Anakinra-induced psoriasis in a patient with Schnitzler syndrome

Sirs,

Schnitzler syndrome is a rare polygenic or multifactorial autoinflammatory disease characterised by urticarial lesions associated with fever, arthralgia, bone pain and laboratory changes, such as increased inflammatory markers and monoclonal gammopathy (1). Among different conventional and biologic immunosuppressive agents, anakinra [a recombinant human interleukin 1 (IL-1) receptor antagonist (IL-1Ra)], has emerged as an effective treatment in most cases (1).

We report a 74-year-old woman with past medical history of hypertension who was referred to our department after 14 years of flares with fever (38.5ºC), arthralgia, headache, legs pain and evanescent, non-pruritic and symmetrically distributed urticarial lesions. The attacks occurred 4–5 times a year and lasted from a few days to several weeks. Laboratory findings included raised acute phase reactants, normocytic anaemia, leukocytosis and thrombocytosis. Serum immunofixation disclosed an IgG lambda monoclonal gammopathy. Genetic analysis of genes responsible for the most common monogenic autoinflammatory diseases (*NRLP3*, *MEFV*, *TNFRSF1A*, *MVK*, *PSTPIP1* and *NOD2)* was negative. An x-ray of the lower limbs showed a cortical thickening of the fibula. A FDG-PET/CT scan revealed a modest hepatosplenomegaly and enlarged axillary, retroperitoneal and inguinal lymph nodes with hypermetabolic uptake. A resected inguinal adenopathy confirmed reactive lymphadenitis and a cutaneous biopsy proved a superficial perivascular lymphocytic and neutrophilic dermatitis, without vascular inflammation.

Prednisone was started and could not be reduced below 10–15 mg/day during the previous years because of cutaneous flares. Different conventional immunosuppressive drugs, including methotrexate and azathioprine, were used without sustained steroid-sparing effect.

The definite diagnosis of Schnitzler syndrome was then achieved according to 2013 Strasbourg diagnostic criteria (1). Anakinra was initiated subcutaneously at a dose of 100 mg/day with a rapid cutaneous improvement. All clinical and laboratory changes became normal within the three following weeks. One month after starting anakinra, the patient developed erythematous-desquamative lesions suggestive of psoriasis on the lower limbs that subsequently spread throughout the body (Fig. 1A-B). No past personal or familial history of any type of erythematous-desquamative dermatosis was recalled. A skin biopsy confirmed the diagnosis of psoriasis (Fig. 1C-D). Acitretin 35 mg/day was added to anakinra with good response (Fig. 1E-F). The patient did not tolerate anakinra reductions of every-other-day doses and has remained well with the two drugs during three years of follow-up.

