EDITORIAL

ORAL LICHENOID LESIONS RELATED TO DRUGS: REVIEW OF CLINICOPATHOLOGICAL FEATURES AND DIFFERENTIAL DIAGNOSIS

E. BARIŞ¹, B. SENGÜVEN¹, T. TÜZÜNERT and S.E. GÜLTEKİN¹

¹Gazi University, Faculty of Dentistry, Department of Oral Pathology, Ankara, Turkey; ²Karadeniz Technical University, Faculty of Dentistry, Department of Pedodontics, Trabzon, Turkey

Received February 27, 2014 – Accepted March 31, 2014

Lichenoid drug reaction is termed as a condition of the oral cavity having an identifiable etiology, which is clinically and histologically similar to oral lichen planus. A number of drugs have been described as a causative factor of those reactive lesions. The aim of this study is to conduct a systematic review on the role of causative drugs in oral lichenoid lesions (OLLD) and the clinico-pathological features of this entity which still has uncertainty in diagnosis. Bibliographic searches were carried out to identify articles published in English on PubMed® Online electronic databases from 1993 to 2013. Available clinical, histological and treatment methods were recorded. A total of 25 articles fulfilled the inclusion criteria with 37 patients. OLLD were detected frequently in patients with a history of zidovudine and imatinib mesylate medication. OLLD occurred significantly in subjects over the age of 30 (p<0.01), mostly on buccal mucosa (42.37%). The most preferable treatment is withdrawal of the drugs and administering a topical steroid regimen. Thirty OLLD cases were confirmed by biopsies which were characterized by diffuse inflammatory infiltrate through the deep side of the lamina propria. Medical history and histological features are the two basic criteria for the differential diagnosis of OLLD.
GAINING MORE INSIGHT INTO THE DETERMINANTS OF CANDIDA SPECIES PATHOGENICITY IN THE ORAL CAVITY

M.H. ARZMI1,2, E. ALSHWAIMI3, W.H.A. WAN HARUN4, F. ABDUL RAZAK4, F. FARINA5,6, M.J. M’CULLOUGH1 and N. CIRILLO1,6

1Melbourne Dental School and Oral Health CRC, The University of Melbourne, Melbourne, VIC, Australia; 2Department of Basic Medical Sciences, Kulliyyah of Dentistry, International Islamic University Malaysia, Kuantan, Pahang, Malaysia; 3Department of Restorative Dental Sciences, College of Dentistry, University of Dammam, KSA; 4Department of Oral Biology, Faculty of Dentistry, University of Malaya, Kuala Lumpur, Malaysia; 5Facultatea de Medicina si Medicina Dentara Titu Maiorescu, Bucharest, Romania; 6Centro per l’Innovazione, la Ricerca, l’Istruzione, la Salute (IRIS), Italy

Received June 26, 2013 – Accepted March 17, 2014

Candida infection (candidiasis) is potentially life threatening and can occur in almost all anatomical sites, including the mouth. Candida species are in fact the most common fungal pathogens isolated from the oral cavity and frequently cause superficial infections such as oral candidiasis and denture-associated erythematous stomatitis. Whilst systemic dissemination of Candida from intraoral foci is rare and largely due to severe deficits of the host immune defenses, the development of localized oral candidiasis is most commonly related to a variety of non-immune determinants such as Candida virulence factors and permissive oral microenvironment. In particular, phenotypic switching and dental biofilm have emerged as major determinants for the pathogenicity of Candida and are currently the subject of intense research. An understanding of the molecular aspects underlying the biological behavior of Candida will be the key to the development of effective preventive as well as therapeutic measures for invasive and oral candidiasis.
EDITORIAL

IS MINIMALLY INVASIVE SPINE SURGERY ALSO MINIMALLY PRO-INFLAMMATORY? MUSCULAR MARKERS, INFLAMMATORY PARAMETERS AND CYTOKINES TO QUANTIFY THE OPERATIVE INVASIVENESS ASSESSMENT IN SPINE FUSION

