III REUNIÓN NACIONAL EN ENFERMEDADES AUTOINMUNES SISTÉMICAS

Juan Jiménez Alonso / Granada

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- Etiopatogenia
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PubMed/SLE: 47.706 citas!!!!

4-6/día

1800 abstracts aprox.
desde septbre 2009
138 diapositivas...

Etiopatogenia

- estudios sobre productos tóxicos/químicos implicados: *pesticidas, disolventes, ...*
- estudios sobre virus *(EB, parvovirus...)*
- numerosos estudios inmunológicos/genéticos

Rheumatology (Oxford). 2010 Jul 31. [Epub ahead of print]

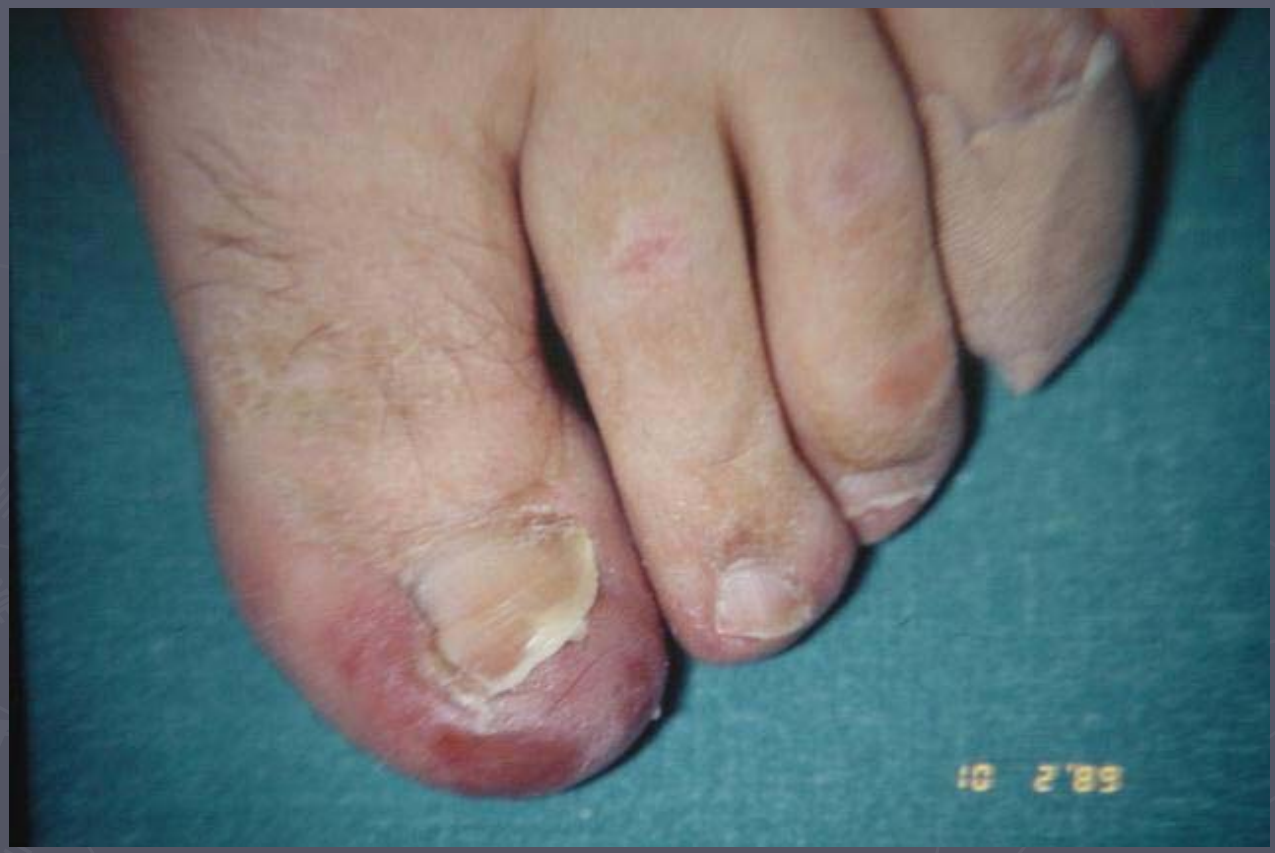
Occupational and environmental exposures and risk of systemic lupus erythematosus: silica, sunlight, solvents.

Cooper GS, Wither J, Bernatsky S, Claudio JO, Clarke A, Rioux JD; CaNIOS GenES Investigators, Fortin PR.