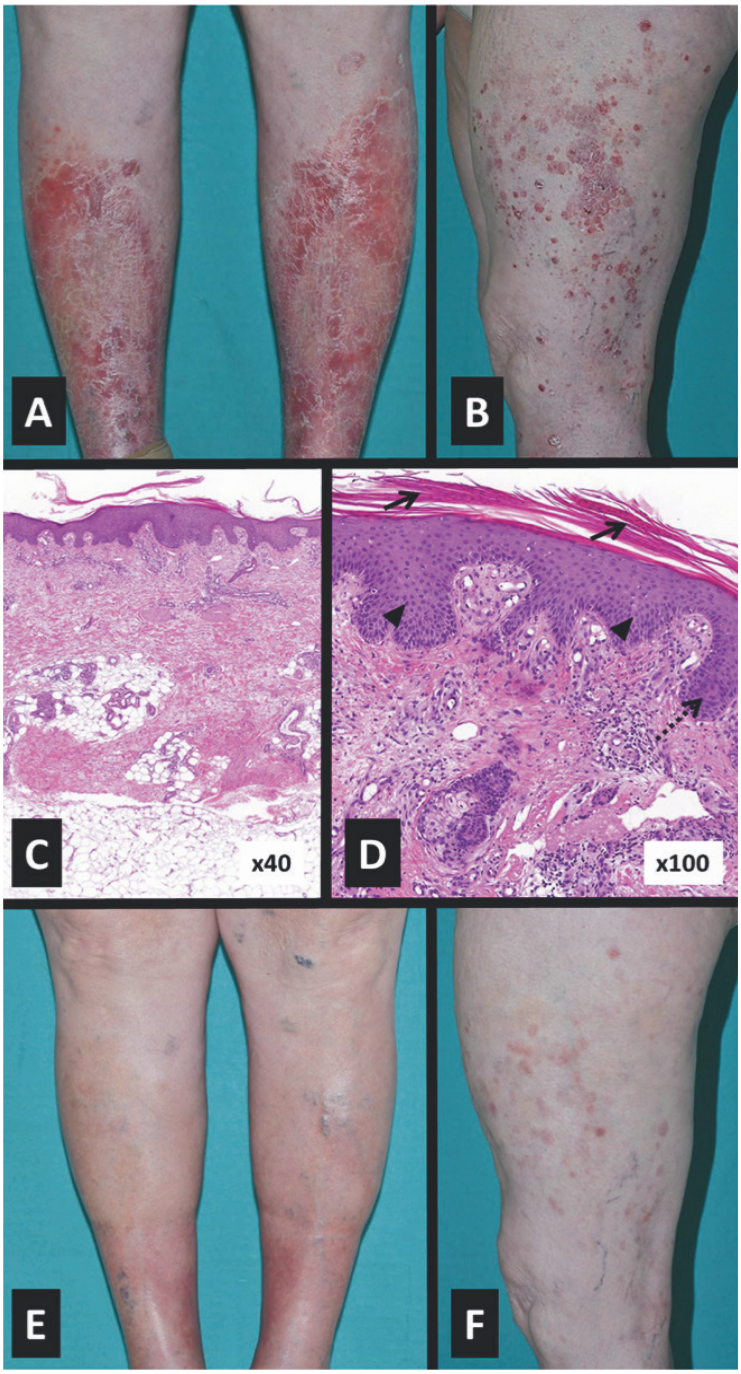

Fig. 1. A-**B**: Psoriasis vulgaris (plaque psoriasis) on lower limbs. **C**-**D**: Cutaneous biopsy confirming psoriasis with irregular epidermal acanthosis (arrow heads), focal parakeratosis (arrows) and occasional subcorneal neutrophils (dashed arrow). **E**-**F**: Clinical response of psoriatic lesions after treatment with acitretin.

The diagnosis of Schnitzler syndrome is a real challenge due to its rarity. In addition, the presence of a monoclonal gammopathy may not be present at the time of the first evaluation and may be developed later during the disease course, which results in undue diagnostic delay (2). Among monogenic autoinflammatory diseases, differential diagnosis must include cryopyrin-associated periodic syndromes (CAPS), since both conditions share clinical, laboratory and histological features. In this regard, some authors have allegedly diagnosed patients with Schnitzler syndrome carrying germline low-penetrance or somatic mutations in the *NLRP3* gene (3, 4),

IL-1 pathogenic role in Schnitzler syndrome is supported by the good response to IL-1 blockade with anakinra (5) and canakinumab (6). Indeed, anakinra is recommended as first line of treatment (1). To the best of our knowledge, the anakinra-in-

duced psoriasis occurring in our patient has been similarly reported in only a previous patient with rheumatoid arthritis, in whom anakinra cessation led to resolution of skin lesions (7). Although anakinra has been described effective in pustular psoriasis (8), it does not seem to be useful in plaque psoriasis (9), probably due to the presence of an overexpression of IL-1Ra in plaque psoriatic lesions (10).

In summary, we report a patient diagnosed with Schnitzler syndrome after 14 years of symptoms onset, in whom anakinra led to good disease control but plaque psoriasis was subsequently developed. Anakinra-induced psoriasis improved with acitretin and cessation of anakinra was not required.

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Competing interests: none declared.

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