G. LOMBARDI¹, D. GRASSO¹, P. BERJANO², G. BANFI¹,³ and C. LAMARTINA⁴

¹Laboratory of Experimental Biochemistry and Molecular Biology, I.R.C.C.S. Istituto Ortopedico Galeazzi, Milan, Italy; ²O.U. Orthopaedics and Traumatology, Spine Surgery IV, I.R.C.C.S. Istituto Ortopedico Galeazzi, Milan, Italy; ³Department of Biomedical Sciences for Health, University of Milan, Milan, Italy; ⁴O.U. Orthopaedics and Traumatology, Spine Surgery II, I.R.C.C.S. Istituto Ortopedico Galeazzi, Milan, Italy

Received July 2, 2013 – Accepted March 4, 2014

Over the last decades, minimally invasive surgery (MIS) techniques entered in the surgical routine due to their major advantage in reducing the unnecessary exposure of tissue and, thus, the trauma. Even in the context of orthopedics and spine surgery these practices have been widely developed and applied. Besides the clinical outcome of the patients, few studies have quantitatively assessed the traumatic and inflammatory effects of a specific surgical technique. Indeed, currently, a universally accepted biological outcome measure, such as a panel of biochemical markers, to define the success of MIS approach is still lacking. We reviewed the literature to collect the published data regarding the quantitative analysis of trauma induced by either conventional or minimally invasive surgery with the aim of highlighting evidence useful to guide future studies. Previous publications show some evidence in support of the hypothesis that MIS approaches are less traumatic, and possibly less pro-inflammatory, than conventional ones. Creatin kinase (as a marker of muscular damage) and C-reactive protein (as a marker of systemic inflammation) seem to reproducibly follow different trends in minimally invasive surgery compared to conventional procedures. Moreover, cytokines, such as interleukin (IL)-6 and IL-10 are also promising markers in this context.
ARTICULAR AND OTHER IMMUNE-MEDIATED EXTRA-INTESTINAL MANIFESTATIONS IN INFLAMMATORY BOWEL DISEASES

R. PELUSO¹, S. IERVOLINO², M. VITIELLO¹, V. BRUNER¹, P. AMBROSINO³, F. MANGUSO⁴, F. CASTIGLIONE⁵ and M.N.D. DI MINNO³

¹Rheumatology Research Unit, Department of Clinical Medicine and Surgery, University Federico II, Naples, Italy; ²Rheumatology and Rehabilitation Research Unit “Salvatore Maugeri” Foundation, Telese Terme (BN), Italy; ³Regional Reference Center for Coagulation Disorders, Department of Clinical Medicine and Surgery, University Federico II, Naples, Italy; ⁴Complex Operating Unit of Gastroenterology, AORN “A.Cardarelli”, Naples, Italy; ⁵Gastroenterology Research Unit, Department of Clinical Medicine and Surgery, University Federico II, Naples, Italy

Received January 10, 2014 – Accepted May 28, 2014

The first two authors equally contributed to the paper

The articular involvement in patients with inflammatory bowel diseases is included in the group of immune-mediated extra-intestinal manifestations, occurring approximately in a range from 6.2-36% of the patients. This group is also made up of the skin and eyes manifestations, that usually but not invariably are correlated with intestinal inflammatory disease activity. Rheumatic manifestations are the most frequent extra-intestinal findings of this group with a prevalence from 20-50%. They are divided into two different clinical subsets: peripheral and axial joint involvement (including sacroiliitis with or without spondylitis). Peripheral arthritis is the most frequent finding in both Crohn’s disease and ulcerative colitis, occurring with a frequency ranging from 17-20%, and it is more common in Crohn’s disease. Axial involvement is more common in Crohn’s disease (5-22%) than in ulcerative colitis (2-6%) and generally the prevalence of sacroiliitis (asymptomatic and symptomatic) is between 12-20% and of spondylitis is between 2-16%. The IBD is also associated with other rheumatic diseases such as rheumatoid arthritis, Sjogren syndrome, Takayasu arteritis and fibromyalgia. The management of patients with EA requires an active cooperation between gastroenterologists and rheumatologists.
ASTHMA AND MAST CELL BIOLOGY