Department of Environmental and Occupational Health, The George Washington University, School of Public Health and Health Services, National Center for Environmental Assessment, US Environmental Protection Agency, Washington, DC, USA, Department of Rheumatology, Toronto Western Hospital, Toronto, ON, Department of Medicine, McGill University Health Centre, Montreal, Health Care Outcomes and Research, Toronto Western Hospital, University Health Network, Laboratoire de génétique et médecine génomique en inflammation, Toronto Western Hospital, University of Toronto, Toronto, ON and University of Toronto, Toronto, ON, Canada.

Abstract

Objectives. We examined occupational and non-occupational exposures in relation to risk of SLE in a case-control study conducted through the Canadian Network for Improved Outcomes in SLE (CaNIOS). Methods. SLE cases (n = 258) were recruited from 11 rheumatology centres across Canada. Controls (without SLE, n = 263) were randomly selected from phone number listings and matched to cases by age, sex and area of residence. Data were collected using a structured telephone interview. Results. An association was seen with outdoor work in the 12 months preceding diagnosis [odds ratio (OR) 2.0; 95% CI 1.1, 3.8]; effect modification by sun reaction was suggested, with the strongest effect among people who reported reacting to midday sun with a blistering sunburn or a rash (OR 7.9; 95% CI 0.97, 64.7). Relatively strong but imprecise associations were seen with work as an artist working with paints, dyes or developing film (OR 3.9; 95% CI 1.3, 12.3) and work that included applying nail polish or nail applications (OR 10.2; 95% CI 1.3, 81.5). Patients were more likely than controls to report participation in pottery or ceramics work as a leisure activity, with an increased risk among individuals with a total frequency of at least 26 days (OR 2.1; 95% CI 1.1, 3.9). Analyses of potential respirable silica exposures suggested an exposure-response gradient (OR 1.0, 1.4. and 2.1 for zero, one and two or more sources of exposure, respectively; trend test P < 0.01). Conclusions. This study supports the role of specific occupational and non-occupational exposures in the development of SLE.



Clínica

- hay todo tipo de artículos, cartas, de mayor o menor interés...
- Artritis erosiva del LES y Ac antiCCP +
- Niveles bajos de Vit. D/actividad lúpica. Fatiga
- Anti U1RNP en LCR y antiRab guanosina en enfermos con afectación del SNC
- Aterosclerosis: *...Acs.antiHDL COL, anti ApoA1, antiPCR...*
- Recurrencias subclínicas de NL tras TX renal*... a vigilar: Tx negros, mujeres y jóvenes.*
- EMBARAZO

Arthritis Rheum. 2010 Apr;62(4):1153-7.

Cutaneous manifestations of neonatal lupus and risk of subsequent congenital heart block.

Izmirly PM, Llanos C, Lee LA, Askanase A, Kim MY, Buyon JP.

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Abstract

OBJECTIVE: Cutaneous disease associated with placental transport of maternal anti-SSA/Ro or anti-SSB/La antibodies is transient, and children often appear to be otherwise healthy. However, the impact of this manifestation of neonatal lupus (NL) on the risk of cardiac disease occurring in a future pregnancy is critical for family counseling and for powering preventive trials. The purpose of this study was to determine the recurrence rates of NL, with specific focus on cardiac NL following cutaneous NL in a child enrolled in the Research Registry for Neonatal Lupus (RRNL). METHODS: Fifty-eight families who were enrolled in the RRNL met the following inclusion criteria for our study: maternal anti-SSA/Ro or anti-SSB/La antibodies, a child with cutaneous NL, and a pregnancy subsequent to the child with cutaneous NL. RESULTS: The majority of the 58 mothers (78%) were Caucasian. Of 77 pregnancies that occurred following the birth of a child with cutaneous NL, the overall recurrence rate for any manifestation of NL was 49% (95% confidence interval [95% CI] 37-62%); 14 pregnancies (18.2%) were complicated by cardiac NL, 23 (29.9%) by cutaneous NL, and 1 (1.3%) by hematologic/hepatic NL. A subset analysis was restricted to the 39 children who were born after the initial child with cutaneous NL had been enrolled in the RRNL. The overall recurrence rate for NL was 36% (95% CI 20-52%); 5 pregnancies (12.8%) were complicated by cardiac NL and 9 (23.1%) by cutaneous NL. There were no significant differences in the following maternal risk factors for having a subsequent child with cardiac or cutaneous NL: age, race/ethnicity, anti-SSB/La status, diagnosis, use of nonfluorinated steroids, or breastfeeding. The sex of the subsequent fetus did not influence the development of cardiac or cutaneous NL. CONCLUSION: Based on data from this large cohort, the identification of cutaneous NL in an anti-SSA/Ro antibody-exposed infant is particularly important, since it predicts a 6-10-fold risk of a subsequent child developing cardiac NL.

