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LETTER TO THE EDITOR

T Cell Large Granular Lymphocyte Leukaemia with Cutaneous Infiltration

سرطان الدم الليمفاوي الناتج عن خلية-ت-الكبيرة مع انتشار المرض في الجلد

Sir,

A 63-year-old woman was referred to the Department of Dermatology of the Complejo Hospitalario de Granada, Granada, Spain, in 2016 with painful erythematous desquamative nodules and papules of three weeks' duration. She had a history of stage I infiltrating ductal carcinoma of the breast, unilinear myelodysplastic syndrome with granulocytic involvement, chronic neutropaenia and a diagnosis of T cell (cluster of differentiation [CD]8^+) large granular lymphocyte (LGL) leukaemia. Upon examination, the papules were distributed mainly on the forehead and right upper and lower limbs [Figures 1A–C]. Some of the lesions were fluctuating and suppurative, while the others were of a solid consistency. The examination also revealed oral *aphthae* which were causing dysphagia [Figure 1D]. At referral, the patient was receiving treatment with 50 mg of low-dose cyclosporine on alternate days and 300 µg of granulocyte-colony stimulating factor per week, to which a partial response was noted.

Given the suspicion of leukaemia *cutis*, a biopsy of the lesions was taken. The findings were compatible with a diagnosis of folliculitis, with polymerase chain reaction and direct immunofluorescence tests negative for *Mycobacterium tuberculosis* and immunoglobulin (Ig) G, IgA, IgM and complement 3 deposits, respectively. Consequently, treatment with 500 mg of cloxacillin every six hours and 15 mg of prednisone per day was initiated; however, there was no evidence of clinical improvement. Successive biopsies indicated systemic vasculitis caused by granulomatosis with polyangiitis. Eventually, nine months after the onset of the symptoms, a final biopsy revealed that the papules represented the cutaneous infiltration of LGL leukaemia [Figure 2], associated with secondary interstitial granulomatous dermatitis. At the time of writing, the patient was being treated with combined cyclophosphamide, vincristine, doxorubicin and prednisone (CHOP) therapy which resulted in the resolution of her cutaneous symptoms [Figure 3]. There was no evidence on computed tomography of any systemic progression to other organs.

LGL leukaemia is a low-grade lymphoproliferative disorder characterised by monoclonal expansion in the peripheral blood and bone marrow with either an activated cytotoxic T lymphocyte (i.e. CD8 or $CD57^+$ cells) or, less frequently, a natural killer ($CD3^-$, $CD8^-$ or $CD56^+$ cells) phenotype.[1] Generally, LGLs represent 10–15% of circulating mononuclear cells and are identified morphologically by their large size and rounded or dentate nuclei and abundant cytoplasm with azurophilic granules.[2] Clonality has been confirmed by T cell receptor gene

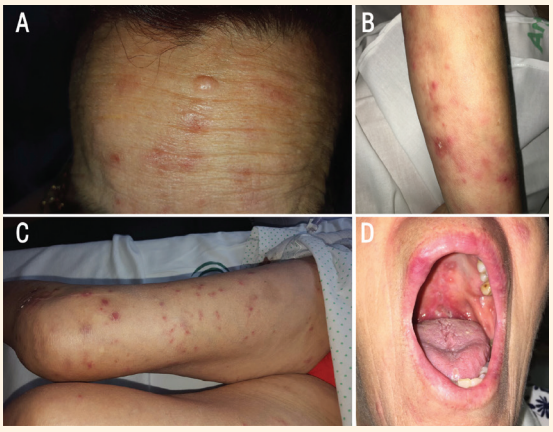

Figure 1: Photographs of infiltrated papules and patches on the (**A**) forehead and right (**B**) upper and (**C**) lower limbs of a 63-year-old woman with large granular lymphocyte leukaemia. The clinical examination also revealed (**D**) major *aphthae* in the oral cavity.

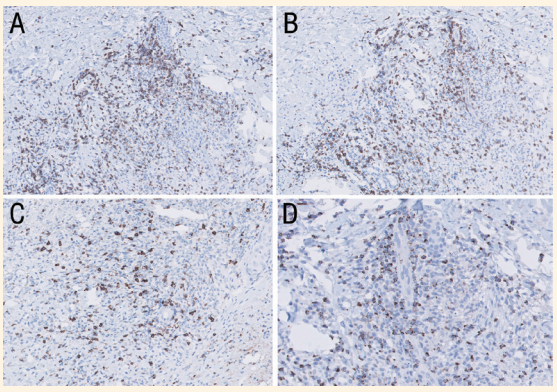

Figure 2: Immunohistochemistry panel at x20 magnification showing positive (**A**) cluster of differentiation (CD)2, (**B**) CD8, (**C**) CD57 and (**D**) T cell intracytoplasmic antigen 1 stains.

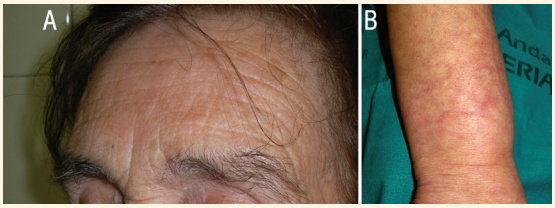

Figure 3: Photographs of the (**A**) forehead and (**B**) upper right limb of a 63-year-old woman showing the resolution of large granular lymphocyte leukaemia-infiltrated papules and patches following chemotherapy treatment.

rearrangement testing.[3] Frequently, LGL leukaemia is related to autoimmune diseases such as Felty's syndrome and has a chronic and indolent course, with a mean survival of 10 years.[4,5] Occasionally, the behaviour of this form of leukaemia can be more aggressive, especially in cases with a natural killer phenotype.[2]

Approximately one-third of patients with LGL leukaemia are clinically asymptomatic, with neutropaenia observed in up to 85% of cases.[3] The disease is sometimes associated with arthritis, cytopaenia and splenomegaly, but only exceptionally with lymphadenopathy.[4] Cutaneous infiltration is rare and usually manifests as papules, nodules or, even less frequently, leg ulcers.[4,6] Other reports have described LGL leukaemia patients presenting with generalised erythema and pruritus, *petechiae* and disseminated granuloma annulare.[6–8] The indolent course of the disease usually permits a 'wait and see' approach, although indications for treatment include recurrent infections, anaemia, symptomatic splenomegaly or severe B symptoms.[5] Immunosuppressants are the first line of treatment, such as methotrexate, cyclosporine, or cyclophosphamide; these monotherapies are effective in almost 50% of patients by correcting cytopaenia without eradicating the leukaemia cells.[9] However, for those with refractory or highly aggressive forms of the disease, CHOP therapy or a similar chemotherapy regimen is recommended. Trials with purine analogues, alemtuzumab, bortezomib, splenectomies or allogeneic bone marrow transplants have resulted in variable outcomes.[1,9]

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