S.K. KRITAS¹, A. SAGGINI², G. CERULLI³, A. SPEZIALI³, A. CARAFFA⁴, P. ANTINOLFI⁴, A. PANTALONE⁵, M. ROSATI⁶, M. TEF⁷, R. SAGGINI⁷ and P. CONTI⁸

¹Department of Microbiology and Infectious Diseases, School of Veterinary Medicine, Aristotle University of Thessaloniki, Macedonia, Greece; ²Department of Dermatology, University of Rome Tor Vergata, Rome, Italy; ³Nicola’s Foundation, Onlus, Arezzo, Italy; ⁴Orthopedic Division, University of Perugia, Perugia, Italy; ⁵Orthopedic Division, University of Chieti-Pescara, Chieti, Italy; ⁶Gynecology Clinic, Pescara Hospital, Pescara, Italy; ⁷Department of Neurosciences and Imaging, Faculty of Medicine and Surgery, G. d’Annunzio University Chieti-Pescara, Chieti, Italy; ⁸Immunology Division, Medical School, University of Chieti-Pescara, Chieti, Italy

Received May 30, 2014 – Accepted July 10, 2014

Asthma is a chronic inflammatory disease of the lung and its pathophysiology is initiated by mast cell activation in response to the antigen binding to IgE receptor as well as by TH2 cell activation. Mast cells are well established effector cells in asthma where they exacerbate the inflammatory response, playing a key role in early phase, degranulating and increasing histamine. Human mast cells possess high affinity IgE receptors and are ubiquitous but predominantly localized in mucosal and connective tissue and are distributed along blood vessels. There are two types of mast cells: connective tissue mast cells (TC) and mucosal mast cells (T mast cells). TC mast cells contain more heparin, whereas T mast cells contain more chondroitin sulfate. In asthma, mast cell activation can trigger degranulation, releasing secretory granule complex and preformed mediators, such as histamine and proteases, along with the synthesis of leukotrienes and prostaglandins, and induction of cytokines and chemokines. Leukotrine inhibitors and omalizumab, which inhibits IgE, both relieve the asthma exacerbation when administered to humans and permit to reduce the use of other drugs. The release of cytokines by mast cells, such as TNF-alpha, IL-1, IL-6 and IL-33, participate in the pathogenesis of asthma. Stress worsens asthma, and this effect is also mediated by mast cell activation through the release of cytokines. Administration of IL-33 in experimental animals provokes pathological effects in the mucosal tissues and augments antibody IgE and IgA in blood vessels. Here, we report the impact of mast cell biology in asthma pathogenesis.
Biomarkers are emerging as important tools in the detection and monitoring of various diseases. A major limitation and challenge to effectively utilize biomarker signals is the limited understanding of factors contributing to their variance. As genetic variation is a major contributor to phenotypic variation, exploring genetic contributions is of great importance. Copy number variants (CNVs) offer an alternative genomic framework to understand contributions to phenotypic variance. A copy-number variation genome-wide association study was performed using 116 serum inflammatory biomarkers as quantitative trait in elderly normal controls to test the hypothesis that CNVs contribute to the phenotypic heterogeneity of serum biomarkers. Three chromosomal regions were associated with four biomarkers in trans. Transforming growth factor alpha (TG-alpha) serum levels were associated with CNV dosage at chr11:5,788 kb, soluble levels of receptor for advanced glycation endproducts (sRAGE) was associated with CNV dosage at chr8:40,183 kb and both thrombospondin-1 and tissue inhibitor of metalloproteinase 1 (TIMP-1) were associated with CNV dosage at chr11:18,961 kb. The CNV at chr11:5,788 kb harbors 2 olfactory genes and the introns of Tripartite motif-containing (TRIM) gene cluster TRIM5&22 while the CNV at chr11:18,961 includes the Mas-related G-protein coupled receptor member X1. These trans associations may identify novel relationships in the relevant pathways and suggest that genetic variation can contribute to biomarker levels. The detected trans-association between MRGPRX1 and thrombospondin-1/TIMP-1 could implicate a novel pathway between pain/itching and inflammation. Cataloguing all genetic variants with an effect on biomarkers will serve as a tool to interpret epidemiological studies and establish causal relationships through Mendelian randomization.
