there appearance forces the clinician to consider the possibility of rhombencephalitis.[4] Regarding immunosuppressive treatment of the patients in the series by Horta-Baas et al., five cases had previously received MMF but none rituximab.[1] Four cases of meningitis/encephalitis due to *L. monocytogenes* associated to rituximab have been published, all of them in adult patients with an underlying hematologic malignant process.[5,6] Infection with *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 *L. monocytogenes*, treated and solved with ampicillin.[7] One aspect that is also interesting in our patient is the subsequent appearance of other severe neurologic infections after the administration of rituximab.

## References


1. Horta-Baas G, Guerrero-Soto O, Barile-Fabris L. Central nervous system infection by *Listeria monocytogenes* in patients with systemic lupus erythematosus: analysis of 26 cases, including the report of a new case. Reumatol Clin. 2013;9:340–7.
2. Mylonakis E, Hohmann EL, Calderwood SB. Central nervous system infection with *Listeria monocytogenes*. 33 years' experience at a general hospital and review of 776 episodes from the literature. Medicine (Baltimore). 1998;77:313–36.
3. Bennett L. *Listeria monocytogenes*. In: Mandell GL, Bennett JE, Dolin R, editors. Mandell, Douglas, and Bennett's principles and practice of infectious diseases. Philadelphia: Elsevier Inc.; 2010. p. 2707–14.
4. Shaffer DN, Drevets DA, Farr RW. *Listeria monocytogenes* rhomboencephalitis with cranial-nerve palsies: a case report. W Va Med J. 1998;94:80–3.
5. Bodro M, Paterson DL. Listeriosis in patients receiving biologic therapies. Eur J Clin Microbiol Infect Dis. 2013;32:1225–30.
6. Lin TS, Donohue KA, Byrd JC, Lucas MS, Hoke EE, Bengtson EM, et al. Consolidation therapy with subcutaneous alemtuzumab after fludarabine and rituximab induction therapy for previously untreated chronic lymphocytic leukemia: final analysis of CALGB 10101. J Clin Oncol. 2010;28:4500–6.
7. Tobón GJ, Serna MJ, Cañas CA. *Listeria monocytogenes* infection in patients with systemic lupus erythematosus. Clin Rheumatol. 2013;32 Suppl. 1: S25–7.



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## Genetic Characteristics of Rheumatic Patients Developing Inflammatory Skin Lesions Induced by Biologic Therapy☆

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

*Dear Editor,*

The appearance of inflammatory skin lesions (ISL), induced by biological drugs, mainly cutaneous psoriasis, has been extensively described.[1–3] The hypothesis is that in patients with genetic susceptibility present an activation of alternative inflammatory pathways such as interferon-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 *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), biologic 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 *late cornified envelope* (LCE), LCE3C_LCE3B-del (with a *multiplex* PCR experiment[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 *vulgaris* and *one with 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%), only 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,[5–7] 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 *vulgaris and guttate* subtypes[5]).

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%).[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%[4,9,10] 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[4] 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 a pattern of genetic susceptibility as in the case of LCE3C_LCE3B deletions.

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**Table 1**
Genetic Characteristics of Patients with Cutaneous Lesions Induced.

| ISL | N.p. Total | N.p. HLA-B27+ | N.p. HLA-CW6+ | N.p. HLA-DR1+ | N.p. HLA-DR4+ | N.p. HLA-DR7+ | LCE 3C-LCE 3B-del D+/D+ | LCE 3C-LCE 3B-del D+/D− |
|---|---|---|---|---|---|---|---|---|
| Skin psoriasis | 7 | 4 | 1 | 1 | 0 | 3 | 3 | 4 |
| Alopecia areata | 3 | 1 | 1 | 0 | 0 | 1 | 1 | 2 |
| Cutaneous lupus | 2 | 0 | 1 | 0 | 0 | 1 | 0 | 2 |
| Eczema | 1 | 1 | 0 | 0 | 0 | 1 | 0 | 1 |
| Hydradenitis | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 1 |
| Erythema multiforme | 1 | 0 | 1 | 0 | 1 | 0 | 0 | 1 |
| Total | 15 | 7 | 4 | 1 | 1 | 6 | 4 | 11 |

LCE 3B-3C-LCE del, deletion of the late cornified envelope; ISL, induced skin lesions; N.p., number of patients; +, positive; D+, deleted; D−, non-deleted.

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## Conflict of Interest

The authors have no conflict of interest to state.

