The treatment of this disease is difficult and disappointing. The remarkable effect of inhibition of IL-1 has led to new expectations for these patients.5,7 There is currently no Anakinra available in Argentina.

The interest of this article lies in the presence of a monoclonal IgG variant, together with the clinical and histological lesions and the subsequent progression to multiple myeloma.

References


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there appearance forces the clinician to consider the possibility of rhombencephalitis.\textsuperscript{4} Regarding immunosuppressive treatment of the patients in the series by Horta-Baas et al., five cases had previously received MMF but none rituximab.\textsuperscript{1} Four cases of meningitis/encephalitis due to \textit{L. monocytogenes} associated to rituximab have been published, all of them in adult patients with an underlying hematologic malignant process.\textsuperscript{5,6} Infection with \textit{L. monocytogenes} in pSLE is rare, found in the literature only in a 5 year old patient with type IV lupus nephritis, neurologic alterations and antiphospholipid syndrome who developed bacteremia due to \textit{L. monocytogenes}, treated and solved with ampicillin.\textsuperscript{7} One aspect that is also interesting in our patient is the subsequent appearance of other severe neurologic infections after the administration of rituximab.

\textbf{References}


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\textbf{Genetic Characteristics of Rheumatic Patients Developing Inflammatory Skin Lesions Induced by Biologic Therapy}\textsuperscript{3-7}

Características genéticas de pacientes reumatológicos que desarrollan lesiones cutáneas inflamatorias inducidas por fármacos biológicos

\textit{Dear Editor,}

The appearance of inflammatory skin lesions (ISL), induced by biological drugs, mainly cutaneous psoriasis, has been extensively described.\textsuperscript{1,2-3} The hypothesis is that in patients with genetic susceptibility present an activation of alternative inflammatory pathways such as interferon-\textit{α} 1.2, but this has not been demonstrated and no genetic studies in these patients exist.

We conducted a prospective observational study analyzing genetic data from patients of the Rheumatology Department of the Hospital del Mar (Barcelona) who developed \textit{de novo} ISL due to biological therapy between January 2008 and December 2012.

The demographic and clinical variables evaluated were: age, sex, diagnosis of ISL, rheumatic disease and duration (in years), biological drug employed and time from onset to the start of the drug (weeks). Genetic variables were the presence of HLA-B27, HLA-DR1, HLA-DR4 and HLA-DR7 alleles (detected by standard PCR), HLA-CW6 (Sanger sequencing using the indirect marker rs4406273) and the deletion of two genes \textit{lute cornified envelope (LCE)}, \textit{LCE3C/LCE3B-del} (with a multiplex PCR experiment\textsuperscript{4}). Fifteen patients who developed ISL (prevalence 2.5%) were included. They had a mean age of 43.9 ± 12.4 years and 73.3% were female. The diagnoses of ISL were: seven skin psoriasis (five palmoplantar pustulosis, one with psoriasis \textit{vulgaris} and one with \textit{guttata})), three alopecia areata, two cutaneous lupus, one eczema, one suppurative hidradenitis and one with erythema multiforme. Rheumatological diagnoses were: three rheumatoid arthritis, ankylosing spondylitis 6, four non-radiological axial spondyloarthritis and two psoriatic arthritis, mean disease duration of 13.1 ± 7.4 years. Biologic drugs were eight cases using adalimumab, etanercept in four, infliximab in two and abatacept in one, with a mean time of onset of 57.1 ± 62.1 weeks.

Genetically, seven patients had HLA-B27, four were HLA-CW6 positive (26%), one with psoriasis, one positive HLA-DR1, another HLA-DR4 and six HLA-DR7 positive patients (40%), three with psoriasis. In four patients (26.7%) two LCE3C/LCE3B deleted alleles were detected and 11 (73.3%) had one deleted allele (Table 1). LCE3C/LCE3B allele frequency was 63.6%.

The low proportion of patients with the presence of HLA-CW6 and HLA-DR7 alleles (especially in cases of psoriasis) stands out, lower than that found in populations of cutaneous psoriasis,\textsuperscript{2,3} which could be due to the predominant type of psoriasis, palmoplantar pustulosis, since the average age of patients was older than 40 years (HLA-CW6 and HLA-DR7 alone have been associated with type I psoriasis, with an onset before 40 years of age, and with the \textit{vulgaris} and \textit{guttata} subtypes\textsuperscript{3}).

In our series, the presence of the deletion of the two LCE genes (allele frequency of 63.6%) was consistent with the frequently seen in population samples with inflammatory diseases (62%–70%) but higher than that reported in control populations (55%–60%).\textsuperscript{4,8-10} But what stands out is that all patients with ISL had at least one copy of the LCE3C/LCE3B deleted alleles (absence of non-deleted homozygous individuals). In the general population, the frequency of non-deleted homozygotes is around 18%\textsuperscript{3,9,10} and disruption of the skin barrier occurs in relation to the number of copies of LCE3C/LCE3B, being undetectable in carriers of the homozygous deletion\textsuperscript{a} and reduced in heterozygotes.

This observational study of a series of cases of ISL induced by biological drugs and is the first to include genetic data, although further studies are needed with larger numbers of patients and a control group to better study this process and help establish if there is a pattern of genetic susceptibility as in the case of LCE3C/LCE3B deletions.