An important role in pathomechanism of Lyme disease is played by the ability of spirochetes to spread within tissues, and to adhere (to platelets, erythrocytes and vascular epithelium). The principal factors regulating that process are chemokines, cytokines and adhesion particles. The aim of this study was to select genes related to the chemokines and their receptors, differentiating the type of infection in the system model, i.e. a culture of normal human diploid fibroblasts infected with three different spirochete genospecies: B. afzelii, B. garinii and B. burgdorferi sensu stricto, by comparing the infected fibroblast culture with that of the control fibroblast. The differences in the expression of genes selected on the basis of a scientific database Affymetrix were analysed by comparing transcriptomes from the four cultures of fibroblasts, using the oligonucleotide microarrays HG_U133A. In the result of infection of fibroblast cultivation with a specific Borrelia genospecies, a variable expression of the chemokines and their receptors, specific for one genospecies was observed. The fibroblast infected with B. afzelii expressed CCL4, CCL1, CCL2 and CCR10; with B. garinii - CXCL12, IL6, CCR3 and CXCR5; and with B. burgdorferi sensu stricto - CCL5, CCR1, CCL3, CCL16, CXCR6, IL8, CXCR7 and CXCR3.
The objective of this study was to evaluate the efficacy of cryosurgery on 134 different benign oral lesions in 90 patients. All lesions were treated every 2 weeks until complete regression of the lesion had been achieved. Patients were examined at 2, 7, and 10 days, 2 and 4 weeks, and 3 and 6 months after the cryosurgery. The relationship between the number of cryosurgery applications to achieve complete regression and the type of lesions was assessed for statistical significance by one-way analysis of variance and with the Scheffé test. The mean application number of the cryosurgery was 1.82±0.49 for fibroma, 2.35±1.44 for vascular lesions, 1.50±0.70 for mucocele, 2.65±1.18 for lichen planus lesions. The difference between the type of the lesion and number of application was statistically significant for all groups (p< 0.05). Our data prove that a significantly fewer number of cryosurgery treatments are required to achieve complete regression for fibroma and mucocele lesions compared to lichen planus lesions. During the follow-up period, only 7 lichen planus lesions of 76 lesions recurred.
The aim of this study was to evaluate diagnostic value of 25-hydroxyvitamin D level, Upar, IL-33 and ST2 in comparison with C-reactive protein, TNF-α and Interleukin-6 in neonatal sepsis. A total of 106 term babies were included 20 of whom were the control group. We used only data of high probable sepsis with blood culture positive infants, therefore 46 infants were excluded. Blood was collected from infants from the first day of sepsis (1.value) and 48-72 hours later (2.value). There were significant differences between the controls and sepsis (1.value) for 25-hydroxyvitamin D levels (35±19ng/ml and 69±7.5ng/ml, p=0.01), for IL-33 levels (90±34 ng/ml and 412±170 ng/ml, p=0.01), for sST2 levels (453±44 ng/ml and 4120±2720ng/ml, p=0.01), for sUpar levels (2.1±1.3 ng/ml and 11.4 ± 5.2 ng/ml, p=0.01), respectively. There were significant differences between sepsis (1.value) and sepsis (2.value.) with reference to 25-hydroxyvitamin D, IL-33, sST2, and suPAR levels, respectively. In the light of these results, it may be suggested that 25-hydroxyvitamin D level, upar, IL-33 and ST2 can be used as an acute phase reactant like C-reactive protein, TNF-α and Interleukin-6 in diagnosis of neonatal sepsis.
We observed that low concentrations of procalcitonin (PCT) in the early stages of bacterial infection among HIV/AIDS patients are not always associated with a good prognosis. Many of our patients developed sepsis despite a PCT level of <0.5 ng/ml on the first days of infection. The aim of our study was to assess whether laboratory standards for PCT in patients with HIV/AIDS correlate with their clinical condition. We analyzed the concentration of PCT and other inflammatory markers in the early stages of bacterial infection among 40 HIV-infected patients and 52 AIDS patients enrolled for the study. The control group consisted of 37 healthy individuals. In comparison with PCT and WBC, PCT proved to be the most reliable in the early stages of bacterial infection. To conclude, we suggest new PCT cut-off ranges for HIV/AIDS patients with bacterial infection.
LOW CD40 EXPRESSION LEVELS IN *LEISHMANIA INFANTUM*-INFECTED BONE MARROW DENDRITIC CELLS EVOKE REGULATORY RESPONSES BY DOWN-REGULATING INTERLEUKIN-12 PRODUCTION: ROLE OF ERK1/2