J Am Coll Cardiol. 2010 Jun 15;55(24):2778-84.

The importance of the level of maternal anti-Ro/SSA antibodies as a prognostic marker of the development of cardiac neonatal lupus erythematosus a prospective study of 186 antibody-exposed fetuses and infants.

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Abstract

OBJECTIVES: The purpose of this study was to determine whether cardiac complications of neonatal lupus erythematosus (NLE) are related to maternal anti-Ro and anti-La autoantibody-levels.

BACKGROUND: Autoantibody-positive mothers are frequently referred for serial echocardiography because of the elevated fetal risk of developing immune-mediated heart block. Little is known why only some and not all offspring are affected.

METHODS: All cases referred since 2000 for serial fetal echocardiography or cardiac complications related to maternal antibodies were included. Patients without cardiac NLE (group 1) and with cardiac NLE (group 2) were compared. Antibody levels were measured by enzyme-linked immunosorbent assay with a cutoff value of 8 U/ml for a positive test result.

RESULTS: Group 1 included 146 serially screened fetuses with normal pregnancy outcomes. Group 2 consisted of 40 fetuses/neonates with a diagnosis of heart block or endocardial fibroelastosis or both, and included 4 fetuses diagnosed during serial screening. All cardiac complications were associated with moderate (>or=50 U/ml; 15%) or high (>or=100 U/ml; 85%) maternal anti-Ro levels, independently of anti-La antibody titres. The event rate of complete heart block was 5% for prospectively screened fetuses with Ro-values >or=50 U/ml (odds ratio: 7.8) and 0% for fetuses with lower titres ($p < 0.0001$). Infants with pre-natal exposure to high-titre anti-La levels >or=100 U/ml were the most likely to have noncardiac features of NLE (event rate: 57%; odds ratio: 4.7).

CONCLUSIONS: Our findings support that the amount of maternal antibodies, rather than their presence, is associated with fetal tissue injury. As anti-Ro levels correlate with the risk of cardiac complications, serial echocardiography should be limited to women with high anti-Ro-titres.

J Rheumatol. 2010 Apr;37(4):754-8. Epub 2010 Mar 15.

The effect of lupus nephritis on pregnancy outcome and fetal and maternal complications.

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Abstract

OBJECTIVE: To evaluate the effect of lupus nephritis on pregnancy with respect to fetal outcome, maternal complications, and lupus activity.

METHODS: All pregnancies seen between 1970 and 2003 in the Lupus Clinic were evaluated for the 3 outcomes. Renal disease was defined as the presence of nephrotic syndrome, dialysis, renal transplant, serum creatinine > 120 mmol/l, proteinuria, sterile hematuria and pyuria, or the presence of casts. Fetal complications were evaluated in pregnancies resulting in either live births or stillbirths. Generalized estimating equations were used to test for differences in outcomes between pregnancies with and without the presence of active renal disease. Repeated measures adjustments were made in the model for multiple pregnancies in the same mother.

RESULTS: There were 193 pregnancies in 104 women. Of these, 81 occurred in the presence of active renal disease during the study period, defined as 6 months prior to conception until the date of pregnancy outcome. One hundred twelve pregnancies were defined as nonrenal. No statistical difference was found in pregnancy outcome. Fetal complications were not different between the 2 groups with the exception of low birth weight and congenital malformations, which were observed more frequently in the renal group. Pregnancy-induced hypertension was more frequent in pregnancies with renal disease. Lupus flares were also more likely to occur in pregnancies with renal disease compared to those without.

CONCLUSION: Lupus nephritis in pregnancy does not lead to worsened pregnancy or fetal outcomes. Active renal disease, however, is associated with pregnancy-induced hypertension, as well as a flare of lupus activity during pregnancy.

