, inhibiting T cell activation and proliferation and selectively induces apoptosis of T cells. Alefacept is indicated for the moderate to severe psoriasis. The overall response rates for the 7.5 mg IV and 15 mg IM of alefacept administered once weekly for 12 weeks were 28% and 33% with a $\geq$75% reduction in PASI, respectively (IV and IM placebo; 8% and 13%, respectively). Second course of alefacept treatment increased the reponse rates (IV 40%, IM 43%). The median duration of a $\geq$50% reduction in PASI was 216 days for patients who achieved a $\geq$75% reduction in PASI during or after treatment and 241 days for patients who achieved a Physician Global Assessment (PGA) of "clear" or "almost clear". The duration of response was longer for patients receiving a second course of alefacept therapy. Patients do not develop tachyphylaxis with repeated courses of therapy. The second course of alefacept can be given any time after the first 12 weeks of treatment-free follow-up after an initial 12-week course of therapy. In terms of the dosage, a rational approach would be to give alefacept for longer courses rather than to increase the dose. Phototherapy would be additive, or possibly synergistic, and therefore compatible with alefacept. Data from clinical trials indicated that the maximum reduction in T cell counts (especially CD4+ and CD8+ CD45RO+ memory T cells) generally occurred within 6 weeks of initiating alefacept. If the current safety profile does not change during postmarketing studies, the monitoring requirements will be less frequent, eg, at baseline and at 2, 4, 8, and 12 weeks. The most serious adverse reactions found in clinical trials of alefacept treatment were lymphopenia, malignancies, serious infections, and hypersensitivity. In summary, alefacept therapy significantly improves psoriasis and produces durable clinical remission with a very favorable safety profile, without rebound following treatment cessation. The safety and incremental effectiveness of a second course of alefacept provides strong support for its use as an intermittent therapy for the moderate to severe recurrent psoriasis.

Efalizumab

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The chronic plaque variety accounts for 85-90% of cases. The management of psoriasis needs to take into account both the physical and psychological aspects of the disease. Treatment of psoriasis is aimed at symptomatic relief and improved quality of life. The current management of psoriasis involves consideration of the severity of disease, quality of life, risk versus benefit of various treatment strategies, and a patient's response to prior treatment. Patients with mild disease normally receive topical therapy and with moderate- to severe, resistant disease are candidates for phototherapy and systemic therapy.

On occasion, the psoriasis patients with limited extent disease can be treated with systemic therapies if there is resistance to therapy and/or overwhelming psychosocial disability from psoriasis. Furthermore, current systemic therapies, though effective, in the most part can not produce clearance of disease without someelement of risk and their long-term use is limited by concerns of toxicity, intolerance, need for frequent laboratory monitoring and published guidelines restricting their use. These limitations and an improved understanding regarding the pathophysiologyof psoriasis have led to the development and testing of biological approaches that specifically target and modulate key pathogenic steps, with the aim of less organ toxicity and safer long-term maintenance therapy.

Efalizumab is a humanized monoclonal IgG1 antibody that is a targeted T-cell modulator.

It binds to CD11a, the alpha chain of the lymphocyte function-associated antigen-1 (LFA-1), thereby preventing LFA-1 from binding to its ligand, intercellular adhesion

molecule-1(ICAM-1). Efalizumab inhibits various T cell processes believed to be important in the pathogenesis of psoriasis, including T cell activation, T cell adhesion to endothelial cells and T cell migration. Efalizumab has been extensively studied more than 2000 patients for the treatment of moderate-to-severe chronic plaque psoriasis.

Subjects treated with efalizumab had fewer psoriatic skin lesions, less itching, and improved quality-of-life as well as sustained benefits while on therapy. Efalizumab is associated with an early onset of action, with improvement noted as early as 14 days.

Few subjects experienced serious adverse effects from efalizumab therpy; the most

common adverse events were milld, self-limiting (headache, chills, nausea, fever, myalgia, and asthenia) and associated with the first two doses. There is no evidence

to suggest that efalizumab affects the overall rate of malignancies and infections compared with placebo. Efalizumab provides a significant new alternative for patients with moderate to severe plaque psoriasis and offer the potential for improved and potentially safer long-term, continuous maintenance therapy.