M. AGALLOU, E. DOTSNIKA and E. KARAGOUNI

Received May 30, 2013 – Accepted June 24, 2014

Department of Microbiology, Hellenic Pasteur Institute, Athens, Greece

Dendritic cells (DCs) play a pivotal role in promoting resistance to leishmaniasis, both by activating CD4+ T cells and endorsing their differentiation into Th1 cells by producing interleukin (IL)-12. High level of IL-12 production, a decisive component of the DC maturation, requires not only microbial stimuli but also strong CD40-CD40L interactions. Until now, the mechanisms by which *Leishmania (L.) infantum* parasites affect DC functional maturation and consequently T cell polarization are not fully understood. In the present study, we investigated the response that is elicited when *L. infantum* promastigote-infected bone marrow-derived DCs (BM-DCs) to CD40 engagement and this way mimicking DC-T cells interactions at the early stages of infection. We found that *L. infantum* promastigotes-infected BM-DCs following CD40 engagement were capable of inducing significant amounts of TNF-α and IL-10, whereas IL-12 production remained unaffected compared to infected untreated cells. Interestingly, infected BM-DCs did not up-regulate CD40 surface expression. On the other hand, BM-DC stimulation with soluble *Leishmania* antigen (SLA) resulted not only in significant increase of co-stimulatory molecule expression but also IL-12 and IL-10 production. CD40 engagement on *L. infantum*-infected BM-DCs sustained ERK1/2 activation induced by the parasite alone. Inhibition of ERK1/2 activation with the use of PD98059 inhibitor prior to CD40 engagement on *L. infantum*-infected BM-DCs resulted in significant up-regulation of p38 MAPK phosphorylation and IL-12 production, whereas it did not affect TNF-α and IL-10 production. These findings suggest that *L. infantum* has evolved specific strategies to avoid efficient DC-T cell interactions by suppressing CD40 expression and consequently leading CD40 signaling pathways to ERK1/2 activation.
TYROSINE KINASE INHIBITOR TYRPHOSTIN AG490 INHIBITS OSTEOCLAST DIFFERENTIATION IN COLLAGENASE-INDUCED OSTEOARTHRITIS

V. GYURKOVSKA, P. DIMITROVA and N. IVANOVSKA

Department of Immunology, Institute of Microbiology, Sofia, Bulgaria

Received March 5, 2014 – Accepted July 1, 2014

The janus kinase (JAK)-signal transducer and activator of transcription (STAT) cascade plays a principal role in the signaling of a vast array of cytokines and growth factors which stimulates diverse cellular functions and immune responses. Osteoarthritis (OA) is the most common joint disease in the adult population. The present study was designed to evaluate the effects of tyrosine kinase inhibitor, tyrphostin AG490 in a mouse model of collagenase-induced osteoarthritis (CIOA). CIOA was provoked by two intraarticular (i.a.) injections of collagenase in mice and intraperitoneally (i.p.) treated with AG490 at a dose of 5 mg/kg at days 0, 5 and 10 and at a dose of 8 mg/kg at day 18. The administration of AG490 in CIOA mice inhibited osteoclast generation in bone and the loss of glycosaminoglycans and proteoglycans in cartilage. Tyrphostin decreased the levels of IFN-\(\gamma\), IL1, IL-6 and IL-17 in the synovial fluid (SF) dependant on the time post AG490 administration. Limited numbers of CD11b positive Ly6G neutrophils in blood and SF along with a decrease of F4/80 positive cells in synovial fluid (SF) were observed in tyrphostin AG490-treated arthritic mice. AG490 inhibited M-CSF+RANKL-induced cytokine production by bone marrow (BM) cells and the differentiation of BM cells in vitro. Because of the findings presented, we argue that tyrphostin AG490 may hold promising therapeutic potential against important clinical conditions such as osteoarthritis (OA).
MAMMALIAN TARGET OF RAPAMYCIN IN INFLAMMATORY SKIN CONDITIONS