Sábado 11.09.10
IDEAL

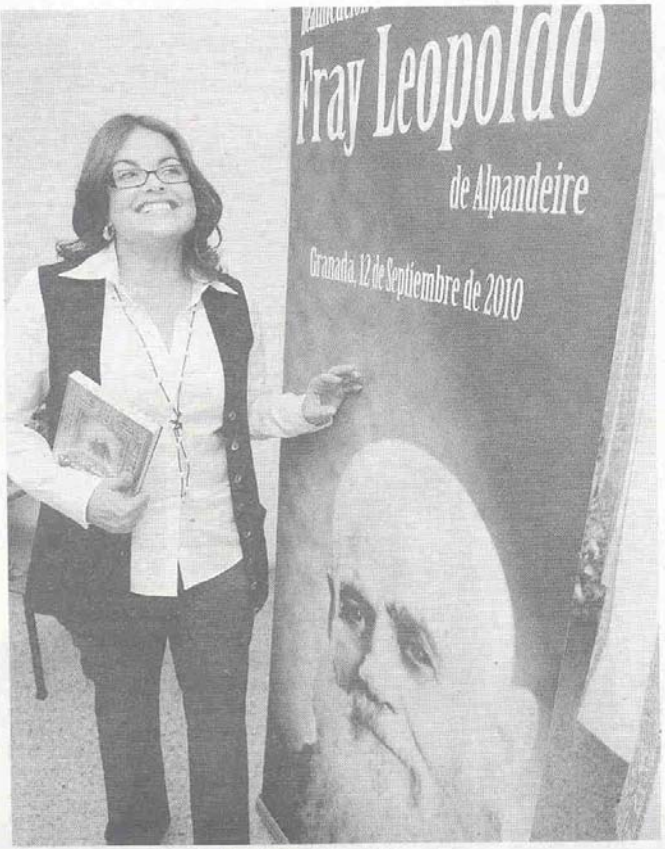
«Estoy aquí gracias a mi Fray Leopoldo de Alpandeire y su milagro»

Ileana Martínez se curó de un peligroso brote de Lupus, y los médicos determinaron que su mejoría repentina no tenía explicación científica alguna

:: CARMEN TÉBAR

GRANADA. La actriz puertorriqueña Ileana Martínez notó por primera vez los síntomas de su enfermedad en el verano de 1994. Le dolía la cabeza como resultado de una anemia hemolítica que le había producido el Lupus. Desde entonces, su cuadro clínico fue aumentando con una gran lista de enfermedades y patologías. Su última analítica fue muy crítica, e incluso el sacerdote acudió a su cama a darle la extremaunción. Pero una amiga suya rezó a Fray Leopoldo, y a la mañana siguiente comenzó a recuperarse de manera espectacular.

Diez días después recibía el alta. Ahora, cuando han pasado tantos años, está en Granada para acudir el próximo domingo a la Beatificación de Fray Leopoldo. Su amigo Alfonso Ramírez, vicepostulador de la causa, le insistió y ella no pudo negarse, ya que, como ella dice, «estoy aquí gracias a mi Fray Leopoldo de Alpandeire y su milagro». Juntos, y con la compañía de Rafael Pozo, el representante provincial de los Capuchinos andaluces, explicaron todo el proceso que vivieron para que esta recuperación de Ileana se reconociera como un milagro. Y no un milagro cualquiera, sino el decisivo para la beatificación del fraile de Alpandeire.



Ileana, frente al cartel de la Beatificación. :: EFE

Una carta como testimonio

Ileana, años después de su ingreso, escribió una carta a sus hijos contándoles todo el favor que le hizo Fray Leopoldo. Esa carta llegó a las manos de Alfonso Ramírez, y comenzó a recoger todos los datos y pruebas necesarios. «Fue un proceso complicado, ya que muchas eran a mano o en italiano, y había que traducir. Era la primera vez que me encontraba con un material así. Pero lo importante es que los médicos determinaron que su recuperación no tenía explicación científica, era un milagro», dijo el vicepostulador. La carta íntegra que Ileana escribió aparece hoy en el especial de 160 páginas que regala IDEAL dedicado a la Beatificación de Fray Leopoldo.

Ileana recibió de repente una llamada: «me preguntaron si estaba bien, y ni siquiera sabía quién era. Empezaban a investigar mi caso

Tratamiento

- No podía faltar la HCQ!!: cada vez más estudios sobre su utilidad: *menos daño orgánico/mejor pronóstico, menos afectación cutánea (LUMINA), menos riesgo de complicaciones fetales en madres portadoras de acs. antiRo/SSA, reducción glucemia...*
- CS*: dosis > 7.5 aumentan IR, pero no bajas (RCV)*
- Dosis intensivas o no de CFM en NL *(protocolo SEMI-SEN), dudas eficacia GnRHanálogos*
- DHEA*: Estudio muy bien diseñado: no eficacia en astenia*

Ann Rheum Dis. 2010 Aug;69(8):1423-9.