## References

1. Russell AS, Rosenbaum JT. Anti-tumor necrosis factor therapies in immune-mediated rheumatic diseases. Other observations from the clinic. J Rheumatol Suppl. 2010;85:53–62.
2. Collamer AN, Battafarano DF. Psoriatic skin lesions induced by tumor necrosis factor antagonist therapy: clinical features and possible immunopathogenesis. Semin Arthritis Rheum. 2010;40:233–40.
3. Ko JM, Gottlieb AB, Kerbleski JF. Induction and exacerbation of psoriasis with TNF-blockade therapy: a review and analysis of 127 cases. J Dermatol Treat. 2009;20:100–8.
4. De Cid R, Riveira-Muñoz E, Zeeuwen PL, Robarge J, Liao W, Dannhauser EN, et al. Deletion of the late cornified envelope LCE3C and LCE3B genes as a susceptibility factor for psoriasis. Nat Genet. 2009;41:211–5.
5. Ikaheimo I, Tiilikainen A, Karvonen J, Silvennoinen-Kassinen S. HLA risk haplotype Cw6, DR7, DQA1*0201 and HLA-Cw6 with reference to the clinical picture of psoriasis vulgaris. Arch Dermatol Res. 1996;288:363–5.
6. Henseler T. Genetics of psoriasis. Arch Dermatol Res. 1998;90:463–76.
7. Asumalahti K, Ameen M, Suomela S, Hagforsen E, Michaëlsson G, Evans J, et al. Genetic analysis of PSORS1 distinguishes guttate psoriasis and palmoplantar pustulosis. J Invest Dermatol. 2003;148:233–5.
8. Riviera-Muñoz E, He SM, Escaramís G, Stuart PE, Hüffmeier U, Lee C, et al. Meta-analysis confirms the LCE3C_LCE3B deletion as a risk factor for psoriasis in several ethnic groups and finds interaction with HLA-Cw6. J Invest Dermatol. 2011;131:1105–9.
9. Docampo E, Giardina E, Riviera-Muñoz E, de Cid R, Escaramís G, Perricone C, et al. Deletion of the LCE3C and LCE3B genes is a susceptibility factor for psoriatic arthritis: a study in Spanish and Italian populations and meta-analysis. Arthritis Rheum. 2011;63:1860–5.
10. Docampo E, Rabionet R, Riviera-Muñoz E, Escaramís G, Julià A, Marsal S, et al. Deletion of the late cornified envelope genes, LCE3C and LCE3B, is associated with rheumatoid arthritis. Arthritis Rheum. 2010;62:1246–51.

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## Usefulness of Ultrasound in Jaccoud's Arthropathy. A Case Report☆

### *La ecografía en la artropatía de Jaccoud. A propósito de un caso*

*To the Editor,*

Joint involvement is one of the initial manifestations in most patients with systemic lupus erythematosus (SLE); ranging from joint pain to severe deforming arthritis.[1] Within the deforming types, non erosive forms, such as *Rhupus* and others such as Jaccoud's arthropathy (JA),[2] non-erosive in principle, occurs in 10%–35% of patients with SLE.[3]

Ultrasound has proven superior to clinical examination in detecting joint and tendon inflammatory activity in patients with SLE.[2] We report a patient with SLE and JA in which this technique was useful in the assessment of disease.

The patient is a 40-year-old woman from Honduras diagnosed with SLE 4 years prior and, has presented during her evolution, joint pain and arthritis of small proximal joints of the hands, wrists, knees and elbows; scarring alopecia; Raynaud's phenomenon and subacute cutaneous lupus erythematosus lesions. She had positive antinuclear antibodies (1/1280), anti-dsDNA, anti-Sm, anti-RNP and anti-CCP (high titers); anemia of chronic diseases and complement consumption. From the onset of the disease she has been treated with hydroxychloroquine, methotrexate and prednisone.

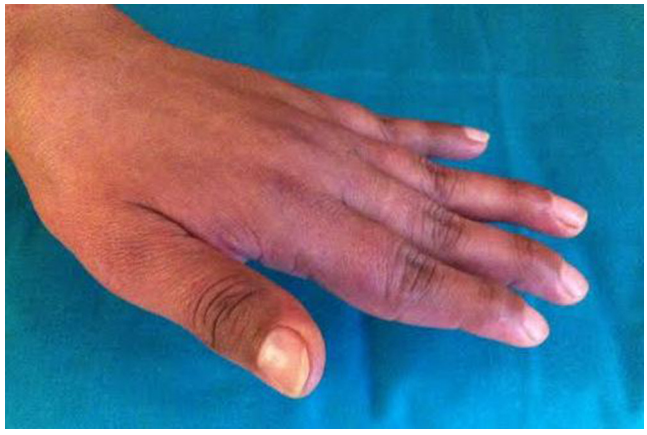

**Fig. 1.** Left hand of the patient with Jaccoud's arthropathy where ulnar deviation of the 5th finger and swan neck deformity of fingers 2–5 is appreciated.

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