A. BALATO¹, R. DI CAPRIO¹, S. LEMBO¹, M. MATTII¹, M. MEGNA¹, M. SCHIATTARELLA¹, G. TARANTINO², N. BALATO¹, F. AYALA¹ and G. MONFRECOLA¹

¹Department of Dermatology, University of Naples Federico II, Naples, Italy; ²Department of Clinical and Experimental Medicine, University of Naples Federico II, Naples, Italy

Received July 18, 2012 – Accepted March 13, 2013

The conserved serine/threonine kinase mammalian target of rapamycin (mTOR) is a major regulator of survival growth, proliferation and motility, in response to mitogens, energy and nutrient levels. Dysregulation of mTOR pathway has been observed in various inflammatory or neoplastic human diseases. To assess the potential involvement of mTOR in some of the most common inflammatory skin diseases, and its interaction with other inflammatory mediators, we investigated mTOR expression in psoriasis, allergic contact dermatitis (ACD) and atopic dermatitis (AD). mTOR gene expression was assessed in the following conditions: i) skin biopsies from 15 patients affected by psoriasis, 5 patients with ACD, 5 patients with AD and 3 patients with EGFR-inhibitor-induced skin rash; ii) in immortalized keratinocytes HaCaT, primary human keratinocytes (KCs) and full thickness skin organ cultures, incubated with tumor necrosis factor (TNF)-α, interleukin (IL) 17A or their combination; iii) in HaCaT cells stimulated with ultraviolet (UV)B; iv) in skin biopsies from 5 psoriatic patients before and after 16 weeks of anti-TNF-α therapy; mTOR expression was also evaluated through immunohistochemistry in lesional and non-lesional skin samples from 5 psoriatic patients. Moreover, mTOR major up-stream and down-stream regulator gene expression was assessed in skin biopsies from 15 patients affected by psoriasis, 5 patients with ACD, 5 patients with AD and 3 patients with EGFR-inhibitor-induced skin rash. All analyzed skin diseases showed an increase of mTOR gene expression whereas mTOR up-stream negative regulators were reduced or not enhanced in all of them. mTOR was strongly expressed in all epidermal layers of lesional and non-lesional psoriatic skin. Conversely, pro-inflammatory conditions, in vitro, were not able to increase mTOR levels, except for UVB. Similarly, anti-TNF-α therapy was not able to reduce mTOR gene expression in patients with psoriasis. Our study provides evidence that mTOR is involved in cutaneous inflammatory process, but through a signalling not directly dependent from Th1-Th17 pathway.
Reactive oxygen species (ROS) are mainly produced by microglia and macrophages during inflammation-driven oxidative burst. However, they can in turn affect the reactivity and function of immune cells. For the first time, the relationship between these two key players involved in Multiple Sclerosis (MS) was evaluated at peripheral level. We performed an in-depth immune-phenotypic and functional analysis of MBP (Myelin Basic Protein)-stimulated Peripheral Blood Mononuclear Cells (PBMCs) by flow-cytometry. In addition, blood Coenzyme-Q10 (CoQ10), total, oxidized and reduced forms of glutathione (GSTot, GSSG, GSH), malondialdehyde (MDA), ROS, anti-oxidized-low-density-lipoproteins antibodies (anti-oxLDL), and anti-oxidant-power (PAO) were studied