Allogenic mesenchymal stem cells transplantation in refractory systemic lupus erythematosus: a pilot clinical study.

Liang J, Zhang H, Hua B, Wang H, Lu L, Shi S, Hou Y, Zeng X, Gilkeson GS, Sun L.

Department of Rheumatology and Immunology, The Affiliated Drum Tower Hospital of Nanjing University Medical School, Nanjing, China.

Comment in:

Ann Rheum Dis. 2010 Aug;69(8):1413-4.

Abstract

OBJECTIVE: To determine the safety and efficacy of allogeneic mesenchymal stem cell transplantation (MSCT) in refractory systemic lupus erythematosus (SLE).

METHODS: A total of 15 patients with persistently active SLE underwent MSCT. Outcome was evaluated by changes in the SLE disease activity index (SLEDAI), serological features (anti-nuclear antibodies and anti-double-stranded DNA (anti-dsDNA)), renal function and percentage of peripheral blood regulatory T cells.

RESULTS: From 11 March 2007 to 4 November 2008, 15 patients with persistently active SLE were enrolled and underwent MSCT. The mean follow-up period was 17.2+/-9.5 months. A total of 13 patients have been followed for more than 12 months. All patients clinically improved following treatment with mesenchymal stem cells with a marked decrease in the SLEDAI score and 24 h proteinuria. At 12-month follow-up, SLEDAI scores decreased from 12.2+/-3.3 to 3.2+/-2.8 and proteinuria decreased from 2505.0+/-1323.9 to 858.0+/-800.7 mg/24 h (all $p<0.05$, by paired t test, n=12). At 1-year follow-up in 13 patients, 2 had a relapse of proteinuria, while the other 11 continue to have decreased disease activity on minimal treatment. Anti-dsDNA levels decreased. Improvement in glomerular filtration rate was noted in two patients in which formal testing was performed. Non-renal-related manifestations also improved significantly. No serious adverse events were reported.

CONCLUSION: Allogeneic MSCT in patients with refractory lupus resulted in amelioration of disease activity, improvement in serological markers and stabilisation of renal function. MSCT appears beneficial in treatment of patients with SLE refractory to conventional treatment options.

J Immunol. 2009 Nov 15;183(10):6346-58. Epub 2009 Oct 19.

Regulatory T cell (Treg) subsets return in patients with refractory lupus following stem cell transplantation, and TGF-beta-producing CD8+ Treg cells are associated with immunological remission of lupus.

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Abstract

Compared with conventional drug therapy, autologous hemopoietic stem cell transplantation (HSCT) can induce very-long-term remission in refractory lupus patients. Herein, we show that in posttransplant patients, both CD4(+)CD25(high)FoxP3(+) and an unusual CD8(+)FoxP3(+) Treg subset return to levels seen in normal subjects; accompanied by almost complete inhibition of pathogenic T cell response to critical peptide autoepitopes from histones in nucleosomes, the major lupus autoantigen from apoptotic cells. In addition to a stably sustained elevation of FoxP3, posttransplant CD8 T cells also maintained markedly higher expression levels of latency-associated peptide (LAP), CD103, PD-1, PD-L1, and CTLA-4, as compared with pretransplant CD8 T cells that were identically treated by a one-time activation and rest in short-term culture. The posttransplant CD8 regulatory T cells (Treg) have autoantigen-specific and nonspecific suppressive activity, which is contact independent and predominantly TGF-beta dependent. By contrast, the pretransplant CD8 T cells have helper activity, which is cell contact dependent. Although CD4(+)CD25(high) Treg cells return during clinical remission of conventional drug-treated lupus, the posttransplant patient's CD8 Treg cells are considerably more potent, and they are absent in drug-treated patients in whom CD4 T cell autoreactivity to nucleosomal epitopes persists even during clinical remission. Therefore, unlike conventional drug therapy, hemopoietic stem cell transplantation generates a newly differentiated population of LAP(high) CD103(high) CD8(TGF-beta) Treg cells, which repairs the Treg deficiency in human lupus to maintain patients in true immunological remission.