Infliximab

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Infliximab is a mouse/human chimeric antibody blocking TNF-α activity by binding it. It has been used to treat rheumatoid arthritis and Crohn's disease. Recently its clinical use has been extended to the treatment of psoriasis vulgaris and psoriatic arthritis. TNF-α is a proinflammatory cytokine, which is known to be elevated in the lesions and the sera of psoriasis patients. TNF-α is also known to stimulate Langerhans cells to mature to activate T cells and induce adhesion molecules in keratinocytes and endothelial cells, which facilitate infiltration of inflammatory cells in the lesions. TNF-α can induce vascular endothelial growth factor, which may increase the amount of blood vessels in the lesions. TNF-αcan stimulate keratinocytes to proliferate and prevent the apoptosis of keratinocytes by elevating plasminogen activator inhibitor type 2. Chaudhari et al first reported the phase II randomized clinical trial results of infliximab treatment for the psoriasis patients, which showed PASI 75 responses in 82% of 5 mg/kg injection group and in 73% of 10 mg/kg injection group, but only in 15% of the control group. Recently Gottlieb et al reported that 10 wk follow-up results of infliximab treatment in 249 patients showed PASI 75 response in 72% of the 3mg/kg injection group and in 88% of the 5 mg/kg injection group, but only in 6% of the control group. Infliximab is also reported to improve psoriatic arthritis, pustular psoriasis and intractable psoriasis. Most commonly reported side effects of infliximab were fever and chilling, and other rare reported side effects were chest pain, hypotension, hypertension and dyspnea. In case of appearance of neutralizing antibody, serum sickness can occur. Therefore, long term use of infliximab may require simultaneous methotrexate treatment to reduce the incidence. Elevated incidence of infections such as tuberculosis was well documented. Therefore, careful evaluation of the patients is necessary before starting the treatment. Considering the reports of lymphoma, demyelinating disease and lupus erythematosus among the patients treated, the usage of infliximab should be restricted to the severe intractable patients by conventional therapy. In summary, infliximab can be an alternative treatment requiring I.V. injections once per two weeks for severe psoriasis, which does not respond to other conventional treatments.

Etanercept

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Increasing data indicate that TNF-α is taking a key role in the pathogenesis of psoriasis and psoriatic arthritis. Elevated level of TNF-α has been found in skin lesions, serum, and joint fluid of psoriasis patients and the levels correlated with PASI scores. TNF-α has also been implicated in the pathogenesis of Crohn's disease and rheumatoid arthritis. It is considered to be important in the activation of both innate and acquired immune response.

Etanercept (Enbrel) is a fully human fusion protein of two TNF-α receptor p75 extracelluar domains with one IgG1 Fc portion. It inhibits activity of TNF-α by competitively binding to this pro-inflammatory cytokine, preventing interaction with its cell surface receptors. It acts just like the naturally occurring soluble forms of TNF-α receptors, which cannot completely inhibit development of psoriasis. Being a dimeric structure, it can bind two free TNF-α molecules with greater affinity, 50-1000 times, than that of soluble monomeric forms of the TNF-α receptor. Despite the presence of Fc portion, it does not induce complement-mediated cytotoxicity. In contrast to infliximab, it has a very low rate of immunogenecity. It is easily administered through SC injections by patients whereas infliximab should be administered via IV infusion, which requires hospital visits. It has been approved by FDA for the treatment of rheumatoid arthritis and psoriatic arthritis.

A phase II trial in psoriasis patients showed that 30% achieved PASI 75 at 12 weeks compared with 2% in placebo group. With 24 weeks of treatment 56% of etanercept group demonstrated PASI 75 improvement. Adverse events from both groups did not show significant differences.

With safety, convenience and acceptable efficacy, etanercept will be used for moderate to severe psoriasis patients especially with psoriatic arthritis.

대한건선학회 임원 및 평의원

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