in 31 untreated MS patients (MSnoTP), 23 MS patients (MSTP) treated with Disease Modifying Drugs (DMDs) and 39 matched controls (HC). The focus of our study was the correlation between oxidative stress biomarkers and distribution of immune-phenotypes across the 3 studied groups. In MSnoTP an inverse correlation between MDA and apoptotic cells (CD4+ AnnexinV+ TIM3+) was detected (rs= - 0.50, p= 0.01). M1 functional phenotype (CD14+ IL6+) and TH17 cells (CD4+ IL22+) inversely (rs= - 0.48) and directly (rs= 0.46) correlated (p = 0.01) with Anti-oxLDL antibodies and GSSG, respectively. The latter direct correlation was shown also in MSTP. Notably, in this group, we also detected a direct correlation between CD4+ IL4+ and CD4+ IL25+ (TH2 phenotype) with CoQ10 (rs= 0.54) and GSH (rs= 0.46) (p< 0.03), two crucial anti-oxidants. Again, a direct correlation was found between CD8+ BDNF+ cells (suppressor phenotype) and anti-oxLDL (rs= 0.48, p= 0.03). Surprisingly, we measured an inverse correlation between CD4+ IL10+ cells (M2 immune-regulatory cells) with GSH (rs= - 0.59, p< 0.001). Our findings endorse the idea of a relationship between pro-inflammatory cells and pro-oxidative environment, even at peripheral level. Interestingly, the correlation between CD4+ IL10+ cells and a defective anti-oxidant equipment might be regarded as evidence of the involvement of these cells during an inflammatory/oxidative phase that they try to control. The finding of this link only in MSTP patients might suggest that DMDs can provide an alternative way to counteract inflammation, regardless of an absolute increase of these immune-regulatory cells.
An increasing number of studies have suggested a key role for low levels of vitamin D in the development of several chronic diseases and bacterial infections. In particular, its role in acute respiratory infection has been clarified, while the potential role of vitamin D for susceptibility to urinary tract infections still remains unexplored. Since the typical symptoms associated with urinary infections or with other conditions, like overactive bladder, include dysuria, urgency and frequency, the aim of this study was to investigate the association between these symptoms and vitamin D status. We conducted a retrospective study on 233 women who, in the previous year, had their serum levels of vitamin D measured. The subjects were queried about the presence of urinary symptoms and their frequency over the previous year. Women with low serum levels of vitamin D had a higher prevalence of symptoms than those with normal levels of vitamin D (p<0.001). In particular, women who reported high frequency of symptoms had a mean vitamin D level of ~27 ng/mL, those with low frequency had a mean vitamin D level of ~24 ng/mL, while asymptomatic women had mean levels of ~37 ng/mL (p=0.004 among group). In this study hypovitaminosis D is associated with urinary symptoms in a population of women, and it may suggest a key role of this vitamin in the development of infections or other conditions affecting the urinary tract.
N-PALMITOYLETHANOLAMINE ADMINISTRATION AMELIORATES THE CLINICAL MANIFESTATION AND PROGRESSION OF EXPERIMENTAL AUTOIMMUNE ENCEPHALOMYELITIS IN RODENTS