A seguir la pista de..

- Estatinas
- Biológicos: *Belimumab*
- Nuevas moléculas:
  - *Inhibidores de topoisomerasa I (irinotecan)*

Arthritis Rheum. 2010 Jul;62(7):2073-85.

Statins, inhibitors of 3-hydroxy-3-methylglutaryl-coenzyme A reductase, function as inhibitors of cellular and molecular components involved in type I interferon production.

Amuro H, Ito T, Miyamoto R, Sugimoto H, Torii Y, Son Y, Nakamichi N, Yamazaki C, Hoshino K, Kaisho T, Ozaki Y, Inaba M, Amakawa R, Fukuhara S.

Kansai Medical University, Moriguchi, Osaka, Japan.

Abstract

OBJECTIVE: Statins, which are used as cholesterol-lowering agents, have pleiotropic immunomodulatory properties. Although beneficial effects of statins have been reported in autoimmune diseases, the mechanisms of these immunomodulatory effects are still poorly understood. Type I interferons (IFNs) and plasmacytoid dendritic cells (PDCs) represent key molecular and cellular pathogenic components in autoimmune diseases such as systemic lupus erythematosus (SLE). Therefore, PDCs may be a specific target of statins in therapeutic strategies against SLE. This study was undertaken to investigate the immunomodulatory mechanisms of statins that target the IFN response in PDCs.

METHODS: We isolated human blood PDCs by flow cytometry and examined the effects of simvastatin and pitavastatin on PDC activation, IFNalpha production, and intracellular signaling.

RESULTS: Statins inhibited IFNalpha production profoundly and tumor necrosis factor alpha production modestly in human PDCs in response to Toll-like receptor ligands. The inhibitory effect on IFNalpha production was reversed by geranylgeranyl pyrophosphate and was mimicked by either geranylgeranyl transferase inhibitor or Rho kinase inhibitor, suggesting that statins exert their inhibitory actions through geranylgeranylated Rho inactivation. Statins inhibited the expression of phosphorylated p38 MAPK and Akt, and the inhibitory effect on the IFN response was through the prevention of nuclear translocation of IFN regulatory factor 7. In addition, statins had an inhibitory effect on both IFNalpha production by PDCs from SLE patients and SLE serum-induced IFNalpha production.

CONCLUSION: Our findings suggest a specific role of statins in controlling type I IFN production and a therapeutic potential in IFN-related autoimmune diseases such as SLE.

Lupus. 2010;19(8):927-34. Epub 2010 Apr 21.

Atorvastatin therapy reduces interferon-regulated chemokine CXCL9 plasma levels in patients with systemic lupus erythematosus.

Ferreira GA, Teixeira AL, Sato EI.

Rheumatology Division, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil.

Abstract

A recent study showed transcriptional levels of interferon-inducible chemokines in peripheral blood cells were associated with disease activity and organ damage in systemic lupus erythematosus, and may be useful in monitoring disease activity and prognosis. Our objective was to evaluate the capacity of atorvastatin to reduce plasma levels of interferon-regulated chemokines (CCL2, CCL3 and CXCL9) and to study the correlation between these chemokines and disease activity in patients with systemic lupus erythematosus. Eighty-eight female patients with systemic lupus erythematosus were divided into two groups: 64 receiving 20 mg/day of atorvastatin (intervention group) and 24 without atorvastatin (control group). All patients were followed for 8 weeks. At baseline and after 8 weeks laboratory tests were performed for all patients. Plasma levels of chemokines were measured by ELISA using commercial kits (DuoSet, R&D Systems, Minneapolis, USA). In a univariate analysis we found correlation between CCL2, CCL3 and CXCL9 plasma levels and SLEDAI score. In the intervention group we observed a significant decrease in CXCL9 plasma levels comparing baseline and levels at the end of the study ($p = 0.04$); however, no differences were observed regarding CCL2 or CCL3 plasma levels in this study. No significant difference was observed in the plasma levels of these chemokines in the control group. We conclude that treatment with atorvastatin was associated with a significant decrease in the plasma levels of CXCL9 in patients with systemic lupus erythematosus. As the plasma levels of CXCL9 correlated with the SLEDAI score, we ask whether reducing levels of this chemokine could help to control systemic lupus erythematosus activity.

J Immunol. 2010 Feb 15;184(4):2175-82. Epub 2010 Jan 18.