D. IMPELLIZZERI1, R. DI PAOLA1, A. AHMAD1, R. CRUPI1, I. PATERNITI1, M. CAMPOLO1, G. BRUSCHETTA1, S. CLEMENTE2, E. ESPOSITO1 and S. CUZZOCREA1,3

1Department of Biological and Environmental Sciences, University of Messina, Italy; 2Macomer Rehabilitation Center of the Nuoro Health Care Center, Sassari, Italy; 3School of Medicine, Manchester Biomedical Research Centre, Manchester Royal Infirmary, University of Manchester, Manchester, United Kingdom

Received October 22, 2013 - Accepted March 25, 2014

Experimental autoimmune encephalomyelitis in rodents (EAE) is an accepted in vivo model for immunopathogenic mechanisms underlying multiple sclerosis (MS) and tests possible treatment options because it mimics many of the disease patterns. The current treatments for delaying MS progression include cytostatic, immunomodulatory drugs such as mitoxantrone, cyclophosphamide (CY), biological agents such as interferon (IFN)-beta, natalizumab and random polymer glatiramer acetate. Unfortunately, all of these compounds have potentially serious side effects, some require systemic administration, and the biological agents are costly and immunogenic, causing response failure during prolonged treatment. With this aim in mind, the purpose of the current research was to examine the effects of endogenous substances such as N-palmitoylethanolamine (PEA). PEA is an endogenous fatty acid amide belonging to the family of the N-acylethanolamines (NAEs). Recently, several studies demonstrated that PEA is an important analgesic, anti-inflammatory and neuroprotective mediator, acting at several molecular targets in both central and sensory nervous systems as well as immune cells. The effect of PEA daily administered was investigated in rats and mice developing EAE. A multidisciplinary approach was employed to study behavior and biochemical parameters. In our study we found that PEA counteracts the clinical course and pathology of monophasic EAE in myelin basic protein-immunized Lewis rats and the progression of EAE induced in C57BL/6 mice by immunization with myelin oligodendrocyte glycoprotein. Our results show that PEA treatment had a beneficial effect on the two different EAE models.
LETTER TO THE EDITOR

SUCCESSFUL WITHDRAWAL OF OMALIZUMAB IN A PATIENT WITH SEVERE ASTHMA: FREE IgE AS A POSSIBLE BIOMONITOR

C. DOMINGO¹², X. POMARES¹², M.-J. AMENGUAL²³ and M. OLLERT⁴

¹ Pneumology Service, Corporació Sanitària Universitària Parc Taulí, Sabadell, Barcelona, Spain; ²Department of Medicine, Universitat Autònoma de Barcelona, Sabadell, Barcelona, Spain; ³Laboratory Departmanet, Immunology Section, UDIAT, Corporació Sanitària Universitària Parc Taulí, Sabadell, Barcelona, Spain; ⁴Clinical Research Division of Molecular and Clinical Allergotoxicology, Department of Dermatology and Allergy, Technische Universität München, Munich, Germany

Received February 22, 2013 – Accepted March 7, 2014

To date, the pharmacological activity and clinical benefits of omalizumab have been well described, however several questions still remain unanswered, such as the moment to withdraw the drug as well as the possible biological markers that may be useful to do so. In the present case report, we describe our experience with our dose-reduction protocol in a middle-aged patient and elucidate the usefulness of free IgE levels.
Rasmussen encephalitis is a chronic inflammatory disease commonly seen in children. Hemispheric atrophy, intellectual disability, and hemiparesis are characteristics of this rare disease. The main pathological findings are chronic meningeal and parenchymal inflammation attributed to T lymphocytes. Plasmapheresis, immunomodulators, and immunosuppressives are commonly used for treatment. In this article, a patient suffering from Rasmussen encephalitis whose seizures were treated with prednisolone is discussed according to the literature.
LETTER TO THE EDITOR

USE OF TOPICAL MINOXIDIL, 17α-ESTRADIOL AND HYDROCORTISONE BUTYRATE IN FRONTAL FIBROSING ALOPECIA

A. ROSSI¹, A. IORIO¹, M. SCARNÒ², M.C. FORTUNA¹, L. PRIOLO¹, D. DI NUNNO¹, M. CARLESIMO¹, S. CALVIERI¹ and E. MARI¹

¹Department of Internal Medicine and Medical Specialities, University of Rome “Sapienza”, Italy; ²CASPUR (Inter-University Consortium for Supercomputing), Rome, Italy; ³Dermatology Sant’Andrea Hospital, University of Rome “Sapienza”, II School, Italy

Received November 27, 2013 – Accepted March 27, 2014

A valid approach to treating frontal fibrosing alopecia (FFA), a scarring alopecia, does not yet exist. The aim of this study is to evaluate the efficacy of a topical application composed of minoxidil, hydrocortisone butyrate, 17α-estradiol, ciclosilicone pentamer, and alcohol in women affected by FFA. Forty women affected by FFA were treated with 2 ml of a topical lotion composed of 2% minoxidil base, 0.08% hydrocortisone butyrate, 0.05% 17α-estradiol, 16% ciclosilicone pentamer, 96° alcohol, applied once a day on the scalp. A score index, based on the comparison of the photos, taken at the beginning (T0) and after 36 months (T36), was used. The topical lotion led to an improvement in 20 patients, stabilization in 15 patients and worsening of the clinical condition in 5 women. This topical lotion induces a considerable improvement or stabilization of frontal fibrosing alopecia.