Reversal of established lupus nephritis and prolonged survival of New Zealand black x New Zealand white mice treated with the topoisomerase I inhibitor irinotecan.

Frese-Schaper M, Zbaeren J, Gugger M, Monestier M, Frese S.

Department of Clinical Research, University Hospital Bern, Bern, Switzerland.

Abstract

Systemic lupus erythematosus is a chronic autoimmune disorder that predominantly affects women of childbearing age. Lupus-associated glomerulonephritis is a major cause of mortality in these patients. Current treatment protocols for systemic lupus erythematosus include cyclophosphamide, prednisolone, azathioprine, and mycophenolate mofetil. However, in mice none of these agents alone or in combination were shown to reverse established proteinuria. Using New Zealand Black x New Zealand White F1 mice, we report that administration of the topoisomerase I inhibitor irinotecan from week 13 completely prevented the onset of proteinuria and prolonged survival up to at least 90 wk without detectable side effects. Furthermore, application of irinotecan to mice with established lupus nephritis, as indicated by grade 3+ (> or =300 mg/dl) and grade 4+ (> or =2000 mg/dl) proteinuria and, according to a median age of 35 wk, resulted in remission rates of 75% and 55%, respectively. Survival was significantly prolonged with 73 wk (grade 3+ and 4+ combined) versus 40 wk for control animals. Although total IgG and anti-dsDNA Abs in the serum and mesangial IgG deposits in the kidneys were not reduced in irinotecan-treated mice, subendothelial immune deposits were considerably diminished, suggesting a prevention of glomerular basement membrane disruption. This effect was accompanied by increased rates of ssDNA breaks and inhibition of renal cell apoptosis being different to what is known about irinotecan in anticancer therapy. In conclusion, our data provide evidence that irinotecan might represent an entirely new strategy for the treatment of systemic lupus erythematosus.

Arthritis Rheum. 2009 Dec;60(12):3744-54.

Amelioration of brain pathology and behavioral dysfunction in mice with lupus following treatment with a tolerogenic peptide.

Lapter S, Marom A, Meshorer A, Elmann A, Sharabi A, Vadai E, Neufeld A, Sztainberg Y, Gil S, Getselter D, Chen A, Mozes E.

The Weizmann Institute of Science, Rehovot, Israel.

Comment in:

Arthritis Rheum. 2009 Dec;60(12):3531-3.

Abstract

OBJECTIVE: Central nervous system (CNS) involvement in systemic lupus erythematosus (SLE) is manifested by neurologic deficits and psychiatric disorders. The aim of this study was to examine SLE-associated CNS pathology in lupus-prone (NZBxNZW)F1 (NZB/NZW) mice, and to evaluate the ameliorating effects of treatment with a tolerogenic peptide, hCDR1 (human first complementarity-determining region), on these manifestations.

METHODS: Histopathologic analyses of brains from lupus-prone NZB/NZW mice treated with vehicle, hCDR1, or a control scrambled peptide were performed. The messenger RNA expression of SLE-associated cytokines and apoptosis-related molecules from the hippocampi was determined. Anxiety-like behavior was assessed by open-field tests and dark/light transfer tests, and memory deficit was assessed using a novel object recognition test.

RESULTS: Infiltration was evident in the hippocampi of the lupus-afflicted mice, and the presence of CD3+ T cells as well as IgG and complement C3 complex deposition was observed. Furthermore, elevated levels of gliosis and loss of neuronal nuclei immunoreactivity were also observed in the hippocampi of the mice with lupus. Treatment with hCDR1 ameliorated the histopathologic changes. Treatment with hCDR1 down-regulated the high expression of interleukin-1beta (IL-1beta), IL-6, IL-10, interferon-gamma, transforming growth factor beta, and the proapoptotic molecule caspase 8 in the hippocampi of the mice with lupus, and up-regulated expression of the antiapoptotic bcl-xL gene. Diseased mice exhibited increased anxiety-like behavior and memory deficit. Treatment with hCDR1 improved these parameters, as assessed by behavior tests.

CONCLUSION: Treatment with hCDR1 ameliorated CNS pathology and improved the tested cognitive and mood-related behavior of the mice with lupus. Thus, hCDR1 is a novel candidate for the treatment of CNS lupus.


SEMI
LA VISIÓN GLOBAL DE LA PERSONA ENFERMA
XXVII
Congreso
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Sademi
Sociedad Andaluza de Medicina Interna
Palacio de Congresos
19-20 Mayo - 2011
Granada